KAISER PERMANENTE
COLORADO HMO
MEDICATION REQUEST GUIDELINES

Administered by

Prior Authorization Required Drugs:

a. Drug products, which are listed as **Prior Authorization (PA) required**, require approval when the member presents a prescription to a network pharmacy. To obtain coverage a physician, member or pharmacist may:
   i. Fax a completed **Prior Authorization Request** to MedImpact at (858) 357-2615.
   ii. Contact MedImpact at (800) 788-2949 and provide all necessary information requested.

b. The request will be reviewed by Kaiser Permanente staff according to Medical Exception criteria approved by the Kaiser Permanente Colorado P&T Committee.

c. If the request meets established criteria, the request will be approved and an authorization given.

d. If the request does not meet the criteria established by the P&T Committee, the request will be sent to the health plan physician for further review.

e. Failure to submit a Prior Authorization for a listed drug will result in non-coverage for the health plan member.

f. If the physician wishes to appeal a denied request, he/she may do so by contacting Kaiser Permanente Member Services at (303) 338-3800 for more information.

ABALOPARATIDE (TYMLOS)

Generic name	Brand name	HICL	GCN/GPID	Other
ABALOPARATIDE	TYMLOS		43334	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:

1. Must be prescribed by an endocrinology or rheumatology provider
2. No history of osteosarcoma
3. Diagnosis of osteoporosis and meets one of the following criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Patient is considered very high risk for fracture with one of the following:
        i. T-score of -2.5 or less, and 1 or more fragility fractures
        ii. BMD with t-score of -3.5 or less
        iii. History of multiple vertebral compression fractures
        iv. History of multiple fragility fractures
    b. Decline in BMD by more than 2% at hip or more than 2.5% at spine per year, after at least one year of oral alendronate or risedronate, IV zoledronic acid, or denosumab (Prolia), with at least 75% adherence to therapy
    c. T-score remains or has dropped to <-3.5 after at least one year of oral alendronate or risedronate, IV zoledronic acid, or denosumab (Prolia)
    d. Experienced 2 or more fragility fractures while adherent (at least 75% proportion days covered) to oral alendronate or risedronate, IV zoledronic acid, or denosumab (Prolia) for at least one year
    e. Unable to use alendronate or risedronate and IV zoledronic acid due to contraindications or adverse effects, or unable to use denosumab (Prolia) due to contraindications or adverse effects
4. Patient has tried and failed, or has an intolerance or contraindication to, teriparatide injection (Forteo), or the patient travels regularly and is unable to refrigerate teriparatide injection (Forteo) within 36 hours due to travel, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve x2 years.
If initial criteria are not met, do not approve.

RENEWAL CONSIDERATIONS: Do not approve. FDA labeling limits to 2 years.

ePA Questions for Provider Outreach

1. Diagnosis/ICD-10 codes associated with this request:_____
2. Has the patient failed other treatments for this indication? If yes, must list medication, strength, dates of treatment, and reason for discontinuation in Provider Comments section below or attach applicable chart notes.
3. Is there reasoning why alternatives are not suitable (i.e. alendronate tablets, IV zoledronic acid)? If yes, must list reasoning in Provider Comments section below or attach applicable chart notes.
4. Does the patient have history of osteosarcoma?
5. Current T-score: _____ Date: _____
6. Number of fragility fractures patient has had: ___
7. Number of vertebral compression fractures patient has had: ___

RATIONALE

Initial criteria -

- For initial therapy in patients at high risk, there is some evidence that teriparatide could be started first and then followed by an antiresorptive agent (e.g., bisphosphonate) because the bone formation effects of teriparatide may be reduced if started after treatment with an antiresorptive agent. Criteria would allow for use in patients who are at highest risk for fracture prior to starting alternative therapy.
- Patients with history of fragility fracture and BMD with initial t-score in osteoporosis range (<-2.5) but without severe osteoporosis (<-3.5) are generally managed in primary care with use of IV or oral bisphosphonates, with evidence to support use in fracture risk reduction with treatment duration of up to 6-10 years as long as no significant declines in BMD or multiple fragility fractures while on bisphosphonate therapy. Evidence that transition to anabolic agent after use of bisphosphonates may not have as much of a robust response in BMD improvements compared to initial treatment. Therefore, for patients without severe disease or evidence of bisphosphonate failure, continuation of initial therapy is reasonable.
- Based on the landmark pivotal trials for teriparatide and abaloparatide, there is no clinically significant difference in efficacy or recommended treatment durations between teriparatide and abaloparatide for postmenopausal women with osteoporosis.
- There is no head-to-head comparative trial between teriparatide and abaloparatide. Each agent has only been compared to placebo. When compared to placebo, both have demonstrated comparable BMD improvements and fracture reduction with similar treatment durations for efficacy.
- Given similar efficacy and teriparatide being more cost effective, reasonable to preferentially use teriparatide over abaloparatide.
- Both teriparatide and abaloparatide are viable options for treatment of osteoporosis in those with contraindications or intolerances to bisphosphonates when other alternatives (ex. denosumab or romosozumab would also be contraindicated such as in the case of osteonecrosis of the jaw and atypical femur fractures).

Renewal criteria -

- In November 2020, the FDA removed the 2-year lifetime limitation to treatment with teriparatide due to the risk of osteosarcoma:
  - The osteosarcoma warning was based upon studies in rats that high doses (3x greater than human dosing) administered over most of the rats' lifespan (about 24 months) increased the risk of osteosarcoma.
  - Since the teriparatide clinical trials were happening at that time, the trials were terminated early (~19 months).

  - In the 18 years since teriparatide was approved, no increase in osteosarcoma risk has been reported in studies in animals with bone remodeling similar to that in humans (e.g., monkeys). However osteosarcoma is rare (about 1 in 250,000 adults per year) so would need very large sample sizes.
  - The observed incidence of osteosarcoma during a 15-year post marketing surveillance study was no different than the background incidence rate.
  - Teriparatide has been studied for up to 3 years for the treatment of glucocorticoid-induced osteoporosis.
- Abaloparatide still has 2-year treatment duration in FDA labeling

FDA APPROVED INDICATIONS

FORTEO (teriparatide)

- **Osteoporosis:** Treatment of osteoporosis in postmenopausal females who are at high risk for fracture (defined as history of osteoporotic fracture or multiple risk factors for fracture); treatment to increase bone mass in males with primary or hypogonadal osteoporosis who are high risk for fracture; treatment of males and females with glucocorticoid-induced osteoporosis associated with chronic systemic glucocorticoids with a prednisone dosage of ≥5 mg/day (or equivalent) at a high risk for fracture. May also be used in patients who have failed or are intolerant to other available osteoporosis therapy.

TYMLOS (abaloparatide)

- **Osteoporosis, postmenopausal, fracture risk reduction:** Indicated to reduce risk of vertebral and nonvertebral fractures in postmenopausal women with osteoporosis at high risk for fracture or who failed or intolerant to other available osteoporosis therapy.
- **Osteoporosis, Men at high risk of fracture or who have failed or are intolerant to other osteoporosis therapy:** Indicated to increase bone density in men with osteoporosis at high risk for fracture (defined as a history of osteoporotic fracture or multiple risk factors for fracture), or patients who have failed or are intolerant to other available osteoporosis therapy.

REFERENCES

1. Eastell R, Rosen CJ, Black DM, Cheung AM, Murad MH, Shoback D. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2019;104(5):1595–1622.
2. Tsai JN, Uihlein AV, Lee H, et al. Teriparatide and denosumab, alone or combined, in women with postmenopausal osteoporosis: the DATA study randomized trial. *Lancet* 2013; 382(9886):50–56.
3. Cosman F, Nieves JW, Dempster DW. Treatment sequence matters: anabolic and
4. antiresorptive therapy for osteoporosis. J Bone Miner Res. 2017;32(2):198–202.
5. Miller PD, Lewiecki EM, Krohn K, Schwartz E. Teriparatide: Label changes and identifying patients for long-term use. *Cleveland Clinic Journal of Medicine*. 2021;88(9):489-493. https://www.ccjm.org/content/88/9/489

Creation Date: 05/2022
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

ABORTIVE MIGRAINE MEDICATIONS: DIHYDROERGOTAMINES

Generic	Brand	HICL	GCN	Exception/Other
DIHYDROERGOTAMINE MESYLATE (DHE)	TRUDHESA	00155	50931	*Route = Nasal Spray* Non-Formulary tier

GUIDELINES FOR COVERAGE

Must have one of the following diagnoses and meet the diagnosis-specific criteria below:

1. For abortive treatment of migraine headaches with or without aura, must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Patient has a history of failure or intolerance to at least one triptan
   b. Patient has a history of failure or intolerance to dihydroergotamine (Migranal) nasal spray
   c. Patient has a history of failure or intolerance to Zavzpret (zavegepant) nasal spray

   If criteria above are met, then approve indefinitely at GPID, max of 8 per 30 days.
   If criteria not met, do not approve.

2. For abortive treatment of cluster headaches, must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. The patient is unresponsive or intolerant to high flow oxygen (100%) via non-rebreather mask
   b. The patient is unresponsive or intolerant to sumatriptan nasal spray (formulary), zolmitriptan nasal spray (non-formulary), and/or injectable sumatriptan
   c. Patient has a history of failure or intolerance to dihydroergotamine (Migranal) nasal spray

   If criteria above are met, then approve indefinitely at GPID, max of 8 per 30 days.
   If criteria not met, do not approve.

RATIONALE

Ensure appropriate criteria are used for the management of requests for DHE nasal spray according to approved indication, dosing, and national treatment guidelines.

Trudhesa, a new intranasal (IN) dihydroergotamine (DHE) product for the acute treatment of migraines with or without aura in adults was approved on September 3, 2021. This is the second IN DHE product for the acute treatment of migraine; Migranal being the first IN DHE product that is generically available. Per the drug company, Trudhesa uses a proprietary delivery device to deliver DHE to the upper nasal space, which allows a lower dose of DHE to be administered and may lower the incidence of adverse

effects. Head-to-head studies between Trudhesa and Migranal have not been performed to show whether this lower dose translates into a difference in efficacy or safety.

** Contraindications & Serious Precautions to DHE nasal spray:*

1) with hemiplegic migraine
2) with migraine with brainstem aura (previously known as basilar artery migraine, basilar migraine and basilar-type migraines)
3) with ischemic heart disease (angina pectoris, history of myocardial infarction, or documented silent ischemia) or to patients who have clinical symptoms or findings consistent with coronary artery vasospasm including Prinzmetal's variant angina
4) with uncontrolled hypertension
5) with concurrent prescriptions for both Dihydroergotamine Mesylate Nasal Spray and either 5-HT1 agonists (e.g., sumatriptan), ergotamine-containing or ergot-type medications or methysergide *should not be used within 24 hours of each other*
6) with concomitant potent CYP 3A4 inhibitors, such as protease inhibitors and macrolide antibiotics, resulting in vasospasm that led to cerebral ischemia and/or ischemia of the extremities. Examples include ritonavir, nelfinavir, indinavir, erythromycin, clarithromycin, troleandomycin, ketoconazole, and itraconazole
7) with concomitant peripheral and central vasoconstrictors (i.e., alpha-adrenergic agonists, vasopressin analogues)
8) with known peripheral arterial disease, sepsis, and following vascular surgery
9) with severely impaired hepatic or renal function

FDA APPROVED INDICATIONS

DHE nasal spray (Migranal and Trudhesa) is an ergot derivative indicated for the acute treatment of migraine headaches with or without aura; not intended for the prophylactic therapy of migraine or for the management of hemiplegic or basilar migraine.

HOW SUPPLIED

INTRANASAL: 4 mg/mL solution

REFERENCES

1. Dihydroergotamine mesylate (Migranal) nasal spray. https://www.bauschhealth.com/Portals/25/Pdf/PI/Migranal-AG-PI.pdf
2. Andersson PG, Jespersen LT. Dihydroergotamine nasal spray in the treatment of attacks of cluster headache. A double-blind trial versus placebo. Cephalalgia. 1986; 6:51-4.
3. https://americanmigrainefoundation.org/resource-library/cluster-headache-treatment-options/
4. The International Headache Society. https://www.ichd-3.org/1-migraine/1-2-migraine-with-aura/1-2-2-migraine-with-brainstem-aura/

Creation date: 5/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

ACUTE MIGRAINE QUANTITY LIMIT PER COPAY

Generic	Brand	HICL	GCN	Exception/Other
N/A	N/A	N/A	N/A	

- There are limitations on products used to treat migraines to ensure patient safety by minimizing adverse side effects (such as rebound headache) and over-utilization of these products.
- Quantity limits ensure appropriate use and decrease the risk of waste.
- These quantity limits are coded within the PBM and limit the quantities allowed to process for benefit.
- The acute migraine quantity limits are limited per copay (or per rx) and 30-day benefit plans are allowed a certain quantity which is less than for 60-day benefit plans. Prescriptions for these agents do not have refills coded within KPHC as a method of alerting the prescriber that the member might be over-using the medication by triggering a refill request. If the prescriber approves a refill the pharmacy will be able to reprocess the prescription.
- If appropriate and refills are available on the prescription, there is no need for an approval as the pharmacy may reprocess the prescription at any time.

Formulary*	30 Day Plan - Qty/Copay	60 Day Plan - Qty/Copay
D.H.E. 45 Soln 1 mg/ml (dihydroergotamine)	8 ampules (vials)	16 ampules (vials)
Eletriptan tabs	12 tablets	24 tablets
ERGOMAR SL tabs	12 SL tablets	24 SL tablets
Ergotamine/caffeine tabs (CAFERGOT)	24 tablets	48 tablets
MIGERGOT SUPP (ergotamine/caffeine)	12 suppositories	24 suppositories
Naratriptan tabs	18 tablets	36 tablets
Rizatriptan ODT tabs	18 tablets	36 tablets
Rizatriptan tabs	18 tablets	36 tablets
Sumatriptan 6mg/0.5ml cartridge	8 doses (4 ML)	16 doses (8 ML)
Sumatriptan 6mg/0.5ml PEN injection	8 doses (4 ML)	16 doses (8 ML)
Sumatriptan 6mg/0.5ml SDV Soln (Single Dose Vials)	10 SDV (5 ML)	20 SDV (10 ML)
Sumatriptan nasal spray (6 units per box)	18 units (3 boxes)	36 units (6 boxes)
Sumatriptan tabs	18 tablets	36 tablets

Non-Formulary*	30 Day Plan - Qty/Copay	60 Day Plan - Qty/Copay
Acetaminophen-isometheptene-dichloralphenazone caps (MIDRIN)	80 caps / 30 days**	160 caps / 60 days**
Almotriptan tabs	12 tablets	24 tablets
AMERGE tabs	18 tablets	36 tablets
AXERT tabs	12 tablets	24 tablets
CAFERGOT tabs	24 tablets	48 tablets
CAMBIA pack	9 packets	9 packets
ELYXYB (celecoxib) oral solution	9 doses (120mg/dose)	18 doses (120mg/dose)
Diclofenac Potassium powder pack	9 packets	9 packets
FROVA tabs	9 tablets	18 tablets
Frovatriptan tabs	9 tablets	18 tablets

IMITREX 6mg/0.5ml cartridge	8 doses (4 ML)	16 doses (8 ML)
IMITREX 6mg/0.5ml PEN injection	8 doses (4 ML)	16 doses (8 ML)
IMITREX 6 mg/0.5ML SDV Soln (Single Dose Vials)	10 SDV (5 ML)	20 SDV (10 ML)
IMITREX nasal spray (6 units per box)	18 units (3 boxes)	36 units (6 boxes)
IMITREX tabs	18 tablets	36 tablets
Isometheptene-caffeine-acetaminophen tabs (PRODRIN)	80 tabs / 30 days**	80 tabs / 60 days**
MAXALT tabs & TBDP	18 tablets	36 tablets
ONZETRA XSAIL EXHP	8 doses (1 kit)	16 doses (2 kits)
PRODRIN tabs (isometheptene-caffeine-acetaminophen)	80 tabs / 30 days**	80 tabs / 60 days**
RELPAX tabs	12 tablets	24 tablets
RIZAFILM 10mg oral film	18 films	36 films
Sumatriptan 4mg/0.5ml pen INJ (Imitrex)	4 doses (2 ML)	8 doses (4 ML)
Sumatriptan 4mg/0.5ml cartridge (Imitrex)	4 doses (2 ML)	8 doses (4 ML)
TOSYMRA (sumatriptan) 10mg Nasal Spray	18 units (3 boxes)	18 units (3 boxes)
ZEMBRACE SYMTOUCH SOAJ	4 syringes (2 ML)	8 syringes (4 ML)
Zolmitriptan tabs & TBDP	12 tablets	24 tablets
ZOMIG nasal spray (6 units per box)	6 units (1 box)	12 units (2 boxes)
ZOMIG tabs & ZMT tabs	12 tablets	24 tablets

RATIONALE
Per Plan.

FDA APPROVED INDICATIONS

REFERENCES
Per Plan.

Creation date: 09/26/2018
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 05/2023

ALIROCUMAB (PRALUENT)

Generic Name	Brand Name	HICL	GPID	Comments
ALIROCUMAB	PRALUENT PEN	42347		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and stable on therapy.
2. Patient has tried and failed an appropriate dose of, experienced adverse events with, or has an allergy or contraindication to, evolocumab (Repatha), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If met, approve indefinitely.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient has a diagnosis of either homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH), or atherosclerotic cardiovascular disease (ASCVD) with a clinical event^^*
2. Has a current LDL level drawn within the last 90 days of greater than or equal to one of the following:
   a) 55 mg/dL for ASCVD at very high risk defined as multiple ASCVD events^^ or 1 ASCVD event and 2 or more high risk conditions (age ≥ 65 years, familial hypercholesterolemia, diabetes, HTN, eGFR 15-59, current smoking)
   b) 70mg/dL for ASCVD not at very high risk
   c) 100 mg/dL for HeFH/HoFH
3. Patient must meet one of the following:
   a) has been taking atorvastatin 80mg or rosuvastatin 40mg daily or statin therapy at the maximally tolerated dose for at least 30 days prior to LDL lab;
   b) has an absolute contraindication to statin therapy (active, decompensated liver disease; nursing female, pregnancy, or plans to become pregnant;
   c) has experienced a hypersensitivity reaction to a statin drug;
   d) has a documented history of CPK>10x ULN or rhabdomyolysis attributed to a statin and not explained by a drug interaction, fall, or prolonged immobility);
   e) is statin intolerant as defined by the National Lipid Association Statin Intolerance Panel**
4. Patient has been taking ezetimibe for at least 30 days prior to LDL lab, or the patient has a contraindication or intolerance to ezetimibe
5. The patient has tried and failed an appropriate dose of, experienced adverse events with, or has an allergy or contraindication to, evolocumab (Repatha), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv)

the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If met, approve at HICL indefinitely, max daily dose of 0.08 (2 per 28 days for syringes/pens).
If not met, do not approve.

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ePA Questions

1. Is the patient stable on alirocumab therapy?
2. For patients noted stable on therapy, start date of therapy (MMDDYY):
3. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH), or atherosclerotic cardiovascular disease (ASCVD) with a clinical event (must list the clinical event in Provider Comment section below or attach applicable chart notes.]
4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
5. Is there reasoning why alternatives (rosuvastatin tablets, atorvastatin tablets, lovastatin tablets, simvastatin tablets, pravastatin tablets; fenofibrate tablets (54 mg, 160 mg); gemfibrozil 600 mg tablets; ezetimibe tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
6. Current LDL:
7. Date of LDL lab (MMDDYY):

REFERENCES

*Requires documentation which may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and laboratory data.

^^**Includes**: MI, ACS, CAD with intervention (e.g., PCI, stent, CABG), ischemic non-cardioembolic stroke, PAD with intervention (e.g., stent, surgery); **Excludes**: High CAC score, AAA, CAD finding on diagnostic cath without MI/ACS/intervention, CAD equivalents (e.g. DM, CKD), primary prevention patients regardless of CV risk score

**Inability to tolerate at least 2 statins, with at least one started at the lowest starting daily dose

For primary prevention for a patient who has NOT been noted to have familial hypercholesterolemia, a PCSK9i would not be appropriate. If they have failed statins (even low dose 1-2 days per week) and ezetimibe, we could offer any formulary, unrestricted lipid-lowering therapy.

RATIONALE

Per Health Plan

Creation Date: 3/15/2017
Effective Date: 4/2024
Reviewed Date: 3/2024
Revised Date: 3/2024

FIRDAPSE (AMIFAMPRIDINE)

Generic	Brand	HICL	GCN/GPID	Other
AMIFAMPRIDINE PHOSPHATE	FIRDAPSE	36930	28457	Non-formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: All the following must be met:
1. Must be prescribed by a Neurologist or if clinically appropriate, an oncologist
2. Patient must have a diagnosis of Lambert-Eaton Myasthenic Syndrome (LEMS)
3. Patient must be age 6 years or older
4. Patient is ambulatory and has weakness that interferes with daily function
5. Has documentation of a baseline clinical muscle strength assessment (examples include either the Quantitative Myasthenia Gravis (QMG) score or the triple-timed up-and-go test (3TUG))
6. Must not have a history of seizure disorder or have active brain metastasis

If initial criteria are met, then approve x 3 months, max dose 8 tablets per day.

RENEWAL CRITERIA: Must meet all the following criteria:
1. Patient has maintained >75% adherence to the medication since last approval
2. The patient's current QMG score or 3TUG test has remained stable or improved compared to baseline
3. Patient is still ambulatory
4. Patient has not developed epileptic seizures

If renewal criteria are met, then approve x 1 year, max dose 8 tablets per day.

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ePA Questions for Provider Outreach
INITIAL REVIEW QUESTIONS
1. Is the patient ambulatory with weakness that interferes with daily function?
2. Current Quantitative Myasthenia Gravis (QMG) score:
3. Date of Current Quantitative Myasthenia Gravis (QMG) score (MMDDYY):
4. Current triple-timed up-and-go test (3TUG) score:
5. Date of Current triple-timed up-and-go test (3TUG) score (MMDDYY):
6. Does the patient have history of seizure disorder or active brain metastasis?

RENEWAL REVIEW QUESTIONS
1. Current Quantitative Myasthenia Gravis (QMG) score:
2. Date of Current Quantitative Myasthenia Gravis (QMG) score (MMDDYY):
3. Current triple-timed up-and-go test (3TUG) score:
4. Date of Current triple-timed up-and-go test (3TUG) score (MMDDYY):
5. Is the patient ambulatory?
6. Has the patient developed epileptic seizures?

RATIONALE
Firdapse is a potassium channel blocker indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.

NOTES:

Given serious teratogenicity risk from this medicine, those members with pregnancy potential should be encouraged to have a negative pregnancy test, to be on highly effective contraception (ie IUD or implant) unless there is a valid reason not to, and should not be breastfeeding.

FDA APPROVED INDICATIONS

- FIRDAPSE is a potassium channel blocker indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.

REFERENCES

1. Firdapse [Prescribing Information]. Coral Gables, FL: Catalyst Pharmaceuticals, Inc: September 2022.
2. Emerging-Therapeutics-Strategy-Program. Inter-regional Practice Recommendations. Last updated 8/29/2019. https://sp-cloud.kp.org/sites/teams-emergingtsc/Firdapse/IR%20Practice%20Recs_amifapridine%20(Firdapse_Ruzurgi)%20FINALv2%2020190829.pdf#search=firdapse Accessed January 31, 2023.

Creation Date:11/2020
Effective Date:04/2024
Reviewed Date: 03/2024
Revised Date: 03/2023

AMLODIPINE 1 MG/ML SUSPENSION AND SOLUTION - AGE RESTRICTION CRITERIA

Generic	Brand	HICL	GCN	Exception/Other
AMLODIPINE SUSPENSION 1 MG/ML	KATERZIA	45864	46652	Formulary
AMLODIPINE SUSPENSION 1 MG/ML	NORLIQVA	06494	46882	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL AND RENEWAL CRITERIA: ONE of the following criteria must be met:
1. Patient must be less than or equal to 10 years old
2. Patient is using an alternative administration route, such as a gastrostomy tube
3. Dose cannot be administered by using half, whole or combo of the amlodipine 5 mg tablet (i.e., 2.5 mg or 7.5 mg)
4. Patient cannot swallow other tablets whole, halved, or crushed tablets (with or without mixing in apple sauce)

If any criterion is met, approve x1 year.
If no criteria are met, do not approve, and suggest either changing to tablet strengths that can be halved or used in combination, or crushing amlodipine tablets before administration and taking with or without applesauce.

RATIONALE
Per Health Plan.

General Clinical Criteria for solutions/suspension
1. Age is less than or equal to 10 years old
2. Presence of gastrostomy
3. Dose does not allow use of halved, whole or combo of tablet
4. Dose does not use whole capsule (cannot “cut” capsules in half)
5. Clinical condition where unable to swallow crushed/opened tablets/capsules (i.e., esophageal stricture)

FDA APPROVAL
1. Treatment of hypertension in patients age > 6 and older
2. Treatment of Chronic Stable Angina, Vasospastic Angina, or Angiographically documented coronary artery disease in patients without heart failure or an ejection fraction < 40%
3. Max dose is 10 mg daily

REFERENCES
Per Health Plan

Creation date: 10/2019
Effective date: 03/2024
Reviewed date: 12/2023
Revised date: 12/2023

AJOVY MD RESTRICTION

Generic	Brand	HICL	GCN	Exception/Other
FREMANEZUMAB-VFRM	AJOVY 225 MG/ML	45236	45306	Acts on ligand

GUIDELINES FOR COVERAGE for Commercial, HIX and Fed:

1. Is the requesting provider a CPMG or an affiliated network neurologist or headache specialist, with appropriate referral if needed?

   If yes, approve the MD restriction at GPID indefinitely.
   If no, do not approve.

RATIONALE
Ajovy is KPCO's preferred CGRP-mAb and cheaper than Botox injections. Ajovy was added to formulary 2/2023.

FDA APPROVED INDICATIONS
Preventative treatment of migraine in adults

REFERENCES

Creation Date:3/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

APALUTAMIDE (ERLEADA)

Generic	Brand	HICL	GCN/GPID	Other
APALUTAMIDE	ERLEADA	44773	44446	

GUIDELINES FOR COVERAGE
Must meet all the following:

1. Patient has a diagnosis of prostate adenocarcinoma
2. Medication is prescribed by an Oncologist
3. Patient does not have a history of seizures or seizure disorder
4. Must have PSA greater than or equal to 2ng/dL
5. Must have a diagnosis of nonmetastatic castration-resistant prostate cancer (M0CRPC) or metastatic castration-sensitive prostate cancer (M1CSPC), and meet all the diagnosis subtype-specific criteria below:
    a. Nonmetastatic Castration Resistant Prostate Cancer (M0CRPC): Must meet all:
        i. No metastasis observable on radiologic scans
        ii. Must have had PSA double in 10 months or less while on at least one ADT (androgen deprivation therapy) including: leuprolide (Eligard, Lupron), goserelin (Zoladex), triptorelin (Trelstar), histrelin (Supprelin, Vantas), degarelix (Firmagon)
        iii. Patient is intolerant of enzalutamide (Xtandi), or has a contraindication to enzalutamide (Xtandi) [ex: currently being treated with a strong CYP3A4 inducer that prohibits the use of enzalutamide (Xtandi)] and darolutamide (Nubeqa), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
    b. Metastatic Castration Sensitive Prostate Cancer (M1CSPC): Must meet all:
        i. Patient has documented metastatic disease that has not progressed on ADT (androgen deprivation therapy) including: leuprolide (Eligard, Lupron), goserelin (Zoladex), triptorelin (Trelstar), histrelin (Supprelin, Vantas), degarelix (Firmagon)
        ii. The patient is intolerant of, or has a contraindication to, enzalutamide (Xtandi), or the patient is currently being treated with a strong CYP3A4 inducer [that prohibits the use of enzalutamide (Xtandi)], or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
        iii. The patient is intolerant of, or has a contraindication to, abiraterone (Zytiga), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient

is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

6. Patient has not experienced disease progression on any of the following: enzalutamide (Xtandi), abiraterone acetate (Zytiga, Yonsa), darolutamide (Nubeqa), docetaxel (Taxotere), or bicalutamide

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve. Alternatives include enzalutamide [Xtandi] for M0CRPC or abiraterone [Zytiga] for patients with M1CSPC.

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ePA Questions

1. Does the patient a diagnosis of prostate adenocarcinoma?
2. Does the patient have a history of seizures or seizure disorder?
3. Has the patient experienced disease progression on any of the following: enzalutamide (Xtandi), abiraterone acetate (Zytiga, Yonsa), darolutamide (Nubeqa), docetaxel (Taxotere), or bicalutamide?
4. Diagnosis subtype associated with this request: [check boxes for all diagnosis-subtypes listed in criteria: nonmetastatic castration-resistant prostate cancer (M0CRPC); metastatic castration-sensitive prostate cancer (M1CSPC)]

QUESTIONS BASED ON DIAGNOSIS SELECTED

Nonmetastatic Castration-Resistant Prostate Cancer (M0CRPC)

1. Does the patient have any observable metastasis on radiologic scans?
2. Has the patient's PSA doubled in 10 months or less while on ADT (androgen deprivation therapy)?
3. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
4. Is there reasoning why alternatives (enzalutamide (Xtandi), darolutamide (Nubeqa)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Metastatic Castration-Sensitive Prostate Cancer (M1CSPC)

1. Does the patient have metastatic disease?
2. Has metastatic disease progressed on ADT (androgen deprivation therapy)?
3. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
4. Is there reasoning why alternatives (enzalutamide (Xtandi), abiraterone (Zytiga)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Health Plan.
Enzalutamide is the KPCO preferred agent for nonmetastatic (M0) castration resistant prostate cancer (CRPC), unless CYP-interacting drugs then apalutamide should be used. If the patient has metastatic castration sensitive prostate cancer (mCSPC), KPCO formulary alternatives of abiraterone or docetaxel are preferred.

FDA APPROVED INDICATIONS

Treatment of non-metastatic, castration-resistant prostate cancer (M0CRPC). Treatment of metastatic castration-sensitive prostate cancer (M1CSPC).

REFERENCES

1. Erleada (apalutamide) [prescribing information]. Horsham, PA: Janssen Products, LP; September 2020.
2. NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer v.1.2023. www.nccn.org

Creation Date: 11/2018
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

ARCALYST (RILONACEPT)

Generic	Brand	HICL	GCN	Exception/Other
RILONACEPT	ARCALYST	35438	99473	Nonformulary Specialty tier

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Arcalyst.

If met, approve indefinitely.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following diagnoses and must meet all diagnosis-specific criteria below:
A. Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS), and Muckle-Wells Syndrome (MWS)
B. Deficiency of Interleukin-1 Receptor Antagonist (DIRA)
C. Recurrent pericarditis

A. For the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS), and Muckle-Wells Syndrome (MWS)
   1. Prescribed by CPMG or affiliated rheumatologist, geneticist, allergist/immunologist, or dermatologist
   2. Patient is 12 years of age or older

   If above initial criteria are met, then approve at HICL indefinitely.
   If above initial criteria are not met, do not approve.

B. For the maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist (DIRA)
   1. Patient's weight is greater than or equal to 10 kg
   2. Diagnosis of DIRA
   3. Genetic testing has confirmed mutation in the ILRN1 gene

   If above initial criteria are met, approve at HICL indefinitely.
   If above initial criteria are not met, do not approve.

C. For the treatment of recurrent pericarditis (RP) and reduction in risk of recurrence
   1. Medication is prescribed by a cardiologist or rheumatologist
   2. Patient is 12 years of age or older
   3. Patient has experienced at least 3 episodes of pericarditis (current episode can count as 1 of the 3 if patient is currently having an episode) with at least 1 of them occurring despite the use of NSAIDs and colchicine (or contraindication or documented intolerance to these agents)
   4. CRP level greater than or equal to 1.0 mg/dL

   If above initial criteria are met, approve at HICL indefinitely.
   If above initial criteria are not met, do not approve.

REFERENCES
Per Health Plan

Creation date: 7/2/2021
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

ASENAPINE (SAPHRIS)

Generic	Brand	HICL	GCN	Exception/Other
ASENAPINESL TABLETS	SAPHRIS	36576		Quantity limits

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO within the past 90 days and is stable on therapy.

If met, approve indefinitely at HICL, max 2 tabs per day.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following diagnoses and meet all related criteria below:

A. Bipolar mania or mixed episodes
B. Schizophrenia

A. Bipolar Mania or Mixed Episodes
   1. Patient is at least 10 years of age
   2. Documented contraindication, intolerance, or treatment failure to the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. One antipsychotic
      b. One mood stabilizer (e.g. lithium, carbamazepine, valproic acid and derivatives)

If criteria are met, approve indefinitely at HICL, max 2 tabs per day.
If criteria are not met, do not approve.

B. Schizophrenia
   1. Patient is at least 18 years of age
   2. Documented contraindication, intolerance, or treatment failure to at least 1 antipsychotic, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If criteria are met, approve indefinitely at HICL, max 2 tabs per day.
If criteria are not met, do not approve.

ESCALATION CRITERIA: Must meet one of the following:
1. Daily dose is below or equal to the maximum approved by FDA unless prescribed by psychiatry.
2. Dose is unable to be met within the quantity limit restriction.

If met, then approve indefinitely at HICL without quantity limits.
If not met, deny quantity requested, maintaining original quantity approved.

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ePA Questions

1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Bipolar mania or mixed episodes; Schizophrenia]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Bipolar mania or mixed episodes

   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules; Lithium capsules, as carbonate: 150 mg, 300 mg; Lithium tablets, as carbonate: 300 mg; Lithium CR tablets, as carbonate (Eskalith CR): 450 mg; Lithium SR tablets, as carbonate (Lithobid): 300 mg; Lamotrigine tablets; Divalproex sodium DR (12 hr) or ER (24 hr) tablets, valproic acid capsules (250 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Schizophrenia

   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Carbamazepine, divalproex, and lithium are teratogenic so avoiding use in women of reproductive potential is not unreasonable (and highly recommended for divalproex). Unfortunately, most of the non-formulary antipsychotics lack reassuring data and absence of evidence of risk is not the same as absence of risk. Lithium may still be continued or started in women that are pregnant as the benefits of use are often considered to outweigh the small absolute risk of cardiac malformation (1-2 extra cases per 100 live births with first trimester in utero exposure compared with no lithium exposure).

FDA APPROVED INDICATIONS

Asenapine

- **Bipolar disorder (sublingual tablet only):** Treatment of acute mania or episodes with mixed features associated with bipolar I disorder (as monotherapy in adult and pediatric patients ≥10 years of age or adjunctive treatment with lithium or valproate in adults) and maintenance treatment in adults (as monotherapy) (max daily dose: 10 mg BID)
- **Schizophrenia (transdermal patch, sublingual tablet):** Treatment of adults with schizophrenia (max daily dose: 10 mg BID)..

APPENDIX A. Formulary antipsychotics

First-generation antipsychotics	Second-generation antipsychotics

Chlorpromazine	Aripiprazole
Fluphenazine	Clozapine
Haloperidol	Lurasidone
Loxapine	Olanzapine
Molindone	Quetiapine
Perphenazine	Risperidone
Pimozide	Ziprasidone
Thioridazine	
Thiothixene	
Trifluoperazine	

HOW SUPPLIED:
Asenapine (Saphris) SL tablets: 2.5 MG, 5 MG, 10 MG

REFERENCES
American Psychiatric Association. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. 3rd ed. Washington, DC: American Psychiatric Association; 2021.

Patorno E, Huybrechts KF, Bateman BT, et al. Lithium use in pregnancy and the risk of cardiac malformations. N Engl J Med. 2017;376:23.

Saphris. Package insert. Allergan, Inc.; October 1, 2021.

Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord 2018;20:97-170.

Creation Date: 3/2023
Effective Date: 4/2024
Reviewed Date: 3/2024
Revised Date: 3/2024

AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD)
TOLVAPTAN (JYNARQUE)

Generic	Brand	HICL	GCN/NDC	Exception/Other
TOLVAPTAN	JYNARQUE PACK		39957, 39958, 39956, 48066, 48068	
TOLVAPTAN	JYNARQUE		59148-0082-13, 59148-0083-13	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all drug specific criteria as follows:

A. JYNARQUE: Must meet all the following criteria:
   1. Prescribed by a nephrologist
   2. Patient has diagnosis of autosomal dominant polycystic kidney disease (ADPKD) confirmed by baseline CT scan or MRI of the kidneys (typical is defined as bilateral/diffuse cyst distribution)
   3. Patient is at high risk of disease progression defined by Mayo ADPKD Classification as "Typical (Class 1) ADPKD" and classified as either 1C, 1D, or 1E
   4. Patient is in one of the following three groups:
      a. Age 18 to 50 years; AND estimated glomerular filtration rate (eGFR) is at least 60 mL/min/1.73m2 AND total kidney volume (TKV) is at least 750 mL
      b. Age 18 to 55 years; AND eGFR is at least 25 to 65 mL/min/1.73m2
      c. Age 56 to 65 years; AND eGFR is at least 25 to 44 mL/min/1.73m2; AND eGFR decline is greater than 2 mL/min/1.73m2 per year

If initial criteria are met, approve x1 year (monitoring for labs is recommended monthly for 18 months).
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet both criteria below:
1. Prescribed by a nephrologist.
2. Prescriber attests to evidence of disease improvement, such as improved eGFR, rate of growth in TKV, and ADPKD Impact Scale.

If renewal criteria are met, approve x1 year (monthly lab monitoring recommended for first 18 months of therapy, and every 3 months thereafter.).
If renewal criteria are not met, do not approve.

RATIONALE
KP Regional and National ADPKD treatment guidance
Samsca for hyponatremia must be started in the hospital due to risk of rapid sodium correction and osmotic demyelination [Black Box Warning].

FDA APPROVED INDICATIONS
ADPKD
Hyponatremia

REFERENCES

..\Chebib A Practical Guide for Treatment of ADPKD with Tolvaptan.pdf
Regional ADPKD Clinic for Tolvaptan.ppt
Tolvaptan for Autosomal Dominant Polycystic Kidney Disease.docx

Samsca [package insert]. Tokyo, Japan; Otsuka Pharmaceutical Co., Ltd. 2018.

Creation date: 3/2019
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 5/2021

AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD)
TOLVAPTAN (SAMSCA)

Generic	Brand	HICL	GCN/NDC	Exception/Other
TOLVAPTAN	SAMSCA 15MG TABLETS, SAMSCA 30MG TABLETS		59148-0020-50, 59148-0021-50	Off Label -Ascites, Heart Failure FDA Approved - ADPKD, Hyponatremia

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all drug specific criteria as follows:

A. SAMSCA: Must meet all the following criteria:
   1. Prescribed by a nephrologist
   2. Samsca started or restarted in the hospital for hyponatremia

If initial criteria are met, approve for a total duration of 30 days, max 2 tablets/day.
If initial criteria are not met, do not approve.

RATIONALE

KP Regional and National ADPKD treatment guidance
Samsca for hyponatremia must be started in the hospital due to risk of rapid sodium correction and osmotic demyelination [Black Box Warning].

FDA APPROVED INDICATIONS

ADPKD
Hyponatremia

REFERENCES

..\Chebib A Practical Guide for Treatment of ADPKD with Tolvaptan.pdf
Regional ADPKD Clinic for Tolvaptan.ppt
Tolvaptan for Autosomal Dominant Polycystic Kidney Disease.docx

Samsca [package insert]. Tokyo, Japan; Otsuka Pharmaceutical Co., Ltd. 2018.

Creation date: 3/2019
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 5/2021

AVAPRITINIB (AYVAKIT)

Generic	Brand	HICL	GCN	Exception/Other
AVAPRITINIB	AYVAKIT	46291		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
1. Patient is new to KPCO within the past 90 days and stable on therapy with Ayvakit

If met, approve indefinitely, max 1 tablet/day.
If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must meet all of the following criteria:
1. Patient must be 18 years of age or older
2. Patient must have unresectable or metastatic GIST (gastrointestinal stromal tumor) with a PDGFRA D842V mutation
   OR advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL)
   OR indolent systemic mastocytosis (ISM)

If initial criteria are met, approve indefinitely, max 1 tablet/day.
If initial criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with GIST study population in which avapritinib was evaluated, majority of whom had a PDGFRA D842V mutation. Ensure all FDA indications are included in the PA criteria.

FDA APPROVED INDICATIONS
Treatment of adults with unresectable or metastatic gastrointestinal stromal tumors that harbor a PDGFRA Exon 18 mutation, including PDGFRA D842V mutation.
Treatment of adults with advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis, systemic mastocytosis with an associated hematological neoplasm, and mast cell leukemia.
Treatment of adults with indolent systemic mastocytosis (ISM).

REFERENCES
1. Avapritinib [Package Insert], Cambridge, MA: Blueprint Medicines Corporation: 2023.

Creation Date: 10/2020
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

AZACITIDINE (ONUREG)

Generic	Brand	HICL	GCN	Exception/Other
AZACITIDINE	ONUREG	26361	48540, 48545	Nonformulary Specialty tier

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all of the following:
1. Patient must be age 18 or older
2. Must be prescribed by an oncology specialist
3. Must have diagnosis of acute myeloid leukemia (AML)
4. Must be in first complete response (CR or Cri, see below) after receiving initial intensive induction therapy (cytarabine + anthracycline) for AML
   - CR=complete response = Blasts <5%, ANC >1000, Platelets ≥100,000, patient currently independent of transfusions
   - CRi = complete response but with incomplete hematologic recovery = all CR criteria met (including current transfusion independence) but with persistent neutropenia (ANC <1000) and/or thrombocytopenia (<100,000)
5. Attained CR/CRi within prior 4 months
6. Must not be a hematopoietic stem cell transplant (HSCT, aka BMT) candidate
7. Does not have an allergy to mannitol or azacitidine

If initial criteria are met, approve at HICL x 1 year, maximum dose #14 tabs per 28 days.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Patient does not have disease relapse of AML (>15% blasts on bone marrow or in blood)
2. Patient has not undergone hematopoietic stem cell transplant (HSCT, aka BMT)

If renewal criteria are met, approve at HICL level x 1 year, maximum dose #14 tabs per 28 days.
If renewal criteria are not met, do not approve.

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ePA Questions for Provider Outreach
Initial Review Questions
1. Has the patient achieved complete response (CR or Cri) after initial intensive induction therapy (cytarabine + anthracycline)?
2. Date of complete response (MMDDYY):
3. Current labs:
   a. Labs: Blasts (%):
   b. Blast Lab Date (MMDDYY):
   c. Labs: ANC:
   d. ANC Lab Date (MMDDYY):
   e. Labs: Platelets:
   f. Platelet Lab Date (MMDDYY):
4. Is the patient currently independent of transfusions?
5. Is the patient a candidate for hematopoietic stem cell transplant (HSCT, aka BMT)?
6. Does the patient have an allergy to mannitol or azacitidine?

Renewal Review Questions
1. Does the patient have disease relapse of AML?

2. Has the patient undergone hematopoietic stem cell transplant since starting azacitidine?

RATIONALE
To promote evidence-based, safe use of oral azacitidine in concordance with FDA approval and NCCN guideline recommendations.

FDA APPROVED INDICATIONS
Continued treatment of AML for adults who achieved first CR or CRi following intensive induction chemotherapy and are not able to complete intensive curative therapy.

REFERENCES
1. NCCN Clinical Practice Guidelines in Oncology. Acute Myeloid Leukemia v.3.2022. www.nccn.org
2. Onureg Prescribing Information. Summit, NJ. Celgene Corporation. 10/2022

Creation Date: 3/2021
Effective Date: 4/2024
Reviewed Date: 3/2024
Revised Date: 3/2024

BECAPLERMIN

Generic	Brand	HICL	GCN	Exception/Other
BECAPLERMIN	REGRANEX	17028		Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA
Must meet either criteria 1, or 2-4 below:
1. Prescription is from a hospital discharge per the member, pharmacy or prescriber
   OR all the following:
2. Patient has a diagnosis of diabetes mellitus with lower extremity diabetic neuropathic ulcer
3. Prescription is written by a vascular surgeon, podiatrist or endocrinologist
4. Patient does not have a diagnosis of a neoplasm (i.e., cancer), necrotic tissue, infection or osteomyelitis at site of application

If initial criteria, either 1, or 2-4 are met, then approve for 3 months, maximum two (2) tubes per month.
If initial criteria are not met, then do not approve.

RENEWAL CRITERIA
1. Patient's wound size has decreased by at least a 30% since starting becaplermin

If renewal criteria are met, then approve for a period of time necessary to complete a 20 week course, including previous approvals, maximum two (2) tubes per month.
If renewal criteria are not met, then do not approve.

RATIONALE
To ensure use consistent with FDA indication of the treatment of diabetic ulcers.

FDA APPROVED INDICATIONS
Becaplermin is indicated for treatment of lower-extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply. To be used as an adjunct to, and not a substitute for, good ulcer care practices, including initial sharp debridement, pressure relief, and infection control.

REFERENCES
1. Regranex. MedImpact P&T Monograph, February 1999.
2. Regranex Package Insert. McNeil Pharmaceutical, Raritan, New Jersey 08869.
3. MICROMEDEX® Healthcare Series Vol. 108.

Creation date: 11/2016
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

BEMPEDOIC ACID (NEXLETOL)

Generic	Brand	HICL	GCN	Exception/Other
BEMPEDOIC ACID	NEXLETOL	46382	47755	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following
1. Diagnosis of heterozygous familial hypercholesterolemia (HeFH) and/or atherosclerotic cardiosvascular disease (ASCVD)
2. Current use of, or documented intolerance/contraindication to maximally tolerated statin, ezetimibe, and PCSK9 inhibitor, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception inhibitor
3. Must have a current LDL level drawn within the last 90 days of greater than or equal to one of the following:
    a. 55 mg/dL for ASCVD at very high risk defined as multiple ASCVD events^^, or 1 ASCVD event and 2 or more high risk conditions (age ≥ 65 years, familial hypercholesterolemia, diabetes, HTN, eGFR 15-59, current smoking)
    b. 70 mg/dL for ASCVD not at very high risk
    c. 100 mg/dL for HeFH/HoFH

If initial criteria are met, approve at HICL x 6 months.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
1. Current LDL was reduced by at least 10% from baseline after starting Nexletol

If met, approve at HICL indefinitely.
If criteria are not met, do not approve.

DEFINITIONS:
ASCVD includes acute coronary syndromes (ACS), coronary artery disease (CAD), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)

Statin intolerance is defined as inability to tolerate at least 2 statins, with at least one started at lowest starting daily dose

RATIONALE:
The current American Heart Association/American College of Cardiology cholesterol guideline, as well at the KP National Cholesterol and Cardiac Risk Guideline, recommend medications with established efficacy in reducing the risk of cardiovascular events first-line in the treatment of hyperlipidemia and atherosclerotic cardiovascular disease. Specifically, these agents are statins, ezetimibe, and the PCSK9 inhibitors, the first 2 or which are on formulary. Bempedoic acid only produces a moderate reduction in LDL, much less than statins and PCSK9 inhibitors and on par with ezetimibe. This is our

rationale for this prior authorization criteria which will allow its use only after using these alternative agents which are recommended ahead of bempedoic acid in the current AHA/ACC cholesterol guidelines. Bempedoic acid's safety profile is comparable to these other agents, as all are well-tolerated and carry low risk of serious adverse reactions.

FDA APPROVED INDICATIONS
Adjunct to diet and statin therapy for the treatment of primary hyperlipidemia in adults with heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease, who require additional lowering of LDL-C

REFERENCES
Per Health Plan

Creation date: 10/14/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

BEMPEDOIC ACID (NEXLIZET)

Generic	Brand	HICL	GCN	Exception/Other
BEMPEDOIC ACID/EZETIMIBE	NEXLIZET	46386	47765	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following
1. Diagnosis of heterozygous familial hypercholesterolemia (HeFH) and/or atherosclerotic cardiosvascular disease (ASCVD)
2. Current use of, or documented intolerance/contraindication to maximally tolerated statin, ezetimibe, and PCSK9 inhibitor, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception inhibitor
3. Must have a current LDL level drawn within the last 90 days of greater than or equal to one of the following:
    a. 55 mg/dL for ASCVD at very high risk defined as multiple ASCVD events^^, or 1 ASCVD event and 2 or more high risk conditions (age ≥ 65 years, familial hypercholesterolemia, diabetes, HTN, eGFR 15-59, current smoking)
    b. 70 mg/dL for ASCVD not at very high risk
    c. 100 mg/dL for HeFH/HoFH

If initial criteria are met, approve at HICL x 6 months.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
1. Current LDL was reduced by at least 10% from baseline after starting Nexlizet

If met, approve at HICL indefinitely.
If criteria are not met, do not approve.

DEFINITIONS:
ASCVD includes acute coronary syndromes (ACS), coronary artery disease (CAD), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)

Statin intolerance is defined as inability to tolerate at least 2 statins, with at least one started at lowest starting daily dose

RATIONALE:
The current American Heart Association/American College of Cardiology cholesterol guideline, as well at the KP National Cholesterol and Cardiac Risk Guideline, recommend medications with established efficacy in reducing the risk of cardiovascular events first-line in the treatment of hyperlipidemia and atherosclerotic cardiovascular disease. Specifically, these agents are statins, ezetimibe, and the PCSK9 inhibitors, the first 2 or which are on formulary. Bempedoic acid only produces a moderate

reduction in LDL, much less than statins and PCSK9 inhibitors and on par with ezetimibe. This is our rationale for this prior authorization criteria which will allow its use only after using these alternative agents which are recommended ahead of bempedoic acid in the current AHA/ACC cholesterol guidelines. Bempedoic acid's safety profile is comparable to these other agents, as all are well-tolerated and carry low risk of serious adverse reactions.

FDA APPROVED INDICATIONS
Adjunct to diet and statin therapy for the treatment of primary hyperlipidemia in adults with heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease, who require additional lowering of LDL-C

REFERENCES
Per Health Plan

Creation date: 10/14/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

BENRALIZUMAB (FASENRA)

Generic	Brand	HICL	GCN	Exception/Other
BENRALIZUMAB	FASENRA	44635	47019, 44088	Formulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
1. Patient is new to KPCO within the past 90 days and noted as stable on therapy with Fasenra or Nucala (transitioning to KPCO preferred product Fasenra) for the treatment of asthma or EGPA
2. Medication is prescribed by an Allergist or Pulmonologist
3. Medication is not being used in combination with another biologic for the same indication

If above criteria are met, approve indefinitely, max 1mL per 28 days.
If above criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the diagnosis-specific criteria below:
A. DIAGNOSIS OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA, i.e. CHURG-STRAUSS SYNDROME): Must meet all the following:
   1. Must be prescribed by an Allergist or Pulmonologist
   2. Medication is not being used in combination with another biologic for the same indication

If initial criteria above are met, approve indefinitely, max 1 per 28 days.
If initial criteria above are not met, do not approve.

B. DIAGNOSIS OF MODERATE-TO-SEVERE PERSISTENT ASTHMA: Must meet all the following:
   1. Must be prescribed by an Allergist or Pulmonologist
   2. Uncontrolled asthma as evidenced by ANY one of the following:
      - Two or more asthma exacerbations requiring systemic corticosteroids (≥3 days each) in the past 12 months
      - one asthma-related hospitalization in the past 12 months
      - Asthma Control Test (ACT) consistently <20
   3. Adherent (≥75% proportion of days covered) to optimized drug therapy (triple drug therapy with high-dose ICS-LABA plus tiotropium (Spiriva Respimat)) for the previous 6 months, OR has contraindications or intolerance to ICS/LABA/tiotropium, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
   4. Medication is not being used in combination with another biologic for the same indication

If initial criteria above are met, approve indefinitely, max 1 per 28 days.
If initial criteria above are not met, do not approve.

C. DIAGNOSIS OF HEMATOLOGIC HYPEREOSINOPHILIC SYNDROMES: Must meet all the following:
   1. Must be prescribed by a hematologist
   2. Medication is not being used in combination with another biologic for the same indication

3. Absolute eosinophil count of >1.5 on 2 occasions >1 month apart or tissue showing 20% involvement on bone marrow or other tissue infiltration
4. Documented end organ dysfunction caused by this syndrome
5. FIP1L1-PDGFRA mut negative
6. Diagnosed at least 6 months prior
7. Disease relapse after at least 2 previous trials of systemic corticosteroids in conjunction with hydroxyurea, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If initial criteria above are met, then approve x8 months.
If initial criteria above are not met, do not approve.

RENEWAL CRITERIA: Must meet the following criteria:
A. Patient previously authorized for coverage of Fasenra for the treatment of asthma.

If met, approve indefinitely, max 1 per 28 days.
If renewal criteria are not met, do not approve. [Fasenra for the treatment of hematologic hyper-eosinophilic syndromes is not designed as an open-ended intervention.]

RATIONALE
Per Health Plan and current treatment guidelines.

Benralizumab has anti-eosinophilic activity that makes it a reasonable choice for EGPA in situations where the physician deems it the best choice for EGPA.

FDA APPROVED INDICATIONS
Asthma (Moderate to Severe)

REFERENCES
Table 1: High-dose ICS and High-dose ICS plus LABA combinations for Age ≥12 years

fluticasone/salmeterol DPI (Advair Diskus) 500/50 mcg, 1 inh twice daily
fluticasone/salmeterol MDI (Advair HFA) 230/21 mcg, 2 puffs twice daily
mometasone/formoterol MDI (Dulera) 200/5 mcg, 2 puffs twice daily
ciclesonide MDI (Alvesco) 160 mcg, 2 puffs twice daily
fluticasone MDI (Flovent HFA) 220 mcg, 2 puffs twice daily
Budesonide DPI (Pulmicort Flexhaler) 180 mcg, 4 inh twice daily
Mometasone MDI (Asmanex HFA) 200 mcg, 2 puffs twice daily
Mometasone DPI (Asmanex Twisthaler) 220 mcg, 2 inh twice daily

Creation Date: 09/2021
Effective Date: 01/2024
Revised Date: 07/2023
Reviewed Date: 07/2023

BEXAGLIFLOZIN (BRENZAVVY)

Generic	Brand	HICL	GCN	Exception/Other
BEXAGLIFLOZIN	BRENZAVVY	48644		NF 4th Preferred

GUIDELINES FOR COVERAGE
Must be used for one of the following indications and meet all related criteria as follows:

A. Adults 25 years of age or older with DM2
B. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat adults 25 years of age or older with type 2 diabetes: Must meet all the following:
   1. Most recent HgbA1c is above, but within 2% of their designated A1c goal
   2. Patient has an eGFR of at least 20 ml/min
   3. Patient has contraindications to, is currently using, or has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. maximum dose metformin IR and subsequently metformin ER
      b. empagliflozin (Jardiance)
      c. maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
         i. h/o bariatric surgery
         ii. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
         iii. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e. sulfonylurea, insulin, pioglitazone)
         iv. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If all criteria met, approve at HICL x6 months, max 1 tablet per day.
If criteria are not met, do not approve.

B. To treat type 2 diabetes in young adult/pediatric patients between 10 and 25 years of age: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Patient has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER
   2. Patient has an eGFR of at least 20 ml/min and has tried and failed, or has an intolerance or contraindication to empagliflozin (Jardiance)
   3. Patient has contraindications to, is currently using, or has failed maximum dose pioglitazone unless the patient has one of the following:

i. h/o bariatric surgery
ii. BMI ≥ 95%ile for age and sex
iii. ≥ 5% increase in body weight after 6 months of starting these medications
iv. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If all criteria met, approve at HICL x6 months, max 1 tablet per day.
If criteria are not met, do not approve.

RENEWAL CRITERIA
1. HgbA1c is either at goal or has decreased by at least 0.5%.

If renewal criteria are met, approve indefinitely at HICL, max 1 tablet per day.
If renewal criteria are not met, do not approve.

RATIONALE
- KP National Diabetes Guidelines recommend using SGLT-2i for people with type 2 diabetes with clinical ASCVD who are already taking metformin to reduce the risk of: (1) cardiovascular events (myocardial infarction or stroke) or cardiovascular death, (2) progression of renal disease and/or (3) death from renal causes, and/or (4) heart failure hospitalizations. The American College of Cardiology (ACC) 2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients with Type 2 Diabetes, which is also endorsed by the American Diabetes Association (ADA), recommends SGLT-2i as a first-line treatment in patients with type 2 diabetes and one or more of the following: ASCVD, HFrEF, HFpEF (empagliflozin only), diabetic kidney disease (DKD), or at high risk for ASCVD.
- Preferred order of agents:
  1) Empagliflozin (Jardiance), formulary without PA, is the preferred agent for ASCVD, CKD, and HF due to strength of clinical trial data, range of approved indications, and cost (1/2 tab regimen)
  2) Canagliflozin (Invokana), non-formulary with PA, is the 2nd preferred option for ASCVD, CKD and DM2 patients without compelling indications. due to broad range of indications and cost (1/2 tab regimen).
  3) Dapagliflozin (Farxiga), non-formulary with PA, is the 2nd preferred option for HF, and the 3rd preferred option for ASCVD, CKD and DM2 patients without compelling indications due to broad range of indications but at high cost.
  4) Ertugliflozin (Steglatro), non-formulary with PA, is least preferred due to high cost, paucity of positive clinical trial data, and lack of additional FDA-approved indications. Specifically, ertugliflozin has been studied in patients with type 2 diabetes and ASCVD and did not improve cardiovascular outcomes while all three other SGLT-2i have demonstrated such benefits in this population.
  5) Bexagliflozin (Brenzavvy): non-formulary with PA, is least preferred due to high cost and lack of additional FDA-approved indications.
  6) Sotagliflozin (Inpefa): non-formulary with PA, is 3rd preferred for HF given shorter history of postmarketing safety data compared to other SGLT2i's approved for HF as well as the need to titrate sotagliflozin dose for when others are fixed-dose regimens. Sotagliflozin (Inpefa) is least preferred for glycemic control due to lack of clinical trial data and FDA-approved indication as well as its high cost.
- Jardiance (empagliflozin) is the preferred sodium glucose co-transporter 2 inhibitor (SGLT-2i) at Kaiser Permanente Colorado (KPCO) and can be used effectively and safely with a GFR down to

20 mL/min. In addition, the dose of 12.5 mg (1/2 of 25mg tablet) is an effective dose for all patients regardless of GFR.

- Based on the available evidence, various organizations endorse SGLT-2is use down to lower GFR levels than indicated in product labels:
  - American College of Cardiology Expert Consensus now recommends empagliflozin in GFR ≥ 20 mL/min (2021).
  - National Kidney Foundation recommends SGLT-2is in GFR ≥ 20 mL/min as long as there are no contraindications (2023).
  - American Diabetes Association recognizes SGLT-2is benefits in patients with GFR ≥ 20 mL/min (2023).

FDA APPROVED INDICATIONS for SGLT2 Inhibitors

Empagliflozin (Jardiance)

1. Improve glycemic control in patients with DM2
2. Reduce the risk of CV death in pts with DM2 + CVD
3. Reduce risk of CVD death and HF hospitalizations in pts with HF
4. Reduce risk of sustained eGFR decline, ESRD, CV death and hospitalizations in adults with CKD at risk of progression

Canagliflozin (Invokana)

1. Improve glycemic control in patients with DM2
2. Reduce risk of MACE in pts with DM2 + CVD
3. Reduce the risk of ESRD, doubling of creatinine, CV death, or HF hospitalization in pts with DM2 + diabetic nephropathy

Dapagliflozin (Farxiga)

1. Improve glycemic control in patients with DM2
2. Reduce risk of HF hosp in pts with DM2 + CVD/multiple CV RFs
3. Reduce the risk of CV death and HF hosp in patients with HFrEF NYHA II-IV
4. Reduce risk of sustained eGFR decline, ESRD, CV death, and hospitalization for HF in adults with CKD at risk of progression

Ertugliflozin (Steglatro)

1. Improve glycemic control in patients with DM2

Bexagliflozin (Brenzavvy)

1. Improve glycemic control in patients with DM2

Sotagliflozin (Inpefa)

1. Reduce the risk of CV death and HF hosp in pts with heart failure
2. Reduce the risk of CV death and HF hosp in pts with DM2 + CKD + CV RF(s)

REFERENCES

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012

3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation date: 01/2024
Effective date: 02/2024
Reviewed date: 01/2024
Revised date:

BLADDER PAIN SYNDROME (BPS)/INTERSTITIAL CYSTITIS (ICS): PENTOSAN POLYSULFATE SODIUM

Generic	Brand	HICL	GCN	Exception/Other
PENTOSAN POLYSULFATE SODIUM	ELMIRON	08734	41229	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: All the following criteria must be met:

1. The requesting provider is a CPMG Urologist or Uro-gynecologist or an affiliated network Urologist/Uro-Gynecologist with active referral, if needed
2. The patient has a diagnosis of interstitial cystitis (ICS)/ bladder pain syndrome (BPS)
3. Patient has had an eye exam with an Ophthalmologist within the past 365 days
4. Patient less than 65 years of age must have an intolerance to or past failure of a TCA, hydroxyzine, or cimetidine, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria above are met, approve indefinitely with max daily dose of 1 capsule (100 mg).
If initial criteria above are not met, do not approve.

For Quantity Limit overrides:
For all requests of pentosan doses > 100 mg/day

- The patient has tried pentosan 100 mg/day with some benefit, such as a decrease in pain, urgency and/or frequency

If meets above criteria, then approve x indefinitely.
If not met, do not approve.

Note: quantity limit of 100mg/day is based on a safety concern regarding an eye condition called maculopathy which can cause a decrease or change in vision and the risk is higher with higher doses.

RATIONALE

Ensure appropriate criteria are used for requests of pentosan according to approved indication, dosing, national treatment guidelines and clinical studies.

FDA APPROVED INDICATIONS:

Relief of bladder pain or discomfort due to Interstitial Cystitis

HOW SUPPLIED:

Capsules - 100 mg

Creation date: 07/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

BOSUTINIB

Generic	Brand	HICL	GCN/GPID	Other
BOSUTINIB	BOSULIF	39590		Nonformulary, 2nd Generation TKI

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

A. Patient is new to KPCO within the past 90 days, and the medication has been prescribed by an Oncologist

If met, approve x 2 years.
If not met, then use Initial Criteria.

INITIAL CRITERIA: Must meet the following criteria based on drug and diagnosis below:

A. Bosutinib (Bosulif) for All Phases of CML and ALL
B. All other indications

A. **Bosutinib (Bosulif) for CML (any phase) or ALL: Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Patient must not have any of the following BCR-ABL1 mutations: T315I, V299L, G250E or F317L
   3. Patient must have Philadelphia Chromosome (aka BCR-ABL) and one of a through c below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient must have a documented intolerance to imatinib (Gleevec, if chronic phase CML), and/or dasatinib (Sprycel), and/or nilotinib (Tasigna) not alleviated by dose reductions (see below)
         i. Imatinib (Gleevec): ≤200 mg/day [adult] or 260mg/m^2 [peds; if this calculates to >200mg/day use adult dose cutoff]
         ii. Nilotinib (Tasigna): 400mg/day, if peds 230mg/m2 daily
         iii. Dasatinib (Sprycel): 70mg/day [If patient developed pulmonary arterial hypertension (PAH) during treatment with dasatinib (Sprycel) (at any dose), patient may be deemed "intolerant"]; for peds use table below

Weight	Dose of dasatinib (Sprycel) which must be tried and failed before deeming patient "intolerant"
10 to <20kg	20mg
20 to <30kg	20mg
30 to <45kg	50mg
45kg+	Use adult dose cutoff

b. Patient must have one of the following BCR-ABL1 mutations: E255K/V, F317L/V/I/C, F359V/C/I, T315A, or Y253H
c. Patient has tried and failed imatinib (Gleevec, if chronic phase CML), and/or dasatinib (Sprycel), and/or nilotinib (Tasigna) with an inadequate response that is not due to patient nonadherence

If criteria are met, approve x 2 years.
If criteria are not met, do not approve.

B. **If for any other diagnosis (e.g., hypereosinophilic syndrome, eosinophilic leukemia, dermatofibrosarcoma, chordoma): Must meet all the following:**
1. Prescribed by an oncology specialist
2. Use must meet the Medicare Compendia criteria as detailed in the following policy: Medicare Benefit Policy Manual Chapter 15 - Covered Medical and Other Health Services Section 50.4.5 - Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

If criteria are met, approve x 1 year.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
A. Patient has been on the TKI for greater than 3 months and one of the following criteria:
1. Disease progression or relapse are not noted in the chart
2. Patient has experienced improvement in disease symptoms since starting the medication

If criteria are met, approve x 2 years.
If criteria are not met, do not approve.

RATIONALE

REFERENCES
1. NCCN Clinical Practice Guidelines in Oncology Chronic Myeloid Leukemia v.2.2023 www.nccn.org
2. NCCN Clinical Practice Guidelines in Oncology Acute Lymphoblastic Leukemia v.1.2022 www.nccn.org
3. NCCN Clinical Practice Guidelines in Oncology Gastrointestinal Stromal Tumors (GISTs) v.1.2023 www.nccn.org

Creation Date: 11/2019
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

BRAND WHEN GENERIC IS AVAILABLE

Generic	Brand	HICL	GCN	Exception/Other
N/A	N/A	N/A	N/A	

GUIDELINES FOR USE OF BRANDS WHEN A GENERIC IS AVAILABLE (NON-AED)

Brand medications (non-AED) when a generic is available, when not excluded from benefit coverage, will be approved when ALL the following criteria are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. An authorized generic is not available
2. Patient has a documented allergic reaction to an inactive ingredient in the generic product (example: dye) not present in the brand name product and other generic equivalents to the brand are not available without the inactive ingredient which caused the allergic reaction
3. Patient has treatment failure, intolerance, or contraindication to at least three other formulary, therapeutic alternatives (Note: In cases where no other alternatives are available, only the generic equivalent needs to have been tried)
4. Patient meets requirements for coverage for generic equivalent, when/if applicable

If 1 through 4 are met, approve the brand indefinitely.
If criteria are not met, do not approve.

GUIDELINES FOR USE OF BRAND ANTIEPILEPTIC DRUGS WHEN A GENERIC IS AVAILABLE

Brand antiepileptic medications when a generic is available, when not excluded from benefit coverage, will be approved when two of the following criteria are met and one of those must be #7, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Patient is less than 18 years of age
2. Patient has a history of status epilepticus
3. Patient has a history of multiple (more than 1) seizures in one day
4. Patient has a history of a seizure in the past 30 days
5. Patient has a documented allergic reaction to an inactive ingredient in the generic product (example: dye) not present in the brand name product and other generic equivalents to the brand are not available without the inactive ingredient which caused the allergic reaction
6. Patient is currently pregnant
7. An authorized generic is not available

If 1, 2, 3, 4, or 5 AND 7 is met, approve the brand antiepileptic indefinitely.
If 6 AND 7 is met, approve the brand antiepileptic x 1 year.

If criteria are not met, do not approve.

RATIONALE

- Per KPCO Health Plan, Pharmacy Benefits Department
- Excerpted from the BWGA FAQ's Clinicians CO Final 11.15.19 and the BWGA FAQ's Member CO Final 11.18.19 documents created and approved by the KPCO Drug Use Management team
- KPNW BWGA guideline, 2020
- Brand to Generic Antiepileptic FAQ, 2018

Background from CO BWGA documents:

- The FDA requires generic drugs to have the same quality and performance as brand name drugs.
- Patients can expect the same quality, performance, safety, and side-effects with the generic as with the brand-name product. In many cases, the generic is even made by the same company ("authorized generics").
- The nonformulary exception process should not apply for brand medications when the equivalent generic medication is available (BWGA) because they contain the same active ingredients. The exception is in very RARE situations where patients have a documented allergy to a specific inactive ingredient in the equivalent generic medication.

Creation date: 07/2021
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 9/2023

BREXPIPRAZOLE (REXULTI)

Generic	Brand	HICL	GCN/GPID	Exception/Other
BREXPIPRAZOLE TABLET	REXULTI	42283		Half-tab approved

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO within the past 90 days and is stable on therapy.

If met, approve indefinitely at HICL.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following diagnoses and meet all related criteria below:

A. Agitation associated with Alzheimer's Disease
B. Major depressive disorder
C. Schizophrenia

A. Agitation associated with Alzheimer's Disease
   1. Agitation related behaviors place patient at risk of harm to themselves or others
   2. Documented intolerance or treatment failure to TWO of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception: aripiprazole, olanzapine, quetiapine, risperidone, citalopram, escitalopram, or sertraline.

If criteria are met, approve x 6 months at HICL.
If criteria are not met, do not approve.

B. Major Depressive Disorder
   1. Patient is at least 18 years of age
   2. Concomitant therapy with an antidepressant
   3. Documented contraindication, intolerance, or treatment failure to the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Two antidepressants
      b. One antipsychotic

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

C. Schizophrenia
   1. Patient is at least 13 years of age
   2. Documented contraindication, intolerance, or treatment failure to at least 1 antipsychotic, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

RENEWAL CRITERIA:
If the medication was initially approved for agitation associated with Alzheimer's Disease, the provider must document that a brexpiprazole (Rexulti) dose reduction trial has been attempted.

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

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ePA Questions
Initial Review Questions
1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Agitation associated with Alzheimer's Disease; Major depressive disorder; Schizophrenia]
   QUESTIONS BASED ON DIAGNOSIS SELECTED
   Agitation associated with Alzheimer's Disease
      1. Do agitation-related behaviors place patient at risk of harm to themselves or others?
      2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
      3. Is there reasoning why alternatives (i.e. aripiprazole tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets; citalopram tablets/solution, escitalopram tablets, sertraline tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
   Major depressive disorder
      1. Will this medication be used as concomitant therapy with an antidepressant?
      2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
      3. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules; citalopram tablets/solution, escitalopram tablets, fluoxetine capsules/solution, paroxetine IR tablets, sertraline tablets; venlafaxine ER capsules (37.5 mg, 75 mg, 150 mg), duloxetine capsules (20 mg, 30 mg, 60 mg); vilazodone tablets; bupropion XL tablets (150 mg, 300 mg), bupropion IR tablets (75 mg); mirtazapine tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
   Schizophrenia

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Renewal Review Questions

1. Has a brexpiprazole (Rexulti) dose reduction trial been attempted?

RATIONALE

Regarding agitation associated with dementia due to Alzheimer's disease indication, non-drug interventions are first line and psychotropic medications should be reserved for those cases when symptoms present a danger to the person and/or others. Brexpiprazole is the only FDA approved antipsychotic for this indication; however, it still has a boxed warning like all other antipsychotics regarding the increased risk of mortality in elderly patients with dementia-related psychosis. Additionally, there is extensive off-label data, including randomized controlled trials and meta-analyses, for use of other antipsychotics and antidepressants, specifically aripiprazole, olanzapine, quetiapine, risperidone, escitalopram, citalopram, and sertraline in the management of various behavioral and psychological symptoms of dementia (BPSD) symptoms. Comparative efficacy data with brexpiprazole and these other off-label treatment options is difficult, since brexpiprazole studies used a different and specific primary outcome measure (eg Cohen-Mansfield Agitation Inventory vs Neuropsychiatric Inventory [NPI]). Off-label antipsychotics have shown 35% reduction in baseline NPI score with small effect size (range = 0.12-0.20 based on one meta-analysis). Brexpiprazole studies found a 31% reduction in baseline CMAI total score compared with patients on placebo with a small effect size 0.18 - 0.25 in primary analyses. Additionally, risperidone is indicated for the short-term treatment of persistent aggression in Alzheimer's Disease in some countries outside the United States. Off-label antidepressants, specifically citalopram (20-30 mg/d), escitalopram (10 mg/d), and sertraline (50-200 mg/d), have been found to work as well as an antipsychotic with better tolerability and safety profile. However, antidepressants may take longer to work. More recent treatment guidelines recommend against the use of haloperidol and other first-generation antipsychotics as first-line agents because of several studies showing a higher risk of mortality compared with second-generation antipsychotics. Carbamazepine and valproate products have limited/mixed evidence for benefit. For any psychotropic used for BPSD, a gradual dose reduction trial is recommended after at least 4 months (assuming symptoms have stabilized or stopped) since BPSD may be temporary. Several studies have shown patients receiving treatment for BPSD and withdrawn from an antipsychotic showed no worsening of behavioral symptoms. A small group of patients may experience worsening of BPSD after withdrawal of the antipsychotic, but it is difficult to identify these patients.

Regarding major depressive disorder (MDD) criteria, both risperidone and ziprasidone have off-label data for treatment of MDD which can be reviewed in Lexicomp.

FDA APPROVED INDICATIONS

Brexpiprazole (Rexulti)

1. **Agitation associated with dementia due to Alzheimer's Disease**: Max daily dose: 3mg.
2. **Major depressive disorder (unipolar):** Adjunctive treatment in adults for the treatment of major depressive disorder (max daily dose: 3 mg).
3. **Schizophrenia:** Treatment of schizophrenia in pediatric patients ≥13 years of age and adults (max daily dose: 4 mg).

APPENDIX A. Formulary antipsychotics

First-generation antipsychotics	Second-generation antipsychotics
Chlorpromazine	Aripiprazole
Fluphenazine	Clozapine
Haloperidol	Lurasidone
Loxapine	Olanzapine
Molindone	Quetiapine
Perphenazine	Risperidone
Pimozide	Ziprasidone
Thioridazine	
Thiothixene	
Trifluoperazine	

HOW SUPPLIED:
Brexpiprazole (Rexulti): 0.25 MG, 0.5 MG, 1 MG 2 MG, 3 MG, 4 MG

***The following are approved for tablet splitting:**
Brexpiprazole (Rexulti) 0.5 mg (use for 0.25 mg doses)
Brexpiprazole (Rexulti) 1 mg (use for 0.5 mg doses)
Brexpiprazole (Rexulti) 2 mg (use for 1 mg doses)
Brexpiprazole (Rexulti) 4 mg (use for 2 mg doses)

REFERENCES
American Psychiatric Association. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. 3rd ed. Washington, DC: American Psychiatric Association; 2021.

Drug FAQs: Antipsychotics in the Elderly. KPCO. 2020.

Grossberg GT, Kohegyi E, Mergel V, et al. Efficacy and safety of brexpiprazole for the treatment of agitation in Alzheimer's Dementia: two 12-week, randomized, double-blind, placebo-controlled trials. Am J Geriatr Psychiatry. 2020;28 (4):383-400.
Mayths M. Pharmacologic management of behavioral and psychological symptoms of major neurocognitive disorder. Ment Health Clin. 2018;B96):284-93.

Rexulti. Package insert. Otsuka America Pharmaceutical, Inc.; November 9, 2022.

Ruelaz Maher A, Maglione M, Bagley S, et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: a systematic review and meta-analysis. JAMA. 2011;306(12):1359-1369.

Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord 2018;20:97-170.

Creation Date: 3/2023
Effective Date: 4/2024
Reviewed Date: 3/2024
Revised Date: 3/2024

BRODALUMAB (SILIQ)

Generic	Brand	HICL	GCN	Exception/Other
BRODALUMAB	SILIQ	44102		Non-formulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on therapy, Medication is not being used in combination with another biologic for the same indication, and meets all indication-specific criteria below:
   1. Patient has a diagnosis of Psoriasis and is being prescribed by a CPMG or affiliated dermatologist

If met, then approve at HICL indefinitely with the following quantity limits:
- Brodalumab (Siliq): 2 syringes per 28 days [MDD 0.11].

If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Psoriasis: All the following must be met:
   1. Patient has a diagnosis of moderate to severe psoriasis and the medication is prescribed by a dermatology provider.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. The patient is 18 years of age or older
   4. Patient has experienced an inadequate response (after at least two months of therapy), intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. A topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus), or the patient is reported as having very high disease activity (ex: > 50% BSA, erythrodermic, pustular psoriasis), disease affecting critical areas (ex: genitals, face), or prior biologic therapy within the past 4 months, skip and proceed to step 4c
      b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Acitretin, Cyclosporine, Methotrexate, Apremilast (Otezla), Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
      c. At least one TNF inhibitor (adalimumab (Amjevita) - preferred [F, PA], infliximab (Inflectra) - preferred [F], etanercept (Enbrel) [F, PA]) - unless the patient has failed an IL-17 inhibitor
      d. At least one IL-17 inhibitor (secukinumab (Cosentyx) - preferred [F])
      e. At least one IL-23 inhibitor: guselkumab (Tremfya) - preferred [NF, PA], risankizumab-rzaa (Skyrizi) [NF, PA]

If criteria are met, approve at HICL with a quantity limit of a max 3 syringes per 28 days [MDD 0.16] x 1 month (loading dose), then max 2 syringes per 28 days [MDD 0.11] (maintenance dose) indefinitely.
If above criteria are not met, do not approve.

RENEWAL CRITERIA:
1. The diagnosis for which the patient was originally authorized medication coverage, has been assessed by the applicable specialist in the past two years.
2. Medication is not being used in combination with another biologic for the same indication.

If met, then approve at HICL indefinitely with a quantity limit of 2 syringes per 28 days [MDD 0.11].
If not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member, Initial, or Renewal PA Criteria prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval.

A. Patient diagnosis of Psoriasis:
   1. Documentation by dermatology provider of the patient resuming therapy after a gap 3 months or longer in treatment (to reload)

If above criteria are met, then approve at HICL with the following quantity limits of max 3 syringes per 28 days [MDD 0.16] x 1 month (loading dose), then max 2 syringes per 28 days [MDD 0.11] (maintenance dose) indefinitely.
If above criteria are not met, deny and offer indefinite approvals of brodalumab (Siliq): 2 syringes per 28 days [MDD 0.11].

RATIONALE
Per Health Plan - CPS in Derm

FDA APPROVED INDICATIONS
1. Siliq: Treatment of moderate to severe plaque psoriasis in adults

REFERENCES
"Currently stable on medication," means patient is tolerating well, medication appears to be effective, and provider wishes to continue therapy.

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (e.g., systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for psoriasis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*

Creation Date: 11/2019
Effective Date: 01/2024
Reviewed Date: 11/2023
Revised Date: 11/2023

BUPRENORPHINE PATCH

Generic	Brand	HICL	GCN	Exception/Other
BUPRENORPHINE	BUTRANS PATCH	23438		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and currently using buprenorphine patch

If met, approve x1 month.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient is 18 years of age or older
2. Patient has a chronic pain diagnosis
3. Medication is not being used for treatment of opioid use disorder
4. Patch is being used x1 as part of a micro-dosing strategy to transition to sublingual buprenorphine; or the patient's daily opioid dose is 80 MME or less and the patient has one of the following:
   - History of or active substance use disorder (including not limited to opioid use disorder, alcohol use disorder, amphetamine use disorder, cocaine use disorder, benzodiazepine use disorder)
   - High risk of opioid misuse or abuse
   - History of or active chronic pulmonary condition (untreated obstructive sleep apnea, COPD, chronic O2 requirement)
   - Failed the following formulary alternatives or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception: Morphine SR tablets, Fentanyl patches, methadone tablets

   If initial criteria are met as part of a micro-dosing strategy, approve x1 fill only. If initial criteria are met for any other use, approve indefinitely at HICL.
   If initial criteria are not met, do not approve.

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ePA Questions for Provider Outreach
1. Diagnosis associated with this request: [check boxes for possible diagnoses listed in criteria: treatment of chronic pain; treatment of opioid use disorder]
   QUESTIONS BASED ON DIAGNOSIS SELECTED
   Treatment Of Chronic Pain
   1. Is the patch being used one time only as part of a micro-dosing strategy to transition to sublingual buprenorphine?
   2. Patient's total daily opioid dose (MME):
   3. Does the patient have any of the following conditions (check any/all boxes that apply):
      a. History of or active substance use disorder (including not limited to opioid use disorder, alcohol use disorder, amphetamine use disorder, cocaine use disorder, benzodiazepine use disorder)

   b. High risk of opioid misuse or abuse
   c. History of or active chronic pulmonary condition (untreated obstructive sleep apnea, COPD, chronic O2 requirement)
4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
5. Is there reasoning why alternatives (Morphine SR tablets, Fentanyl patches, methadone tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

FDA APPROVED INDICATIONS

Pain management: Management of pain severe enough to require around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Creation Date: 07/2023
Effective Date: 08/2023
Reviewed Date: 03/2024
Revised Date: 03/2024

CABOTEGRAVIR (VOCABRIA)

Generic	Brand	HICL	GCN	Exception/Other
CABOTEGRAVIR SODIUM	VOCABRIA	46411		Oral cabotegravir is an option for starting Cabenuva treatment of HIV. It can also be used in instances where patients have missed a scheduled Cabenuva administration to restart therapy.

GUIDELINES FOR COVERAGE

INITIAL CRITERIA
Must meet all the following:
1. Patient must be 12 years of age or older
2. Must be prescribed by an Infectious Disease provider
3. Patient has HIV and the virus shows no evidence of resistance to integrase strand inhibitors (INSTIs - raltegravir, dolutegravir, elvitegravir, bictegravir, cabotegravir) or nonnucleoside reverse-transcriptase inhibitors (NNRTIs - efavirenz, delavirdine, nevirapine, rilpivirine)
4. Patient has no history of treatment failure (i.e., failure to consistently suppress viral load to undetectable levels) with previous HIV regimens
5. Current HIV viral suppression is documented by an HIV-1 RNA less than 50 copies per mL for at least the past 6 months
6. Patient has had no treatment interruptions lasting two weeks or more in the past 6 months

If initial criteria are met, approve x3 fills only x1 year.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA
Must meet the following:
1. Patient has not missed more than 2 scheduled administrations of cabotegravir/rilpivirine (Cabenuva) by 7 days or more in the past 12 months.

If met, approve x3 fills only x1 year.
If not met, do not approve.

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ePA questions for Provider Outreach
INITIAL REVIEW QUESTIONS
1. Does the patient's virus show evidence of resistance to integrase strand inhibitors (INSTIs – raltegravir, dolutegravir, elvitegravir, bictegravir, cabotegravir) or nonnucleoside reverse-transcriptase inhibitors (NNRTIs – efavirenz, delavirdine, nevirapine, rilpivirine)?
2. Does the patient have history of treatment failure (i.e. failure to consistently suppress viral load to undetectable levels) with previous HIV regimens?
3. 2 most recent HIV-1 RNA Lab values (copies per mL):
    a. Lab 1:
    b. Lab 2:
4. Dates of HIV-1 RNA Lab values (MMDDYY):
    a. Date of Lab 1:
    b. Date of Lab 2:
5. How many treatment interruptions lasting two weeks or more has the patient had in the past 6 months?

RENEWAL REVIEW QUESTIONS

1. How many scheduled administrations of cabotegravir/rilpivirine (Cabenuva) has the patient missed by 7 days or more in the past 12 months?

RATIONALE

Per Health Plan.

FDA APPROVED INDICATIONS

HIV-1 infection:
Preexposure prophylaxis: Oral: As oral lead-in to assess tolerability of cabotegravir prior to administration of IM cabotegravir or as oral bridging therapy for missed cabotegravir injections.

Treatment: Oral: Short-term treatment of HIV-1 infection (in combination with rilpivirine) in adults and adolescents ≥12 years of age weighing ≥35 kg who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known or suspected resistance to cabotegravir or rilpivirine, as an oral lead-in to assess tolerability of cabotegravir prior to initiating IM cabotegravir and rilpivirine, or an oral bridging therapy for missed cabotegravir injections.

REFERENCES

NNRTI - nonnucleoside reverse transcriptase inhibitor
INSTI - integrase strand transfer inhibitor

Vocabria (cabotegravir) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2022.

Creation Date: 07/2021
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

CALCIPOTRIENE CREAM (DOVONEX)

Generic	Brand	HICL	GCN	Exception/Other
CALCIPOTRIENE CREAM	DOVONEX		1851	Nonformulary

GUIDELINES FOR COVERAGE

Must have one of the following indications and meet all indication specific criteria:
A. Actinic Keratosis
B. Psoriasis

A. Actinic Keratosis:
   1. Medication is prescribed by a CPMG or affiliated dermatology provider.

If above criteria are met, approve at GPID indefinitely.
If above criteria are not met, do not approve.

B. Psoriasis:
   1. Patient with inadequate response or intolerance to calcitriol ointment or calcipotriene solution, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If above criteria are met, approve at GPID indefinitely.
If above criteria are not met, do not approve.

RATIONALE

Per Health Plan and current treatment guidelines

Creation Date: 07/2022
Effective Date: 01/2024
Revised Date: 07/2023
Reviewed Date: 07/2023

CANAGLIFLOZIN (INVOKANA)

Generic	Brand	HICL	GCN	Exception/Other
CANAGLIFLOZIN	INVOKANA	40171		NF 1st Preferred – 0.5 tab of 300mg (150mg/day)

GUIDELINES FOR COVERAGE
Must be used for one of the following indications and meet all related criteria as follows:

A. Adults 25 years of age or older with DM2 and ASCVD
C. Adults 25 years of age or older with DM2 with Nephropathy
D. Adults 25 years of age or older with DM2 without ASCVD or diabetic nephropathy
E. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat adults 25 years of age or older with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD) [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    1. Patient has contraindication or intolerance to, is currently using, or has failed maximum doses of metformin IR and/or metformin ER, or the patient's A1c is at goal and SGLT-2i is more appropriate for ASCVD, CKD and/or HF benefit
    2. Patient has an eGFR of at least 20 ml/min and has tried and failed, or has an intolerance or contraindication to empagliflozin (Jardiance)

If all criteria met, approve at HICL indefinitely, max 0.5 tablet per day.
If criteria are not met, do not approve.

B. To treat adults 25 years of age or older with type 2 diabetes with nephropathy: Must meet all the following:
    1. eGFR is at least 20 ml/min, and eGFR is less than 60 ml/min and/or urinary albumin-to-creatinine ratio greater than 300
    2. The patient has contraindication to, is currently using, or has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        a. Maximum doses of metformin IR and/or metformin ER, or the patient’s A1c is at goal and SGLT-2i is more appropriate for ASCVD, CKD and/or HF benefit
        b. ACE-I or ARB
        c. empagliflozin (Jardiance)

If all criteria met, approve at HICL indefinitely, max 0.5 tablet per day.
If criteria are not met, do not approve.

C. To treat adults 25 years of age or older with type 2 diabetes without ASCVD or diabetic nephropathy: Must meet all the following:
   1. Most recent HgbA1c is above, but within 2% of their designated A1c goal
   2. Patient has an eGFR of at least 20 ml/min
   3. Patient has contraindications to, is currently using, or has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. maximum dose metformin IR and subsequently metformin ER
      b. empagliflozin (Jardiance)
      c. maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
         i. h/o bariatric surgery
         ii. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
         iii. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e. sulfonylurea, insulin, pioglitazone)
         iv. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If all criteria met, approve at HICL x6 months, max 0.5 tablet per day.
If criteria are not met, do not approve.

D. To treat type 2 diabetes in young adult/pediatric patients between 10 and 25 years of age: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Patient has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER
   2. Patient has an eGFR of at least 20 ml/min and has tried and failed, or has an intolerance or contraindication to empagliflozin (Jardiance)
   3. Patient has contraindications to, is currently using, or has failed maximum dose pioglitazone unless the patient has one of the following:
      a. h/o bariatric surgery
      b. BMI ≥ 95%ile for age and sex
      c. ≥ 5% increase in body weight after 6 months of starting these medications
      d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If all criteria met, approve at HICL x6 months, max 0.5 tablet per day.
If criteria are not met, do not approve.

RENEWAL CRITERIA
1. HgbA1c is either at goal or has decreased by at least 0.5%.

If renewal criteria are met, approve indefinitely at HICL, max 0.5 tablet per day.
If renewal criteria are not met, do not approve.

RATIONALE
- KP National Diabetes Guidelines recommend using SGLT-2i for people with type 2 diabetes with clinical ASCVD who are already taking metformin to reduce the risk of: (1) cardiovascular events (myocardial infarction or stroke) or cardiovascular death, (2) progression of renal disease and/or (3) death from renal causes, and/or (4) heart failure hospitalizations. The American College of Cardiology (ACC) 2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients with Type 2 Diabetes, which is also endorsed by the American Diabetes Association (ADA), recommends SGLT-2i as a first-line treatment in patients with type 2 diabetes and one or more of the following: ASCVD, HFrEF, HFpEF (empagliflozin only), diabetic kidney disease (DKD), or at high risk for ASCVD.
- Preferred order of agents:
    1) Empagliflozin (Jardiance), formulary without PA, is the preferred agent for ASCVD, CKD, and HF due to strength of clinical trial data, range of approved indications, and cost (1/2 tab regimen)
    2) Canagliflozin (Invokana), non-formulary with PA, is the 2nd preferred option for ASCVD, CKD and DM2 patients without compelling indications. due to broad range of indications and cost (1/2 tab regimen).
    3) Dapagliflozin (Farxiga), non-formulary with PA, is the 2nd preferred option for HF, and the 3rd preferred option for ASCVD, CKD and DM2 patients without compelling indications due to broad range of indications but at high cost.
    4) Ertugliflozin (Steglatro), non-formulary with PA, is least preferred due to high cost, paucity of positive clinical trial data, and lack of additional FDA-approved indications. Specifically, ertugliflozin has been studied in patients with type 2 diabetes and ASCVD and did not improve cardiovascular outcomes while all three other SGLT-2i have demonstrated such benefits in this population.
    5) Bexagliflozin (Brenzavvy): non-formulary with PA, is least preferred due to high cost and lack of additional FDA-approved indications.
    6) Sotagliflozin (Inpefa): non-formulary with PA, is 3rd preferred for HF given shorter history of postmarketing safety data compared to other SGLT2i's approved for HF as well as the need to titrate sotagliflozin dose for when others are fixed-dose regimens. Sotagliflozin (Inpefa) is least preferred for glycemic control due to lack of clinical trial data and FDA-approved indication as well as its high cost.
- Jardiance (empagliflozin) is the preferred sodium glucose co-transporter 2 inhibitor (SGLT-2i) at Kaiser Permanente Colorado (KPCO) and can be used effectively and safely with a GFR down to 20 mL/min. In addition, the dose of 12.5 mg (1/2 of 25mg tablet) is an effective dose for all patients regardless of GFR.
- Based on the available evidence, various organizations endorse SGLT-2is use down to lower GFR levels than indicated in product labels:
    - American College of Cardiology Expert Consensus now recommends empagliflozin in GFR ≥ 20 mL/min (2021).

- National Kidney Foundation recommends SGLT-2is in GFR ≥ 20 mL/min as long as there are no contraindications (2023).
- American Diabetes Association recognizes SGLT-2is benefits in patients with GFR ≥ 20 mL/min (2023).

FDA APPROVED INDICATIONS for SGLT2 Inhibitors

Empagliflozin (Jardiance)

1. Improve glycemic control in patients with DM2
2. Reduce the risk of CV death in pts with DM2 + CVD
3. Reduce risk of CVD death and HF hospitalizations in pts with HF
4. Reduce risk of sustained eGFR decline, ESRD, CV death and hospitalizations in adults with CKD at risk of progression

Canagliflozin (Invokana)

1. Improve glycemic control in patients with DM2
2. Reduce risk of MACE in pts with DM2 + CVD
3. Reduce the risk of ESRD, doubling of creatinine, CV death, or HF hospitalization in pts with DM2 + diabetic nephropathy

Dapagliflozin (Farxiga)

Improve glycemic control in patients with DM2
Reduce risk of HF hosp in pts with DM2 + CVD/multiple CV RFs
Reduce the risk of CV death and HF hosp in patients with HFrEF NYHA II-IV
Reduce risk of sustained eGFR decline, ESRD, CV death, and hospitalization for HF in adults with CKD at risk of progression

Ertugliflozin (Steglatro)

Improve glycemic control in patients with DM2

Bexagliflozin (Brenzavvy)

Improve glycemic control in patients with DM2

Sotagliflozin (Inpefa)

Reduce the risk of CV death and HF hosp in pts with heart failure
Reduce the risk of CV death and HF hosp in pts with DM2 + CKD + CV RF(s)

REFERENCES

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class

were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation date: 09/26/18
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

CARIPRAZINE (VRAYLAR)

Generic	Brand	HICL	GCN/GPID	Exception/Other
CARIPRAZINE CAPSULE	VRAYLAR	42552		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO within the past 90 days and is stable on therapy.

If met, approve indefinitely at HICL.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following diagnoses and meet all related criteria below:

A. Bipolar depression
B. Bipolar mania or mixed episodes
C. Major depressive disorder
D. Schizophrenia

A. Bipolar Depression
   1. Patient is at least 18 years of age.
   2. Documented contraindication, intolerance, or treatment failure to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Lurasidone (Latuda)
      b. One mood stabilizer: lamotrigine, lithium, valproic acid and derivatives

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

B. Bipolar Mania or Mixed Episodes
   1. Patient is at least 18 years of age.
   2. Documented contraindication, intolerance, or treatment failure to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. One antipsychotic
      b. One mood stabilizer (eg lithium, carbamazepine, valproic acid and derivatives)

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

C. Major Depressive Disorder
   1. Patient is at least 18 years of age.
   2. Concomitant therapy with an antidepressant
   3. Documented contraindication, intolerance, or treatment failure to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Two antidepressants
      b. One antipsychotic

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

D. Schizophrenia
   1. Patient is at least 18 years of age.
   2. Documented contraindication, intolerance, or treatment failure to at least 1 antipsychotic, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

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ePA Questions

1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Bipolar depression; Bipolar mania or mixed episodes; Major depressive disorder; Schizophrenia]
   QUESTIONS BASED ON DIAGNOSIS SELECTED
   Bipolar depression
      1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
      2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules; Lithium capsules, as carbonate: 150 mg, 300 mg; Lithium tablets, as carbonate: 300 mg; Lithium CR tablets, as carbonate (Eskalith CR): 450 mg; Lithium SR tablets, as carbonate (Lithobid): 300 mg; Lamotrigine tablets; Divalproex sodium DR (12 hr) or ER (24 hr) tablets, valproic

acid capsules (250 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Bipolar mania or mixed episodes

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules; Lithium capsules, as carbonate: 150 mg, 300 mg; Lithium tablets, as carbonate: 300 mg; Lithium CR tablets, as carbonate (Eskalith CR): 450 mg; Lithium SR tablets, as carbonate (Lithobid): 300 mg; carbamazepine ER tablets (100 mg, 200 mg, 400 mg), carbamazepine IR tablets (200 mg), carbamazepine chewable tablets (100 mg); Divalproex sodium DR (12 hr) or ER (24 hr) tablets, valproic acid capsules (250 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Major depressive disorder

1. Will this medication be used as concomitant therapy with an antidepressant?
2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
3. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules; citalopram tablets/solution, escitalopram tablets, fluoxetine capsules/solution, paroxetine IR tablets, sertraline tablets; venlafaxine ER capsules (37.5 mg, 75 mg, 150 mg), duloxetine capsules (20 mg, 30 mg, 60 mg); vilazodone tablets; bupropion XL tablets (150 mg, 300 mg), bupropion IR tablets (75 mg); mirtazapine tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Schizophrenia

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Regarding bipolar depression criteria, cariprazine (Vraylar), lumateperone (Caplyta), and lurasidone all have low risk of metabolic side effects. Lurasidone is the only formulary antipsychotic option that has both low risk of metabolic side effects and a labeled FDA indication for treatment of bipolar depression as quetiapine and olanzapine have moderate and high metabolic risk, respectively. As such, if patient has trialed formulary lurasidone and one formulary mood stabilizer, nonformulary criteria will be met for bipolar depression treatment.

Regarding major depressive disorder (MDD) criteria, both risperidone and ziprasidone have off-label data for treatment of MDD which can be reviewed in Lexicomp.

Carbamazepine, divalproex, and lithium are teratogenic so avoiding use in women of reproductive potential is not unreasonable (and highly recommended for divalproex). Unfortunately, most of the non-formulary antipsychotics lack reassuring data and absence of evidence of risk is not the same as absence of risk. Lithium may still be continued or started in women that are pregnant as the benefits of

use are often considered to outweigh the small absolute risk of cardiac malformation (1-2 extra cases per 100 live births with first trimester in utero exposure compared with no lithium exposure).

FDA APPROVED INDICATIONS

Cariprazine (Vraylar)

- **Bipolar disorder:** Acute treatment of mania or episodes with mixed features and major depression associated with bipolar I disorder.
- **Major depressive disorder (unipolar):** Adjunctive therapy in adults with an inadequate response to antidepressants for the treatment of unipolar major depressive disorder.
- **Schizophrenia:** Treatment of schizophrenia.

APPENDIX A. Formulary antipsychotics

First-generation antipsychotics	Second-generation antipsychotics
Chlorpromazine	Aripiprazole
Fluphenazine	Clozapine
Haloperidol	Lurasidone
Loxapine	Olanzapine
Molindone	Quetiapine
Perphenazine	Risperidone
Pimozide	Ziprasidone
Thioridazine	
Thiothixene	
Trifluoperazine	

HOW SUPPLIED:

Cariprazine (Vraylar): 1.5 MG, 3 MG, 4.5 MG 6 MG; capsule therapy pack, 1.5 MG AND 3 MG

REFERENCES

American Psychiatric Association. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. 3rd ed. Washington, DC: American Psychiatric Association; 2021.

Patorno E, Huybrechts KF, Bateman BT, et al. Lithium use in pregnancy and the risk of cardiac malformations. N Engl J Med. 2017;376:23.

Vraylar. Package insert. Allergan Inc; December 2022.

Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord 2018;20:97-170.

Creation Date: 3/2023
Effective Date: 4/2024
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Revised Date: 3/2024

XCOPRI (CENOBAMATE)

Generic	Brand	HICL	GCN	Exception/Other
CENOBAMATE	XCOPRI	46241	47409, 47413, 47414, 47394, 47395, 47416, 49574, 47396, 47397	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and is stable on cenobamate (Xcopri)
2. Patient has a diagnosis of Partial Onset Seizures and is being managed by a CPMG or affiliated neurologist or epileptologist

If New Member Criteria are met, approve indefinitely.
If New Member Criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Medication is prescribed by a CMPG or affiliated neurologist or epileptologist
2. Patient is 18 years of age or older. [This drug has not been studied in pediatric populations.]
3. Patient has a diagnosis of partial onset seizures (also known as focal onset aware or impaired awareness)
4. The patient is stable on cenobamate (Xcopri), or the patient has failed at least **2** of the medications, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event:
    - Carbamazepine [preferred formulary]
    - Lacosamide [preferred formulary]
    - Lamotrigine [preferred formulary]
    - Levetiracetam [preferred formulary]
    - Oxcarbazepine [preferred formulary]
    - Topiramate [preferred formulary]
    - Zonisamide [preferred formulary]
    - Valproic acid derivative [formulary]
    - Felbamate [formulary]
    - Gabapentin [formulary]
    - Phenobarbital [formulary]
    - Phenytoin [formulary]
    - Pregabalin [formulary]
    - Primidone [formulary]

- Brivaracetam (Briviact) [non-formulary]
- Eslicarbazepine (Aptiom) [non-formulary]
- Tiagabine [non-formulary]
- Vigabatrin [non-formulary]

If met, approve indefinitely at HICL.
If not met, do not approve.

FDA APPROVED INDICATIONS
Xcopri is indicated for the treatment of partial-onset seizures in adult patients.

REFERENCES
1. Xcopri Prescribing Information. Paramus, NJ: SK Life Science, Inc.; 2022. Available at: https://www.xcopri.com.
2. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: efficacy and tolerability of the new antiepileptic drugs I: treatment of new-onset epilepsy. Neurology. 2018;91(2):74-81.
3. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: efficacy and tolerability of the new antiepileptic drugs II: treatment-resistant epilepsy. Neurology. 2018;91(2):82-90.

Creation Date: 07/2023
Effective Date: 01/2024
Reviewed Date:
Revised Date:

CGRP MONOCLONAL ANTIBODY INHIBITORS
AIMOVIG

Generic	Brand	HICL	GCN/GPID	Exception/Other
ERENUMAB	AIMOVIG	44923	46116 140mg, 44753 70mg	Acts on receptor

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
A. Patient is new to KPCO within the past 90 days
B. Patient is stable on CGRP-mAb for migraine prevention

If New Member criteria are met for migraine prevention, approve current therapy x 3 months (to allow time for consideration of formulary preferred alternatives then must meet Initial Criteria for ongoing coverage).
If New Member criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the following:
A. Requesting provider is a CPMG or an affiliated network neurologist or headache specialist (with an appropriate referral if needed)
B. If the patient has a diagnosis of medication overuse headache (MOH), prescriber attests to having a treatment plan to taper off offending MOH medication
C. Patient is not taking another CGRP-directed medication for migraine prevention
D. Must meet drug and diagnosis specific criteria (1, 2, or 3) below:
   1. Provider notes that Aimovig was previously effective, and the patient has now failed Ajovy due to side effects, or due to lack of efficacy after taking for at least 2 monthly doses

      If initial criteria are met, then approve Aimovig at HICL indefinitely.
      If initial criteria are not met, do not approve.

   2. For Episodic Migraine diagnosis: The patient must meet all the following criteria:
      a. Patient has a diagnosis of episodic migraine (less than 15 migraine days per month)
      b. Patient with failure of (after at least 6-8 weeks at maximally tolerated dose), intolerance to, or contraindication to, at least one medication from each of the three migraine preventive classes, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
         i. Anticonvulsants: divalproex, valproate, topiramate
         ii. Beta blockers: atenolol, metoprolol, nadolol, propranolol, timolol
         iii. Antidepressants: amitriptyline, nortriptyline, venlafaxine, duloxetine
      c. Patient has completed a Migraine Disability Assessment (MIDAS) or has documentation of headache days per month for at least one month in the past three months
      d. Meets medication specific criteria below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on

known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

i. Patient has tried and failed one CGRP-mAb that acts on the ligand (examples: fremanezumab (Ajovy), galcanezumab (Emgality), eptinezumab (Vyepti))

If initial criteria are met, then approve at HICL x3 months.
If initial criteria are not met, do not approve. If patient has not tried and failed a CGRP-mAb that acts on the ligand, deny and recommend Ajovy 225 mg monthly or 675 mg every 3 months.

3. For Chronic Migraine diagnosis: The patient must meet all the following criteria:
   a. Patient has a diagnosis of chronic migraine (defined as 15 or more headache days [migraine-like or tension-like] per month for the past 3 months, of which at least 8 days are migraines)
   b. Patient has documented intolerance, contraindication, or inadequate response after an adequate trial* to at least one medication from at least three migraine preventive classes, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      i. Anticonvulsants: divalproex, valproate, topiramate
      ii. Beta blockers: atenolol, metoprolol, nadolol, propranolol, timolol
      iii. Antidepressants: amitriptyline, nortriptyline, venlafaxine, duloxetine
      iv. Botulinum toxin: onabotulinumtoxinA
   c. Patient has completed a Migraine Disability Assessment (MIDAS) or has documentation of headache days per month for at least one month in the past three months
   d. Meets medication specific criteria below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      i. Patient has tried and failed a CGRP-mAb that acts on the ligand (examples: fremanezumab (Ajovy), galcanezumab (Emgality), eptinezumab (Vyepti)

      If initial criteria are met, then approve at HICL x3 months.
      If initial criteria are not met, do not approve. If patient has not tried and failed a CGRP-mAb that acts on the ligand, deny and recommend Ajovy 225 mg monthly or 675 mg every 3 months.

RENEWAL CRITERIA: Review based on diagnosis specific criteria:

A. For episodic or chronic migraine indications: All the following criteria must be met:
   1. If the patient has/had a diagnosis of medication overuse headache (MOH), the prescriber attests that frequency of use of the offending MOH medication has decreased or stopped
   2. Patient has demonstrated improvement after at least 3 months of starting CGRP-mAb, by one of the following:
      a. At least 30% reduction in headache days per month
      b. At least 50% improvement in MIDAS score

      If criteria are met, then approve Aimovig at HICL indefinitely.
      If criteria are not met, do not approve.

** Adequate trials of non-CGRP mAb preventive medication trials FOR MIGRAINE:*

- Oral migraine preventive medicaton: at least 6-8 weeks at maximally tolerated dose
- OnabotulinumtoxinA: at least two quarterly injections with response assessed 6 months after initiation

CGRP-Directed Migraine Medications

Generic (Brand)	Route CGRP "class"	Acute Migraine Approval	Preventive Migraine Approval
Eptinezumab (Vyepti)	IV, CGRP-mAb	X	100 mg or 300 mg Q 3 mo
Erenumab (Aimovig)	SC, CGRP-mAb	X	70 mg or 140 mg Q mo
Fremanezumab (Ajovy)	SC, CGRP-mAb	X	225 mg Q mo, OR 675 mg Q 3 mo
Galcanezumab (Emgality)	SC, CGRP-mAb	X	240 mg loading dose, then 120 mg Q mo
Atogepant (Qulipta)	Oral, CGRP antagonist "gepant"	X	10 mg, 30 mg or 60 mg daily
Rimegepant (Nurtec ODT)	Orally disintegrating tablet, CGRP antagonist "gepant"	75 mg at onset do NOT repeat dose	75 mg every OTHER day
Ubrogepant (Ubrelvy)	Oral, CGRP antagonist "gepant"	50 mg or 100 mg at onset, may repeat in 2 hours	X
Zavegepant (Zavzpret)	Intranasal, CGRP antagonist "gepant"	10 mg at onset do NOT repeat dose	X

ePA Questions for Provider Outreach

1. Diagnosis/ICD-10 codes associated with this request: _____
2. Has the patient failed other treatments for this indication? If yes, must list medication, strength, dates of treatment, and reason for discontinuation in Provider Comments section below or attach applicable chart notes.
3. Is there reasoning why alternatives are not suitable (i.e. Ajovy prefilled syringes or auto-injector; divalproex sodium DR or ER tablets, valproic acid capsules (250 mg); topiramate IR tablets;

atenolol, metoprolol IR or ER, propranolol IR or ER; amitriptyline, nortriptyline; venlafaxine ER capsules; Botox)? If yes, must list reasoning in Provider Comments section below or attach applicable chart notes.
4. Number of headache days per month for this patient over the past 3 months? _____
5. Migraine Disability Assessment (MIDAS) score for this patient: _____
6. Does the patient have a diagnosis of Medication Overuse Headaches? If yes, must describe taper plan in Provider Comments section below or attach applicable chart notes.

RATIONALE

Ensure appropriate criteria are used for the management of requests for all CGRP inhibitors according to approved indication and national treatment guidelines. There are no head-to-head studies with other treatments for migraine prophylaxis. However, CGRP inhibitors appears to have similar efficacy to other pharmacologic options, with no clinically significant differences in number needed to treat or reductions in monthly migraine or headache days. Data are limited to healthy subjects as patients with cardiovascular comorbidities were excluded from the clinical trials. Given the limited clinical trial data and lack of long-term safety data, exceedingly judicious prescribing and monitoring of therapy are warranted.

^^ Original intent of D.1 was to allow patients who were previously stable on Emgality and in May/June 2021 were converted to Ajovy (KP's preferred agent) which resulted in a loss of stability (migraines returned while on Ajovy) to be able to convert back to Emgality. This has been updated to include Aimovig so patients who had been stable and achieved migraine reduction on Aimovig, who have tried Ajovy but failed, are able to easily transition back to Aimovig without significant delay in care that could result in further worsening of migraines.

Results from erenumab trials did not show the 140 mg monthly dose to be superior to 70 mg monthly, however, both 70 mg monthly and 140 mg monthly are FDA approved doses.

FDA APPROVED INDICATIONS

Preventive treatment of migraine in adults
Episodic cluster headache treatment (Emgality 100 mg only)

REFERENCES

1. The American Headache Society position statement on integrating new migraine treatments into clinical practice. Headache 2019;59:1-18.
2. Kaiser Permanente Inter-regional Practice Recommendations. CGRP Inhibitors. 10/19/2018.
3. Aimovig [package insert]. Thousand Oaks, CA: Amgen Inc; 2018.
4. Steiner TJ, Stovner LJ, Birbeck GL. Migraine: the seventh disabler. Headache: The Journal of Head and Face Pain. 2013 Feb 1;53(2):227-9.
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6. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013; 33:629-808.
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9. Ashina M, Dodick D, Kudrow D, et al. A phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of erenumab in migraine prevention: primary results of the ARISE trial. Eur J Neurol. 2017;24(S1):470.
10. Tepper S, Ashina M, Reuter U, et al. Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomised, double-blind, placebo-controlled phase 2 trial. Lancet Neurol. 2017; 16:425-434.
11. Silberstein SD, Dodick DW, Bigal ME, et al. Fremanezumab for the preventive treatment of chronic migraine. N Engl J Med. 2017 Nov 30;377(22):2113-22.
12. Ashina M, Dodick D, Goadsby PJ, et al. Erenumab (AMG 334) in episodic migraine: Interim analysis of an ongoing open-label study. Neurology. 2017; 89:1237-1243.
13. Silberstein SD, Neto W, Schmitt J, Jacobs D. Topiramate in migraine prevention: results of a large controlled trial. Archives of Neurology. 2004 Apr 1;61(4):490-5.
14. Storey JR, Calder CS, Hart DE, Potter DL. Topiramate in migraine prevention: a double-blind, placebo-controlled study. *Headache: The Journal of Head and Face Pain*. 2001 Dec 1;41(10):968-75.
15. Jackson JL, Cogbill E, Santana-Davila R, et al. A comparative effectiveness meta-analysis of drugs for the prophylaxis of migraine headache. *PLoS One*. 2015 Jul 14;10(7): e0130733.
16. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. *Neurology*. 2012 Apr 24;78(17):1337-45.
17. Gonzales E, Smith J, Nudelman K, Potrebic S, and Langer-Gould A. Improving Patient-Centeredness of Headache Questionnaires. *Neurology.* 2018 Apr:90(15 Supplement):136. (Kaiser Permanente Southern California, Department of Research & Evaluation).
18. Kounis NG, Soufras GD, Tsigkas G, Hahalis G. Adverse cardiac events to monoclonal antibodies used for cancer therapy: The risk of Kounis syndrome. *Oncoimmunology*. 2014 Feb 14; 3:e27987.
19. MaassenVanDenBrink A, Meijer J, Villalón CM, Ferrari MD. Wiping Out CGRP: Potential Cardiovascular Risks. *Trends Pharmacol Sci*. 2016 Sep;37(9):779- 788.
20. Holland PR, Goadsby PJ. Targeted CGRP Small Molecule Antagonists for Acute Migraine Therapy. *Neurotherapeutics*. 2018 Apr;15(2):304-312.
21. Ajovy [package insert]. North Wales, PA: Teva Pharmaceuticals USA Inc.; 2018.
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23. Dodick DW, Silberstein SD, Bigal ME, et al. Effect of Fremanezumab Compared with Placebo for Prevention of Episodic Migraine: A Randomized Clinical Trial. *JAMA*. 2018 May 15;319(19):1999-2008.
24. Summary Review for Erenumab-aooe (Aimovig). Center for Drug Evaluation and Research, U.S. Food and Drug Administration. May 15, 2018. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/761077Orig1s000TOC.cfm. Accessed September 23, 2018.
25. Emgality [package insert]. Indianapolis, IN: Eli Lilly and Company; 2018.
26. Stauffer VL, Dodick DW, Zhang Q, Carter JN, Ailani J, Conley RR. Evaluation of Galcanezumab for the Prevention of Episodic Migraine: The EVOLVE-1 Randomized Clinical Trial. *JAMA Neurol*. 2018 Sep 1;75(9):1080-1088.
27. Skljarevski V, Matharu M, Millen BA, Ossipov MH, Kim BK, Yang JY. Efficacy and safety of galcanezumab for the prevention of episodic migraine: Results of the EVOLVE-2 Phase 3 randomized controlled clinical trial. *Cephalalgia*. 2018 Jul;38(8):1442-1454.
28. Zhang Q, Ruff DD, Pearlman EM, Govindan S, Aurora SK. Efficacy of Galcanezumab in Patients Who Failed to Respond to Preventives Previously: Results from EVOLVE-1, EVOLVE-2 and REGAIN Studies (S20.004). *Neurology.* Apr 2018, 90 (15 Supplement) S20.004

29. Goadsby PJ, Dodick DW, Leone M, Bardos JN, Oakes TM, Millen BA, Zhou C, Dowsett SA, Aurora SK, Ahn AH, Yang JY, Conley RR, Martinez JM. Trial of Galcanezumab in Prevention of Episodic Cluster Headache. N Engl J Med. 2019 Jul 11;381(2):132-141.
30. Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, Schwedt TJ. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. Headache. 2016 Jul;56(7):1093-106 Botox in combination with CGRP-mAb
31. Cohen F, Armand C, Lipton RB, et al. Efficacy and tolerability of calcitonin gene-related peptide targeted monoclonal antibody medications as add-on therapy to onabotulinumtoxinA in patients with chronic migraine. Pain Med 2021.
32. Pellesi L, Do TP, Ashina H, et al. Dual therapy with anti-CGRP monoclonal antibodies and botulinum toxin for migraine prevention: Is there a rationale? Headache 2020;60:1056-65.
33. Suri H. Combination of erenumab (Aimovig) and onabotulinum toxin a (BoNT-A or Botox) is safe and effective. 62nd Annual Scientific Meeting American Headache Society. Headache: The Journal of Head and Face Pain 2020;60:1-156.

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CGRP MONOCLONAL ANTIBODY INHIBITORS
EMGALITY

Generic	Brand	HICL	GCN/GPID	Exception/Other
GALCANEZUMAB	EMGALITY	45281	46397, 40418, 40419	Acts on ligand

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:

A. Patient is new to KPCO within the past 90 days
B. Either the patient is stable on CGRP-mAb for migraine prevention, or the patient is in an active cluster headache and prior cluster headaches were treated with Emgality 300 mg

If New Member criteria are met for migraine prevention, approve current therapy x 3 months (to allow time for consideration of formulary preferred alternatives then must meet Initial Criteria for ongoing coverage).
If New Member criteria are met for cluster headache, approve Emgality 100 mg x 2 months (to allow time for consideration of formulary preferred alternatives then must meet Initial Criteria for ongoing coverage).
If New Member criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the following:

A. Requesting provider is a CPMG or an affiliated network neurologist or headache specialist (with an appropriate referral if needed)
B. If the patient has a diagnosis of medication overuse headache (MOH), prescriber attests to having a treatment plan to taper off offending MOH medication
C. Patient is not taking another CGRP-directed medication for migraine prevention
D. Must meet drug and diagnosis specific criteria (1, 2, 3, or 4) below:
    1. Provider notes that Emgality was previously effective, and the patient has now failed Ajovy due to side effects, or due to lack of efficacy after taking for at least 2 monthly doses

    If initial criteria are met, then approve Emgality at GPID indefinitely.
    If initial criteria are not met, do not approve.

    2. For Episodic Migraine diagnosis: The patient must meet all the following criteria:
        a. Patient has a diagnosis of episodic migraine (less than 15 migraine days per month)
        b. Patient with failure of (after at least 6-8 weeks at maximally tolerated dose), intolerance to, or contraindication to, at least one medication from each of the three migraine preventive classes, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
            ii. Anticonvulsants: divalproex, valproate, topiramate
            iii. Beta blockers: atenolol, metoprolol, nadolol, propranolol, timolol
            iv. Antidepressants: amitriptyline, nortriptyline, venlafaxine, duloxetine

c. Patient has completed a Migraine Disability Assessment (MIDAS) or has documentation of headache days per month for at least one month in the past three months
d. Meets medication specific criteria below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

    i. Galcanezumab (Emgality) 120 mg: Patient has tried and failed, or has a contraindication to, at least one CGRP-mAb that acts on the ligand (examples: fremanezumab (Ajovy), eptinezumab (Vyepti))

    If initial criteria are met, then approve at GPID x3 months.
    If initial criteria are not met, do not approve. If patient has not tried and failed a CGRP-mAb that acts on the ligand, deny and recommend Ajovy 225 mg monthly or 675 mg every 3 months.

    ii. Galcanezumab (Emgality) 100 mg: Do not approve. No indication.

3. For Chronic Migraine diagnosis: The patient must meet all the following criteria:
    a. Patient has a diagnosis of chronic migraine (defined as 15 or more headache days [migraine-like or tension-like] per month for the past 3 months, of which at least 8 days are migraines)
    b. Patient has documented intolerance, contraindication, or inadequate response after an adequate trial* to at least one medication from at least three migraine preventive classes, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        i. Anticonvulsants: divalproex, valproate, topiramate
        ii. Beta blockers: atenolol, metoprolol, nadolol, propranolol, timolol
        iii. Antidepressants: amitriptyline, nortriptyline, venlafaxine, duloxetine
        iv. Botulinum toxin: onabotulinumtoxinA
    c. Patient has completed a Migraine Disability Assessment (MIDAS) or has documentation of headache days per month for at least one month in the past three months
    d. Meets medication specific criteria below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

i. Galcanezumab (Emgality) 120 mg: Patient has tried and failed, or has a contraindication to, at least one CGRP-mAb that acts on the ligand (examples: fremanezumab (Ajovy), eptinezumab (Vyepti))

If initial criteria are met, then approve at GPID x3 months.
If initial criteria are not met, do not approve. If patient has not tried and failed a CGRP-mAb that acts on the ligand, deny and recommend Ajovy 225 mg monthly or 675 mg every 3 months.

ii. Galcanezumab (Emgality) 100 mg: Do not approve. No indication.

4. For Episodic Cluster Headache diagnosis: The patient must meet all the following criteria:
   a. Patient has not received coverage approval for Emgality in the past for cluster headache (if they have, use renewal criteria)
   b. Patient has a diagnosis of episodic cluster headache (cluster attacks that occur in periods lasting from 7 days to 1 year, with remission periods greater than 3 months between attacks)
   c. Patient does not have a diagnosis of chronic cluster headache (cluster attacks that occur for one year or longer without remission, or with remission periods lasting less than 3 months)
   d. Request is for galcanezumab (Emgality) 100 mg/mL syringes and patient is not using another CGRP-mAb or oral CGRP antagonist (ubrogepant, rimegepant, atogepant, etc.)
   e. Patient has documented intolerance, contraindication, or inadequate response to at least 2 other acute/abortive medication/therapy trials (including triptans, oxygen, intranasal dihydroergotamine, and intranasal lidocaine) and at least 2 standard cluster headache therapies (lithium, verapamil, melatonin, prednisone, occipital nerve block, topiramate, valproate, memantine), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

   If initial criteria are met, then approve at GPID x2 months (2 doses of 300 mg Q month).
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Review based on diagnosis specific criteria in either A or B below:

A. For episodic or chronic migraine indications: All the following criteria must be met:
   1. If the patient has/had a diagnosis of medication overuse headache (MOH), the prescriber attests that frequency of use of the offending MOH medication has decreased or stopped
   2. Patient has demonstrated improvement after at least 3 months of starting CGRP-mAb, by one of the following:
      a. At least 30% reduction in headache days per month
      b. At least 50% improvement in MIDAS score

   If criteria are met, then approve Emgality at GPID indefinitely.
   If criteria are not met, do not approve.

B. For episodic cluster headache indication: All the following criteria must be met:

1. Request is for galcanezumab (Emgality) 100 mg/ml syringes
2. Patient's prior cluster headache period for which galcanezumab (Emgality) was approved to treat has resolved, and the patient is now in a new cluster headache period
3. Patient had an adequate response to galcanezumab (Emgality) 300 mg monthly for cluster headache (adequate response: at least 30% reduction in cluster headache frequency from baseline after 4 weeks)
4. Patient has not used consecutive monthly doses of Emgality in the last two months [Note: galcanezumab (Emgality) should not be used for more than 2 months total per cluster headache period]

   If criteria are met, then approve at GPID x 2 months (2 doses of 300 mg Q month).
   If criteria are not met, do not approve.

** Adequate trials of non-CGRP mAb preventive medication trials FOR MIGRAINE:*

- Oral migraine preventive medicaton: at least 6-8 weeks at maximally tolerated dose
- OnabotulinumtoxinA: at least two quarterly injections with response assessed 6 months after initiation

CGRP-Directed Migraine Medications

Generic (Brand)	Route CGRP "class"	Acute Migraine Approval	Preventive Migraine Approval
Eptinezumab (Vyepti)	IV, CGRP-mAb	X	100 mg or 300 mg Q 3 mo
Erenumab (Aimovig)	SC, CGRP-mAb	X	70 mg or 140 mg Q mo
Fremanezumab (Ajovy)	SC, CGRP-mAb	X	225 mg Q mo, OR 675 mg Q 3 mo
Galcanezumab (Emgality)	SC, CGRP-mAb	X	240 mg loading dose, then 120 mg Q mo
Atogepant (Qulipta)	Oral, CGRP antagonist "gepant"	X	10 mg, 30 mg or 60 mg daily
Rimegepant (Nurtec ODT)	Orally disintegrating tablet, CGRP antagonist "gepant"	75 mg at onset do NOT repeat dose	75 mg every OTHER day
Ubrogepant (Ubrelvy)	Oral, CGRP antagonist "gepant"	50 mg or 100 mg at onset, may repeat in 2 hours	X
Zavegepant (Zavzpret)	Intranasal, CGRP antagonist "gepant"	10 mg at onset do NOT repeat dose	X

RATIONALE

Ensure appropriate criteria are used for the management of requests for all CGRP inhibitors according to approved indication and national treatment guidelines. There are no head-to-head studies with other treatments for migraine prophylaxis. However, CGRP inhibitors appears to have similar efficacy to other pharmacologic options, with no clinically significant differences in number needed to treat or reductions in monthly migraine or headache days. Data are limited to healthy subjects as patients with cardiovascular comorbidities were excluded from the clinical trials. Given the limited clinical trial data and lack of long-term safety data, exceedingly judicious prescribing and monitoring of therapy are warranted.

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Results from erenumab trials did not show the 140 mg monthly dose to be superior to 70 mg monthly, however, both 70 mg monthly and 140 mg monthly are FDA approved doses.

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4. Steiner TJ, Stovner LJ, Birbeck GL. Migraine: the seventh disabler. Headache: The Journal of Head and Face Pain. 2013 Feb 1;53(2):227-9.
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6. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013; 33:629-808.
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9. Ashina M, Dodick D, Kudrow D, et al. A phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of erenumab in migraine prevention: primary results of the ARISE trial. Eur J Neurol. 2017;24(S1):470.
10. Tepper S, Ashina M, Reuter U, et al. Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomised, double-blind, placebo-controlled phase 2 trial. Lancet Neurol. 2017; 16:425-434.
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12. Ashina M, Dodick D, Goadsby PJ, et al. Erenumab (AMG 334) in episodic migraine: Interim analysis of an ongoing open-label study. Neurology. 2017; 89:1237-1243.
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14. Storey JR, Calder CS, Hart DE, Potter DL. Topiramate in migraine prevention: a double-blind, placebo-controlled study. *Headache: The Journal of Head and Face Pain*. 2001 Dec 1;41(10):968-75.
15. Jackson JL, Cogbill E, Santana-Davila R, et al. A comparative effectiveness meta-analysis of drugs for the prophylaxis of migraine headache. *PLoS One*. 2015 Jul 14;10(7): e0130733.
16. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. *Neurology*. 2012 Apr 24;78(17):1337-45.

17. Gonzales E, Smith J, Nudelman K, Potrebic S, and Langer-Gould A. Improving Patient-Centeredness of Headache Questionnaires. *Neurology.* 2018 Apr:90(15 Supplement):136. (Kaiser Permanente Southern California, Department of Research & Evaluation).
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19. MaassenVanDenBrink A, Meijer J, Villalón CM, Ferrari MD. Wiping Out CGRP: Potential Cardiovascular Risks. *Trends Pharmacol Sci*. 2016 Sep;37(9):779- 788.
20. Holland PR, Goadsby PJ. Targeted CGRP Small Molecule Antagonists for Acute Migraine Therapy. *Neurotherapeutics*. 2018 Apr;15(2):304-312.
21. Ajovy [package insert]. North Wales, PA: Teva Pharmaceuticals USA Inc.; 2018.
22. Silberstein SD, Dodick DW, Bigal ME, et al. Fremanezumab for the preventive treatment of chronic migraine. *N Engl J Med*. 2017 Nov 30;377(22):2113-22.
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24. Summary Review for Erenumab-aooe (Aimovig). Center for Drug Evaluation and Research, U.S. Food and Drug Administration. May 15, 2018. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/761077Orig1s000TOC.cfm. Accessed September 23, 2018.
25. Emgality [package insert]. Indianapolis, IN: Eli Lilly and Company; 2018.
26. Stauffer VL, Dodick DW, Zhang Q, Carter JN, Ailani J, Conley RR. Evaluation of Galcanezumab for the Prevention of Episodic Migraine: The EVOLVE-1 Randomized Clinical Trial. *JAMA Neurol*. 2018 Sep 1;75(9):1080-1088.
27. Skljarevski V, Matharu M, Millen BA, Ossipov MH, Kim BK, Yang JY. Efficacy and safety of galcanezumab for the prevention of episodic migraine: Results of the EVOLVE-2 Phase 3 randomized controlled clinical trial. *Cephalalgia*. 2018 Jul;38(8):1442-1454.
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30. Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, Schwedt TJ. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. Headache. 2016 Jul;56(7):1093-106 Botox in combination with CGRP-mAb
31. Cohen F, Armand C, Lipton RB, et al. Efficacy and tolerability of calcitonin gene-related peptide targeted monoclonal antibody medications as add-on therapy to onabotulinumtoxinA in patients with chronic migraine. Pain Med 2021.
32. Pellesi L, Do TP, Ashina H, et al. Dual therapy with anti-CGRP monoclonal antibodies and botulinum toxin for migraine prevention: Is there a rationale? Headache 2020;60:1056-65.
33. Suri H. Combination of erenumab (Aimovig) and onabotulinum toxin a (BoNT-A or Botox) is safe and effective. 62nd Annual Scientific Meeting American Headache Society. Headache: The Journal of Head and Face Pain 2020;60:1-156.

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CIMZIA (CERTOLIZUMAB)

Generic	Brand	HICL	GCN	Exception/Other
CERTOLIZUMAB	CIMZIA	35554	99615, 23471	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on Cimzia, medication is not being used in combination with another biologic for the same indication, and has one of the following indications managed by the appropriate specialist as noted below:
   1. Patient has a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), or Ankylosing Spondylitis or subtype and is being managed by a CPMG or affiliated rheumatologist.
   2. The patient has a diagnosis of Crohn's Disease and is being managed by a CPMG or affiliated gastroenterology specialist.
   3. The patient has a diagnosis of Psoriasis and is being managed by a CPMG or affiliated dermatology specialist.

   If met, approve indefinitely.
   If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Rheumatoid Arthritis (RA)
B. Psoriatic Arthritis (PsA)
C. Ankylosing Spondylitis or subtype
D. Crohn's Disease
E. Psoriasis

A. RHEUMATOID ARTHRITIS: All the following must be met:
   1. Patient has a diagnosis of RA, and medication is prescribed by a rheumatologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least 2 DMARDs (including methotrexate)
      b. at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred [F], adalimumab-atto (Amjevita)-preferred [F, PA])
      c. at least 2 non-TNF inhibitor biologics

   If above criteria are met, approve indefinitely.
   If above criteria are not met, do not approve.

B. PSORIATIC ARTHRITIS (PsA): All the following must be met:
   1. Patient has a diagnosis of PsA, and medication is prescribed by a rheumatologist or dermatologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least two DMARDs (including methotrexate), or the patient has documented high disease activity in which the medications below would not be suitable treatment
      b. at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred [F], adalimumab-atto (Amjevita)-preferred [F, PA])
      c. secukinumab (Cosentyx) [F]
      d. guselkumab (Tremfya) [NF, PA]
      e. at least 1 of the following:
         i. ustekinumab (Stelara) [NF, PA]
         ii. abatacept (Orencia) [F, PA]
         iii. risankizumab (Skyrizi)
         iv. JAK inhibitor [e.g., tofacitinib (Xeljanz)]

   If above criteria are met, approve indefinitely.
   If above criteria are not met, do not approve.

C. ANKYLOSING SPONDYLITIS: All the following must be met:
   1. Medication must be prescribed by a rheumatologist, and the patient has a diagnosis of ankylosing spondylitis or one of the following subtype diagnoses: spondyloarthritis (SpA), axial SpA, nonradiographic axial SpA, radiographic axial SpA, sacroiliitis, undifferentiated spondyloarthropathy, spondyloarthropathy, or enteropathic arthropathy.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. secukinumab (Cosentyx) [F]
      b. at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred [F], adalimumab-atto (Amjevita)-preferred [F, PA])

   If above criteria are met, approve indefinitely.
   If above criteria are not met, do not approve.

D. CROHN'S DISEASE: All the following must be met:
   1. Patient has a diagnosis of Crohn's disease or indeterminant colitis with Crohn's features, and the medication is prescribed by a gastroenterologist.
   2. Patient is 18 years of age or older.
   3. Medication is not being used in combination with another biologic for the same indication.
   4. Patient with failure, intolerance, or contraindication to at least one TNF inhibitor (e.g. infliximab [F], and adalimumab (Amjevita) [F, PA], or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If above criteria are met, approve indefinitely.
   If above criteria are not met, do not approve.

E. PSORIASIS: All the following must be met:
   1. Patient has a diagnosis of moderate to severe psoriasis, and medication is prescribed by a CPMG or affiliated dermatology provider.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response (after at least 2 months of therapy), intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. One topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus), or the patient is reported as having very high disease activity (ex: > 50% BSA, erythrodermic, pustular psoriasis), disease affecting critical areas (ex: genitals, face), or past biologic therapy within the past 4 months [skip and proceed to step 3c]
      b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Acitretin, Cyclosporine, Methotrexate, Apremilast (Otezla), Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
      c. One TNF inhibitor [adalimumab (Amjevita preferred, other biosimilar, or Humira), infliximab (Inflectra or other biosimilar, Remicade), or etanercept (Enbrel)]
      d. One IL17 inhibitor [secukinumab (Cosentyx) - preferred]
      e. One IL-23 inhibitor [guselkumab (Tremfya) - preferred or risankizumab-rzaa (Skyrizi)]
      f. Ustekinumab (Stelara) [NF, PA]

   If above criteria are met, approve indefinitely.
   If above criteria are not met, do not approve.

CONTINUED ON NEXT PAGE

CIMZIA (CERTOLIZUMAB)

GUIDELINES FOR COVERAGE (CONTINUED)

RENEWAL CRITERIA: Review based on indication outlined A-C below:

A. Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), or Ankylosing Spondylitis and subtypes
B. Crohn's Disease
C. Psoriasis

A. Patient's RA, PsA, or Ankylosing Spondylitis (or subtype) has been assessed by a rheumatologist in the past 2 years, and Medication is not being used in combination with another biologic for the same indication.
B. Patient's Crohn's Disease has been assessed by a gastroenterologist in the last 2 years, and Medication is not being used in combination with another biologic for the same indication.
C. Patient's Psoriasis has been assessed by a dermatologist in the last 2 years, and Medication is not being used in combination with another biologic for the same indication.

If met, approve 2 pens/syringes/vials per 28 days indefinitely.
If not met, do not approve.

REFERENCES

Currently stable on medication means patient is tolerating well, appears to be effective and provider wishes to continue.

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (e.g., systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for psoriasis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Caution in women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*

Created: 11/2020
Effective: 01/2024
Reviewed: 11/2023
Revised: 11/2023

COMBINATION INHALED CORTICOSTEROID AND LONG-ACTING BETA-AGONIST FLUTICASONE-SALMETEROL (ADVAIR HFA)

Generic	Brand	HICL	GCN	Exception/Other
FLUTICASONE PROPION/SALMETEROL	ADVAIR HFA		97135, 97136, 97137	Formulary

GUIDELINES FOR COVERAGE

A. Diagnosis of Asthma or Asthma with COPD or other indication(s) supported in the CMS approved compendia: Must meet criteria listed below based on medication requested and instruction for use or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [listed below in preferential order]:

1. Request is for Advair HFA 230/21 mcg with sig 2 inhalations BID: Must meet one of the following criteria:
   a. Patient is less than 12 years of age and is unable to manipulate brand or generic Advair Diskus device
   b. Patient has tried and failed or has contraindications [inability to use dry powder due to poor inspiratory force or severe milk protein allergy] to, brand or generic Advair Diskus

   If criteria are met, approve Advair HFA 230/21 mcg inhaler indefinitely.
   If criteria are not met, do not approve.

2. Request is for Advair HFA 45/21 mcg, 115/21 mcg or 230/21 mcg with any other sig: Must meet a, and/or b or c below:
   a. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to budesonide or formoterol] to brand or generic Symbicort HFA
   b. Patient is less than 12 years of age and is unable to manipulate brand or generic Advair Diskus device
   c. Patient has tried and failed, or has contraindications [inability to use dry powder due to poor inspiratory force or severe milk protein allergy] to, brand or generic Advair Diskus

   If criteria are met, approve requested inhaler indefinitely.
   If criteria are not met, do not approve.

B. Diagnosis of COPD or other indication(s) supported in the CMS approved compendia: Must meet criteria listed below based on medication requested and instructions for use, or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and

the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [listed below in preferential order]:

1. Request is for Advair HFA: Must meet a, and b, c, or d below:
   a. Patient has tried and failed, or has contraindications to, at least one LAMA/LABA combination inhaler [formulary option: Stiolto Respimat], or one LAMA [formulary option: Spiriva Respimat 2.5 mcg] and one LABA [formulary option: Striverdi Respimat]
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to budesonide or formoterol] to brand or generic Symbicort HFA
   c. Patient is less than 12 years of age and is unable to manipulate brand or generic Advair Diskus device or patient has tried and failed
   d. Patient has tried and failed, or has contraindications [inability to use dry powder due to poor inspiratory force or severe milk protein allergy] to, brand or generic Advair Diskus

   If criteria are met, approve Advair HFA indefinitely.
   If criteria are not met, do not approve.

RATIONALE
Per Health Plan.

- Wixela Inhub (generic Advair Diskus) and Breyna (generic Symbicort) HFA are first- and second-line KPCO formulary ICS/LABA medications
- Advair HFA is the third-line ICS/LABA on formulary. Dulera HFA, AirDuo or Breo Ellipta should only be considered in patients who are not candidates for Wixela Inhub, Breyna HFA, and Advair HFA.
- Patients on high dose ICS/LABA for asthma [Advair HFA 230/21 mcg 2 inhalations BID, Dulera HFA 200/5 mcg 2 inhalations BID, Breo Ellipta 200/25 mcg 1 inhalation QD and AirDuo 232/14 mcg 2 inhalations BID] are only candidates for Wixela Inhub or Advair HFA. Symbicort/Breyna HFA is not available in a high ICS dose formulation based on FDA approved dosing.
- For COPD management, initial therapy consist of regular treatment with a long-acting bronchodilator, either LAMA and/or LABA.
- Formoterol based inhalers, Symbicort/Breyna HFA (40.8gms/4 inhalers per 90 days) and Dulera HFA (52gms/4 inhalers per 90 days), have a quantity limit to avoid medication overuse (≥ 2 rescue doses per week indicates poorly controlled asthma and need to address therapy) with SMART therapy.

FDA APPROVED INDICATIONS
See individual medications.

REFERENCES
Per Health Plan.

Creation date: 03/18/2019
Effective date: 01/2024
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Revised date: 11/2023

COMBINATION INHALED CORTICOSTEROID AND LONG-ACTING BETA-AGONIST
FLUTICASONE-SALMETEROL (AIRDUO)

Generic	Brand	HICL	GCN	Exception/Other
FLUTICASONE PROPION/SALMETEROL	AIRDUO		48494, 48495, 48489, 42957, 42958, 42956	Nonformulary

GUIDELINES FOR COVERAGE

A. Diagnosis of Asthma or Asthma with COPD or other indication(s) supported in the CMS approved compendia: Must meet criteria listed below based on medication requested and instruction for use or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [listed below in preferential order]:

1. Request is for AirDuo 232/14 mcg with sig 2 inhalations BID: Must meet at least one of the following criteria:
   a. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to Advair HFA

   If criteria are met, approve requested inhaler indefinitely.
   If criteria are not met, do not approve.

2. Request is for AirDuo 55/14 mcg, AirDuo 113/14 mcg or other strengths with other sigs not listed in #1: Must meet at least one of the following criteria:
   a. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to budesonide or formoterol] to, brand or generic Symbicort HFA
   c. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to, Advair HFA

   If criteria are met, approve requested inhaler indefinitely.
   If criteria are not met, do not approve.

B. Diagnosis of COPD or other indication(s) supported in the CMS approved compendia: Must meet criteria listed below based on medication requested and instructions for use, or the

provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [listed below in preferential order]:

1. Must meet a, and b, c, or d below:
   a. Patient has tried and failed, or has contraindications to, at least one LAMA/LABA combination inhaler [formulary option: Stiolto Respimat], or one LAMA [formulary option: Spiriva Respimat 2.5 mcg] and one LABA [formulary option: Striverdi Respimat]
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to budesonide or formoterol] to, brand or generic Symbicort HFA
   c. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   d. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to, Advair HFA

   If criteria are met, approve requested inhaler indefinitely.
   If criteria are not met, do not approve.

RATIONALE
Per Health Plan.

- Wixela Inhub (generic Advair Diskus) and Breyna (generic Symbicort) HFA are first- and second-line KPCO formulary ICS/LABA medications
- Advair HFA is the third-line ICS/LABA on formulary. Dulera HFA, AirDuo or Breo Ellipta should only be considered in patients who are not candidates for Wixela Inhub, Breyna HFA, and Advair HFA.
- Patients on high dose ICS/LABA for asthma [Advair HFA 230/21 mcg 2 inhalations BID, Dulera HFA 200/5 mcg 2 inhalations BID, Breo Ellipta 200/25 mcg 1 inhalation QD and AirDuo 232/14 mcg 2 inhalations BID] are only candidates for Wixela Inhub or Advair HFA. Symbicort/Breyna HFA is not available in a high ICS dose formulation based on FDA approved dosing.
- For COPD management, initial therapy consist of regular treatment with a long-acting bronchodilator, either LAMA and/or LABA.
- Formoterol based inhalers, Symbicort/Breyna HFA (40.8gms/4 inhalers per 90 days) and Dulera HFA (52gms/4 inhalers per 90 days), have a quantity limit to avoid medication overuse (≥ 2 rescue doses per week indicates poorly controlled asthma and need to address therapy) with SMART therapy.

FDA APPROVED INDICATIONS
See individual medications.

REFERENCES
Per Health Plan.

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COMBINATION INHALED CORTICOSTEROID AND LONG-ACTING BETA-AGONIST
FLUTICASONE-VILANTEROL (BREO ELLIPTA)

Generic	Brand	HICL	GCN	Exception/Other
FLUTICASONE/VILANTEROL	BREO ELLIPTA	40319	34647, 35808, 54747	Nonformulary

GUIDELINES FOR COVERAGE

A. Diagnosis of Asthma or Asthma with COPD or other indication(s) supported in the CMS approved compendia: Must meet criteria listed below based on medication requested and instruction for use or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [listed below in preferential order]:

1. Request is for Breo Ellipta 200/25 mcg with sig 1 inhalation QD: Must meet at least one of the following criteria:
   a. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to Advair HFA

   If criteria are met, approve requested inhaler indefinitely.
   If criteria are not met, do not approve.

2. Request is for Breo Ellipta 100/25 mcg or other strengths with other sig not listed in #1: Must meet at least one of the following criteria:
   a. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to budesonide or formoterol] to, brand or generic Symbicort HFA
   c. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to, Advair HFA

   If criteria are met, approve requested inhaler indefinitely.
   If criteria are not met, do not approve.

B. Diagnosis of COPD or other indication(s) supported in the CMS approved compendia: Must meet criteria listed below based on medication requested and instructions for use, or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical

characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [listed below in preferential order]:

1. Must meet a, and b, c, or d below:
   a. Patient has tried and failed, or has contraindications to, at least one LAMA/LABA combination inhaler [formulary option: Stiolto Respimat], or one LAMA [formulary option: Spiriva Respimat 2.5 mcg] and one LABA [formulary option: Striverdi Respimat]
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to budesonide or formoterol] to, brand or generic Symbicort HFA
   c. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   d. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to, Advair HFA

   If criteria are met, approve requested inhaler indefinitely.
   If criteria are not met, do not approve.

RATIONALE
Per Health Plan.

- Wixela Inhub (generic Advair Diskus) and Breyna (generic Symbicort) HFA are first- and second-line KPCO formulary ICS/LABA medications
- Advair HFA is the third-line ICS/LABA on formulary. Dulera HFA, AirDuo or Breo Ellipta should only be considered in patients who are not candidates for Wixela Inhub, Breyna HFA, and Advair HFA.
- Patients on high dose ICS/LABA for asthma [Advair HFA 230/21 mcg 2 inhalations BID, Dulera HFA 200/5 mcg 2 inhalations BID, Breo Ellipta 200/25 mcg 1 inhalation QD and AirDuo 232/14 mcg 2 inhalations BID] are only candidates for Wixela Inhub or Advair HFA. Symbicort/Breyna HFA is not available in a high ICS dose formulation based on FDA approved dosing.
- For COPD management, initial therapy consist of regular treatment with a long-acting bronchodilator, either LAMA and/or LABA.
- Formoterol based inhalers, Symbicort/Breyna HFA (40.8gms/4 inhalers per 90 days) and Dulera HFA (52gms/4 inhalers per 90 days), have a quantity limit to avoid medication overuse (≥ 2 rescue doses per week indicates poorly controlled asthma and need to address therapy) with SMART therapy.

FDA APPROVED INDICATIONS
See individual medications.

REFERENCES
Per Health Plan.

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COMBINATION INHALED CORTICOSTEROID AND LONG-ACTING BETA-AGONIST MOMETASONE-FORMOTEROL (DULERA)

Generic	Brand	HICL	GCN	Exception/Other
MOMETASONE/FORMOTEROL	DULERA		28766, 28767	Nonformulary

GUIDELINES FOR COVERAGE

A. Diagnosis of Asthma or Asthma with COPD or other indication(s) supported in the CMS approved compendia: Must meet criteria listed below based on medication requested and instruction for use or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [listed below in preferential order]:

1. Request is for Dulera HFA 200/5 mcg with sig 2 inhalations BID: Must meet at least one of the following criteria:
   a. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to Advair HFA

   If criteria are met, approve with a max of 2 inhalers per 30 days, 3 inhalers per 60 days and 4 inhalers per 90 days.
   If criteria are not met, do not approve.

2. Request is for Dulera HFA 100/5 mcg or other strengths with other sig not listed in #1: Must meet at least one of the following criteria:
   a. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to budesonide or formoterol] to, brand or generic Symbicort HFA
   c. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to, Advair HFA

   If criteria are met, approve with a max of 52gms/4 inhalers per 90 days.
   If criteria are not met, do not approve.

B. Diagnosis of COPD or other indication(s) supported in the CMS approved compendia: Must meet criteria listed below based on medication requested and instructions for use, or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical

characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [listed below in preferential order]:

1. Request is for Dulera HFA: Must meet a, and b, c, or d below:
   a. Patient has tried and failed, or has contraindications to, at least one LAMA/LABA combination inhaler [formulary option: Stiolto Respimat], or one LAMA [formulary option: Spiriva Respimat 2.5 mcg] and one LABA [formulary option: Striverdi Respimat]
   b. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to budesonide or formoterol] to, brand or generic Symbicort HFA
   c. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, milk protein allergy, concomitant use of strong CYP3A4 inhibitor] to, brand or generic Advair Diskus
   d. Patient has tried and failed, or has contraindications [allergy (anaphylaxis, hives) to fluticasone or salmeterol, concomitant use of strong CYP3A4 inhibitor] to, Advair HFA

   If criteria are met, approve with a max of 52gms/4 inhalers per 90 days.
   If criteria are not met, do not approve.

RATIONALE

Per Health Plan.

- Wixela Inhub (generic Advair Diskus) and Breyna (generic Symbicort) HFA are first- and second-line KPCO formulary ICS/LABA medications
- Advair HFA is the third-line ICS/LABA on formulary. Dulera HFA, AirDuo or Breo Ellipta should only be considered in patients who are not candidates for Wixela Inhub, Breyna HFA, and Advair HFA.
- Patients on high dose ICS/LABA for asthma [Advair HFA 230/21 mcg 2 inhalations BID, Dulera HFA 200/5 mcg 2 inhalations BID, Breo Ellipta 200/25 mcg 1 inhalation QD and AirDuo 232/14 mcg 2 inhalations BID] are only candidates for Wixela Inhub or Advair HFA. Symbicort/Breyna HFA is not available in a high ICS dose formulation based on FDA approved dosing.
- For COPD management, initial therapy consist of regular treatment with a long-acting bronchodilator, either LAMA and/or LABA.
- Formoterol based inhalers, Symbicort/Breyna HFA (40.8gms/4 inhalers per 90 days) and Dulera HFA (52gms/4 inhalers per 90 days), have a quantity limit to avoid medication overuse (≥ 2 rescue doses per week indicates poorly controlled asthma and need to address therapy) with SMART therapy.

FDA APPROVED INDICATIONS

See individual medications.

REFERENCES

Per Health Plan.

Creation date: 03/18/2019
Effective date: 01/2024
Reviewed date: 11/2023
Revised date: 11/2023

COMBO SHORT PLUS LONGER-ACTING INSULIN PENS
HUMALOG 50/50

Generic	Brand	HICL	GCN	Exception/Other
INSULIN LISPRO PROTAMINE/INSULIN LISPRO	HUMALOG MIX 50/50 KWIKPEN		50461	

GUIDELINES FOR COVERAGE

A. Must meet either 1 or 2, plus step-therapy criteria from 3:
   1. Prescription is written by an Endocrinology specialist
   2. Patient is under 18 years of age, or the patient is 18 years or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination
   3. Patient has failed* Humulin 70/30, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If above criteria are met, approve indefinitely.
      If above criteria are not met, do not approve.

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RATIONALE
The use of insulin pens at KPCO is reserved for patients age < 18 years and patients with physical and/or cognitive impairment.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

COMBO SHORT PLUS LONGER-ACTING INSULIN PENS
HUMALOG 75/25

Generic	Brand	HICL	GCN	Exception/Other
INSULIN LISPRO PROTAMINE/INSULIN LISPRO	HUMALOG MIX 75/25 KWIKPEN		93717	

GUIDELINES FOR COVERAGE

Must meet criteria based on requested product:

A. Must meet either 1 or 2, plus step-therapy criteria from 3:
   1. Prescription is written by an Endocrinology specialist
   2. Patient is under 18 years of age, or the patient is 18 years or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination
   3. Patient has failed* Humulin 70/30, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If above criteria are met, approve indefinitely.
      If above criteria are not met, do not approve.

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RATIONALE
The use of insulin pens at KPCO is reserved for patients age < 18 years and patients with physical and/or cognitive impairment.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

COMBO SHORT PLUS LONGER-ACTING INSULIN PENS
HUMULIN 70/30

Generic	Brand	HICL	GCN	Exception/Other
INSULIN NPH HUMAN ISOPHANE/REG INSULIN HUMAN	HUMULIN 70/30 PEN		890	**Preferred product**

GUIDELINES FOR COVERAGE

A. Must meet one of the following criteria:
   1. Prescription is written by an Endocrinology specialist
   2. Patient is under 18 years of age, or the patient is 18 years or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination

      If met, approve indefinitely.
      If above criteria are not met, do not approve.

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RATIONALE
The use of insulin pens at KPCO is reserved for patients age < 18 years and patients with physical and/or cognitive impairment.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

COMBO SHORT LONGER-ACTING INSULIN PENS
NOVOLOG 70/30

Generic	Brand	HICL	GCN	Exception/Other
INSULIN ASPART PROTAMINE/INSULIN ASPART	NOVOLOG MIX 70/30 FLEXPEN		17075	

GUIDELINES FOR COVERAGE

Must meet criteria based on requested product:

A. Must meet either 1 or 2, plus step-therapy criteria from 3 and 4 unless the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Prescription is written by an Endocrinology specialist
   2. Patient is under 18 years of age, or the patient is 18 years or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination
   3. Patient has failed* Humulin 70/30
   4. Patient has failed* Humalog Mix 75/25

      If above criteria are met, approve indefinitely.
      If above criteria are not met, do not approve.

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RATIONALE

The use of insulin pens at KPCO is reserved for patients age < 18 years and patients with physical and/or cognitive impairment.

FDA APPROVED INDICATIONS

Diabetes type 1 and type 2 treatment

REFERENCES

Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

COMT-INHIBITOR: OPICAPONE (ONGENTYS)

Generic Name	Brand Name	HICL	GPID	Comments
OPICAPONE	ONGENTYS	45536	45838	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:

1. Patient must be age 18 or older
2. Must be prescribed by a Neurologist or given in consultation with a neurologist
3. Must have a diagnosis of Parkinson's disease
4. Patient is experiencing at least 2 hours 'off' time per day despite maximally tolerated levodopa/carbidopa
5. Patient has failed two of the following adjunct drugs prescribed in combination with levodopa/carbidopa, unless contraindicated or clinically significant adverse effects are experienced, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a) COMT inhibitor: entacapone (Comtan®, Stalevo® or their generics) AND
   b) MAO-B inhibitor: selegiline OR
   c) Dopamine agonist: ropinirole, pramipexole

If initial criteria are met, then approve at GPID x6 months.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:

1. Patient has shown improvement of symptoms since starting on the drug

If renewal criteria above are met, then approve indefinitely.
If renewal criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS

Ongentys is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes.

CONTINUED ON NEXT PAGE

COMT-INHIBITOR: OPICAPONE (ONGENTYS)

FDA APPROVED INDICATIONS (CONTINUED)

Appendix A: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
COMT Inhibitors		
carbidopa/levodopa/ entacapone	PO: Dose should be individualized based on therapeutic response; doses may be adjusted by changing strength or adjusting interval. Fractionated doses are not recommended and only 1 tablet should be given at each dosing interval.	1,200 mg/day (divided doses)
entacapone	PO: 200 mg with each dose of levodopa/carbidopa	1,600 mg/day (divided doses)
tolcapone	PO: 100 mg 3 times daily, as adjunct to levodopa/carbidopa	300 mg/day
MAO-B Inhibitors		
rasagiline	PO: Monotherapy or adjunctive therapy (not including levodopa): 1 mg once daily. Adjunctive therapy with levodopa: Initial: 0.5 mg once daily; may increase to 1 mg once daily based on response and tolerability.	1 mg/day
selegiline	PO: monotherapy or adjunctive therapy (not including levodopa): 5mg twice daily. Adjunctive therapy with levodopa: 5mg twice daily.	5mg twice daily (not to exceed 10mg/day)
Dopamine Agonists		
pramipexole	PO: Initial dose: 0.125 mg 3 times daily, increase gradually every 5 to 7 days; maintenance (usual): 0.5 to 1.5 mg 3 times daily	4.5 mg/day (divided doses)
pramipexole ER	PO: Initial dose: 0.375 mg once daily; increase gradually not more frequently than every 5 to 7 days to 0.75 mg once daily and then, if necessary, by 0.75 mg per dose	4.5 mg/day
ropinirole	PO: Recommended starting dose: 0.25 mg 3 times/day. Based on individual patient response, the dosage should be titrated with weekly increments: Week 1: 0.25 mg 3 times/day; total daily dose: 0.75mg; week 2: 0.5 mg 3 times/day; total daily dose: 1.5 mg; week 3: 0.75 mg 3 times/day; total daily dose: 2.25 mg; week 4: 1 mg 3 times/day; total daily dose: 3 mg. After week 4, if necessary, daily dosage may be increased by 1.5 mg/day on a weekly basis up to a dose of 9 mg/day, and then by up to 3 mg/day weekly to a total of 24 mg/day.	24 mg/day (divided doses)
ropinirole ER	PO: Initial dose: 2 mg once daily for 1 to 2 weeks, followed by increases of 2 mg/day at weekly or longer intervals based on therapeutic response and tolerability	24 mg/day

Appendix B: Contraindications/Boxed Warnings

- Contraindication(s):
  - Concomitant use of non-selective MAO inhibitors.
  - History of pheochromocytoma, paraganglioma, or other catecholamine secreting neoplasms.
- Boxed warning(s): none reported

Appendix C: General Information

- Off time/episodes represent a return of PD symptoms (bradykinesia, rest tremor or rigidity) when the L-dopa treatment effect wears off after each dosing interval.
- PD symptoms, resulting from too little levodopa (L-dopa), are in contrast with dyskinesia which typically results from too much L-dopa. The alterations between “on” time (the time when PD symptoms are successfully suppressed by L-dopa) and “off” time is known as “motor fluctuations”.
- The addition of carbidopa to L-dopa prevents conversion of L-dopa to dopamine in the systemic circulation and liver.

CONTINUED ON NEXT PAGE

COMT-INHIBITOR: OPICAPONE (ONGENTYS)

REFERENCES

1. Ongentys Prescribing Information. San Diego, CA: Neurocrine Biosciences, Inc.; April 2020. Available at: https://www.neurocrine.com/assets/ONGENTYS-PI.pdf. January 4, 2021.
2. Pahwa MD, Factor SA, Lyons KE, et al. Practice Parameter: Treatment of Parkinson disease with motor fluctuations and dyskinesia (an evidence-based review): [RETIRED] Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006 Apr;66:983-995.
3. Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and Movement Disorder Society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. Mov Disord. 2018 Aug;33(8):1248-1266.

Creation Date: 01/2021
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 09/2023

CORTICOTROPIN

Generic	Brand	HICL	GCN	Exception/Other
CORTICOTROPIN	ACTHAR HP GEL, CORTROPHIN	02830	26016	Formulary

Length of approval applies to Federal Group

GUIDELINES FOR COVERAGE

Must meet all criteria for the applicable diagnosis:
A. INFANTILE SPASMS
B. MULTIPLE SCLEROSIS
C. ANY/ALL OTHER DIAGNOSES – NOT COVERED

A. TO TREAT INFANTILE SPASMS: Must meet ALL the following:
   1. Patient has a diagnosis of infantile spasms
   2. Request is for Acthar (Cortrophin does NOT have FDA approval for infantile spasms)
   3. The corticotropin must NOT be administered within a medical office setting. It must be administered in a home setting by non-healthcare persons
   4. Patient is less than 2 years old

If criteria are met, approve for 28 days, at NDC-9 (63004-8710), maximum of 8 vials (each 5mL vial contains 400 units) [applies to FEDERAL Group].
If criteria are not met, do not approve.

B. TO TREAT ACUTE EXACERBATION OF MULTIPLE SCLEROSIS: Must meet the following:
   1. Patient has a diagnosis of multiple sclerosis
   2. Request is for Cortrophin (preferred corticotropin product outside of infantile spasms)
   3. The corticotropin must NOT be administered within a medical office setting. It must be administered in a home setting by non-healthcare persons
   4. Must be prescribed by Neurology
   5. Must meet ONE of the following criteria as follows, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has a contraindication (documented hypersensitivity) to prednisone, methylprednisolone, and dexamethasone
      b. Patient failed a 3-day course of PO prednisone of at least 500mg daily, with or without a short PO prednisone taper afterwards, for this current exacerbation
      c. Patient failed a 7-day course of IV or PO dexamethasone of at least 8mg daily, with or without a short PO prednisone or dexamethasone taper afterwards, for this current exacerbation
      d. Patient failed a 3-day course of IV methylprednisolone of at least 500mg daily, with or without a short oral prednisone taper afterwards, for this current exacerbation

If criteria are met, approve 120 units/day at NDC-9 (62559-0860) for up to 21 days (each 5mL vial contains 400 units) [applies to FEDERAL Group].
If criteria are not met, do not approve.

C. Any/all other indications are not covered. [Per Lexi-Comp - although FDA approved for other indications, there is little evidence to support the use of corticotropin and relevant national guidelines do not recommend the use of corticotropin.]

RATIONALE

Ensure appropriate therapeutic use of this long acting corticotropin formulation.
The recommended regimen for use in infantile spasms is a daily dose of 150 units/m2 (divided into twice daily intramuscular injections of 75 units/ m2) then a gradual taper over a 2-week period. A suggested taper schedule is 30 units/ m2 every morning for 3 days, 15 units/ m2 every morning for 3 days, 10 units/ m2 every morning for 3 days, and then 10 units/ m2 every other morning for 6 days.
8 vials per 28 days supply based on dosage of 150 units/m2/day with an estimate of 0.7m2 body surface area, estimated maximum for a child less than 40 pounds (two years old).
The American Academy of Neurology guidelines for treatment of infantile spasms state that response is usually within 2 weeks and current clinical data is insufficient to determine optimum dosage and duration.
Questcor states that the H.P. Acthar Gel vial expires 28 days after initial puncture, when stored under ideal conditions (per USP standard guidelines).

Contraindications to Acthar
A. concomitant use of live or live attenuated vaccines when receiving immunosuppressive corticotropin dose (also a contraindication to prednisone and methylprednisolone)
B. congenital infection in infants
C. congestive heart failure
D. hypertension, uncontrolled
E. intravenous administration
F. ocular herpes simplex infection
G. osteoporosis
H. peptic ulcers, history or presence of
I. primary adrenocortical insufficiency or adrenocortical hyperactivity
J. scleroderma
K. sensitivity to porcine protein
L. surgery, recent
M. systemic fungal infection (also a contraindication to prednisone, methylprednisolone and dexamethasone)

FDA APPROVED INDICATIONS

Brand corticotrophin	FDA approved indictions
Acthar Gel	• Monotherapy for the treatment of infantile spasms in infants and chidren under 2 years of age • Treatment of exacerbations of MS in adults • May be used for the following disorders and disease: rheumatic, collogen, dermatologic, allergic states, opthalmic, respiratory, and edematous state

Purified Cortrophin Gel	• Nervous system (acute MS exacerbation), rheumatic disorders, collagen disease, dermatologic diseases, allergic states, opthalmic diseases, respiratory disease, and edmatous states.

REFERENCES

1. Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thompson Healthcare. Available at: http://www.thomsonhc/com/micromedex2/librarian. [Accessed: September 13, 2013].
2. Milanese C, La Mantia L, Salmaggi A, et al. Double-blind randomized trial of ACTH versus dexamethasone versus methylprednisolone in multiple sclerosis bouts. Clinical, cerebrospinal fluid and neurophysiological results. Eur Neurol. 1989;29(10):10-4.
3. Thompson AJ, Kennard C, Swash M, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. Neurology. 1989;39(7):969-71.
4. Abbruzzese G, Gandolfo C, and Loeb C. “Bolus” methylprednisolone versus ACTH in the treatment of multiple sclerosis. Ital J Neurol Sci. 1983 Jun;4(2):169-72.
5. KDIGO Clinical Practice Guideline for Glomerulonephritis (GN) http://www.kidney-international.org. 2012
6. KPMAS Acthar guidelines

Creation date: 07/25/2018
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

DABRAFENIB (TAFINLAR)

Generic Name	Brand Name	HICL	GPID	Comments
DABRAFENIB	TAFINLAR	40360	34723, 34724	Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
1. Patient is new to KPCO within the past 90 days and is stable on therapy.

   If met, approve based on the following:
   - For adjuvant setting: Approve for duration needed to complete a total of 12 months of adjuvant treatment, max 4 per day.
   - For unresectable or metastatic setting: Approve x indefinitely, max 4 per day.

   If not met, review by Initial Criteria below.

INITIAL CRITERIA: Must meet all the following criteria:
A. Must be prescribed by an oncologist
B. Must have a BRAF V600 activating mutation positive tumor
C. Must meet the diagnosis-specific criteria below:
   1. Cutaneous Melanoma (Adjuvant Setting)
      a. Must be requested in the adjuvant treatment setting

      If initial criteria above are met, approve x 12 months, max 4 per day.
      If initial criteria are not met, do not approve.

   2. Cutaneous Melanoma (Unresectable or Metastatic Setting): Must meet both a and b, plus either c or d below:
      a. Must be requested in unresectable or metastatic (advanced) setting
      b. Must have confirmed brain metastasis, or the patient has tried and is unable to tolerate vemurafenib (Zelboraf) due to unacceptable toxicities despite adequate dose reductions, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
      c. If the request is for dabrafenib (Tafinlar) monotherapy: Must not have progressed through other BRAF-targeted therapies (ex: vemurafenib (Zelboraf), encorafenib (Braftovi)) in the unresectable or metastatic (advanced) setting
      d. If the request is for dabrafenib (Tafinlar)/trametinib (Mekinist) combination therapy: Must not have progressed through other BRAF/MEK combination therapy (ex: vemurafenib (Zelboraf)/cobimetinib (Cotellic), encorafenib (Braftovi)/binimetinib (Mektovi)) in the unresectable or metastatic (advanced) setting

      If initial criteria above are met, approve x indefinitely, max 4 per day.
      If initial criteria are not met, do not approve. Use specific notations below for denial as applicable:

- If initial criteria are met other than C.2.b, deny noting patient must use vemurafenib.
- If initial criteria are met other than C.2.c, deny noting that there is not enough evidence to support use of dabrafenib monotherapy after progression on other BRAF-targeted therapies in the unresectable or metastatic (advanced) setting.
- If initial criteria are met other than C.2.d, deny noting there is not enough evidence to support use of dabrafenib/trametinib combination therapy after progression on other BRAF/MEK combination therapies in the unresectable or metastatic (advanced) setting.

3. Non-small cell lung cancer
   a. Must be requested in the unresectable or metastatic setting
   b. Must have BRAF V600E mutation positive tumor

   If initial criteria above are met, approve x indefinitely, max 4 per day.
   If initial criteria are not met, do not approve.

4. Thyroid cancer
   a. Must be requested in the locally advanced or metastatic setting
   b. Must have anaplastic thyroid cancer
   c. Must have BRAF V600E mutation positive tumor

   If initial criteria above are met, approve x indefinitely, max 4 per day.
   If initial criteria are not met, do not approve.

5. Solid tumors
   a. Must be requested in the unresectable or metastatic setting
   b. Must have BRAF V600E mutation positive tumor
   c. Must have progressed through prior treatment and have no satisfactory alternative treatment options

   If initial criteria above are met, approve x indefinitely, max 4 per day.
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA

1. Request for continued coverage is in the unresectable or metastatic setting only. [No indication for treatment beyond 12 months in the adjuvant setting.]
2. Patient's disease has not progressed since treatment initiation, or the treating provider believes patient is deriving significant clinical benefit to justify treatment continuation [Note: provider does not need to prove lack of progression via imaging. Clinical evaluation suffices.]

   If renewal criteria are met, approve x indefinitely, max 4 per day.
   If renewal criteria are not met, do not approve.

RATIONALE

FDA labeling
Steering use toward preferred products

FDA APPROVED INDICATIONS

Melanoma (adjuvant, unresectable/metastatic), NSCLC (metastatic), anaplastic thyroid cancer (locally advanced, metastatic), solid tumors (unresectable, metastatic) with BRAF V600 activating mutations.

Creation Date: 3/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

DAPAGLIFLOZIN (FARXIGA)

Generic	Brand	HICL	GCN	Exception/Other
DAPAGLIFLOZIN	FARXIGA	40137		NF 2nd Preferred

GUIDELINES FOR COVERAGE
Must be used for one of the following indications and meet all related criteria as follows:

A. General criteria for any/all requests
B. Adults 25 years of age or older with DM2 and ASCVD
C. Adults 25 years of age or older with DM2 with Nephropathy
D. Adults 18 years of age or older with Heart Failure
E. Adults 18 years of age or older with CKD (without type 2 diabetes)
F. Adults 25 years of age or older with DM2 without ASCVD, Nephropathy, or Heart Failure
G. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. General criteria for any/all requests:
   - Request must be for generic dapagliflozin [authorized generic available].

If not met, do not approve.

B. To treat adults 25 years of age or older with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD) [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Patient has contraindication or intolerance to, is currently using, or has failed maximum doses of metformin IR and/or metformin ER, or the patient's A1c is at goal and SGLT-2i is more appropriate for ASCVD, CKD and/or HF benefit
   2. Patient has an eGFR of at least 20 ml/min and has tried and failed, or has an intolerance or contraindication to empagliflozin (Jardiance)

If all criteria met, approve at HICL indefinitely, max 1 tablet per day.
If criteria are not met, do not approve.

C. To treat adults 25 years of age or older with type 2 diabetes with nephropathy: Must meet all the following:
   1. eGFR is at least 20 ml/min, and eGFR is less than 60 ml/min and/or urinary albumin-to-creatinine ratio greater than 300
   2. The patient has contraindication to, is currently using, or has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to

lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Maximum doses of metformin IR and/or metformin ER, or the patient's A1c is at goal and SGLT-2i is more appropriate for ASCVD, CKD and/or HF benefit
   b. ACE-I or ARB
   c. empagliflozin (Jardiance)

If all criteria met, approve at HICL indefinitely, max 1 tablet per day.
If criteria are not met, do not approve.

D. To treat adults 18 years of age or older with HF (with or without type 2 diabetes): Must meet all the following:
   1. NYHA Class II-IV
   2. Patient has eGFR of at least 25 ml/min
   3. Has contraindications to, is currently using, or has failed all of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. ACE-I or ARB or ARNI (Entresto)
      b. Beta blocker
      c. Aldosterone antagonist (e.g., spironolactone, eplerenone)
      d. empagliflozin (Jardiance)

If all criteria met, approve at HICL indefinitely, max 1 tablet per day.
If criteria are not met, do not approve.

E. To treat adults 18 years of age or older with CKD (without type 2 diabetes): Must meet all the following:
   1. eGFR of at least 20 ml/min, and eGFR is less than 60 ml/min and/or Urinary albumin-to-creatinine ratio of at least 300
   2. Has contraindications to, is currently using or has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. ACE-I or ARB
      b. empagliflozin (Jardiance)

If all criteria met, approve at HICL indefinitely, max 1 tablet per day.
If criteria are not met, do not approve.

F. To treat adults 25 years of age or older with type 2 diabetes without ASCVD, nephropathy, or HF: Must meet all the following:
   1. Most recent HgbA1c is above, but within 2% of their designated A1c goal
   2. Patient has an eGFR of at least 20 ml/min
   3. Patient has contraindications to, is currently using, or has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. maximum dose metformin IR and subsequently metformin ER
      b. empagliflozin (Jardiance)
      c. maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
         i. h/o bariatric surgery
         ii. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
         iii. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e. sulfonylurea, insulin, pioglitazone)
         iv. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If all criteria met, approve at HICL x6 months, max 1 tablet per day.
If criteria are not met, do not approve.

G. To treat type 2 diabetes in young adult/pediatric patients between 10 and 25 years of age: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Patient has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER
   2. Patient has an eGFR of at least 20 ml/min and has tried and failed, or has an intolerance or contraindication to empagliflozin (Jardiance)
   3. Patient has contraindications to, is currently using, or has failed maximum dose pioglitazone unless the patient has one of the following:
      a. h/o bariatric surgery
      b. BMI ≥ 95%ile for age and sex
      c. ≥ 5% increase in body weight after 6 months of starting these medications
      d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If all criteria met, approve at HICL x6 months, max 1 tablet per day.
If criteria are not met, do not approve.

RENEWAL CRITERIA
1. HgbA1c is either at goal or has decreased by at least 0.5%.

If renewal criteria are met, approve indefinitely at HICL, max 1 tablet per day.
If renewal criteria are not met, do not approve.

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ePA Questions
Initial Review Questions
1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Adults 25 years of age or older with DM2 and ASCVD; Adults 25 years of age or older with DM2 with Nephropathy; Adults 18 years of age or older with Heart Failure; Adults 18 years of age or older with CKD (without type 2 diabetes); Adults 25 years of age or older with DM2 without ASCVD, Nephropathy, or Heart Failure; Pediatrics/Young Adults between 10 and 25 years of age with DM2]
   QUESTIONS BASED ON DIAGNOSIS SELECTED
   Adults 25 years of age or older with DM2 and ASCVD
   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (metformin IR (500 mg, 850 mg, 1000 mg) or ER (500 mg, 750 mg); Jardiance tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
   3. Lab: Current eGFR:
   4. Date of eGFR lab (MMDDYY):

   Adults 25 years of age or older with DM2 with Nephropathy
   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (metformin IR (500 mg, 850 mg, 1000 mg) or ER (500 mg, 750 mg); Jardiance tablets; losartan tablets; lisinopril, benazepril, captopril) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
   3. Lab: Current eGFR:
   4. Date of eGFR lab (MMDDYY):
   5. Lab: Current Albumin to Creatinine Ratio:
   6. Date of Albumin to Creatinine lab (MMDDYY):

   Adults 18 years of age or older with Heart Failure
   1. Patient's NYHA Functional Class (1-4):
   2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   3. Is there reasoning why alternatives (Jardiance tablets; losartan tablets; lisinopril, benazepril, captopril; Entresto tablets; atenolol tablets, metoprolol IR/ER tablets, bisoprolol tablets, carvedilol tablets, labetalol tablets, acebutolol capsules, propranolol ER capsules (60 mg, 80 mg, 120 mg, 160 mg) or IR tablets; spironolactone tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
   4. Lab: Current eGFR:
   5. Date of eGFR lab (MMDDYY):

   Adults 18 years of age or older with CKD (without type 2 diabetes)

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (Jardiance tablets; losartan tablets; lisinopril, benazepril, captopril) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
3. Lab: Current eGFR:
4. Date of eGFR lab (MMDDYY):
5. Lab: Current Albumin to Creatinine Ratio:
6. Date of Albumin to Creatinine lab (MMDDYY):

Adults 25 years of age or older with DM2 without ASCVD, Nephropathy, or Heart Failure

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (metformin IR (500 mg, 850 mg, 1000 mg) or ER (500 mg, 750 mg); glipizide, glimepiride, glyburide (1.25 mg. 2.5 mg, 5 mg) immediate-release tablets; pioglitazone tablets; Jardiance tablets; vials of glargine-yfgn (interchangeable biosimilar to Lantus), Humulin N, Humulin R) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
3. Lab: Current eGFR:
4. Date of eGFR lab (MMDDYY):
5. Lab: Current A1c:
6. Date of A1c (MMDDYY):
7. Patient's current BMI:
8. Has the patient had bariatric surgery?

Pediatrics/Young Adults between 10 and 25 years of age with DM2

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (metformin IR (500 mg, 850 mg, 1000 mg) or ER (500 mg, 750 mg); pioglitazone tablets; Jardiance tablets; vials of glargine-yfgn (interchangeable biosimilar to Lantus), Humulin N, Humulin R) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
3. Lab: Current eGFR:
4. Date of eGFR lab (MMDDYY):
5. Lab: Current A1c:
6. Date of A1c (MMDDYY):
7. Patient's current BMI:
8. Has the patient had bariatric surgery?

Renewal Review Questions

1. Lab: Current A1c:
2. Date of A1c (MMDDYY):

RATIONALE

- KP National Diabetes Guidelines recommend using SGLT-2i for people with type 2 diabetes with clinical ASCVD who are already taking metformin to reduce the risk of: (1) cardiovascular events (myocardial infarction or stroke) or cardiovascular death, (2) progression of renal disease and/or (3) death from renal causes, and/or (4) heart failure hospitalizations. The American College of Cardiology (ACC) 2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients with Type 2 Diabetes, which is also endorsed by the

American Diabetes Association (ADA), recommends SGLT-2i as a first-line treatment in patients with type 2 diabetes and one or more of the following: ASCVD, HFrEF, HFpEF (empagliflozin only), diabetic kidney disease (DKD), or at high risk for ASCVD.

- Preferred order of agents:
  1) Empagliflozin (Jardiance), formulary without PA, is the preferred agent for ASCVD, CKD, and HF due to strength of clinical trial data, range of approved indications, and cost (1/2 tab regimen)
  2) Canagliflozin (Invokana), non-formulary with PA, is the 2nd preferred option for ASCVD, CKD and DM2 patients without compelling indications. due to broad range of indications and cost (1/2 tab regimen).
  3) Dapagliflozin (Farxiga), non-formulary with PA, is the 2nd preferred option for HF, and the 3rd preferred option for ASCVD, CKD and DM2 patients without compelling indications due to broad range of indications but at high cost.
  4) Ertugliflozin (Steglatro), non-formulary with PA, is least preferred due to high cost, paucity of positive clinical trial data, and lack of additional FDA-approved indications. Specifically, ertugliflozin has been studied in patients with type 2 diabetes and ASCVD and did not improve cardiovascular outcomes while all three other SGLT-2i have demonstrated such benefits in this population.
  5) Bexagliflozin (Brenzavvy): non-formulary with PA, is least preferred due to high cost and lack of additional FDA-approved indications.
  6) Sotagliflozin (Inpefa): non-formulary with PA, is 3rd preferred for HF given shorter history of postmarketing safety data compared to other SGLT2i's approved for HF as well as the need to titrate sotagliflozin dose for when others are fixed-dose regimens. Sotagliflozin (Inpefa) is least preferred for glycemic control due to lack of clinical trial data and FDA-approved indication as well as its high cost.
- Jardiance (empagliflozin) is the preferred sodium glucose co-transporter 2 inhibitor (SGLT-2i) at Kaiser Permanente Colorado (KPCO) and can be used effectively and safely with a GFR down to 20 mL/min. In addition, the dose of 12.5 mg (1/2 of 25mg tablet) is an effective dose for all patients regardless of GFR.
- Based on the available evidence, various organizations endorse SGLT-2is use down to lower GFR levels than indicated in product labels:
  - American College of Cardiology Expert Consensus now recommends empagliflozin in GFR ≥ 20 mL/min (2021).
  - National Kidney Foundation recommends SGLT-2is in GFR ≥ 20 mL/min as long as there are no contraindications (2023).
  - American Diabetes Association recognizes SGLT-2is benefits in patients with GFR ≥ 20 mL/min (2023).

FDA APPROVED INDICATIONS for SGLT2 Inhibitors

Empagliflozin (Jardiance)

1. Improve glycemic control in patients with DM2
2. Reduce the risk of CV death in pts with DM2 + CVD
3. Reduce risk of CVD death and HF hospitalizations in pts with HF
4. Reduce risk of sustained eGFR decline, ESRD, CV death and hospitalizations in adults with CKD at risk of progression

Canagliflozin (Invokana)

1. Improve glycemic control in patients with DM2
2. Reduce risk of MACE in pts with DM2 + CVD

3. Reduce the risk of ESRD, doubling of creatinine, CV death, or HF hospitalization in pts with DM2 + diabetic nephropathy

Dapagliflozin (Farxiga)
1. Improve glycemic control in patients with DM2
2. Reduce risk of HF hosp in pts with DM2 + CVD/multiple CV RFs
3. Reduce the risk of CV death and HF hosp in patients with HFrEF NYHA II-IV
4. Reduce risk of sustained eGFR decline, ESRD, CV death, and hospitalization for HF in adults with CKD at risk of progression

Ertugliflozin (Steglatro)
1. Improve glycemic control in patients with DM2

Bexagliflozin (Brenzavvy)
1. Improve glycemic control in patients with DM2

Sotagliflozin (Inpefa)
1. Reduce the risk of CV death and HF hosp in pts with heart failure
2. Reduce the risk of CV death and HF hosp in pts with DM2 + CKD + CV RF(s)

REFERENCES

Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation date: 09/26/18
Effective date: 04/2024
Reviewed date: 01/2024
Revised date: 03/2024

JESDUVROQ (DAPRODUSTAT)

Generic	Brand	HICL	GCN	COMMENTS
DAPRODUSTAT	JESDUVROQ	48668		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
1. Patient is new to KPCO within the past 90 days and stable on therapy.

If met, approve indefinitely at HICL, max #3 per day.
If not met, Use Initial Criteria for review.

INITIAL CRITERIA: Must meet all the following:
1. The patient has a diagnosis of anemia due to chronic kidney disease (CKD).
2. The patient is 18 years of age or older.
3. Therapy is prescribed by a nephrologist.
4. The patient has been receiving dialysis for at least 4 months.
5. The patient has an eGFR of less than 60mL/min/1.73m2 corresponding to stage 3, 4, or 5 chronic kidney disease (CKD).
6. Patient has a hemoglobin level less than 12 g/dL.
7. Medication will not be used in combination with an erythropoiesis-stimulating agent (ESA) (e.g., Epogen, Procrit).

If met, approve at HICL x24 weeks, max #3 per day.
If not met, do not approve.

RENEWAL CRITERIA: Must meet one of the following:
1. The patient has a hemoglobin level of greater than or equal to 10 g/dL.
2. The patient's hemoglobin level has increased by at least 2 g/dL from their baseline level.

If met, approve indefinitely at HICL, max #3 per day.
If not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS
Indicated for the treatment of anemia due to chronic kidney disease in adults who have been receiving dialysis for at least four months.

REFERENCES
Jesduvroq [Prescribing Information]. Durham, NC: GlaxoSmithKline; February 2023.

Creation Date: 11/2023
Effective Date: 12/2023
Reviewed Date:
Revised Date:

DARIDOREXANT (QUVIVIQ)

Generic Name	Brand Name	HICL	GPID	Comments
DARIDOREXANT	QUVIVIQ	47751		Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all General Criteria and all Age Criteria in applicable age section

A. **General Criteria for All Requests:** Must meet all the following:
   1. Medication is prescribed by Behavioral Health or Sleep Medicine provider
   2. Patient must be age 18 or older
   3. Diagnosis of insomnia characterized by difficulties with sleep onset and/or sleep maintenance
   4. Potential factors contributing to sleep disturbances have been addressed (e.g., inappropriate sleep hygiene, sleep environment issues and co-morbid conditions contributing to insomnia)
   5. Patient has no history of substance abuse
   6. Patient has no history of narcolepsy

B. **Age 65 Years or Older:** Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to trazodone
   2. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to ramelteon or OTC melatonin
   3. Trial and failure of, contraindication, or intolerance to lemborexant (Dayvigo) and/or Suvorexant (Belsomra)

   If initial criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.
   If initial criteria are not met, do not approve.

C. **Age Less Than 65 Years:** Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to trazodone
   2. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to ramelteon or OTC melatonin
   3. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to at least ONE of the following sedative-hypnotic alternatives: zolpidem (F), zaleplon (NF), eszopiclone (NF)

4. Trial and failure of, contraindication, or intolerance to lemborexant (Dayvigo) and/or Suvorexant (Belsomra)

   If initial criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.
   If initial criteria are not met, do not approve.

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ePA Questions

1. Have factors that could contribute to sleep disturbances been addressed (e.g., inappropriate sleep hygiene, sleep environment issues and co-morbid conditions contributing to insomnia)?
2. Does the patient have history of substance abuse?
3. Does the patient have history of narcolepsy?
4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
5. Is there reasoning why alternatives (OTC melatonin, trazodone, zolpidem IR tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

FDA APPROVED INDICATIONS

Dayvigo (lemborexant) and Belsomra (suvorexant), and Quviviq (daridorexant) are indicated for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.

REFERENCES

Per Health Plan

Creation Date: 03/2021
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

DARIFENACIN (ENABLEX)

Generic	Brand	HICL	GCN	Exception/Other
DARIFENACIN ER	ENABLEX	26820	24043, 24044	Max daily dose 1 tab per day

GUIDELINES FOR COVERAGE

Review based on patient cognitive status noted in section A or B:

A. Patients with a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin and/or trospium IR, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely (max daily dose of 1 tab/day).
      If criteria are not met, do not approve.

B. Patients WITHOUT a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin, and/or trospium IR, and/or oxybutynin tablet/syrup, the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely (max daily dose of 1 tab/day).
      If criteria are not met, do not approve.

RATIONALE

Per Health Plan.

- An adequate response is defined as one less episode of frequency or incontinence per day after an adequate trial of 4-6 weeks.
- Preferred formulary agents, in order: oxybutynin ER, oxybutynin IR, solifenacin, trospium IR and oxybutynin syrup.

- Preferred nonformulary agents in order: tolterodine IR, tolterodine ER, darifenacin, fesoterodine, trospium ER, mirabegron and vibegron. Oxybutynin gel (Gelnique) and oxybutynin patch (Oxytrol) are excluded from coverage.
- Agents preferred in cognitive impairment include, in order: solifenacin, trospium IR, darifenacin ER, trospium ER.

Creation date: 01/15/2019
Effective date: 01/2024
Reviewed date: 09/2023
Revised date: 09/2023

DAROLUTAMIDE (NUBEQA)

Generic	Brand	HICL	GCN/GPID	Other
DAROLUTAMIDE	NUBEQA	45909	46746	

GUIDELINES FOR COVERAGE
Must meet all the following:

1. Patient has a diagnosis of prostate adenocarcinoma
2. Medication is prescribed by an Oncologist
3. Must have PSA greater than or equal to 2ng/dL
4. Patient has not experienced disease progression on any of the following: enzalutamide (Xtandi), abiraterone acetate (Zytiga, Yonsa), apalutamide (Erleada), docetaxel (Taxotere), or bicalutamide
5. Must have a diagnosis of nonmetastatic castration-resistant prostate cancer (M0CRPC) or metastatic castration-sensitive prostate cancer (M1CSPC), and meet all the diagnosis subtype-specific criteria below:
    a. Nonmetastatic Castration Resistant Prostate Cancer (M0CRPC): Must meet all:
        i. No metastasis observable on radiologic scans
        ii. Must have had PSA double in 10 months or less while on at least one ADT (androgen deprivation therapy) including: leuprolide (Eligard, Lupron), goserelin (Zoladex), triptorelin (Trelstar), histrelin (Supprelin, Vantas), degarelix (Firmagon)
        iii. Patient is intolerant of, or has a contraindication to, enzalutamide (Xtandi), or the patient is currently being treated with a strong CYP3A4 inducer [that prohibits the use of enzalutamide (Xtandi)], or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
    b. Metastatic Castration Sensitive Prostate Cancer (M1CSPC): Must meet all:
        i. Patient has documented metastatic disease that has not progressed on ADT (androgen deprivation therapy) including: leuprolide (Eligard, Lupron), goserelin (Zoladex), triptorelin (Trelstar), histrelin (Supprelin, Vantas), degarelix (Firmagon)
        ii. The patient will receive concurrent docetaxel x6 cycles, planned to start within 6 weeks of starting darolutamide
        iii. The patient is intolerant of, or has a contraindication to, abiraterone (Zytiga), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve. Alternatives include enzalutamide [Xtandi] for M0CRPC or abiraterone [Zytiga] for patients with M1CSPC.

ePA Questions

1. Does the patient a diagnosis of prostate adenocarcinoma?
2. Lab: Current PSA:
3. Date of PSA Lab (MMDDYY):
4. Has the patient experienced disease progression on any of the following: enzalutamide (Xtandi), abiraterone acetate (Zytiga, Yonsa), darolutamide (Nubeqa), docetaxel (Taxotere), or bicalutamide?
5. Diagnosis subtype associated with this request: [check boxes for all diagnosis-subtypes listed in criteria: nonmetastatic castration-resistant prostate cancer (M0CRPC); metastatic castration-sensitive prostate cancer (M1CSPC)]

QUESTIONS BASED ON DIAGNOSIS SELECTED

Nonmetastatic Castration-Resistant Prostate Cancer (M0CRPC)

1. Does the patient have any observable metastasis on radiologic scans?
2. Has the patient's PSA doubled in 10 months or less while on ADT (androgen deprivation therapy)?
3. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
4. Is there reasoning why alternatives (enzalutamide (Xtandi)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Metastatic Castration-Sensitive Prostate Cancer (M1CSPC)

1. Does the patient have metastatic disease?
2. Has metastatic disease progressed on ADT (androgen deprivation therapy)?
3. Will the patient receive concurrent docetaxel x6 cycles, planned to start within 6 weeks of starting darolutamide?
4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
5. Is there reasoning why alternatives (abiraterone (Zytiga)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Health Plan.
Enzalutamide is the KPCO preferred agent for nonmetastatic (M0) castration resistant prostate cancer (CRPC), unless history of seizures then darolutamide or apalutamide should be used. If the patient has metastatic castration sensitive prostate cancer (mCSPC), KPCO formulary alternatives of abiraterone or docetaxel are preferred.

FDA APPROVED INDICATIONS

Treatment of non-metastatic, castration-resistant prostate cancer (M0CRPC). Treatment of metastatic castration-sensitive prostate cancer (M1CSPC, in combination with docetaxel if darolutamide).

REFERENCES

1. Nubeqa (darolutamide) [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; July 2019.
2. NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer v.1.2023. www.nccn.org

Creation Date: 11/2018
Effective Date: 04/2024
Reviewed Date: 03/2024

Revised Date: 03/2024

DASATINIB

Generic	Brand	HICL	GCN/GPID	Other
DASATINIB	SPRYCEL	33855		Formulary, 2nd Generation TKI

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

A. Patient is new to KPCO within the past 90 days, and the medication has been prescribed by an Oncologist

If met, approve x 2 years.
If not met, then use Initial Criteria.

INITIAL CRITERIA: Must meet the following criteria based on drug and diagnosis below:

A. Dasatinib (Sprycel) for Chronic Phase of Chronic Myeloid Leukemia (CML)
B. Dasatinib (Sprycel) for Accelerated or Blast Phase of Chronic Myeloid Leukemia (CML)
C. Dasatinib (Sprycel) for Acute Lymphoblastic Leukemia (ALL)
D. Dasatinib (Sprycel), Nilotinib (Tasigna) for Gastrointestinal Stromal Tumor (GIST)
E. All other indications

A. **Dasatinib (Sprycel) for CML - Chronic Phase: Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Must not have any of the following BCR-ABL1 mutations: T315I/A, F317L/V/I/C or V299L
   3. Patient must have Philadelphia Chromosome (aka BCR-ABL) and one of a through e below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has tried and failed imatinib (Gleevec) with an inadequate response that is not due to patient nonadherence
      b. Patient must have a documented intolerance to imatinib (Gleevec) not alleviated by dose reductions (≤200 mg/day [adult] or 260mg/m^2 [peds; if this calculates to >200mg/day use adult dose cutoff])
      c. Patient has a contraindication to imatinib (Gleevec)
      d. Patient has Intermediate or High Sokal Score (0.8 or greater)
      e. Patient has one of the following BCR-ABL1 mutations: Y253H, E255K/V or F359V/C/I

If criteria are met, approve x 2 years.
If criteria are not met, do not approve [direct to imatinib (Gleevec) as appropriate].

B. **Dasatinib (Sprycel) for CML - Accelerated or Blast Phase: Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Must not have any of the following BCR-ABL1 mutations: T315I/A, F317L/V/I/C or V299L
   3. Patient must have Philadelphia Chromosome (aka BCR-ABL)

4. Must meet criteria below based on Accelerated Phase or Blast Phase:
   a. Accelerated Phase: Must meet one of the following:
      i. Peripheral blood myeloblasts ≥15% and <30%
      ii. Peripheral blood myeloblasts and promyelocytes combined ≥30%
      iii. Peripheral blood basophils ≥20%
      iv. Platelet count ≤100 x 10^9/L unrelated to therapy
      v. Additional clonal cytogenetic abnormalities in Ph+ cells
   b. Blast Phase: Must meet one of the following:
      i. ≥30% blasts in the blood, marrow, or both
      ii. Extramedullary infiltrates of leukemic cells

If criteria are met, approve x 2 years.
If criteria are not met, do not approve.

C. **Dasatinib (Sprycel) for Acute Lymphoblastic Leukemia (ALL): Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Patient must have Philadelphia Chromosome (aka BCR-ABL)
   3. Must not have any of the following BCR-ABL1 mutations: T315I/A, F317L/V/I/C or V299L

If criteria are met, approve indefinitely.
If criteria are not met, do not approve.

D. **Dasatinib (Sprycel) for Gastrointestinal Stromal Tumor (GIST): Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Patient must have metastatic or unresectable GIST
   3. Patient has had disease progression, documented intolerance, or contraindications to all of the following medications in a through d below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a) imatinib (Gleevec)
      b) sunitinib (Sutent)
      c) regorafenib (Stivarga)
      d) ripretinib (Qinlock)
   4. Dasatinib (Sprycel) only: Patient must have PDGFRA D842V mutation.

If criteria are met, approve indefinitely.
If criteria are not met, do not approve.

E. **If for any other diagnosis (e.g., hypereosinophilic syndrome, eosinophilic leukemia, dermatofibrosarcoma, chordoma): Must meet all the following:**
   1. Prescribed by an oncology specialist
   2. Use must meet the Medicare Compendia criteria as detailed in the following policy: Medicare Benefit Policy Manual Chapter 15 - Covered Medical and Other Health Services Section 50.4.5 - Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

If criteria are met, approve x 1 year.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:

A. Patient has been on the TKI for greater than 3 months and one of the following criteria:
   1. Disease progression or relapse are not noted in the chart
   2. Patient has experienced improvement in disease symptoms since starting the medication

If criteria are met, approve x 2 years.
If criteria are not met, do not approve.

RATIONALE

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology Chronic Myeloid Leukemia v.2.2023 www.nccn.org
2. NCCN Clinical Practice Guidelines in Oncology Acute Lymphoblastic Leukemia v.1.2022 www.nccn.org
3. NCCN Clinical Practice Guidelines in Oncology Gastrointestinal Stromal Tumors (GISTs) v.1.2023 www.nccn.org

Creation Date: 11/2019
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

DEFLAZACORT (EMFLAZA)

Generic	Brand	HICL	GCN	Exception/Other
DEFLAZACORT	EMFLAZA 18MG	11668	43012	GSN 77113
DEFLAZACORT	EMFLAZA 22.75MG/ML SUSP	11668	43016	GSN 77117
DEFLAZACORT	EMFLAZA 30MG	11668	23762	GSN 27605
DEFLAZACORT	EMFLAZA 36MG	11668	43015	GSN 77116
DEFLAZACORT	EMFLAZA 6MG	11668	23761	GSN 27604

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: All the following must be met:
1. Patient is equal to or greater than 2 years old
2. Patient has a diagnosis of Duchenne Muscular Dystrophy (DMD)
3. Patient had onset of weakness associated with DMD that occurred before 5 years of age
4. Patient has tried continuous prednisone for at least 12 months and experienced 'clinically significant' weight gain during the first 2 years of prednisone use, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If all initial criteria are met, approve at HICL x 1 year.
   If criteria are not met, do not approve.

RENEWAL CRITERIA: All the following must be met:
1. Patients weight gain must not be persisting or worsening

   If met, approve at HICL x 2 years.
   If criteria are not met, do not approve.

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ePA Questions
Initial Review Questions
1. Has the patient had onset of weakness associated with DMD that occurred before 5 years of age?
2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
3. Is there reasoning why alternatives (prednisone) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Renewal Review Questions
1. Has the patient had persistent or worsening weight gain since starting deflazacort?

RATIONALE
Prednisone is recommended as the first-line corticosteroid for use in patients with DMD. Prednisone and deflazacort are considered comparable in efficacy with regards to improving muscle strength and function in patients with DMD.

The American Academy of Neurology concluded that prednisone may be associated with a greater weight gain within the first 12 months of treatment (5 kg vs. 2 kg, respectively), with no significant difference in weight gain observed with longer-term use. Deflazacort treatment, however, may be associated with an increased risk of cataracts compared to prednisone. These differences have been supported by a Cochrane Review noting very low quality of evidence. Deflazacort may be associated with less weight gain than prednisone in the short-term, but differences in weight gain with long-term use as well as any differences in other side effects, such as behavior changes, risk for fractures, cataracts, or effects on glucose control are not clearly known.

*Clinically significant weight gain is defined as crossing at least two stanines on the weight growth chart during the first 2 years of prednisone use (new weight gain after several years of prednisone use is likely due to multiple factors such as inactivity and persistence of appetite.
A 2022 study in 196 boys with DMD compared efficacy and safety outcomes of three different corticosteroid dosing regimens: daily prednisone, daily deflazacort, and intermittent prednisone. Across measures of motor function, both daily prednisone and daily deflazacort were more effective than intermittent prednisone and the daily regimens did not differ significantly.

FDA APPROVED INDICATIONS
Treatment of Duchenne muscular dystrophy (DMD) in patients 2 years and older

REFERENCES
KP InterRegional Practice Recommendations for Deflazacort final 20170822
Guglieri M, Bushby K, McDermott MP, et al. Effect of Different Corticosteroid Dosing Regimens on Clinical Outcomes in Boys With Duchenne Muscular Dystrophy: A Randomized Clinical Trial. JAMA. 2022 Apr 19;327(15):1456-1468.

Created: 9/26/2018
Effective: 04/2024
Last revised: 03/2024
Last reviewed: 03/2024

DESMOPRESSIN (NOCDURNA)

Generic Name	Brand Name	HICL	GPID	Comments
DESMOPRESSIN	NOCDURNA	02841	35296, 37509	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:

1. Patient must be age 18 years or older
2. Must have a diagnosis of nocturia due to nocturnal polyuria that has been confirmed with a 24-hour urine collection and the patient meets one of the following:
   a. The nocturnal urine volume exceeds 20% of the total 24-hour urine volume if the patient is less than 65 years of age
   b. The nocturnal urine volume exceeds 33% of the total 24-hour urine volume if the patient is 65 years of age or older
3. Patient awakens at least two times per night to void
4. Must have baseline sodium (Na) level within the past 30 days that is within normal limits (135 -145 mmol/L)
5. Requested dose does not exceed 27.7 mcg per day for women or 55.3 mcg per day for men
6. Patient has tried or had an intolerance to desmopressin oral tablets and oral solution, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If initial criteria are met, approve x1 year, max 1 tab per day.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:

1. Patient has shown improvement or decrease in nocturia episodes since starting on the drug
2. Patient has routine monitoring for serum sodium levels with normal level (135 -145 mmol/L) since initiating therapy and within the past 6 months

If renewal criteria are met, approve indefinitely, max 1 tab per day.
If renewal criteria are not met, do not approve.

RATIONALE

Desmopressin acetate has a black box warning regarding potential for hyponatremia. Serum sodium levels should be normal prior to prescribing and should be remeasured within 7 days and one month after starting. Patient 65 years or older should be monitored more frequently since they are at higher risk of hyponatremia. Desmopressin SL tablets have only been studied in adult patients.

FDA APPROVED INDICATIONS

Desmopressin SL tablets (Nocdurna) is FDA approved for treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void.

QUANTITY LIMITS: 1 SL tablet per day (either strength)

REFERENCES:

1. Nocdurna [package insert]. Parsippany, NJ: Ferring Pharmaceuticals: 2018.

Creation Date: 1/2022
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 9/2023

DIACOMIT (STIRIPENTOL)

Generic	Brand	HICL	GCN	Exception/Other
STIRIPENTOL	DIACOMIT	35461		Nonformulary, Specialty Tier with Quantity Limit

GUIDELINES FOR COVERAGE

All the following must be met:
1. Medication is prescribed by a CMPG or affiliated neurologist or epileptologist
2. Patient has a diagnosis of Dravet Syndrome (DS)
3. Patient is 2 years of age or older
4. The patient is stable on stiripentol (Diacomit), or the patient has failed all the following medications, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. a valproic acid derivative
   b. clobazam
   c. Epidiolex [Nonformulary requires Prior Authorization]

If initial criteria are met, approve at HICL indefinitely, max 6 capsules/packets per day.
If initial criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS
Treatment of seizures associated Dravet syndrome (DS) in patients ≥2 years of age taking clobazam. There are no clinical data to support the use of DIACOMIT as monotherapy in Dravet syndrome .

NOTES:
Given serious teratogenicity risk from this medicine, those members with pregnancy potential should be encouraged to have a negative pregnancy test, to be on highly effective contraception (ie IUD or implant) unless there is a valid reason not to and should not be lactating.

REFERENCES
Diacomit [Package Insert], Beauvais, France: Biocodex; 2022.

Creation date: 11/18/2020
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

DIFICID (FIDAXOMICIN)

Generic	Brand	HICL	GCN	Exception/Other
FIDAXOMICIN	DIFICID		30035	

GUIDELINES FOR USE

INITIAL CRITERIA: Must meet all of the following:
1. Patient has a diagnosis of *C. difficile* infection
2. Patient is intolerant to vancomycin or has had no improvement/worsening of symptoms after a 6-12 week regimen consisting of standard dose treatment (e.g. at least 125 mg four times daily for 10-14 days) with a gradual reduction in dosing frequency over the following 4-10 weeks, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If all the above are met then approve x1 fill, max qty: 20 tablets.
If all the above are not met, do not approve.

RENEWAL CRITERIA: Must meet all of the following:
1. Diagnosis of C. difficile infection
2. Previous course of fidaxomicin resolved symptoms of C. difficile infection
3. Patient with C. difficile infection (relapse or recurrence) after course of Dificid
4. Patient did not have any improvement in symptoms while previously taking oral vancomycin, or the patient has a contraindication or intolerance to vancomycin, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If all the above are met then approve x1 fill, max qty: 20 tablets.
If all the above are not met, do not approve.

RATIONALE
To ensure appropriate utilization of Dificid.

Renewal criteria considerations: If a patient receives vancomycin initially, improves, and then when vancomycin stops their symptoms return, AND the patient has the same issue with Dificid (things improve, only to return after Dificid course ends), then the two drugs have both shown to work, but not long-term. Dificid should not be given long-term in that case, go back to vancomycin. For cases where the patient's symptoms did not improve or worsened while on vancomycin initially, and a course of Dificid worked in that patient, only to have symptoms return upon end of Dificid course, then it is reasonable to renew.

FDA APPROVED INDICATIONS
Treatment of C. difficile infection

REFERENCES

Creation date: 11/2021
Effective date: 12/2023
Reviewed date: 11/2023
Revised date: 11/2023

DIHYDROERGOTAMINE NASAL SRAY - STEP THERAPY

Generic	Brand	HICL	GCN	Exception/Other
DIHYDROERGOTAMINE MESYLATE (DHE) NASAL SPRAY	MIGRANAL	00155	24732	GENERIC ONLY - formulary

Step Therapy Criteria

Patient has tried and failed, or had an intolerance/allergy to any triptan product, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If met, override restriction only for generic dihydroergotamine nasal spray (Migranal) at GPID-G indefinitely.
If not met, do not approve.

RATIONALE
Per Health Plan

REFERENCE
Note: this product does have a quantity limit per fill applied to it. The claims will look for the quantity limit first and if that is met will begin the step therapy look back for triptan use with the following HICLs in the claim history:

Generic Name	HICL Code
RIZATRIPTAN BENZOATE	18535
SUMATRIPTAN SUCCINATE	6587
NARATRIPTAN HCL	13266
SUMATRIPTAN	12779
ZOLMITRIPTAN	12958
ELETRIPTAN HYDROBROMIDE	23093
SUMATRIPTAN-NAPROXEN SODIUM	35534
ALMOTRIPTAN MALATE	21894
FROVATRIPTAN SUCCINATE	22988
SUMATRIPTAN SUCCINATE & CAMPHOR-MENTHOL	43394

Since Migranal is available as a generic, the Brand Migranal will remain non-formulary.

Creation date: 01/2024
Effective date: 02/2024
Reviewed date:
Revised date:

DPP-4 INHIBITORS
JANUVIA

Generic	Brand	HICL	GCN	Exception/Other
SITAGLIPTIN	JANUVIA	34126		NF - 4th Preferred

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on age criteria below:

A - DM2 in adults older than 25 years old
B - DM2 in pediatrics/young adults age 10 to 25 years

A. To treat type 2 diabetes in adults older than 25 years of age: Must meet all the following:
   1. Patient is at least 25 years old
   2. Most recent HgbA1c is within 1% or less from their designated goal
   3. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
   4. Has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER, maximum dose sulfonylurea, maximum dose pioglitazone, Jardiance, and all possible combinations thereof, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
   5. If on insulin, unable to adjust insulin regimen to achieve better control
   6. If DPP-4 is approved, the patient's current diabetes treatment regimen will not contain four or more medications
   7. Meets the following criteria based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has tried and failed or has an intolerance or contraindication to linagliptin (Tradjenta), alogliptin (Nesina), and/or saxagliptin (Onglyza)

      If initial criteria are met, approve x 6 months.
      If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in young adult/pediatric patients 10 years of age to less than 25 years of age: Must meet all the following:
   1. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
   2. Has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER, maximum dose pioglitazone, Jardiance, and all possible

combinations thereof, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

3. Meets the following criteria based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Patient has tried and failed or has an intolerance or contraindication to linagliptin (Tradjenta), alogliptin (Nesina), and/or saxagliptin (Onglyza)

If initial criteria are met, approve x 6 months.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:

1. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
2. HgbA1c is at goal

If renewal criteria are met, approve x 12 months.
If renewal criteria are not met, do not approve.

RATIONALE

- DPP-4 inhibitors [i.e., linagliptin (Tradjenta), alogliptin (Nesina), sitagliptin (Januvia), saxagliptin (Onglyza)] are not considered first- or second-line medications for the treatment of type 2 diabetes due to minimal A1c lowering (0.5% to 0.7%), lack of positive outcomes data (i.e., ASCVD, CKD, HF), undetermined long-term safety and high cost compared to other agents.
- SGLT-2 inhibitors (such as empagliflozin and canagliflozin) are preferred over DPP-4 inhibitors due to extra benefits in HF, chronic kidney disease, and ASCVD.
- Kaiser Permanente does not promote combination medications [i.e., Jentadueto (linagliptin/metformin)] and are excluded from coverage (not eligible for NF review) for several reasons:
  - lack of medical advantage
  - ease of dosage adjustment and discontinuation of a single medication
  - ease of identification and management of a side effect or an allergy of a single medication

FDA APPROVED INDICATIONS

All DPP-4 inhibitors are indicated to improve glycemic control in adults with type 2 diabetes mellitus

REFERENCES

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation date: 09/26/2018
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

DPP-4 INHIBITORS
NESINA

Generic	Brand	HICL	GCN	Exception/Other
ALOGLIPTIN	NESINA	39968		NF - 2nd Preferred

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on age criteria below:

A - DM2 in adults older than 25 years old
B - DM2 in pediatrics/young adults age 10 to 25 years

A. To treat type 2 diabetes in adults older than 25 years of age: Must meet all the following:
   1. Patient is at least 25 years old
   2. Most recent HgbA1c is within 1% or less from their designated goal
   3. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
   4. Has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER, maximum dose sulfonylurea, maximum dose pioglitazone, Jardiance, and all possible combinations thereof, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
   5. If on insulin, unable to adjust insulin regimen to achieve better control
   6. If DPP-4 is approved, the patient's current diabetes treatment regimen will not contain four or more medications
   7. Meets the following criteria based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has tried and failed or has an intolerance or contraindication to linagliptin (Tradjenta)

      If initial criteria are met, approve x 6 months.
      If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in young adult/pediatric patients 10 years of age to less than 25 years of age: Must meet all the following:
   1. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
   2. Has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER, maximum dose pioglitazone, Jardiance, and all possible combinations thereof, or the provider has submitted justification and supporting clinical

documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

3. Meets the following criteria based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Patient has tried and failed or has an intolerance or contraindication to linagliptin (Tradjenta)

   If initial criteria are met, approve x 6 months.
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:

1. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
2. HgbA1c is at goal

   If renewal criteria are met, approve x 12 months.
   If renewal criteria are not met, do not approve.

RATIONALE

- DPP-4 inhibitors [i.e., linagliptin (Tradjenta), alogliptin (Nesina), sitagliptin (Januvia), saxagliptin (Onglyza)] are not considered first- or second-line medications for the treatment of type 2 diabetes due to minimal A1c lowering (0.5% to 0.7%), lack of positive outcomes data (i.e., ASCVD, CKD, HF), undetermined long-term safety and high cost compared to other agents.
- SGLT-2 inhibitors (such as empagliflozin and canagliflozin) are preferred over DPP-4 inhibitors due to extra benefits in HF, chronic kidney disease, and ASCVD.
- Kaiser Permanente does not promote combination medications [i.e., Jentadueto (linagliptin/metformin)] and are excluded from coverage (not eligible for NF review) for several reasons:
  - lack of medical advantage
  - ease of dosage adjustment and discontinuation of a single medication
  - ease of identification and management of a side effect or an allergy of a single medication

FDA APPROVED INDICATIONS

All DPP-4 inhibitors are indicated to improve glycemic control in adults with type 2 diabetes mellitus

REFERENCES

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.

2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation date: 09/26/2018
Effective date: 02/2024
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DPP-4 INHIBITORS
ONGLYZA

Generic	Brand	HICL	GCN	Exception/Other
SAXAGLIPTIN	ONGLYZA	36471		NF - 3rd Preferred

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on age criteria below:

A - DM2 in adults older than 25 years old
B - DM2 in pediatrics/young adults age 10 to 25 years

A. To treat type 2 diabetes in adults older than 25 years of age: Must meet all the following:
   1. Patient is at least 25 years old
   2. Most recent HgbA1c is within 1% or less from their designated goal
   3. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
   4. Has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER, maximum dose sulfonylurea, maximum dose pioglitazone, Jardiance, and all possible combinations thereof, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
   5. If on insulin, unable to adjust insulin regimen to achieve better control
   6. If DPP-4 is approved, the patient's current diabetes treatment regimen will not contain four or more medications
   7. Meets the following criteria based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has tried and failed or has an intolerance or contraindication to linagliptin (Tradjenta) and/or alogliptin (Nesina)

      If initial criteria are met, approve x 6 months.
      If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in young adult/pediatric patients 10 years of age to less than 25 years of age: Must meet all the following:
   1. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
   2. Has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER, maximum dose pioglitazone, Jardiance, and all possible

combinations thereof, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

3. Meets the following criteria based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Patient has tried and failed or has an intolerance or contraindication to linagliptin (Tradjenta) and/or alogliptin (Nesina)

If initial criteria are met, approve x 6 months.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:

1. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
2. HgbA1c is at goal

If renewal criteria are met, approve x 12 months.
If renewal criteria are not met, do not approve.

RATIONALE

- DPP-4 inhibitors [i.e., linagliptin (Tradjenta), alogliptin (Nesina), sitagliptin (Januvia), saxagliptin (Onglyza)] are not considered first- or second-line medications for the treatment of type 2 diabetes due to minimal A1c lowering (0.5% to 0.7%), lack of positive outcomes data (i.e., ASCVD, CKD, HF), undetermined long-term safety and high cost compared to other agents.
- SGLT-2 inhibitors (such as empagliflozin and canagliflozin) are preferred over DPP-4 inhibitors due to extra benefits in HF, chronic kidney disease, and ASCVD.
- Kaiser Permanente does not promote combination medications [i.e., Jentadueto (linagliptin/metformin)] and are excluded from coverage (not eligible for NF review) for several reasons:
  - lack of medical advantage
  - ease of dosage adjustment and discontinuation of a single medication
  - ease of identification and management of a side effect or an allergy of a single medication

FDA APPROVED INDICATIONS

All DPP-4 inhibitors are indicated to improve glycemic control in adults with type 2 diabetes mellitus

REFERENCES

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

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DPP-4 INHIBITORS
TRADJENTA

Generic	Brand	HICL	GCN	Exception/Other
LINAGLIPTIN	TRADJENTA	37576		Non-Formulary Preferred

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on age criteria below:

A - DM2 in adults older than 25 years old
B - DM2 in pediatrics/young adults age 10 to 25 years

A. To treat type 2 diabetes in adults older than 25 years of age: Must meet all the following:
   1. Patient is at least 25 years old
   2. Most recent HgbA1c is within 1% or less from their designated goal
   3. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
   4. Has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER, maximum dose sulfonylurea, maximum dose pioglitazone, Jardiance, and all possible combinations thereof, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
   5. If on insulin, unable to adjust insulin regimen to achieve better control
   6. If DPP-4 is approved, the patient's current diabetes treatment regimen will not contain four or more medications

   If initial criteria are met, approve x 6 months.
   If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in young adult/pediatric patients 10 years of age to less than 25 years of age: Must meet all the following:
   1. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
   2. Has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER, maximum dose pioglitazone, Jardiance, and all possible combinations thereof, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

   If initial criteria are met, approve x 6 months.

If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Not currently using a GLP-1 +/- GIP receptor agonist (medications containing semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide)
2. HgbA1c is at goal

If renewal criteria are met, approve x 12 months.
If renewal criteria are not met, do not approve.

RATIONALE
- DPP-4 inhibitors [i.e., linagliptin (Tradjenta), alogliptin (Nesina), sitagliptin (Januvia), saxagliptin (Onglyza)] are not considered first- or second-line medications for the treatment of type 2 diabetes due to minimal A1c lowering (0.5% to 0.7%), lack of positive outcomes data (i.e., ASCVD, CKD, HF), undetermined long-term safety and high cost compared to other agents.
- SGLT-2 inhibitors (such as empagliflozin and canagliflozin) are preferred over DPP-4 inhibitors due to extra benefits in HF, chronic kidney disease, and ASCVD.
- Kaiser Permanente does not promote combination medications [i.e., Jentadueto (linagliptin/metformin)] and are excluded from coverage (not eligible for NF review) for several reasons:
  - lack of medical advantage
  - ease of dosage adjustment and discontinuation of a single medication
  - ease of identification and management of a side effect or an allergy of a single medication

FDA APPROVED INDICATIONS
All DPP-4 inhibitors are indicated to improve glycemic control in adults with type 2 diabetes mellitus

REFERENCES
Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

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DRY EYE DISEASE MEDICATIONS
MIEBO

Generic	Brand	HICL	GCN	Exception/Other
PERFLUOROHEXYLOCTANE/PF	MIEBO	45391		Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all of the following:

1. Prescribed by an optometrist or ophthalmologist
2. Patient has a diagnosis of dry eye disease (DED)
3. Patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. over-the-counter (OTC) artificial tears
    b. at least 3 consecutive months of therapy with cyclosporin ophthalmic drops
4. Step therapy criteria based on drug requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Patient must have tried and failed or have contraindication to Xiidra and Tyrvaya.

If initial criteria above are met, then approve indefinitely.
If initial criteria not met, do not approve.

RATIONALE
To ensure appropriate utilization of Xiidra, Tyrvaya, and Miebo.

FDA APPROVED INDICATIONS
Treatment of the signs and symptoms of dry eye disease (DED)

REFERENCES
1. Xiidra (lifitegrast) [prescribing information]. Lexington, MA: Shire US Inc; December 2017.
2. Tyrvaya (varenicline) [prescribing information]. Princeton, NJ: Oyster Point Pharma; October 2021.

Creation date: 09/26/2018
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DRY EYE DISEASE MEDICATIONS
TYRVAYA

Generic	Brand	HICL	GCN	Exception/Other
VARENICLINE NASAL SPRAY	TYRVAYA	33766		Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all of the following:

1. Prescribed by an optometrist or ophthalmologist
2. Patient has a diagnosis of dry eye disease (DED)
3. Patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. over-the-counter (OTC) artificial tears
    b. at least 3 consecutive months of therapy with cyclosporin ophthalmic drops
4. Step therapy criteria based on drug requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Patient must have tried and failed or have contraindication to Xiidra.

If initial criteria above are met, then approve indefinitely.
If initial criteria not met, do not approve.

RATIONALE

To ensure appropriate utilization of Xiidra, Tyrvaya, and Miebo.

FDA APPROVED INDICATIONS

Treatment of the signs and symptoms of dry eye disease (DED)

REFERENCES

1. Xiidra (lifitegrast) [prescribing information]. Lexington, MA: Shire US Inc; December 2017.
2. Tyrvaya (varenicline) [prescribing information]. Princeton, NJ: Oyster Point Pharma; October 2021.

Creation date: 09/26/2018
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DRY EYE DISEASE MEDICATIONS
XIIDRA

Generic	Brand	HICL	GCN	Exception/Other
LIFITEGRAST	XIIDRA	43610		Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all of the following:
1. Prescribed by an optometrist or ophthalmologist
2. Patient has a diagnosis of dry eye disease (DED)
3. Patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. over-the-counter (OTC) artificial tears
    b. at least 3 consecutive months of therapy with cyclosporin ophthalmic drops

If initial criteria above are met, then approve indefinitely.
If initial criteria not met, do not approve.

RATIONALE
To ensure appropriate utilization of Xiidra, Tyrvaya, and Miebo.

FDA APPROVED INDICATIONS
Treatment of the signs and symptoms of dry eye disease (DED)

REFERENCES
1. Xiidra (lifitegrast) [prescribing information]. Lexington, MA: Shire US Inc; December 2017.
2. Tyrvaya (varenicline) [prescribing information]. Princeton, NJ: Oyster Point Pharma; October 2021.

Creation date: 09/26/2018
Effective date: 01/2024
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DUPILUMAB (DUPIXENT)

Generic	Brand	HICL	GCN	Exception/Other
DUPILUMAB	DUPIXENT	44180	43222, 45522, 48277	Formulary, Specialty Tier

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

1. Medication is prescribed by a dermatologist, allergist, pulmonologist, gastroenterologist, or ENT specialist
2. Patient is new to KPCO within the past 90 days, noted as stable on therapy, and has one of the following indications:
   a. Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP)
   b. Asthma (Moderate/Severe)
   c. Atopic Dermatitis (Moderate/Severe)
   d. Eosinophilic Esophagitis
   e. Prurigo Nodularis
3. Medication is not being used in combination with another biologic for the same indication

If above criteria are met, approve indefinitely, with the following quantity limits based on indication:
EoE: max 8 mL (4 syringes/pens) per 28 days [max qty: 8, min ds: 28]
All other above indications: max 4 mL (2 syringes/pens) per 28 days [max qty: 4, min ds: 28].
If above criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet General Criteria and the Diagnosis-Specific Criteria below:

A. GENERAL CRITERIA FOR ALL REQUESTS
B. CHRONIC RHINOSINUSITIS WITH NASAL POLYPOSIS (CRSwNP)
C. ASTHMA (MODERATE/SEVERE)
D. ATOPIC DERMATITIS (MODERATE/SEVERE)
E. EOSINOPHILIC ESOPHAGITIS
F. PRURIGO NODULARIS

A. GENERAL CRITERIA FOR ALL REQUESTS:
   1. Must be prescribed by a CPMG or an affiliated dermatologist, allergist, pulmonologist, gastroenterologist, or ENT specialist
   2. Medication is not being used in combination with another biologic for the same indication

B. DIAGNOSIS OF CHRONIC RHINOSINUSITIS WITH NASAL POLYPOSIS (CRSwNP): Must meet all the following:
   1. Persistent rhinosinusitis symptoms (lasting longer than 12 weeks) with severe nasal obstruction and rhinorrhea or reduced sense of smell
   2. Patient has had sinus surgery
   3. Failure of normalization of mucosa after sinus surgery and despite medical management (e.g., nasal saline irrigation, intranasal corticosteroids [e.g., fluticasone, mometasone, etc.], antileukotriene antagonists [e.g., montelukast, zafirlukast, zileuton])
   4. Received two or more courses of oral corticosteroids in the past year

If criteria are met, approve indefinitely, max 4mL (2 pens/syringes) per 28 days [max qty: 4, min ds: 28].
If criteria are not met, do not approve.

C. DIAGNOSIS OF MODERATE/SEVERE ASTHMA: Must meet all the following:
   1. Uncontrolled asthma as evidenced by ANY one of the following:
      a. Two or more asthma exacerbations requiring systemic corticosteroids (≥3 days each) in the past 12 months
      b. one asthma-related hospitalization in the past 12 months
      c. Asthma Control Test (ACT) consistently <20
   2. Adherent (>75% proportion of days covered) to optimized drug therapy (triple drug therapy with high-dose ICS-LABA plus tiotropium (Spiriva Respimat)) for the previous 6 months, OR has contraindications or intolerance to ICS/LABA/tiotropium, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
   3. Patient meets one of the following classifications:
      a. Patient has concurrent CRSwNP
      b. Patient does not have CRSwNP and does not have eosinophilic asthma
      c. Patient has eosinophilic asthma without CRSwNP and has failed therapy with Fasenra, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria are met, approve at HICL x1 fill, max 4mL (2 pens/syringes) per 14 days (loading dose) [max qty: 4, min ds: 14], then 4mL (2 pens/syringes) per 28 days (maintenance dose) indefinitely [max qty: 4, min ds: 28].
If criteria are not met, do not approve.

D. DIAGNOSIS OF MODERATE/SEVERE ATOPIC DERMATITIS: Must meet all the following based on patient age, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Patient is 6 years of age or younger with inadequate response or intolerance to 2 topical therapies including topical corticosteroid, topical calcineurin inhibitor, or crisaborole (Eucrisa) 2% ointment [trials can be in the same drug class, one must be a topical steroid]

If criteria are met, approve at HICL x1 fill, max 4mL (2 pens/syringes) per 14 days (loading dose) [max qty: 4, min ds: 14], then 4mL (2 pens/syringes) per 28 days (maintenance dose) [max qty: 4, min ds: 28] indefinitely.
If criteria are not met, do not approve.

2. Patient is between 7-17 years of age with inadequate response or intolerance to a topical corticosteroid OR topical calcineurin inhibitor and meets ONE of the following:
   a. Patient with inadequate response (after at least 2 months), intolerance, or contraindication (see table 2) to at least one of the following pre-biologic therapies:
      i. Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
      ii. Azathioprine
      iii. Cyclosporine
      iv. Methotrexate
      v. Mycophenolate
   b. Patient reported as having very high disease activity (i.e., > 50% BSA), or reported as being on a prior atopic dermatitis biologic or oral JAK inhibitor therapy within the past 4 months

If criteria are met, approve at HICL x1 fill, max 4mL (2 pens/syringes) per 14 days (loading dose) [max qty: 4, min ds: 14], then 4mL (2 pens/syringes) per 28 days (maintenance dose) [max qty: 4, min ds: 28] indefinitely.
If criteria are not met, do not approve.

3. Patient is 18 years of age or older with inadequate response or intolerance to a topical corticosteroid OR topical calcineurin inhibitor and meets ONE of the following:
   a. Patient with inadequate response (after at least 2 months) or intolerance to at least one, or contraindication (see table 2) to at least two of the following pre-biologic therapies:
      i. Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
      ii. Azathioprine
      iii. Cyclosporine
      iv. Methotrexate
      v. Mycophenolate
   b. Patient reported as being on a prior atopic dermatitis biologic or oral JAK inhibitor therapy within the past 4 months

If criteria are met, approve at HICL x1 fill, max 4mL (2 pens/syringes) per 14 days (loading dose) [max qty: 4, min ds: 14], then 4mL (2 pens/syringes) per 28 days (maintenance dose) [max qty: 4, min ds: 28] indefinitely.
If criteria are not met, do not approve.

E. DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS
1. Age 1 year and older and weighing at least 15 kg
2. Two or more episodes of dysphagia per week
3. Inadequate response after at least 8-week trial, or intolerance/contraindication to all the following therapies, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Twice daily PPI therapy
   b. Swallowed ICS (inhaled corticosteroid) therapy

If criteria are met, approve indefinitely, max 8mL (4 pens/syringes) per 28 days [max qty: 8, min ds: 28].
If criteria are not met, do not approve.

F. DIAGNSOSIS OF PRURIGO NODULARIS: Must meet age criteria and all the following step therapy requirements, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Age 18 years of age or older
   2. Patient with inadequate response (after at least 3 months) or intolerance to ONE of the following:
      a. Topical corticosteroid
      b. Topical calcineurin inhibitor
      c. Intralesional corticosteroid (at least 2 administrations)
   3. Patient with inadequate response (after at least 3 months), intolerance, or contraindication to phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
   4. Patient with inadequate response (after at least 2 months) or intolerance to at least TWO of the following:
      a. Methotrexate
      b. Cyclosporine
      c. Gabapentinoid: gabapentin or pregabalin
      d. Antidepressant: tricyclic antidepressant, selective serotonin reuptake inhibitor (SSRI), or serotonin and norepinephrine reuptake inhibitor (SNRI)
      e. Naltrexone
      f. Thalidomide
      g. Topical vitamin D analogue (calcipotriene, calcitriol)
      h. Topical capsaicin
      i. Topical lidocaine (with or without topical amitriptyline and gabapentin)

If criteria are met, approve at HICL x1 fill, max 4mL (2 pens/syringes) per 14 days (loading dose) [max qty: 4, min ds: 14], then 4mL (2 pens/syringes) per 28 days (maintenance dose) [max qty: 4, min ds: 28] indefinitely.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:
1. Patient previously authorized for coverage of Dupixent

If met, approve indefinitely, max 4mLs (2 syringes/pens) per 28 days [max qty: 4, min ds: 28], or max 8mLs (4 syringes/pens) per 28 days [max qty: 8, min ds: 28] for Eosinophilic Esophagitis.
If renewal criteria are not met, do not approve.

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ePA Questions
1. Is the patient using another biologic for the same indication?
2. Is the patient stable on therapy with dupilumab?
3. For patients noted stable on therapy, start date of therapy (MMDDYY):

4. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP); Asthma (Moderate/Severe); Atopic Dermatitis (Moderate/Severe); Eosinophilic Esophagitis; Prurigo Nodularis]

QUESTIONS BASED ON DIAGNOSIS SELECTED

CHRONIC RHINOSINUSITIS WITH NASAL POLYPOSIS (CRSwNP)

1. Does the patient have persistent rhinosinusitis symptoms (lasting longer than 12 weeks) with severe nasal obstruction and rhinorrhea or reduced sense of smell?
2. Has the patient had sinus surgery?
3. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
4. Is there reasoning why alternatives (nasal saline irrigation, intranasal corticosteroids [e.g., fluticasone, mometasone, etc.], antileukotriene antagonists [e.g., montelukast]) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
5. How many courses of oral corticosteroids has the patient taken for this indication in the past year?

DIAGNOSIS OF MODERATE/SEVERE ASTHMA

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (triple drug therapy with high-dose ICS-LABA plus tiotropium (Spiriva Respimat)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
3. Has the patient experienced any of the following (check any/all boxes that apply):
    a. Two or more asthma exacerbations requiring systemic corticosteroids (≥3 days each) in the past 12 months
    b. one asthma-related hospitalization in the past 12 months
    c. Asthma Control Test (ACT) consistently <20
4. Patient meets one of the following classifications (check any/all boxes that apply):
    a. Patient has concurrent CRSwNP
    b. Patient does not have CRSwNP and does not have eosinophilic asthma
    c. Patient has eosinophilic asthma without CRSwNP and has failed therapy with Fasenra

DIAGNOSIS OF MODERATE/SEVERE ATOPIC DERMATITIS

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (topical corticosteroids, tacrolimus ointment, phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy, azathioprine, cyclosporine, methotrexate, mycophenolate) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
3. Percent body surface area (BSA) impacted:

DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS

1. Current weight (in kg):
2. Date of current weight (MMDDYY):
3. Number of episodes of dysphasia per week:
4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.

5. Is there reasoning why alternatives (twice daily PPI therapy, swallowed ICS therapy [budesonide respules (0.25 mg/2 ml, 0.5 mg/2 ml), Alvesco HFA (2 puffs swallowed), Asmanex HFA (2 puffs swallowed)]) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

DIAGNSOSIS OF PRURIGO NODULARIS

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (ex: topical corticosteroids, tacrolimus ointment, intralesional corticosteroid, cyclosporine, methotrexate, SNRI, SSRI, TCA, gabapentin or pregabalin, naltrexone, topical lidocaine, thalidomide, topical vitamin D analogue, topical capsaicin) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Health Plan and current treatment guidelines.

1. Dupilumab has activity against a broad range of asthma phenotypes including atopic and eosinophilic phenotypes.

FDA APPROVED INDICATIONS

Asthma (Moderate to Severe)
Atopic Dermatitis (Moderate to Severe)
Chronic Rhinosinusitis with Nasal Polyposis
Prurigo Nodularis

REFERENCES

1. Dupixent [Prescribing Information]. Tarrytown, NY. Regeneron Pharmaceuticals, Inc., October 2022.

Table 1: High-dose ICS and High-dose ICS plus LABA combinations for Age ≥12 years

fluticasone/salmeterol DPI (Advair Diskus) 500/50 mcg, 1 inh twice daily
fluticasone/salmeterol MDI (Advair HFA) 230/21 mcg, 2 puffs twice daily
mometasone/formoterol MDI (Dulera) 200/5 mcg, 2 puffs twice daily
ciclesonide MDI (Alvesco) 160 mcg, 2 puffs twice daily
fluticasone MDI (Flovent HFA) 220 mcg, 2 puffs twice daily
Budesonide DPI (Pulmicort Flexhaler) 180 mcg, 4 inh twice daily
Mometasone MDI (Asmanex HFA) 200 mcg, 2 puffs twice daily
Mometasone DPI (Asmanex Twisthaler) 220 mcg, 2 inh twice daily

Table 2: Relative contraindications of various treatments

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (ex: systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for dermatology indications.*

Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*
Mycophenolate	*Hypersensitivity to mycophenolate, active malignancy, pregnancy, breastfeeding, women of childbearing age not using highly effective contraceptive methods. Mycophenolate requires REMS program for females of childbearing age.*

Table 3: Home UV phototherapy criteria and contracted provider information (Daavlin)

KPCO home phototherapy contracted provider: Daavlin
KPCO contracts with Daavlin for home phototherapy units Submit orders to Daavlin (see form link below), and they will work with the patient directly and help coordinate insurance coverage, billing, shipping, and technical support if needed Daavlin Phone: 1-800-322-8546; Daavlin Fax: 1-419-636-1739 https://www.daavlin.com/physicians/ https://www.daavlin.com/wp-content/uploads/2017/08/Home-Phototherapy-Order-Packet-042017.pdf Units: DermaPal: hand-held scalp spot unit 1 Series: small panel unit (ideal for patients with limited disease [ex: only hand / foot involvement]) 4 Series: mid-sized panel unit (ideal for patients with regional disease [ex: those with lower leg, arm involvement) 7 Series: large 6' panel unit (most used unit, allows for full body treatment)

Creation Date: 4/2020
Effective Date: 04/2024
Revised Date: 03/2024
Reviewed Date: 03/2024

EDARAVONE (RADICAVA ORS)

Generic	Brand	HICL	GCN	Exception/Other
EDARAVONE (ORAL)	RADICAVA ORS ORAL SUSPENSION		52318	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and stable on therapy

If met, approve x3 months.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Medication is prescribed by a CPMG or affiliated neurologist
2. The patient has a diagnosis of clinical ALS and is 2 years or less from onset of first symptom
3. Normal Respiratory Function defined as a Forced Vital Capacity (FVC) greater than or equal to 80% obtained within past two months
4. The patient has an ALS Functional Rating Scale-Revised (ALSFRS-R) score of 2 points or better on each of the 12 items within past two months (e.g., speech, salivation, swallowing, handwriting, cutting food, dressing and hygiene, turning in bed, walking, climbing stairs, dyspnea, respiratory insufficiency)
5. The patient has a score of greater than 3 on ALSFRS-R for dyspnea, orthopnea, or respiratory insufficiency
6. The patient is currently taking riluzole or has previously tried riluzole, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve x 1 year at GPID.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
1. The patient is not dependent on invasive ventilation or tracheostomy

If met, approve x 1 year at GPID.
If not met, do not approve.

RATIONALE
Promote appropriate utilization of Radicava ORS based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS
Radicava ORS is an orally administered formulation of edaravone indicated for the treatment of amyotrophic lateral sclerosis (ALS).

DOSAGE AND ADMINISTRATION

The recommended dosage of Radicava ORS is an orally administered suspension of 105 mg (5 mL) given according to the same schedule as the infusion:

- An initial treatment cycle with daily dosing for 14 consecutive days, followed by a 14-day drug-free period.
- Subsequent treatment cycles with daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods
- Radicava ORS should be taken on an empty stomach in the morning after overnight fasting
    - Patients should not consume any food or drink (except water) for 1 hour after administration

ADDENDUM

The ALSFRS-R is a validated questionnaire-based scale designed to be a clinical rating tool to monitor the progression of patients in clinical practice as well as an outcome measure in clinical trials. The rate of progression of ALS patient population is typically linear, however it is not homogenous, therefore it is difficult to ascertain the general rate of progression for the patient population. The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS (speech, salivation, swallowing, handwriting, cutting food, dressing/hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency). There are four domains: bulbar, fine motor, gross motor and breathing. Each questionnaire item is scored from 0-4, with higher scores representing greater functional ability; the total possible score is 48 points.

Figure 1: ALSFRS-R Questionnaire

Bulbar	Fine Motor	Gross Motor	Breathing

1. Speech
4. Normal speech processes
3. Detectable speech disturbance
2. Intelligible with repeating
1. Speech combined with nonvocal communication
0. Loss of useful speech

2. Salivation
4. Normal
3. Slight but definite excess of saliva in mouth; may have nighttime drooling
2. Moderately excessive saliva; may have minimal drooling
1. Marked excess of saliva with some drooling
0. Marked drooling; requires constant tissue or handkerchief

3. Swallowing
4. Normal eating habits
3. Early eating problems-occasional choking
2. Dietary consistency changes
1. Needs supplemental tube feeding
0. NPO (exclusively parenteral or enteral feeding)

4. Handwriting
4. Normal
3. Slow or sloppy; all words are legible
2. Not all words are legible
1. Able to grip pen but unable to write
0. Unable to grip pen

5a. Cutting Food / Handling Utensils
4. Normal
3. Somewhat slow and clumsy, but no help needed
2. Can cut most foods, although clumsy and slow; some help needed
1. Food must be cut by someone, but can still feed slowly
0. Needs to be fed

5b. Cutting Food / Handling Utensils (Alt. for patients with Gastrostomy)
4. Normal
3. Clumsy but able to perform all manipulations independently
2. Some help needed with closures and fasteners
1. Provides minimal assistance to caregiver
0. Unable to perform any aspect of task

6. Dressing and hygiene
4. Normal function
3. Independent and complete self-care with effort or decreased efficiency
2. Intermittent assistance or substitute methods
1. Needs attendant for self-care
0. Total dependence

7. Turning in bed
4. Normal
3. Somewhat slow and clumsy, but no help needed
2. Can turn alone or adjust sheets, but with great difficulty
1. Can initiate, but not turn or adjust sheets alone
0. Helpless

8. Walking
4. Normal
3. Early ambulation difficulties
2. Walks with assistance
1. Non-ambulatory functional movement only
0. No purposeful leg movement

9. Climbing stairs
4. Normal
3. Slow
2. Mild unsteadiness or fatigue
1. Needs assistance
0. Cannot do

10. Dyspnea
4. None
3. Occurs when walking
2. Occurs with one or more of the following: eating, bathing, dressing (ADL)
1. Occurs at rest, difficulty breathing when either sitting or lying
0. Significant difficulty, considering using mechanical respiratory support

11. Orthopnea
4. None
3. Some difficulty sleeping at night due to shortness of breath. Does not routinely use more than two pillows
2. Needs extra pillow in order to sleep (more than two)
1. Can only sleep sitting up
0. Unable to sleep

12. Respiratory insufficiency
4. None
3. Intermittent use of BiPAP
2. Continuous use of BiPAP
1. Continuous use of BiPAP during the night and day
0. Invasive mechanical ventilation by intubation or tracheostomy

REFERENCES

- Radicava and Radicava ORS [prescribing information]. Jersey City, NJ: MT Pharma America, Inc.; May 2022.
- Cedarbaum J, Stambler N, Malt E et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. J Neurol Sci. 1999 Oct 31;169(1-2):13-21.
- Cedarbaum J, Mitsumoto H, Pestronk A, et al. The ALSFRS @ 20: Evolution of the ALSFRS-R, history, clinimetric properties and future directions [Poster]. Available at: https://cytokinetics.com/wp-content/uploads/2015/10/2011ALS_MND_ASLFRS20.pdf

Creation Date: 07/2022
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

ELAGOLIX SODIUM (ORILISSA)

Generic	Brand	HICL	GCN/GPID	Other
ELAGOLIX SODIUM 150MG	ORILISSA	45108	45026	
ELAGOLIX SODIUM 200MG	ORILISSA	45108	45028	

****Length of approval applies to Federal Group**

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:

1. Patient is new to KPCO within the past 90 days and is stable on elagolix (Orilissa)
2. Patient has had at least 50% improvement of symptoms since starting treatment with elagolix (Orilissa)
3. Must meet the following based on indication:
   a. For endometriosis with dyspareunia: Patient has not yet completed 6 months of treatment (FDA-approved duration)

      If met, approve GPID 45028 x number of months to meet and not exceed 6 total months of therapy [**Use for FEDERAL Group]
      If not met, review by Initial Criteria.

   b. For endometriosis: Patient has not yet completed 24 months of treatment (FDA-approved duration)

      If met, then approve GPID 45026 x1 fill, to allow time for evaluation by Ob/Gyn [**Use for Federal Group]
      If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:

1. Patient is a female <u>at least</u> 18 years of age
2. Medication is prescribed by an obstetrician/gynecologist (with an appropriate referral, if required)
3. Patient has a surgically confirmed diagnosis of endometriosis with or without dyspareunia
4. Patient has tried and failed or has an absolute contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. At least one NSAID
   b. At least one estrogen-progestin combination contraceptives (pills, patch, or ring) taken in a continuous fashion (skipping placebo tablets)
   c. Depo-medroxyprogesterone acetate injection, norethindrone acetate oral, medroxyprogesterone acetate oral, levonorgestrel intrauterine device, or etonorgestrel implant
   d. GnRH agonist (nafarelin, leuprolide, goserelin or triptorelin) with add-back hormonal therapy (norethindrone [to counteract estrogen suppression effect of GnRH agonist])
5. Patient has had a BMD screening within the last 12 months
6. Patient cannot be currently on a strong organic anion transporting polypeptide 1b1 inhibitor (most common: cyclosporine, gemfibrozil, see comprehensive list in footnote)[4]

7. Provider attests to counselling patient on multiple forms of contraception and associated routine labs

If initial criteria are met, then approve per diagnosis: [**Use for FEDERAL Group]
- Endometriosis with dyspareunia: GPID 45028, 200mg twice daily for 6 months (FDA-approved duration).
- Endometriosis: GPID 45026, 150mg once daily for 12 months.

If initial criteria not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Patient has had at least 50% improvement of symptoms since starting treatment with elagolix (Orilissa)
2. Must meet the following based on indication:
   a. For endometriosis with dyspareunia:
      i. Patient has not yet completed 6 months of treatment (FDA-approved duration)
      ii. Patient has normal LFTs (checked while on therapy with elagolix)

      If renewal criteria are met, approve GPID 45028 x number of months to meet and not exceed 6 total months of therapy [**Use for FEDERAL Group].
      If renewal criteria not met, do not approve.

   b. For endometriosis:
      i. Patient has not yet completed 24 months of treatment (FDA-approved duration)
      ii. Patient has a BMD after 12 months of elagolix therapy that shows no more than 8% decrease in T-score in spine, femoral neck, and total hip
      iii. Patient has a current a negative pregnancy test and is willing to come back to confirm not pregnant with repeat urine pregnancy test in fourteen days, or had sterilization procedure
      iv. Patient has normal LFTs (checked while on therapy with elagolix)

      If renewal criteria are met, approve GPID 45026 for the number of months to meet the maximum of 24 total months of treatment (surgically proven endometriosis) or 6 total months of treatment (surgically proven endometriosis with primary symptom of dyspareunia). If no start date is submitted in review but other renewal criteria are met, approve x1 month only. [**Use for FEDERAL GROUP]

      If renewal criteria not met, do not approve.

RATIONALE
Ensure appropriate utilization and safety criteria are used for the management of requests for Orilissa (elagolix).
Insufficient data for use in breastfeeding.

FDA APPROVED INDICATIONS
Orilissa (elagolix) is a non-peptide, oral gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for management of moderate to severe pain associated with endometriosis. Through suppression of pituitary and ovarian hormone function, concentrations of LH, FSH, and estradiol are decreased during therapy, which reduces dysmenorrhea and nonmenstrual pelvic pain.

NOTES
1. Elagolix can cause increased HDL, LDL, total cholesterol or triglycerides.

2. Osteoporosis, a contraindication to using elagolix, is defined as a T score of -2.5 and below.
3. Osteopenia is defined as a T score of -1.0 to -2.5. Risk factors for fracture are weight < 157lbs, BMI < 21, history of fragility fracture after age 50, parental history of hip fracture, rheumatoid arthritis, corticosteroids (> 3 months at > 5mg), alcohol > 3 drinks/day, and current cigarette smoking. Risk factors requires supplementation with calcium and vitamin D.
4. OATP inhibitors may increase the serum concentration of elagolix: atazanavir, clarithromycin, cobicistat, cyclosporine, daclatasvir, darolutamide, elbasvir, eltrombopag, eluxadoline, gemfibrozil, grazoprevir, ledipasvir, leflunomide, letermovir, lopinavir, simeprevir, teriflunomide, velpatasvir, voxilaprevir. Additional category X interactions are those with CYP3A4 metabolism (fusidic acid, idelalisib), and drugs reliant on PGP. The concentrations of these may be increased to toxic levels if administered with PGP inhibitor elagolix: pazopanib, IV topotecan, vincristine (liposomal).

REFERENCES

1. Surrey E, Taylor HS, Giudice L, et al. Long-term outcomes of elagolix in women with endometriosis: results form two extension studies. Obstet Gynecol. 2018 Jul;132(1):147-160. doi: 10.1097/AOG.0000000000002675.
2. Taylor HS, Giudice LC, Lessey BA, et al. Treatment of endometriosis-associated pain with elagolix, an oral GnRH antagonist. N Engl J Med. 2017 Jul 6;377(1):28-40. doi: 10.1056/NEJMoa1700089. Epub 2017 May 19.
3. Ng J, Chwalisz K, Carter DC, Klein CE. Dose-dependent suppression of gonadotropins and ovarian hormones by elagolix in healthy premenopausal women. J Clin Endocrinol Metab. 2017 May 1;102(5):1683-1691. doi: 10.1210/jc.2016-3845.
4. Ben-Meir A, Sarajari S. Endometriosis. In: DeCherney AH, Nathan L, Laufer N, Roman AS. eds. CURRENT Diagnosis & Treatment: Obstetrics & Gynecology, 12e New York, NY: McGraw-Hill; . http://accessmedicine.mhmedical.com/content.aspx?bookid=2559&sectionid=206967961. Accessed November 12, 2019
5. Elagolix. Lexi-Drugs. [updated 2023 Nov 16; cited 2023 Nov 17] In Lexicomp Online [Internet]. Wolters Kluwer Clinical Drug Information, Inc. Hudson, Ohio. Available at: http://online.lexi.com/lco/action/home
6. ACOG Practice Bulletin No. 110: noncontraceptive uses of hormonal contraceptives. Obstet Gynecol. 2010 Jan;115(1):206-18.
7. Endometriosis: Treatment of pelvic pain. UpToDate [cited 2023 Nov 17] In UpToDate [Internet]. Wolters Kluwer Clinical Drug Information, Inc. Hudson, Ohio. Available at: http://www.uptodate.com/contents/search

Creation Date: 03/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

ELEXACAFTOR/IVACAFTOR/TEZACAFTOR (TRIKAFTA)

Generic	Brand	HICL	GCN	Exception/Other
ELEXACAFTOR/IVACAFTOR/TEZACAFTOR	TRIKAFTA	46112		

GUIDELINES FOR USE

Requests for ELEXACAFTOR/IVACAFTOR/TEZACAFTOR will be approved if ALL the following are met:

1. Prescribed by a pulmonologist
2. Patient has a diagnosis of cystic fibrosis (CF) and
    a. has at least one *F508del* mutation in the CFTR gene
    OR
    b. has a mutation in the CFTR gene that is responsive based on *in vitro* data [Consult Trikafta website to check eligible mutations: https://www.trikafta.com/who-trikafta-is-for]
3. Patient is at least 2 years old

If above criteria are met, then approve indefinitely, max #3/day.
If above criteria are not met, do not approve.

RATIONALE

Per Health Plan

REFERENCES

1. Kaiser Permanente Inter-regional Practice Recommendations 01/2020
2. Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Incorporated; 2021.
3. Trikafta website to check eligible mutations: https://www.trikafta.com/who-trikafta-is-for

Creation date: 07/2020
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

ELIGLUSTAT (CERDELGA)

Generic	Brand	HICL	GCN/GPID	Other
ELIGLUSTAT	CERDELGA	41346		Specialty Non-formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:

A. Must be prescribed by, or in consultation with a specialist in the area of the patient's diagnosis (e.g., endocrinologist, hematologist or geneticist).
B. Must be prescribed as monotherapy and is not given in combination with other SRT agents or enzyme replacement therapies [velaglucerase (Vpriv), imiglucerase (Cerezyme), or taliglucerase (Elelyso)].
C. Must have one of the following diagnoses and meet the disease specific criteria below:
   1. **Gaucher Disease Type 1.** Must meet all the following:
      a. Patient must be age 18 or older
      b. Prior to any treatment for the intended diagnosis, patient has had at least ONE of the following clinical presentations:
         - Anemia (Hgb <13 g/dL in men, <12 g/dL in women)
         - Thrombocytopenia (platelet count <100,000/µL)
         - Hepatomegaly
         - Splenomegaly
         - Growth failure
         - Evidence of bone disease not due to other causes
      c. Must meet the drug specific criteria below:
         i. Cerdelga: Must meet all the following
            - Provider specifies, providing results detected by an FDA-cleared test that the patient is one of the following:
              - CYP2D6 extensive metabolizer (EM)
              - CYP2D6 intermediate metabolizer (IM)
              - CYP2D6 poor metabolizer (PM)

              AND is NOT an ultra rapid metabolizer (URM)
            - Cerdelga is not used concomitantly with any of the following:

CYP2D6 EM or IM	Moderate or strong CYP2D6 inhibitor (e.g., paroxetine, terbinafine) with a moderate or strong CYP3A inhibitor (e.g., ketoconazole)
CYP2D6 IM	Moderate or strong CYP3A inhibitor (e.g., ketoconazole, fluconazole)
CYP2D6 PM	Weak, moderate, or strong CYP3A inhibitor (e.g., ranitidine, ketoconazole, fluconazole)
CYP2D6 EM, IM, or PM	Strong CYP3A4 inducers (e.g., rifampin, phenytoin)

If initial criteria is met, approve x12 months at HICL/GPID as twice daily dosing (max 60 capsules per 30 days) for CYP2D6 extensive/intermediate metabolizer, OR once daily dosing (max 30 capsules per 30 days) for CYP2D6 poor metabolizer.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following disease specific criteria:

1. Gaucher Disease Type 1: Patient has demonstrated clinical symptom improvement or stability since starting on the drug, and no new contraindications to use, to at least one of the following:
   a. Hemoglobin level
   b. Platelet count
   c. Liver volume
   d. Spleen volume
   e. Growth
   f. Bone pain or crisis

   If renewal criteria are met, approve x12 months at HICL/GPID as twice daily dosing (max 60 capsules per 30 days) for CYP2D6 extensive/intermediate metabolizer, OR once daily dosing (max 30 capsules per 30 days) for CYP2D6 poor metabolizer.
   If renewal criteria are not met, do not approve.

RATIONALE

Cerdelga (eliglustat) has been shown to be non-inferior to enzyme replacement therapy (ERT) and is a first-line option for Gaucher Disease. Zavesca (miglustat) is a second-line alternative to ERT.

Per the 2018 consensus guidelines for Niemann-Pick Disease Type C (NPC), miglustat is the only disease modifying medication that may be used in the treatment of neurological manifestations of NPC. Miglustat may halt or attenuate disease progression in some patients. Miglustat is currently used off-label in treatment of NPC in the United States.

FDA APPROVED INDICATIONS

Cerdelga (eliglustat): Treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers, intermediate metabolizers, or poor metabolizers.

REFERENCES

1. Bennett LL, Fellner C. Pharmacotherapy of Gaucher Disease: Current and Future Options. *P T*. 2018;43(5):274-309.
2. Rosenbloom BE, Cox TM, Drelichman GI, et al. Encore - a randomized, controlled, open-label non-inferiority study comparing ELIGLUSTAT to imiglucerase in Gaucher disease type 1 patients stabilized on enzyme replacement therapy: 24-month results. *Blood*. 2014;124(21):1406-1406. doi:10.1182/blood.v124.21.1406.1406
3. Geberhiwot T, Moro A, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. Orphanet J Rare Dis. 2018;13(1):50. Published 2018 Apr 6. doi:10.1186/s13023-018-0785-7

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Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

ELUXADOLINE

Generic	Brand	HICL	GCN/GPID	Exception/Other
ELUXADOLINE	VIBERZI	42445		

GUIDELINES FOR COVERAGE
Must meet all the following:
1. Patient has a diagnosis of irritable bowel syndrome with diarrhea (IBS-D)
2. The patient is 18 years of age or older
3. Therapy is prescribed by a gastroenterologist
4. The patient has tried and failed or has an intolerance or contraindication to all of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    - diphenoxylate and atropine (generic Lomotil) or OTC loperamide
    - at least one tricyclic antidepressant (e.g., amitriptyline, desipramine) [if patient is less than 65 years of age]
    - dicyclomine [if patient less than 65 years of age]
    - Xifaxan (NF, PA required)

   If criteria are met, approve indefinitely, max 2 per day.
   If criteria are not met, do not approve.

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ePA Questions
1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (diphenoxylate and atropine (generic Lomotil); OTC loperamide; dicyclomine; amitriptyline tablets, desipramine tablets, nortriptyline capsules) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
The 2021 American College of Gastroenterology (ACG) guidelines for the treatment of IBS list eluxadoline as a treatment option in its algorithm for IBS-D. Eluxadoline was approved based on two randomized, multicenter (MC), multinational, double-blind (DB), placebo controlled (PC) Phase 3 trials (IBS-3001 and IBS-3002) that evaluated the efficacy and safety of eluxadoline for IBS-D. The primary endpoint for both studies was the percentage of participants who were composite responders based on improvements from baseline in daily worst abdominal pain (WAP) and daily stool consistency scores for at least 50% of days with diary entry during 12 weeks of treatment. A statistically significantly higher proportion of patients treated with eluxadoline achieved the primary endpoint compared to PBO over a 12-week treatment period (23.9% and 28.9% on eluxadoline vs. 17.1% and 16.2% in the placebo group).
Based on the limited treatment effect over placebo, no head-to-head trials and high cost with less costly options available we recommend utilizing eluxadoline last line. Eluxadoline should be reserved last line for IBS-D symptoms that have not previously responded to over-the-counter loperamide, low-dose tricyclic antidepressants, or at least one course of rifaximin.

REFERENCES

Viberzi [Prescribing Information]. Madison, NJ: Allergan USA, Inc; June 2018.

Creation Date: 03/2023
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

EMTRICITABINE/TENOFOVIR (DESCOVY)

Generic	Brand	HICL	GCN/GPID	Exception/Other
EMTRICITABINE / TENOFOVIR ALAFENAMIDE	DESCOVY	43241	51964, 40953	Nonformulary

GUIDELINES FOR COVERAGE

NOTE: All requests for Descovy are treated as urgent requests

INITIAL CRITERIA: Must meet one of the following:
1. Patient has a diagnosis of HIV infection
2. Patient has a CrCL or eGFR between 30 and 60 mL/min
3. Patient has a diagnosis of a metabolic bone disease, such as osteoporosis
4. Patient has suspected renal toxicity to emtricitabine/tenofovir disoproxil fumarate (Truvada), defined as worsening serum Cr, proteinuria or glucosuria that developed while taking emtricitabine/tenofovir disiproxil fumarate (Truvada)
5. Patient had an intolerance to emtricitabine/tenofovir disoproxil fumarate (Truvada), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If any of the above criteria are met, approve indefinitely at GPID level.
If no criteria are met, do not approve.

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ePA Questions for Provider Outreach
1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (Truvada) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
3. Does the patient have a diagnosis of metabolic bone disease, such as osteoporosis?
4. Current eGFR:
5. Date of Current eGFR (MMDDYY):

RATIONALE
To ensure appropriate use of Descovy

REFERENCES
Note: the adjudication systems are built to automatically send a $0 cost share if no other HIV drug is present, besides Truvada, in the claims history (assumed as PrEP) and will apply the applicable cost share for all other claims (assume treatment of HIV).

Creation date: 03/2022
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Revised date: 03/2024

EPIDIOLEX (CANNABIDIOL)

Generic	Brand	HICL	GCN	Exception/Other
CANNABIDIOL	EPIDIOLEX	45006		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and is stable on cannabidiol (Epidiolex)
2. Patient has a diagnosis of Lennox-Gastaut Syndrome, Dravet Syndrome, or Tuberous Sclerosis and is being managed by a CPMG or affiliated neurologist or epileptologist

If New Member Criteria are met, approve indefinitely.
If New Member Criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Review based on diagnosis-specific criteria below:
A. To treat Lennox-Gastaut Syndrome (LGS): All the following must be met:
   1. Medication is prescribed by a CPMG or affiliated neurologist or epileptologist
   2. Patient has a diagnosis of Lennox-Gastaut Syndrome (LGS)
   3. Patient is 1 year of age or older
   4. This medication will be used as adjunctive therapy with at least one other anti-seizure drug
   5. The patient is stable on cannabidiol (Epidiolex), or the patient has failed a valproic acid derivative, and lamotrigine, and either topiramate or rufinamide, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If initial criteria are met, approve indefinitely.
      If initial criteria are not met, do not approve.

B. To treat Dravet Syndrome (DS): All the following must be met:
   1. Medication is prescribed by a CPMG or affiliated neurologist or epileptologist
   2. Patient has a diagnosis of Dravet Syndrome (DS)
   3. Patient is 1 year of age or older
   4. The patient is stable on cannabidiol (Epidiolex), or the patient has failed a valproic acid derivative product and clobazam, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If initial criteria are met, approve indefinitely.
      If initial criteria are not met, do not approve.

C. To treat Tuberous Sclerosis Complex (TSC) associated seizures: All the following must be met:
   1. Medication is prescribed by a CPMG or affiliated neurologist or epileptologist
   2. Patient has a diagnosis of TSC either by confirmed genetic testing or meeting clinical criteria for definitive diagnosis outline by the 2012 International Tuberous Sclerosis Complex Consensus Group
   3. Patient is 1 year of age or older
   4. Patient is treatment refractory to optimal dosing of at least two antiepileptic drugs (AEDs) that are appropriate for the epilepsy diagnosis
   5. Patient has experienced the following over the past 4 weeks:
      a. At least 8 seizures
      b. At least 1 focal seizure ocurring in at least 3 of the 4 weeks
   6. This medication will be used as adjunctive therapy with at least one other anti-seizure drug

   If initial criteria are met, approve indefinitely.
   If initial criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS
Treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or Tuberous Sclerosis Complex (TSC) in patients ≥1 year of age.

REFERENCES
1. Epidiolex [Package Insert], Carlsbad, CA: Greenwich Biosciences, Inc.; 2023.
2. Northrup H, Krueger DA; International Tuberous Sclerosis Complex Consensus Group. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. Pediatr Neurol. 2013;49(4):243-254. doi:10.1016/j.pediatrneurol.2013.08.001

Creation date: 11/28/2018
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

EPINEPHRINE AUTO-INJECTOR NON-FORMULARY GUIDELINE

Generic	Brand	HICL	GCN	Exception/Other
EPINEPHRINE 0.3MG/0.3ML SOAJ	EPIPEN AUTH GENERIC		19862	Non-Formulary – Preferred
EPINEPHRINE 0.15MG/0.3ML SOAJ	EPIPEN JR AUTH GENERIC		19861	Non-Formulary - Preferred
EPINEPHRINE 0.3/0.3ML SOAJ	EPIPEN BRAND		19862	Non-Formulary - Least Preferred
EPINEPHRINE 0.15MG/0.3ML SOAJ	EPIPEN JR BRAND		19861	Non-Formulary – Least Preferred

Non-Formulary Criteria (NCQA reviewable): Must meet the following:

1. Patient is unable to utilize epinephrine 0.15mg/0.3mL or 0.3mg/0.3mL (Adrenaclick generic - 00115-1694-49 or Adrenaclick Jr generic 00115-1695-49) due to any of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Unable to use the device
   b. Institution (school, daycare, group home) requires other device (example retractable needle)

If met, approve indefinitely.
If not met, do not approve.

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ePA Questions

1. Is there reasoning why generic epinephrine 0.15mg/0.3mL or 0.3mg/0.3mL is not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Health Plan.

- Epinephrine auto-injector (Adrenaclick and Adrenaclick Jr generic) is KPCO first-line formulary epinephrine auto-injector.
- The authorized generic for EpiPen or EpiPen Jr should be reserved as the preferred non-formulary option for patients unable to utilize generic Adrenaclick or Adrenaclick Jr to documented allergy, intolerance, or clinical failure.
- Brand EpiPen and EpiPen Jr should be reserved as the non-formulary option for patients unable to utilize epinephrine auto-injector (Adrenaclick and Adrenaclick Jr generic) or the authorized generic for EpiPen or EpiPen Jr.

FDA APPROVED INDICATIONS

See individual medications.

REFERENCES

00115-1694-49 is generic Adrenaclick (pref)
00115-1695-49 is generic Adrenaclick Jr (pref)
49502-0102-02 is authorized generic for EpiPen

49502-0101-02 is authorized generic for EpiPen Jr
49502-0500-02 is brand EpiPen
49502-0501-02 is brand EpiPen Jr

Creation date: 05/2021
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 09/2023

ERTUGLIFLOZIN (STEGLATRO)

Generic	Brand	HICL	GCN	Exception/Other
ERTUGLIFLOZIN	STEGLATRO	44709		NF 3rd Preferred

GUIDELINES FOR COVERAGE
Must be used for one of the following indications and meet all related criteria as follows:

A. Adults 25 years of age or older with DM2
B. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat adults 25 years of age or older with type 2 diabetes: Must meet all the following:
   1. Most recent HgbA1c is above, but within 2% of their designated A1c goal
   2. Patient has an eGFR of at least 20 ml/min
   3. Patient has contraindications to, is currently using, or has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. maximum dose metformin IR and subsequently metformin ER
      b. empagliflozin (Jardiance)
      c. maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
         i. h/o bariatric surgery
         ii. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
         iii. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e. sulfonylurea, insulin, pioglitazone)
         iv. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If all criteria met, approve at HICL x6 months, max 1 tablet per day.
If criteria are not met, do not approve.

B. To treat type 2 diabetes in young adult/pediatric patients between 10 and 25 years of age: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Patient has contraindications to, is currently using, or has failed maximum doses of metformin IR and subsequently metformin ER
   2. Patient has an eGFR of at least 20 ml/min and has tried and failed, or has an intolerance or contraindication to empagliflozin (Jardiance)
   3. Patient has contraindications to, is currently using, or has failed maximum dose pioglitazone unless the patient has one of the following:

a. h/o bariatric surgery
b. BMI ≥ 95%ile for age and sex
c. ≥ 5% increase in body weight after 6 months of starting these medications
d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If all criteria met, approve at HICL x6 months, max 1 tablet per day.
If criteria are not met, do not approve.

RENEWAL CRITERIA

1. HgbA1c is either at goal or has decreased by at least 0.5%.

If renewal criteria are met, approve indefinitely at HICL, max 1 tablet per day.
If renewal criteria are not met, do not approve.

RATIONALE

- KP National Diabetes Guidelines recommend using SGLT-2i for people with type 2 diabetes with clinical ASCVD who are already taking metformin to reduce the risk of: (1) cardiovascular events (myocardial infarction or stroke) or cardiovascular death, (2) progression of renal disease and/or (3) death from renal causes, and/or (4) heart failure hospitalizations. The American College of Cardiology (ACC) 2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients with Type 2 Diabetes, which is also endorsed by the American Diabetes Association (ADA), recommends SGLT-2i as a first-line treatment in patients with type 2 diabetes and one or more of the following: ASCVD, HFrEF, HFpEF (empagliflozin only), diabetic kidney disease (DKD), or at high risk for ASCVD.
- Preferred order of agents:
  1) Empagliflozin (Jardiance), formulary without PA, is the preferred agent for ASCVD, CKD, and HF due to strength of clinical trial data, range of approved indications, and cost (1/2 tab regimen)
  2) Canagliflozin (Invokana), non-formulary with PA, is the 2nd preferred option for ASCVD, CKD and DM2 patients without compelling indications. due to broad range of indications and cost (1/2 tab regimen).
  3) Dapagliflozin (Farxiga), non-formulary with PA, is the 2nd preferred option for HF, and the 3rd preferred option for ASCVD, CKD and DM2 patients without compelling indications due to broad range of indications but at high cost.
  4) Ertugliflozin (Steglatro), non-formulary with PA, is least preferred due to high cost, paucity of positive clinical trial data, and lack of additional FDA-approved indications. Specifically, ertugliflozin has been studied in patients with type 2 diabetes and ASCVD and did not improve cardiovascular outcomes while all three other SGLT-2i have demonstrated such benefits in this population.
  5) Bexagliflozin (Brenzavvy): non-formulary with PA, is least preferred due to high cost and lack of additional FDA-approved indications.
  6) Sotagliflozin (Inpefa): non-formulary with PA, is 3rd preferred for HF given shorter history of postmarketing safety data compared to other SGLT2i's approved for HF as well as the need to titrate sotagliflozin dose for when others are fixed-dose regimens. Sotagliflozin (Inpefa) is least preferred for glycemic control due to lack of clinical trial data and FDA-approved indication as well as its high cost.
- Jardiance (empagliflozin) is the preferred sodium glucose co-transporter 2 inhibitor (SGLT-2i) at Kaiser Permanente Colorado (KPCO) and can be used effectively and safely with a GFR down to

20 mL/min. In addition, the dose of 12.5 mg (1/2 of 25mg tablet) is an effective dose for all patients regardless of GFR.

- Based on the available evidence, various organizations endorse SGLT-2is use down to lower GFR levels than indicated in product labels:
  - American College of Cardiology Expert Consensus now recommends empagliflozin in GFR ≥ 20 mL/min (2021).
  - National Kidney Foundation recommends SGLT-2is in GFR ≥ 20 mL/min as long as there are no contraindications (2023).
  - American Diabetes Association recognizes SGLT-2is benefits in patients with GFR ≥ 20 mL/min (2023).

FDA APPROVED INDICATIONS for SGLT2 Inhibitors

Empagliflozin (Jardiance)

1. Improve glycemic control in patients with DM2
2. Reduce the risk of CV death in pts with DM2 + CVD
3. Reduce risk of CVD death and HF hospitalizations in pts with HF
4. Reduce risk of sustained eGFR decline, ESRD, CV death and hospitalizations in adults with CKD at risk of progression

Canagliflozin (Invokana)

1. Improve glycemic control in patients with DM2
2. Reduce risk of MACE in pts with DM2 + CVD
3. Reduce the risk of ESRD, doubling of creatinine, CV death, or HF hospitalization in pts with DM2 + diabetic nephropathy

Dapagliflozin (Farxiga)

1. Improve glycemic control in patients with DM2
2. Reduce risk of HF hosp in pts with DM2 + CVD/multiple CV RFs
3. Reduce the risk of CV death and HF hosp in patients with HFrEF NYHA II-IV
4. Reduce risk of sustained eGFR decline, ESRD, CV death, and hospitalization for HF in adults with CKD at risk of progression

Ertugliflozin (Steglatro)

1. Improve glycemic control in patients with DM2

Bexagliflozin (Brenzavvy)

1. Improve glycemic control in patients with DM2

Sotagliflozin (Inpefa)

1. Reduce the risk of CV death and HF hosp in pts with heart failure
2. Reduce the risk of CV death and HF hosp in pts with DM2 + CKD + CV RF(s)

REFERENCES

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012

3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation date: 09/26/18
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

ENBREL (ETANERCEPT)

Generic	Brand	HICL	GCN/GPID	Other
ETANERCEPT	ENBREL	18830		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on Enbrel, medication is not being used in combination with another biologic for the same indication, and has one of the following indications managed by the appropriate specialist as noted below:
   1. Patient has a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Ankylosing Spondylitis or subtype, or Polyarticular Juvenile Idiopathic Arthritis (JIA) and is being managed by a CPMG or affiliated rheumatologist
   2. Patient has a diagnosis of Psoriasis and is being managed by a CPMG or affiliated dermatology specialist

   For Enbrel 50 mg: If met, approve x 4 pens/syringes per 28 days indefinitely.
   For Enbrel 25 mg: If met, approve x 8 vials/syringes per 28 days indefinitely.
   If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Rheumatoid Arthritis
B. Psoriatic Arthritis (PsA)
C. Ankylosing Spondylitis
D. Psoriasis
E. Polyarticular Juvenile Idiopathic Arthritis (JIA)

A. RHEUMATOID ARTHRITIS (RA): All the following must be met:
   1. Patient has a diagnosis of RA, and medication is prescribed by a CPMG or affiliated rheumatologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least 2 DMARDs (including methotrexate)
      b. infliximab (Inflectra, Remicade, or other biosimilar), unless documented by prescriber that patient has a barrier to infusion

   For Enbrel 50 mg: If above criteria are met, approve x 4 pens/syringes per 28 days indefinitely.
   For Enbrel 25 mg: If above criteria are met, approve x 8 vials/syringes per 28 days indefinitely.
   If above criteria are not met, do not approve.

B. PSORIATIC ARTHRITIS (PsA): All the following must be met:
   1. Patient has a diagnosis of PsA, and medication is prescribed by CPMG or affiliated rheumatologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least two DMARDs (including methotrexate), or the patient has high disease activity in which traditional DMARDs would not be suitable treatment
      b. infliximab (Inflectra, Remicade, or other biosimilar), unless documented by prescriber that patient has a barrier to infusion

   For Enbrel 50 mg: If above criteria, are met, approve x 4 pens/syringes per 28 days indefinitely.
   For Enbrel 25 mg: If above criteria, are met, approve x 8 vials/syringes per 28 days indefinitely.
   If above criteria are not met, do not approve.

C. ANKYLOSING SPONDYLITIS:
   A. Medication must be prescribed by a rheumatologist, and the patient has a diagnosis of ankylosing spondylitis or one of the following subtype diagnoses: spondyloarthritis (SpA), axial SpA, nonradiographic axial SpA, radiographic axial SpA, sacroiliitis, undifferentiated spondyloarthropathy, spondyloarthropathy, or enteropathic arthropathy.
   B. Medication is not being used in combination with another biologic for the same indication.
   C. Patient with failure, intolerance, or contraindication to infliximab (Inflectra, Remicade, or other biosimilar), unless documented by prescriber that patient has a barrier to infusion, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   For Enbrel 50 mg: If above criteria are met, approve x 4 pens/syringes per 28 days indefinitely.
   For Enbrel 25 mg: If above criteria are met, approve x 8 vials/syringes per 28 days indefinitely.
   If above criteria are not met, do not approve.

D. PSORIASIS: All the following must be met:
   1. Patient has a diagnosis of moderate to severe psoriasis, and medication is prescribed by a CPMG or affiliated dermatology provider.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response (after at least two months of therapy), intolerance, or has a contraindication to, all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective

based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

a. One topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus) [or if the patient is reported as having very high disease activity (ex: > 50% BSA, erythrodermic, pustular psoriasis), disease affecting critical areas (ex: genitals, face), or prior biologic therapy within the past 4 months, skip and proceed to step 3c]
b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Acitretin, Cyclosporine, Methotrexate, Apremilast (Otezla), Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
c. At least one TNF inhibitor (adalimumab (Amjevita) – preferred [F, PA], infliximab (Inflectra) – preferred [F])
d. At least one IL-17 inhibitor (secukinumab (Cosentyx) – preferred [F])

For Enbrel 50 mg: If above criteria are met, approve 8 syringes/pens per 28 days x 3 months (loading dose), then 4 syringes/pens per 28 days (maintenance dose) indefinitely.
For Enbrel 25 mg: If above criteria are met, approve 16 vials/syringes per 28 days x 3 months (loading dose), then 8 vials/syringes per 28 days (maintenance dose) indefinitely.
If above criteria are not met, do not approve.

E. POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS (JIA): All the following must be met
1. Patient has a diagnosis of JIA, and medication is prescribed by CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to at least 1 DMARD, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

For Enbrel 50 mg: If met, approve x 4 pens/syringes per 28 days indefinitely.
For Enbrel 25 mg: If met, approve x 8 vials/syringes per 28 days indefinitely.
If not met, do not approve.

RENEWAL CRITERIA:
1. The diagnosis for which the patient was originally authorized medication coverage, has been assessed by the applicable specialist in the past two years.
2. Medication is not being used in combination with another biologic for the same indication.

For Enbrel 50 mg: If met, approve x 4 pens/syringes per 28 days indefinitely.
For Enbrel 25 mg: If met, approve x 8 vials/syringes per 28 days indefinitely.
If not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member, Initial, or Renewal PA Criteria prior to review of Quantities. Escalation criteria review only the quantities authorized upon PA approval.

Applicable only to patients with a diagnosis of Psoriasis:

1. Dermatology provider notes the patient is resuming therapy after a gap of 3 months or longer in treatment (to reload)

   For Enbrel 50 mg: If above criteria are met, approve 8 syringes/pens per 28 days x 3 months (loading dose), then 4 syringes/pens per 28 days (maintenance dose) indefinitely.
   For Enbrel 25 mg: If above criteria are met, approve 16 vials/syringes per 28 days x 3 months (loading dose), then 8 vials/syringes per 28 days (maintenance dose) indefinitely.
   If not met, deny and offer maximum 4 pens/syringes (for Enbrel 50 mg) or 8 vials/syringes (for Enbrel 25 mg) per 28 days per original approval.

References:

Currently stable on medication means patient is tolerating well, appears to be effective and provider wishes to continue.

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (ex: systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for psoriasis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*

Created: 01/2021
Effective: 01/2024
Reviewed: 11/2023
Revised: 11/2023

ESTRADIOL VAG INSERT (IMVEXXY)

Generic	Brand	HICL	GCN/GPID	Exception/Other
ESTRADIOL VAGINAL INSERT	IMVEXXY		44813, 44814	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Patient has benefit coverage for sexual dysfunction medications
2. Patient has tried and failed or has an intolerance or a contraindication to at least one of the following three KPCO-preferred products (listed in preferred order), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. estradiol vaginal cream
   b. estradiol vaginal tablet (Yuvafem) (nonformulary with PA restriction)
   c. estradiol vaginal ring (Estring) (nonformulary with PA restriction)

If all the above are met then approve x1 year at GPID level.
If all the above are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
1. Patient has benefit coverage for sexual dysfunction medications

If all the above are met then approve x1 year at GPID level.
If all the above are not met, do not approve.

RATIONALE
To ensure appropriate utilization of nonformulary Imvexxy.
Imvexxy is categorized as Category 1 – Drugs to treat impotency.

FDA APPROVED INDICATIONS
IMVEXXY is an estrogen indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.

REFERENCES
Imvexxy Package Insert

Creation date: 11/2021
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 09/2023

ETHACRYNIC ACID (EDECRIN)

Generic	Brand	HICL	GCN/GPID	Other
ETHACRYNIC ACID	EDECRIN	03659	34910	Nonformulary

GUIDELINES FOR COVERAGE: Must meet one of the following:

1. Patient has tried and failed, or has an intolerance to or a contraindication to at least 1 of the preferred loop diuretics, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception: Furosemide, Torsemide, Bumetanide
2. Patient has experienced a severe drug reaction to a sulfonamide, including but not limited to: Stevens-Johnson Syndrome (SJS), Drug Reaction with Eosinophilia and System Symptoms (DRESS), Toxic Epidermal Necrolysis (TEN), or anaphylaxis

If either of the above are met, approve generic only at GPID level indefinitely.
If neither criterion is met, do not approve.

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ePA Questions

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (furosemide tablets, torsemide tablets, bumetanide tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
3. Has the patient experienced any of the following reactions to a sulfonamide (check any/all that apply):
    a. Stevens-Johnson Syndrome (SJS)
    b. Drug Reaction with Eosinophilia and System Symptoms (DRESS)
    c. Toxic Epidermal Necrolysis (TEN)
    d. anaphylaxis

FDA APPROVED INDICATIONS

Management of edema associated with congestive heart failure, hepatic cirrhosis or renal disease; short-term management of ascites due to malignancy, idiopathic edema and lymphedema; short term management of hospitalized pediatric patients, other than infants, with congenital heart disease or nephrotic syndrome.

Creation Date: 4/22/2021
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

EVOLOCUMAB (REPATHA)

Generic Name	Brand Name	HICL	GPID	Comments
EVOLOCUMAB	REPATHA SURECLICK, REPATHA SYRINGE, REPATHA PUSHTRONEX	42378		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
1. Patient is new to KPCO within the past 90 days and stable on therapy.

If met, approve indefinitely.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient has a diagnosis of either homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH), or atherosclerotic cardiovascular disease (ASCVD) with a clinical event^^*
2. Has a current LDL level drawn within the last 90 days of greater than or equal to one of the following:
   a) 55 mg/dL for ASCVD at very high risk defined as multiple ASCVD events^^ or 1 ASCVD event and 2 or more high risk conditions (age ≥ 65 years, familial hypercholesterolemia, diabetes, HTN, eGFR 15-59, current smoking)
   b) 70mg/dL for ASCVD not at very high risk
   c) 100 mg/dL for HeFH/HoFH
3. Patient must meet one of the following:
   a) have been taking atorvastatin 80mg or rosuvastatin 40mg daily or statin therapy at the maximally tolerated dose for at least 30 days prior to LDL lab;
   b) have an absolute contraindication to statin therapy (active, decompensated liver disease; nursing female, pregnancy, or plans to become pregnant;
   c) a hypersensitivity reaction;
   d) a documented history of CPK>10x ULN or rhabdomyolysis attributed to a statin and not explained by a drug interaction, fall, or prolonged immobility);
   e) or the patient is statin intolerant as defined by the National Lipid Association Statin Intolerance Panel**
4. Patient has been taking ezetimibe for at least 30 days prior to LDL lab, or the patient has a contraindication or intolerance to ezetimibe

If met, approve at HICL indefinitely, max daily dose of 0.08 (2 per 28 days for syringes/pens) or max daily dose of 0.13 (3.5 per 28 days for Pushtronex).
If not met, do not approve.

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ePA Questions
1. Is the patient stable on evolocumab therapy?
2. For patients noted stable on therapy, start date of therapy (MMDDYY):
3. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH), or atherosclerotic cardiovascular disease (ASCVD) with a clinical event (must list the clinical event in Provider Comment section below or attach applicable chart notes.]

4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
5. Is there reasoning why alternatives (rosuvastatin tablets, atorvastatin tablets, lovastatin tablets, simvastatin tablets, pravastatin tablets; fenofibrate tablets (54 mg, 160 mg); gemfibrozil 600 mg tablets; ezetimibe tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
6. Current LDL:
7. Date of LDL lab (MMDDYY):

REFERENCES

*Requires documentation which may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and laboratory data.

^^**Includes**: MI, ACS, CAD with intervention (e.g., PCI, stent, CABG), ischemic non-cardioembolic stroke, PAD with intervention (e.g., stent, surgery); **Excludes**: High CAC score, AAA, CAD finding on diagnostic cath without MI/ACS/intervention, CAD equivalents (e.g. DM, CKD), primary prevention patients regardless of CV risk score

**Inability to tolerate at least 2 statins, with at least one started at the lowest starting daily dose

For primary prevention for a patient who has NOT been noted to have familial hypercholesterolemia, a PCSK9i would not be appropriate. If they have failed statins (even low dose 1-2 days per week) and ezetimibe, we could offer any formulary, unrestricted lipid-lowering therapy.

RATIONALE

Per Health Plan

Creation Date: 3/15/2017
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

EXTENDED-RELEASE STIMULANT QUANTITY LIMIT CRITERIA

GUIDELINES FOR QUANTITY LIMIT OVERRIDES

Meeting any one of the criteria below qualifies for an override:

A) Doses above FDA approval when prescribed by a CPMG or affiliated behavioral health provider
B) Requests due to patients needing different doses in am vs pm (i.e., Adderall XR 20mg qam and 30mg qpm), if copay for different strengths is cost prohibitive for the member
C) Lack of efficacy (drug not lasting long enough) with daily dosing (i.e., Vyvanse 10 mg BID)
   a. Ensure provider tried adding an IR stimulant dose in pm prior to dosing extended-release product twice daily, however, if 2 copays cost prohibitive approve request
D) Allow one time approval for dextroamphetamine/amphetamine XR capsule titration sigs at the start of therapy. All other medication must have dose titrations prescriptions set within the quantity limits.

	Drug	Strengths	CM/MP	Max FDA approved dose per Day	Qty Limit per 30 days
GPID: 14635, 17468, 14636, 17469, 14637, 17459	Dextroamphetamine/ amphetamine (Adderall XR) capsules	5, 10, 15, 20, 25, 30 mg	F	60 mg	60 caps
GPID : 43538, 43539, 43542, 43543	Dextroamphetamine/amphetamine (Mydayis) capsules	12.5, 25, 37.5, 50 mg	NF	50 mg	30 caps
GPID: 12567, 17123, 12568, 12248	Methylphenidate (Concerta) tablets	18, 26, 36, 54 mg	F	72 mg	60 tabs
GPID: 20384, 13176, 20386, 26734, 26735, 26736	Methylphenidate (Metadate CD) capsules	10, 20, 30, 40, 50, 60 mg	F	60 mg	60 caps
GPID: 21763, 20387, 20388, 20391, 36195	Methylphenidate (Ritalin LA) capsules	10, 20, 30, 40 mg	NF	60 mg	60 caps
GPID: 26801, 26802, 26803, 26804	Methylphenidate (Daytrana) patch	10, 15, 20, 30 mg	NF	60 mg	30 patches
GPID: 33887	Methylphenidate (Quillivant XR) suspension	25 mg/5 mL	NF	60 mg	360 mL (1800 mg)
GPID: 40289, 40292, 40293	Methylphenidate (Quillichew ER) chewable tablet	20, 30, 40 mg	NF	60 mg	30 tabs
GPID: 37674, 99366, 98071, 99367, 98072, 99368, 98073	Lisdexamfetamine (Vyvanse) capsules	10, 20, 30, 40, 50, 60, 70 mg	NF	70 mg	30 caps

	Drug	Strengths	CM/MP	Max FDA approved dose per Day	Qty Limit per 30 days
GPID: 42969, 43058, 43059, 43063, 43064, 43065	Lisdexamfetamine (Vyvanse) chewable tablets	10, 20, 30, 40, 50, 60 mg	NF	70 mg	30 tabs
GPID: 24734, 97111, 24735, 30305, 28035, 30306, 28933, 24733	Dexmethylphenidate (Focalin XR) capsules	5, 15, 20, 25, 30 mg	NF	40 mg	60 caps

RATIONALE
Quantity limits help to reduce pill burden for patients, help reduce costs and since stimulants are controlled substances; it further helps to limit controlled substances in society.

FDA APPROVED INDICATIONS
Stimulants are FDA approved for treatment of attention-deficit/hyperactivity disorder (ADHD)

REFERENCES

Creation Date: 7/2020
Effective Date: 01/2024
Reviewed Date: 9/2023
Revised Date: 9/2023

FEBUXOSTAT (ULORIC) - STEP THERAPY

Generic	Brand	HICL	GCN	Exception/Other
FEBUXOSTAT	ULORIC	36106		Formulary

Step Therapy Criteria

1. Patient has failed or has a contraindication to allopurinol, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If met, approve generic feboxustat at HICL indefinitely.
If not met, do not approve.

Note: if request for brand Uloric, the member must not only meet step therapy, but also meet the Brand When Generic is Available nonformulary guidance.]

RATIONALE

The 2020 ACR guidelines strongly recommend allopurinol over all other ULT as the preferred first-line agent for all patients, including in those with CKD stage >3.

REFERENCE

FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology guideline for the management of gout. Arthritis Care Res (Hoboken). 2020;72(6):744-760.

Creation date: 11/2020
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

FECAL MICROBIOTA (VOWST)

Generic	Brand	HICL	GCN	Exception/Other
FECAL MICROBIOTA, LIVE ORAL	VOWST	48888	54053	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Patient is 18 years of age or older.
2. Must be prescribed by a provider specializing in gastroenterology or infectious diseases.
3. Patient has a diagnosis of recurrent CDI with at least 3 total CDI episodes.
4. Patient will have completed standard of care treatment of CDI (i.e. vancomycin or fidaxomicin) with administration 2-4 days after completion.
5. Bowel cleanse with either 296 ml of magnesium citrate OR polyethylene glycol electrolyte solution (250ml) will occur on the day before the first dose of Vowst.
6. Patient has failed fecal microbiota transplant (FMT) or has a contraindication to colonoscopy/EGD required for FMT.

If initial criteria are met, approve x1 fill only, max 12 capsules (1 bottle).
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Patient had treatment failure, defined as the presence of CDI diarrhea within 8 weeks of completing Vowst AND a positive stool test for C difficile.
2. Patient has not received more than 1 dose of Vowst.

If renewal criteria are met, approve x1 fill only, max 12 capsules (1 bottle).
If renewal criteria are not met, do not approve.

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ePA Questions for Provider Outreach
Initial Review Questions
1. Number of *Clostridioides difficile* infections the patient has had:
2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
3. Is there reasoning why alternatives (i.e. fecal microbiota transplant (FMT)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
4. Completion date of most recent vancomycin or fidaxomicin treatment (MMDDYY):
5. Planned start date for Vowst treatment (MMDDYY):
6. Will the patient complete a bowel cleanse with either 296 ml of magnesium citrate OR polyethylene glycol electrolyte solution (250ml) on the day before the first dose of Vowst?

Renewal Review Questions
1. How many courses of Vowst has the patient received?
2. Has the patient experienced treatment failure, defined as the presence of CDI diarrhea within 8 weeks of completing Vowst AND a positive stool test for C difficile?

RATIONALE

While we expect utilization to be low, we want to ensure appropriate use of this high cost therapy with: (1) prescribing restricted to gastroenterology and infectious disease providers, (2) diagnosis of recurrent CDI with at least 3 total CDI episodes (in line with current guideline recommendations for use

of FMT) (3) patient completing standard of care treatment for CDI prior to administration (since FML oral is approved for prevention of recurrent CDI but not treatment), and (4) patient having trial and failure or intolerance to FMT OR has contraindication colonoscopy/EGD required for FMT (FML oral has not demonstrated any efficacy or safety advantage over non-FDA approved FMT. Given the limited efficacy data for FML oral, and its high-cost relative to non-FDA approved FMT, FML oral should be positioned after FMT when appropriate). In contrast, we do not propose to require a trial of bezlotoxumab prior to FML given limitations with timely infusion access.

FDA APPROVED INDICATIONS
Clostridioides difficile infection, prophylaxis: Prevention of recurrence of *C. difficile* infection (CDI) in patients ≥18 years of age following antibiotic treatment of recurrent CDI.
Limitations of use: Not indicated for treatment of CDI.

Creation Date: 3/2024
Effective Date: 4/2024
Reviewed Date:
Revised Date:

FENFLURAMINE (FINTEPLA)

Generic	Brand	HICL	GCN	Exception/Other
FENFLURAMINE ORAL SOLUTION	FINTEPLA	02116	48284	Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and is stable on fenfluramine (Fintepla)
2. Patient has a diagnosis of Lennox-Gastaut Syndrome or Dravet Syndrome and is being managed by a CPMG or affiliated neurologist or epileptologist

If New Member Criteria are met, approve indefinitely.
If New Member Criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Review based on diagnosis-specific criteria below:
A. To treat Lennox-Gastaut Syndrome (LGS): All the following must be met:
   1. Medication is prescribed by a CPMG or affiliated neurologist or epileptologist
   2. Patient has a diagnosis of Lennox-Gastaut Syndrome (LGS)
   3. Patient is 2 years of age or older
   4. The medication will be used as adjunctive therapy with at least one other anti-seizure drug
   5. The patient is stable on fenfluramine (Fintepla), or the patient has failed a valproic acid derivative, and lamotrigine, and at least 2 of the following medications, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. clobazam
      b. topiramate
      c. rufinamide [nonformulary]
   6. Patient has failed or is concomitantly receiving Epidiolex [Nonformulary requires Prior Authorization]

      If initial criteria are met, approve indefinitely.
      If initial criteria are not met, do not approve.

B. To treat Dravet Syndrome (DS): All the following must be met:
   1. Medication is prescribed by a CPMG or affiliated neurologist or epileptologist
   2. Patient has a diagnosis of Dravet Syndrome (DS)
   3. Patient is 2 years of age or older
   4. The patient is stable on fenfluramine (Fintepla), or the patient has failed all the following medications, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is

stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
a. a valproic acid derivative
b. clobazam
c. Epidiolex [Nonformulary requires Prior Authorization]
d. Diacomit [Nonformulary requires Prior Authorization]

If initial criteria are met, approve indefinitely.
If initial criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS
Treatment of seizures associated Dravet syndrome (DS) and Lennox-Gastaut Syndrome (LGS) in patients ≥2 years of age.

NOTES: As of December 2022, Fintepla is no longer a controlled substance.

REFERENCES
1. Fintepla [Package Insert], Emeryville, CA: Zogenix; 2023.

Creation date: 01/2021
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

FESOTERODINE (TOVIAZ)

Generic	Brand	HICL	GCN	Exception/Other
FESOTERODINE	TOVIAZ	35606	99711, 99712	Max daily dose 1 tab per day

GUIDELINES FOR COVERAGE

Review based on patient cognitive status noted in section A or B:

A. Patients with a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin and/or trospium IR, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely (max daily dose of 1 tab/day).
      If criteria are not met, do not approve.

B. Patients WITHOUT a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin, and/or trospium IR, and/or oxybutynin tablet/syrup, the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely (max daily dose of 1 tab/day).
      If criteria are not met, do not approve.

RATIONALE

Per Health Plan.

- An adequate response is defined as one less episode of frequency or incontinence per day after an adequate trial of 4-6 weeks.
- Preferred formulary agents, in order: oxybutynin ER, oxybutynin IR, solifenacin, trospium IR and oxybutynin syrup.

- Preferred nonformulary agents in order: tolterodine IR, tolterodine ER, darifenacin, fesoterodine, trospium ER, mirabegron and vibegron. Oxybutynin gel (Gelnique) and oxybutynin patch (Oxytrol) are excluded from coverage.
- Agents preferred in cognitive impairment include, in order: solifenacin, trospium IR, darifenacin ER, trospium ER.

Creation date: 01/15/2019
Effective date: 01/2024
Reviewed date: 09/2023
Revised date: 09/2023

FEZOLINETANT

Generic	Brand	HICL	GCN	COMMENTS
FEZOLINETANT	VEOZAH	48921		

GUIDELINES FOR COVERAGE

Must meet all the following:
1. The patient has a diagnosis of moderate to severe menopausal vasomotor symptoms (VMS)
2. The patient has had an adequate trial* of or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Hormonal therapy (e.g., oral estradiol, transdermal patch [Climara, Dotti] with oral medroxyprogesterone or micronized progesterone [Prometrium] if needed).
    b. At least three preferred non-hormonal therapies (e.g., citalopram/escitalopram, venlafaxine/desvenlafaxine, paroxetine, gabapentin, clonidine).

*Adequate trial is defined as a trial at maximum tolerated dose for at least a 4 week duration.

If met, approve indefinitely at HICL with a quantity limit of #1 per day.
If not met, do not approve.

RATIONALE
Per OB/Gyn
For further information, please refer to the Prescribing Information and/or Drug Monograph for Veozah.

FDA APPROVED INDICATIONS:
Treatment of moderate to severe vasomotor symptoms due to menopause.

REFERENCES
Veozah [Prescribing Information]. Northbrook, IL: Astellas Pharma US, Inc.; May 2023.

Creation Date: 11/2023
Effective Date: 12/2023
Reviewed Date:
Revised Date:

FILGRASTIM-AYOW (RELEUKO)

Generic	Brand	HICL	GPID	Comments
FILGRASTIM-AYOW	RELEUKO VIAL	47848	51978, 51987	NF
FILGRASTIM-AYOW	RELEUKO PREFILLED SYRINGE	47848	51988, 51989	NF - PI does not include latex warning; manufacturer did not confirm

GUIDELINES FOR COVERAGE

1. Must have failed Nivestym due to adverse drug reaction, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii**) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event**; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If met, approve indefinitely.
If not met, do not approve.

RATIONALE

Adults: Nivestym prefilled syringes and vials are the preferred GCSF products for all patients.

Pediatrics: Fulphila is the preferred GCSF product in pediatrics for the indication of febrile neutropenia prevention with chemotherapy. However, if short acting GCSF is requested by a provider, Nivestym is available.

Creation Date: 09/2021
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

FILGRASTIM (NEUPOGEN)

Generic	Brand	HICL	GPID	Comments
FILGRASTIM	NEUPOGEN VIAL	06070	26001, 13206	NF - LATEX FREE
FILGRASTIM	NEUPOGEN PREFILLED SYRINGE	06070	13308, 13309	NF

GUIDELINES FOR COVERAGE

1. Must have failed Nivestym due to adverse drug reaction, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii**) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event**; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If met, approve indefinitely.
If not met, do not approve.

RATIONALE

Adults: Nivestym prefilled syringes and vials are the preferred GCSF products for all patients.

Pediatrics: Fulphila is the preferred GCSF product in pediatrics for the indication of febrile neutropenia prevention with chemotherapy. However, if short acting GCSF is requested by a provider, Nivestym is available.

Creation Date: 09/2021
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

FILGRASTIM-SNDZ (ZARXIO)

Generic	Brand	HICL	GPID	Comments
FILGRASTIM-SNDZ	ZARXIO PREFILLED SYRINGE	41814	38082, 38083	NF – preferred after formulary Nivestym

GUIDELINES FOR COVERAGE

1. Must have failed Nivestym due to adverse drug reaction, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii**) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event**; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If met, approve indefinitely.
If not met, do not approve.

RATIONALE

Adults: Nivestym prefilled syringes and vials are the preferred GCSF products for all patients.

Pediatrics: Fulphila is the preferred GCSF product in pediatrics for the indication of febrile neutropenia prevention with chemotherapy. However, if short acting GCSF is requested by a provider, Nivestym is available.

Creation Date: 09/2021
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

TBO-FILGRASTIM (GRANIX)

Generic	Brand	HICL	GPID	Comments
TBO-FILGRASTIM	GRANIX VIAL	40426	45674, 45673	NF - LATEX FREE
TBO-FILGRASTIM	GRANIX SYRINGE	40426	35575, 35576	NF - LATEX FREE

GUIDELINES FOR COVERAGE

1. Must have failed Nivestym due to adverse drug reaction, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii**) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event**; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If met, approve indefinitely.
If not met, do not approve.

RATIONALE

Adults: Nivestym prefilled syringes and vials are the preferred GCSF products for all patients.

Pediatrics: Fulphila is the preferred GCSF product in pediatrics for the indication of febrile neutropenia prevention with chemotherapy. However, if short acting GCSF is requested by a provider, Nivestym is available.

Creation Date: 09/2021
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

FINERENONE (KERENDIA)

Generic	Brand	HICL	GCN	Exception/Other
FINERENONE	KERENDIA	47487		

GUIDELINES FOR COVERAGE

Must meet all the following:

1. Prescriber is a nephrologist
2. Patient has a diagnosis of Type 2 Diabetes
3. Patient has a diagnosis of chronic kidney disease defined as either:
    a. Urinary albumin-to-creatinine ration (UACR) of 30 or less than 300 mg/g and an estimated glomerular filtration rate (eGFR) of 25 to 60 mL/minute/1.73m2 and diabetic retinopathy
    b. UACR of 300 to 5,000 mg/g and an eGFR of 25-75 mL/minute/1.73m2
4. Patient is currently treated with a maximum tolerated dose of ACE inhibitor or ARB or has documented allergy, intolerance, or contraindication to both, the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
5. Patient has an allergy, intolerance, or contraindication to empagliflozin (Jardiance), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
6. Patient has a baseline serum potassium of 5 mEq/L or less
7. Patient does NOT have chronic heart failure with reduced ejection fraction of < or equal to 40%

If criteria are met, approve indefinitely at HICL with a max of 1 tab/day.
If criteria are not met, do not approve.

Note: Intolerance excludes adverse drug reactions that are expected, mild in nature, resolve

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RATIONALE

Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS

To reduce the risk of sustained eGFR decline, end stage kidney disease, cardiovascular death, non-fatal myocardial infarction and hospitalization in adult patients with chronic kidney disease (CKD) associated with Type 2 Diabetes.

REFERENCES

1. Kerendia [Package Insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; 2021.

Creation Date: 09/2022
Effective Date: 01/2024
Reviewed Date: 9/2023
Revised Date:

FIXED-DOSE ICS/LABA/LAMA TRIPLE COMBINATION INHALERS: BUDESONIDE/GLYCOPYRROLATE/FORMOTEROL (BREZTRI AEROSPHERE)

Generic name	Brand name	HICL	GPID	Comments
BUDESONIDE/GLYCOPYRROLATE/ FORMOTEROL FUMARATE	BREZTRI AEROSPHERE		48435	COPD only

GUIDELINES FOR COVERAGE

Must have one of the following indications and meet all criteria associated with that diagnosis:

A. Medication is requested for the maintenance treatment of COPD and meets all the following criteria, or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Patient must be age 18 years or older.
   2. Must be prescribed by Pulmonology.
   3. Persistent symptoms and/or COPD exacerbation despite combined dual LAMA/LABA or ICS/LABA therapy.
   4. Patient has tried and failed or has an intolerance or a contraindication to at least one of the following combination regimens in each category resulting in triple ingredients:
      - LAMA + ICS/LABA
        - Spiriva Respimat (tiotropium) + Wixela Inhub (fluticasone/salmeterol)
        - Spiriva Respimat (tiotropium) + brand or generic Symbicort HFA (budesonide/formoterol)
      - LAMA/LABA + ICS
        - Stiolto Respimat (tiotropium/olodaterol) + Alvesco HFA (ciclesonide)
        - Stiolto Respimat (tiotropium/olodaterol) + Asmanex HFA (mometasone)

If all criteria are met, approve at HICL indefinitely.
If all criteria are not met, do not approve.

RATIONALE

Trelegy Ellipta is a combination of fluticasone furoate, an inhaled corticosteroid (ICS); umeclidinium, an anticholinergic; and vilanterol, a long-acting beta2-adrenergic agonist (LABA). Budesonide/glycopyrrolate/formoterol fumarate (Breztri Aerosphere) is a combination of an ICS, LAMA, and LABA.

Breztri Aerosphere and Trelegy Ellipta have not been shown to be safer or more cost-effective than use of open triple combination therapy via two separate inhalers (e.g., ICS/LABA plus LAMA).

FDA APPROVED INDICATIONS

Trelegy Ellipta is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema and the maintenance treatment of asthma in patients aged 18 years and older.

Breztri Aerosphere is indicated for the maintenance treatment of patients with COPD. Breztri Aerosphere is NOT indicated for the treatment of asthma.

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 11/2023
Revised Date: 11/2023

FIXED-DOSE ICS/LABA/LAMA TRIPLE COMBINATION INHALERS: FLUTICASONE FUROATE/UMECLIDINIUM/VILANTEROL (TRELEGY ELLIPTA)

Generic name	Brand name	HICL	GPID	Comments
FLUTICASONE FUROATE/UMECLIDINIUM/ VILANTEROL	TRELEGY ELLIPTA		43921, 48708	Asthma and COPD - Breztri preferred over Trelegy for COPD

GUIDELINES FOR COVERAGE

Must have one of the following indications and meet all criteria associated with that diagnosis:

A. Chronic Obstructive Pulmonary Disease (COPD) indication
B. Asthma indication

A. Medication is requested for the maintenance treatment of COPD and meets all the following criteria, or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Patient must be age 18 years or older.
   2. Must be prescribed by Pulmonology.
   3. Persistent symptoms and/or COPD exacerbation despite combined dual LAMA/LABA or ICS/LABA therapy.
   4. Patient has tried and failed or has an intolerance or a contraindication to at least one of the following combination regimens in each category resulting in triple ingredients:
      - LAMA + ICS/LABA
        - Spiriva Respimat (tiotropium) + Wixela Inhub (fluticasone/salmeterol)
        - Spiriva Respimat (tiotropium) + brand or generic Symbicort HFA (budesonide/formoterol)
      - LAMA/LABA + ICS
        - Stiolto Respimat (tiotropium/olodaterol) + Alvesco HFA (ciclesonide)
        - Stiolto Respimat (tiotropium/olodaterol) + Asmanex HFA (mometasone)
   5. Patient must have tried and failed, or has an intolerance or a contraindication to, Breztri Aerosphere.

If all criteria are met, approve at HICL indefinitely.
If all criteria are not met, do not approve.

B. Medication requested is for the maintenance treatment of asthma and meets all the following criteria, or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the

patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Patient must be age 18 years or older.
2. Must be prescribed by Asthma/Allergy or Pulmonology.
3. Persistent symptoms and/or asthma exacerbation despite combination medium-to-high dose ICS/LABA therapy.
4. Patient has tried and failed or has an intolerance or a contraindication to at least one of the following combination regimens resulting in triple ingredients:
   - ICS/LABA + LAMA
     - Wixela Inhub (fluticasone/salmeterol) + Spiriva Respimat (tiotropium)
     - Brand or generic Symbicort HFA (budesonide/formoterol) + Spiriva Respimat (tiotropium)
     - Advair HFA (fluticasone/salmeterol) + Spiriva Respimat (tiotropium)

If all criteria are met, approve indefinitely at HICL.
If all criteria are not met, do not approve.

RATIONALE

Trelegy Ellipta is a combination of fluticasone furoate, an inhaled corticosteroid (ICS); umeclidinium, an anticholinergic; and vilanterol, a long-acting beta2-adrenergic agonist (LABA).
Budesonide/glycopyrrolate/formoterol fumarate (Breztri Aerosphere) is a combination of an ICS, LAMA, and LABA.

Breztri Aerosphere and Trelegy Ellipta have not been shown to be safer or more cost-effective than use of open triple combination therapy via two separate inhalers (e.g., ICS/LABA plus LAMA).

FDA APPROVED INDICATIONS

Trelegy Ellipta is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema and the maintenance treatment of asthma in patients aged 18 years and older.
Breztri Aerosphere is indicated for the maintenance treatment of patients with COPD. Breztri Aerosphere is NOT indicated for the treatment of asthma.

REFERENCES

Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 11/2023
Revised Date: 11/2023

FLUTICASONE 44 MCG (FLOVENT)

Generic	Brand	HICL	GCN	Exception/Other
FLUTICASONE PROPIONATE 44 MCG	FLOVENT HFA	07873	53638	Formulary

GUIDELINES FOR COVERAGE

1. Patient is under 5 years of age.

If above criteria are met, approve until patient turns the age of 5.
If above criteria are not met, do not approve.

RATIONALE

1. Flovent HFA 44 mcg/inhalation inhaler should be reserved for patients < 5 years of age who require a low dose ICS
2. Patients 5 years of age and older on Flovent HFA 44 mcg/inhalation inhaler may be receiving suboptimal ICS dose or utilizing multiple inhalations to achieve therapeutic dose which is not cost-effective
3. Alvesco HFA is our preferred ICS inhaler for patients 5 years and older. Alvesco HFA use in pediatric patients age 5-11 years is supported by National Asthma Guidelines and data from randomized, controlled trials

REFERENCES

Per Health Plan

Creation date: 10/2019
Effective date: 01/2024
Reviewed date: 5/2023
Revised date: 5/2023

FOSTAMATINIB

Generic Name	Brand Name	HICL	GPID	Comments
FOSTAMATINIB 100MG	TAVALISSE 100MG	44895	44702	
FOSTAMATINIB 150MG	TAVALISSE 150MG	44895	44703	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following criteria or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

1. Must be prescribed by a CPMG or affiliated Hematologist/Oncologist
2. Diagnosis of Idiopathic Thrombocytopenic Purpura (ITP)
3. Patient has tried and failed each of the following for the treatment of ITP:
   a. at least one prior systemic corticosteroid
   b. rituximab
   c. IVIG
   d. romiplostim
   e. eltrombopag

If initial criteria are met, approve x3 months, max 2 tablets per day.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:

1. Prescriber must have evaluated for a response to fostamatinib after the patient completed at least 11 weeks of fostamatinib therapy
2. Patient's platelet count increased above baseline to a level which has been sufficient to avoid clinically important bleeding

If renewal criteria are met, approve x1 year, max 2 tablets per day.
If renewal criteria are not met, do not approve.

RATIONALE

Multiple treatment options are available for management of ITP that may have a more tolerable side effect profile than fostamatinib.

FDA APPROVED INDICATIONS

Fostamatinib is a kinase inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

REFERENCES

Tavalisse prescribing information: https://tavalisse.com/downloads/pdf/Tavalisse-Full-Prescribing-Information.pdf

Creation Date: 5/2019
Effective Date: 01/01/2024
Reviewed Date: 5/2023
Revised Date: 5/2023

GANAXOLONE

Generic	Brand	HICL	GCN	Exception/Other
GANAXOLONE	ZTALMY	47912		

GUIDELINES FOR COVERAGE
Must meet all the following:
1. The patient has a diagnosis of seizures
2. The patient is 2 years of age or older
3. The patient's seizures are associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD)

If yes, approve indefinitely at HICL, max #36 mL per day.
If no, do not approve.

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Ztalmy.

REFERENCES
Ztalmy [Prescribing Information]. Radnor, PA: Marinus Pharmaceuticals, Inc.; June 2022.

Creation date: 09/2022
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

GLASDEGIB (DAURISMO)

Generic Name	Brand Name	HICL	GPID	Comments
GLASDEGIB	DAURISMO 25MG, 100MG TABLET	45502	45798, 45797	Not indicated for BCC; Non-preferred for AML

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO in the past 90 days and stable on therapy.

If new member criteria are met, approve x1 year.
If new member criteria are not met, proceed to Initial Criteria.

INITIAL CRITERIA: Must meet all of the following criteria below:
A. Medication is prescribed by a CPMG or affiliated Oncologist
B. Patient has the FDA-labeled indication for use: newly diagnosed with AML, medication will be used in combination with low-dose cytarabine, and either the patient is 75 years or older or the patient has comorbidities that preclude the use of an intensive induction chemotherapy
C. Patient is unable to use an AML regimen that includes venetoclax

If initial criteria above are met, then approve x1 year.
If initial criteria above are not met, do not approve.

RENEWAL CRITERIA:
Patient's disease has not progressed since treatment initiation as assessed by treating physician OR treating physician believes patient is deriving significant clinical benefit to justify treatment continuation.

If renewal criteria above are met, then approve x1 year.
If renewal criteria are not met, do not approve.

RATIONALE
Per KPCO treatment guidelines
Glasdegib combination therapy would be nonpreferred compared to venetoclax combination therapies in newly diagnosed AML for majority of cases, unless patient has a contraindication or ineligibility to venetoclax combination therapies.

FDA APPROVED INDICATIONS
DAURISMO™(glasdegib) is a hedgehog pathway inhibitor indicated for the treatment of newly diagnosed acute myeloid leukemia, in combination with low-dose cytarabine, in adults 75 years of age or older or who have comorbidities that preclude use of intensive induction chemotherapy.

REFERENCES
Ekim Ekinci

Creation Date: 3/8/2019
Effective Date: 1/2024
Reviewed Date: 1/2024
Revised Date: 1/2024

GIP/GLP-1 AGONISTS
MOUNJARO

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
TIRZEPATIDE	MOUNJARO		52333, 52334, 52335, 52336, 52337, 52338	NF Specialty tier	DM2 GIP/GLP-1 agonist

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must have one of the following indications and meet indication-specific criteria as follows:

A. Adults 25 years of age or older with DM2 without ASCVD
B. Adults 25 years of age or older with DM2 with ASCVD
C. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat type 2 diabetes in patients without ASCVD: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor
4. Has contraindications to, is currently using, or has failed maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
   c. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e., sulfonylurea, insulin, pioglitazone)
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus), and/or exenatide ER (Bydureon BCise), and/or exenatide IR (Byetta)

   If initial criteria are met, approve at HICL x 6 months, max 1 box/4 pens/2 mL per 28 days [max daily dose of 0.08].
   If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in patients with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
3. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus), and/or exenatide ER (Bydureon BCise), and/or exenatide IR (Byetta)

   If initial criteria are met, approve at HICL indefinitely, max 1 box/4 pens/2 mL per 28 days [max daily dose of 0.08].
   If initial criteria are not met, do not approve.

C. To treat type 2 diabetes in pediatric patients > 10 but <25 years of age. Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor or the patient has an intolerance to any SGLT-2 inhibitor
4. Patient has contraindications to, is currently using, or has failed maximum dose of pioglitazone unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 95%ile for age and sex
   c. ≥ 5% increase in body weight after 6 months of starting these medications
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus), and/or exenatide ER (Bydureon Bcise), and/or exenatide IR (Byetta)

   If initial criteria are met, approve at HICL x 6 months, max 1 box/4 pens/2 mL per 28 days [max daily dose of 0.08].
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. HgbA1c is either at goal or has decreased by at least 1% or more from baseline prior to starting GLP-1 therapy unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day.

If renewal criteria are met, approve indefinitely at HICL, max 1 box/4 pens/2 mL per 28 days [max daily dose of 0.08].
If renewal criteria are not met, do not approve.

RATIONALE
- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.
- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.
- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS
All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.
Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of
- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:
- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES
Per Health Plan

Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation Date: 11/16/2016
Effective Date: 02/2024
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Revised Date: 01/2024

GIP/GLP-1 AGONISTS
ZEPBOUND

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
TIRZEPATIDE	ZEPBOUND		54991, 54992, 54993, 54994, 54988, 54989	NF Specialty tier	Weight loss GIP/GLP-1 agonist

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Medication is being used for weight loss in patients 12 years of age or older.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
3. Patient must have benefit plan with coverage for weight loss medications.
4. Patient must have an initial body mass index (BMI) of greater than or equal to 30 kg/m2, OR an initial BMI of greater than or equal to 27 kg/m2 AND at least one weight-related comorbid condition, such as hypertension, dyslipidemia, type 2 diabetes.
5. Provider attests to patient being on a reduced calorie diet and has increased physical activity.
6. Meets medication specific step therapy criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
   a. Patient has tried and failed or has a contraindication to all the following: phentermine or diethylpropion, Qsymia, Contrave, and either Ozempic or Wegovy.

If initial criteria are met, approve x4 months at HICL, max 1 box/4 pens/2mL per 28 days [max daily dose of 0.08].
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Not currently using a DPP-4 (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. Patient must have achieved and maintained at least a 5% weight loss from baseline (objectively measured with in-office weight checks).

If renewal criteria are met, approve x 1 year at HICL, max 1 box/4 pens/2mL per 28 days [max daily dose of 0.08].
If renewal criteria are not met, do not approve.

RATIONALE
- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (I.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.

- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.
- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS
All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.
Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of
- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:
- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES
Per Health Plan

Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.

2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation Date: 11/16/2016
Effective Date: 02/2024
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Revised Date: 01/2024

GLP-1 AGONISTS
TRULICITY

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
DULAGLUTIDE	TRULICITY	41421			DM2

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must have one of the following indications and meet indication-specific criteria as follows:

A. Adults 25 years of age or older with DM2 without ASCVD
B. Adults 25 years of age or older with DM2 with ASCVD
C. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat type 2 diabetes in patients without ASCVD: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor
4. Has contraindications to, is currently using, or has failed maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
   c. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e., sulfonylurea, insulin, pioglitazone)
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed, has an intolerance or a contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus), and/or exenatide ER (Bydureon BCise), and/or exenatide IR (Byetta), and/or tirzepatide (Mounjaro)

If initial criteria are met, approve at HICL x 6 months, max daily dose of 0.08 (1 box/4 pens/2mL per 28 days).
If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in patients with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
3. Patient has tried and failed, has an intolerance or a contraindication to semaglutide (Ozempic) and/or liraglutide (Victoza)

If initial criteria are met, approve at HICL indefinitely, max 1 box/4 pens/2mL per 30 days [max daily dose of 0.08].
If initial criteria are not met, do not approve.

C. To treat type 2 diabetes in pediatric patients > 10 but <25 years of age. Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor or the patient has an intolerance to any SGLT-2 inhibitor
4. Patient has contraindications to, is currently using, or has failed maximum dose of pioglitazone unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 95%ile for age and sex
   c. ≥ 5% increase in body weight after 6 months of starting these medications
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus), and/or exenatide ER (Bydureon BCise), and/or exenatide IR (Byetta)

If initial criteria are met, approve at HICL x 6 months, max daily dose of 0.08 (1 box/4 pens/2mL per 28 days).
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. HgbA1c is either at goal or has decreased by at least 1% or more from baseline prior to starting GLP-1 therapy unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day.

If renewal criteria are met, approve indefinitely at HICL, max 1 box/4 pens/2 mL per 28 days [max daily dose of 0.08].
If renewal criteria are not met, do not approve.

RATIONALE
- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.
- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.
- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS
All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.

Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of
- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:
- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES
Per Health Plan

Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

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GLP-1 AGONISTS
BYDUREON BCISE

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
EXENATIDE ER	BYDUREON BCISE	38451			DM2

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must have one of the following indications and meet indication-specific criteria as follows:

A. Adults 25 years of age or older with DM2 without ASCVD
B. Adults 25 years of age or older with DM2 with ASCVD
C. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat type 2 diabetes in patients without ASCVD: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor
4. Has contraindications to, is currently using, or has failed maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
   c. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e., sulfonylurea, insulin, pioglitazone)
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus)

   If initial criteria are met, approve at HICL x 6 months, max 1 box/4 pens per 28 days [max daily dose of 0.13].
   If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in patients with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial

revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
3. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus)

   If initial criteria are met, approve at HICL indefinitely, max 1 box/4 pens per 28 days [max daily dose of 0.13].
   If initial criteria are not met, do not approve.

C. **To treat type 2 diabetes in pediatric patients > 10 but <25 years of age.** Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor or the patient has an intolerance to any SGLT-2 inhibitor
4. Patient has contraindications to, is currently using, or has failed maximum dose of pioglitazone unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 95%ile for age and sex
   c. ≥ 5% increase in body weight after 6 months of starting these medications
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus)

If initial criteria are met, approve at HICL x 6 months, max 1 box/4 pens per 28 days [max daily dose of 0.13].
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. HgbA1c is either at goal or has decreased by at least 1% or more from baseline prior to starting GLP-1 therapy unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day.

If renewal criteria are met, approve indefinitely at HICL, max 1 box/4 pens per 28 days [max daily dose of 0.13].
If renewal criteria are not met, do not approve.

RATIONALE

- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.
- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.
- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS

All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.
Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of
- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:
- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES
Per Health Plan

Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

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GLP-1 AGONISTS
BYETTA

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
EXENATIDE IR	BYETTA	32893			DM2

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must have one of the following indications and meet indication-specific criteria as follows:

A. Adults 25 years of age or older with DM2 without ASCVD
B. Adults 25 years of age or older with DM2 with ASCVD
C. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat type 2 diabetes in patients without ASCVD: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor
4. Has contraindications to, is currently using, or has failed maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
   c. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e., sulfonylurea, insulin, pioglitazone)
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus), and/or exenatide ER (Bydureon BCise)

   If initial criteria are met, approve at HICL x 6 months, max daily dose of 0.09 (1 box/1 pen/2.4mL per 28 days).
   If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in patients with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
3. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus)

   If initial criteria are met, approve at HICL indefinitely, max daily dose of 0.09 (1 box/1 pen/2.4mL per 28 days).
   If initial criteria are not met, do not approve.

C. To treat type 2 diabetes in pediatric patients > 10 but <25 years of age. Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor or the patient has an intolerance to any SGLT-2 inhibitor
4. Patient has contraindications to, is currently using, or has failed maximum dose of pioglitazone unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 95%ile for age and sex
   c. ≥ 5% increase in body weight after 6 months of starting these medications
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic), and/or liraglutide (Victoza), and/or semaglutide oral (Rybelsus), and/or exenatide ER (Bydureon BCise)

   If initial criteria are met, approve at HICL x 6 months, max daily dose of 0.09 (1 box/1 pen/2.4mL per 28 days).
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. HgbA1c is either at goal or has decreased by at least 1% or more from baseline prior to starting GLP-1 therapy unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day.

If renewal criteria are met, approve indefinitely at HICL, with a max 1 box/1 pen/2.4 mL per 28 days [max daily dose of 0.09].
If renewal criteria are not met, do not approve.

RATIONALE
- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.
- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.
- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS
All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.

Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of
- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:
- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES
Per Health Plan

Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

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GLP-1 AGONISTS
SAXENDA

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
LIRAGLUTIDE	SAXENDA		37637	NF Specialty tier	Weight loss

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Medication is being used for weight loss in patient 12 years of age or older.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
3. Patient must have benefit plan with coverage for weight loss medications.
4. Patient must have an initial body mass index (BMI) of greater than or equal to 30 kg/m2, OR an initial BMI of greater than or equal to 27 kg/m2 AND at least one weight-related comorbid condition, such as hypertension, dyslipidemia, type 2 diabetes.
5. Provider attests to patient being on a reduced calorie diet and has increased physical activity.
6. Meets medication specific step therapy criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
   a. Patient has tried and failed or has a contraindication to all the following: phentermine or diethylpropion, Qsymia, Contrave, Ozempic or Wegovy, and Zepbound.

If initial criteria are met, approve x4 months at HICL, max 1 box/1 pen/15mL per 30 days [max daily dose of 0.5].
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Not currently using a DPP-4 (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. Patient must have achieved and maintained at least a 5% weight loss from baseline (objectively measured with in-office weight checks).

If renewal criteria are met, approve x 1 year at HICL, with a max 1 box/1 pen/15mL per 30 days [max daily dose of 0.5].
If renewal criteria are not met, do not approve.

RATIONALE
- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.
- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an

adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.

- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS
All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.
Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of
- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:
- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES
Per Health Plan

Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.

3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation Date: 11/16/2016
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

GLP-1 AGONISTS
VICTOZA

Generic	Brand	GCN	Exception/Other	Indication
LIRAGLUTIDE 2-pack 1.2 mg/d (NDC: 00169-4060-12) 3-pack 1.8 mg/d (NDC: 00169-4060-13)	VICTOZA	26189	NF - 2nd PREFERRED Qty Limits: Non-ASCVD: 1.2 mg/day (2-pk) ASCVD: 1.8 mg/day (3-pk)	DM2

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Patient has one of the following diagnoses and meets all diagnosis specific criteria as follows:

A. DM2 without ASCVD: Patient is new to KPCO in the past 90 days and is currently using a GLP1 agonist for the management of DM2 without ASCVD and meets the following:
    1. Patient has lab history showing A1c above 7% prior to GLP1 therapy
    2. Current clinical presentation falls into one of the following categories:
        a. A1c is at or below goal
        b. A1c is above goal but the patient has failed as least two other diabetes medications (including metformin, unless contraindicated).
    3. Patient has intolerance or contraindication to Ozempic and provider is requesting Victoza.
B. DM2 with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Patient is new to KPCO in the past 90 days and is currently using a GLP1 agonist for the management of DM2 with ASCVD and meets the following:
    1. Patient has intolerance or contraindication to Ozempic and the provider is requesting Victoza.

If met, approve indefinitely with the following quantity limits:
- Liraglutide (Victoza) for all non-ASCVD indications at NDC (00169-4060-12), max 1 box/2 pens/6mL per 28 days [max daily dose of 0.21].
- Liraglutide (Victoza) for ASCVD indications at GPID, max 1 box/3 pens/9mL per 28 days [max daily dose of 0.32].

If New Member Criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following indications and meet indication-specific criteria as follows:

A. Adults 25 years of age or older with DM2 without ASCVD
B. Adults 25 years of age or older with DM2 with ASCVD
C. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat type 2 diabetes in patients without ASCVD: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack

of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor
4. Has contraindications to, is currently using, or has failed maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
   c. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e., sulfonylurea, insulin, pioglitazone)
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide injection (Ozempic)

   If initial criteria are met, approve 2-pack at NDC level x 6 months (00169-4060-12), max 1 box/2 pens/6mL per 28 days [max daily dose of 0.21].
   If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in patients with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
3. Patient has tried and failed or has an intolerance or contraindication to semaglutide injection (Ozempic)

   If initial criteria are met, approve indefinitely at GPID, max 1 box/3 pens/9mL per 28 days [max daily dose of 0.32].

If initial criteria are not met, do not approve.

C. To treat type 2 diabetes in pediatric patients > 10 but <25 years of age. Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor or the patient has an intolerance to any SGLT-2 inhibitor
4. Patient has contraindications to, is currently using, or has failed maximum dose of pioglitazone unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 95%ile for age and sex
   c. ≥ 5% increase in body weight after 6 months of starting these medications
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide injection (Ozempic)

   If initial criteria are met, approve 2-pack at NDC level x 6 months (00169-4060-12), max 1 box/2 pens/6mL per 28 days [max daily dose of 0.21].
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. HgbA1c is either at goal or has decreased by at least 1% or more from baseline prior to starting GLP-1 therapy unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day.

If renewal criteria are met, approve indefinitely at NDC (00169-4060-12), with a max 1 box/2 pens/6mL per 28 days [max daily dose of 0.21].
If renewal criteria are not met, do not approve.

RATIONALE

- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular

events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.

- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.
- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS

All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.
Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of

- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:

- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES

Per Health Plan

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

Creation Date: 11/16/2016
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

GLP-1 AGONISTS
OZEMPIC

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
SEMAGLUTIDE INJECTION	OZEMPIC		53536, 48208, 52125	1st PREFERRED regardless of ASCVD; FORMULARY	DM2 may use off-label for weight loss per PA criteria

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Patient has one of the following diagnoses and meets all diagnosis specific criteria as follows:

A. DM2 without ASCVD: Patient is new to KPCO in the past 90 days and is currently using a GLP1 agonist for the management of DM2 without ASCVD and meets the following:
    1. Patient has lab history showing A1c above 7% prior to GLP1 therapy
    2. Current clinical presentation falls into one of the following categories:
        a. A1c is at or below goal
        b. A1c is above goal but the patient has failed as least two other diabetes medications (including metformin, unless contraindicated).
B. DM2 with ASCVD: Patient is new to KPCO in the past 90 days and is currently using a GLP1 agonist for the management of DM2 with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]

If met, approve and override restriction only at HICL indefinitely, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
If New Member Criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following indications and meet indication-specific criteria as follows:

A. Adults 25 years of age or older with DM2 without ASCVD
B. Adults 25 years of age or older with DM2 with ASCVD
C. Pediatrics/Young Adults between 10 and 25 years of age with DM2
D. Patients 12 years of age or older for weight loss

A. To treat type 2 diabetes in patients without ASCVD: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
    1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
    2. Has contraindications to, is currently using, or has failed maximum dose metformin

3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor
4. Has contraindications to, is currently using, or has failed maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
   c. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e., sulfonylurea, insulin, pioglitazone)
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

   If initial criteria are met, approve and override restriction only at HICL x 6 months, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
   If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in patients with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)

   If initial criteria met, approve and override restriction only at HICL indefinitely, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
   If initial criteria are not met, do not approve.

C. To treat type 2 diabetes in pediatric patients > 10 but <25 years of age. Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an

adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor or the patient has an intolerance to any SGLT-2 inhibitor
4. Patient has contraindications to, is currently using, or has failed maximum dose of pioglitazone unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 95%ile for age and sex
   c. ≥ 5% increase in body weight after 6 months of starting these medications
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day

If initial criteria are met, approve and override restriction only at HICL x 6 months, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
If initial criteria are not met, do not approve.

D. To treat weight loss in patients 12 years of age or older. Must meet all the following:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Patient must have benefit plan with coverage for weight loss medications
3. Patient must have an initial body mass index (BMI) of greater than or equal to 30 kg/m2, OR an initial BMI of greater than or equal to 27 kg/m2 AND at least one weight-related comorbid condition, such as hypertension, dyslipidemia, type 2 diabetes.
4. Provider attests to patient being on a reduced calorie diet and has increased physical activity
5. Meets medication specific step therapy criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
   a. Patient has tried and failed or has a contraindication to all the following: phentermine or diethylpropion, Qsymia, and Contrave.

If initial criteria are met, approve and override restriction only x4 months at HICL, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following criteria based on diagnosis and age:

A. To treat type 2 diabetes in patients without ASCVD: Must meet all the following:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. HgbA1c is either at goal or has decreased by at least 1% or more from baseline prior to starting GLP-1 therapy unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day.

If renewal criteria are met, approve and override restriction only indefinitely at HICL, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
If renewal criteria are not met, do not approve.

B. To treat type 2 diabetes in pediatric patients between 10 and 25 years of age: Must meet all the following:

1. Not currently using a DPP-4 (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. HgbA1c is either at goal or at least has decreased by 1% or more unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day.

If renewal criteria are met, approve and override restriction only indefinitely at HICL, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
If renewal criteria are not met, do not approve.

C. To treat weight loss in patients 12 years of age or older: Must meet all the following:

1. Not currently using a DPP-4 (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. Patient must have achieved and maintained at least a 5% weight loss from baseline (objectively measured with in-office weight checks).

If renewal criteria are met, approve and override restriction only x 1 year at HICL, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
If renewal criteria are not met, do not approve.

RATIONALE

- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.
- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the

treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.

- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS

All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.
Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of

- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:

- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES

Per Health Plan

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

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Effective Date: 02/2024
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Revised Date: 01/2024

GLP-1 AGONISTS
WEGOVY

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
SEMAGLUTIDE INJECTION	WEGOVY		49748, 49749, 49752, 49753, 49754	NF Specialty tier	Weight loss

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Medication is being used for weight loss in patient 12 years of age or older.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
3. Patient must have benefit plan with coverage for weight loss medications.
4. Patient must have an initial body mass index (BMI) of greater than or equal to 30 kg/m2, OR an initial BMI of greater than or equal to 27 kg/m2 AND at least one weight-related comorbid condition, such as hypertension, dyslipidemia, type 2 diabetes.
5. Provider attests to patient being on a reduced calorie diet and has increased physical activity.
6. Meets medication specific step therapy criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
   a. Patient has tried and failed or has a contraindication to all the following: phentermine or diethylpropion, Qsymia, Contrave, and Ozempic.

If initial criteria are met, approve x4 months at HICL, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Not currently using a DPP-4 (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. Patient must have achieved and maintained at least a 5% weight loss from baseline (objectively measured with in-office weight checks).

If renewal criteria are met, approve x 1 year at HICL, max 1 box/1 pen/3mL per 28 days [max daily dose of 0.11].
If renewal criteria are not met, do not approve.

RATIONALE
- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.

- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.
- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS
All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.
Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of
- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:
- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES
Per Health Plan

Medication use in Pediatric/Young Adults:
1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.

2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

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GLP-1 AGONISTS
RYBELSUS

Generic	Brand	HICL	GCN	Exception/Other	FDA Indication
SEMAGLUTIDE ORAL	RYBELSUS		46964, 46965, 46966	Max daily dose is 1 tab/day	DM2

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must have one of the following indications and meet indication-specific criteria as follows:

A. Adults 25 years of age or older with DM2 without ASCVD
B. Adults 25 years of age or older with DM2 with ASCVD
C. Pediatrics/Young Adults between 10 and 25 years of age with DM2

A. To treat type 2 diabetes in patients without ASCVD: Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor
4. Has contraindications to, is currently using, or has failed maximum dose sulfonylurea, maximum dose pioglitazone, and all possible combinations thereof unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 35 (≥ 30 for Asian American/Pacific Islanders)
   c. ≥ 5% increase in body weight after 6 months of starting diabetes medications associated with weight gain (i.e., sulfonylurea, insulin, pioglitazone)
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic) and/or liraglutide (Victoza)

   If initial criteria met, approve at HICL x 6 months, max 1 tablet/day.
   If initial criteria are not met, do not approve.

B. To treat type 2 diabetes in patients with ASCVD [acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, ischemic stroke, transient ischemic attack (TIA), or symptomatic peripheral arterial disease (PAD)]: Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor, or the patient has an intolerance to any SGLT-2 inhibitor.
2. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
3. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic) and/or liraglutide (Victoza)

   If initial criteria are met, approve at HICL indefinitely, max 1 tablet/day.
   If initial criteria are not met, do not approve.

C. To treat type 2 diabetes in pediatric patients > 10 but <25 years of age. Must meet all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin)
2. Has contraindications to, is currently using, or has failed maximum dose metformin
3. Patient has tried and failed to reach A1C goals with any SGLT-2 inhibitor for 3 months, or has a contraindication (including but not limited to UTI, mycotic infections) to any SGLT-2 inhibitor or the patient has an intolerance to any SGLT-2 inhibitor
4. Patient has contraindications to, is currently using, or has failed maximum dose of pioglitazone unless the patient has one of the following:
   a. h/o bariatric surgery
   b. BMI ≥ 95%ile for age and sex
   c. ≥ 5% increase in body weight after 6 months of starting these medications
   d. patient is either on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
5. Most recent HgbA1c is above but within 2% of patient's designated A1c goal unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day
6. Patient has tried and failed or has an intolerance or contraindication to semaglutide (Ozempic) and/or liraglutide (Victoza)

If initial criteria are met, approve at HICL x 6 months (44675), max 1 tablet/day.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Not currently using a DPP-4 inhibitor (medications containing alogliptin, linagliptin, saxagliptin, or sitagliptin).
2. HgbA1c is either at goal or has decreased by at least 1% or more from baseline prior to starting GLP-1 therapy unless the patient is on basal insulin at a dose of ≥ 0.5 units/kg/day or basal/bolus regimen at a dose ≥ 1.5 units/kg/day.

If renewal criteria are met, approve indefinitely at HICL, max 1 tablet/day.
If renewal criteria are not met, do not approve.

RATIONALE
- The 2023 KP National Diabetes Guidelines recommend Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) for people with type 2 diabetes on metformin monotherapy, with clinical ASCVD who cannot take SGLT-2 inhibitors (i.e., empagliflozin), to reduce the risk of cardiovascular events (myocardial infarction or stroke) or cardiovascular death. There is insufficient evidence to recommend GLP-1 agonists for other indications such as renal disease or heart failure.
- The 2022 KP National Overweight and Obesity Guidelines recommend pharmacotherapy for patients who have a history of being unable to successfully lose weight and maintain body weight loss and have a BMI ≥ 30 kg/m2 or a BMI ≥ 27 kg/m2 with an obesity associated comorbidity, as an adjunct to lifestyle modification. The guidelines also recommend offering continued use of medication for weight maintenance for those patients who have achieved an initial weight loss goal of at least 5% of initial body weight and have not experienced serious or intolerable side effects. Ozempic is the KP preferred GLP-1RA for either diabetes or weight loss based on its wide market use for both indications and preferential cost RAs, such as Wegovy and Saxenda, have demonstrated efficacy in weight loss trials involving obese and overweight patients with and without diabetes and are FDA approved for weight loss. Ozempic contains the same active drug, semaglutide, as Wegovy but in a slightly lower strength. Ozempic is FDA approved for the treatment of type 2 diabetes but also has been shown in clinical trials to result in weight loss and thus is commonly used off label for weight management in patients with and without type 2 diabetes.
- Note on DPP-4 inhibitor restriction in weight loss sections: while concomitant use of GLP1 agonists and DPP-4 inhibitors are not duplicative therapy in clinical aspects of weight loss, if the patient is using a DPP-4 for DM2, with the addition of a GLP1 for either weight loss or DM2, the benefits of the DPP-4 in DM2 are no longer present as this represents duplicative therapy in A1c management, and the DPP-4 inhibitor should be discontinued with the start of a GLP1 agonist.

FDA APPROVED INDICATIONS
All GLP-1 agonists, except semaglutide (Wegovy), tirzepatide (Zepbound) and liraglutide (Saxenda), are approved for glycemic control in adults with type 2 diabetes mellitus.
Semaglutide injection (Ozempic) and liraglutide (Victoza) have an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dulaglutide has an additional indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

Tirzepatide (Mounjaro) is indicated to improve glycemic control in patients with type 2 diabetes.

Semaglutide (Wegovy), Tirzepatide (Zepbound), and liraglutide (Saxenda) are indicated as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in:
Adult patients with an initial body mass index (BMI) of

- 30 kg/m2 or greater (obese), or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:

- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m2 or greater for adults (obese) by international cut-offs.

REFERENCES
Per Health Plan

Medication use in Pediatric/Young Adults:

1. Tamborlane WV, Barrientos-Pérez M., Fainberg U et al. Liraglutide in children and adolescents with type 2 diabetes. NEJM. 381;7. Aug. 2019.
2. Zeitler P, Hirst K, Pyle L et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. NEJM. 366;24: June 2012.
3. Nadeau KJ, Hannon TS, Edelstein SL, et al. Impact of insulin and metformin versus metformin alone on b-cell function in youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. Diabetes Care 2018;41:1717–1725.
4. An email (MM Kelsey, 2020, personal communication and power point included March 3) LM2 TD2 Medical Management July 2019 at Children's Hospital Colorado validates use of off-label use of SGLT-2s, DPP-4 inhibitors, GLP-1 Agonists, and pioglitazone.
5. Children's Hospital use of off-label SGLT-2 inhibitors, DPP-4 inhibitors, pioglitazone use and GLP-1 agonists and lack of preference of one agent over another in a specific class were confirmed during a phone interview (M Alonzo, PharmD 2020, personal communication, 20 November).

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GLUCOSE TEST STRIPS & LANCETS

GUIDELINES FOR EXCEPTIONS TO QUANTITY LIMITS

COMMERCIAL LINES OF BUSINESS:
STRIPS and LANCETS:

A. Patient is using insulin; the limit is 300 strips/lancets per 30-day supply (testing 10 times per day)
   1. If refill history demonstrates the patient is consistently testing more than 10 times per day
   AND
   2. The prescriber provides clinical reasoning supporting the need to test more than 10 times per day on a routine, regular basis

If above criteria are met, then approve the quantity with an appropriate max daily dose for the expected duration of the need.

B. Patient is not on insulin; the limit is 100 strips/lancets per 30-day supply (testing 3 times per day)
   1. If refill history demonstrates the patient is consistently testing more than 3 times per day
   AND
   2. The prescriber provides clinical reasoning supporting the need to test more than 3 times per day on a routine, regular basis

If above criteria are met, then approve the quantity with an appropriate max daily dose for the expected duration of the need.

C. Patient has Gestational diabetes, approve max daily dose of 10 per day (#300 strips/30-day supply) for the expected duration of the pregnancy

MEDICARE LINE OF BUSINESS under Part B:
STRIPS:

D. The limit is 300 strips/30-day supply (testing 10 times per day)
   1. If refill history demonstrates the patient is consistently testing more than 10 times per day
   AND
   2. The prescriber provides clinical reasoning supporting the need to test more than 10 times per day on a routine, regular basis

If above criteria are met, then approve the quantity for the remainder of the year.
If denying, then use the Part B denial notification template.

RATIONALE
Per Plan.

FDA APPROVED INDICATIONS

REFERENCES
Per Plan.

Creation date: 09/26/2018
Effective date: 10/2023
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Revised date: 04/2020

GUSELKUMAB (TREMFYA)

Generic	Brand	HICL	GCN	Exception/Other
GUSELKUMAB	TREMFYA	44418		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on therapy, medication is not being used in combination with another biologic for the same indication, and has one of the following indications prescribed by the appropriate specialist as noted:
   1. Patient has a diagnosis of Psoriatic Arthritis (PsA) prescribed by a CPMG or affiliated rheumatologist.
   2. Patient has a diagnosis of Psoriasis prescribed by a CPMG or affiliated dermatologist.

   If met, approve indefinitely, based on indication and medication:
   PsA:
   - Tremfya: 1 pen/syringe per 56 days [max qty: 1, min ds: 56]

   Psoriasis:
   - Tremfya: 1 pen/syringe per 56 days [max qty: 1, min ds: 56]

   If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Psoriatic Arthritis (PsA)
B. Psoriasis

A. Psoriatic Arthritis: All the following must be met:
   1. Patient has a diagnosis of psoriatic arthritis and medication is prescribed by a rheumatology provider
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response, intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. At least 2 DMARDs (including methotrexate) or has documented high disease activity in which traditional DMARDs would not be suitable treatment
      b. At least 1 TNF inhibitor (e.g., adalimumab-atto (Amjevita)-preferred [F, PA], etanercept (Enbrel) [F, PA], infliximab-dyyb (Inflectra)-preferred [F])
      c. Cosentyx [F]

   If criteria are met, approve at HICL with the following quantity limits: x 1 month, max 1 pen/syringe per 28 days (loading dose) [max qty: 1, min ds: 28], then 1 pen/syringe per 56 days (maintenance dose) indefinitely [max qty: 1, min ds: 56].
   If criteria are not met, do not approve.

B. Psoriasis: All the following must be met:
   1. Patient has a diagnosis of moderate to severe psoriasis and medication is prescribed by a dermatology provider.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response (after at least 2 months), intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. A topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus), or the patient is reported as having very high disease activity (ex: > 50% BSA, erythrodermic, pustular psoriasis), disease affecting critical areas (ex: genitals, face), or prior biologic therapy within the past 4 months, skip and proceed to step 3c
      b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Acitretin, Cyclosporine, Methotrexate, Apremilast (Otezla), Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
      c. At least one TNF inhibitor (adalimumab (Amjevita) - preferred [F, PA], infliximab (Inflectra) - preferred [F], etanercept (Enbrel) [F, PA]) - unless the patient has failed an IL-17 inhibitor
      d. At least one IL-17 inhibitor (secukinumab (Cosentyx) - preferred [F])

   If criteria are met, approve at HICL with the following quantity limits: x 1 month, max 1 pen/syringe per 28 days (loading dose) [max qty: 1, min ds: 28], then 1 pen/syringe per 56 days (maintenance dose) indefinitely [max qty: 1, min ds: 56].
   If criteria are not met, do not approve.

RENEWAL CRITERIA
1. The diagnosis for which the patient was originally authorized medication coverage, has been assessed by the applicable specialist in the past two years.
2. Medication is not being used in combination with another biologic for the same indication.

   If met, approve indefinitely based on indication and medication:
   PsA:
   - Tremfya: 1 pen/syringe per 56 days [max qty: 1, min ds: 56]

   Psoriasis:
   - Tremfya: 1 pen/syringe per 56 days [max qty: 1, min ds: 56]

   If not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

FDA APPROVED INDICATIONS
Plaque Psoriasis
Psoriatic Arthritis

REFERENCES
Currently stable on medication means patient is tolerating well, appears to be effective and provider wishes to continue

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (ex: systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for psoriasis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*

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Revised Date: 11/2023

HEPATITIS C MEDICATIONS: DIRECT ACTING ANTIVIRALS

Generic	Brand	HICL	GCN	Exception/Other
DASABUVIR/OMBITASVIR/PARITAPREVIR/RITONAVIR	VIEKIRA PAK, VIEKIRA XR	41644		
ELBASVIR/GRAZOPREVIR	ZEPATIER	43030		
GLECAPREVIR/ PIBRENTASVIR	MAVYRET	44453		
LEDIPASVIR/SOFOSBUVIR	HARVONI	41457		Generic is Formulary
SOFOSBUVIR/ VELPATASVIR	EPCLUSA	43561		Generic is Formulary
SOFOSBUVIR/VELPATAS/VOXILAPREV	VOSEVI	44428		Formulary
SOFOSBUVIR	SOVALDI	40795		Formulary

GUIDELINES FOR COVERAGE

Patient must meet criteria #1 OR #2-4:
1. Patient is receiving or has received an HCV positive transplant.

OR
2. Patient has a detectable HCV RNA level. (If the patient has evidence of prescriptions for past HCV treatment, the detectable HCV RNA level must be from at least 12 weeks after completion of the previous treatment.)
AND

3. Patient does not have a suspected acute HCV exposure in the last 6 months.
AND

4. Provider attests to the best of their knowledge that patient is NOT abusing/misusing alcohol and/or illegal drugs (per Colorado state law) OR if patient is abusing/misusing alcohol and/or illegal drugs (per Colorado state law), provider attests that the patient is receiving or will be enrolled in counseling or substance use treatment program prior to initiating HCV treatment.

AND Patient must meet all criteria #5-8:

5. Patient is at least 3 years old and currently supervised by a gastroenterologist, infectious disease specialist, provider specializing in the treatment of hepatitis (for example, a hepatologist), or a specially trained group such as ECHO (Extension for Community Healthcare Outcomes) model.

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HEPATITIS C MEDICATIONS: DIRECT ACTING ANTIVIRALS

GUIDELINES FOR COVERAGE (CONTINUED)

6. Patient is not currently taking any medications that have a clinically significant interaction with the Hepatits C medication ordered.*

7. Patient does not have a limited life expectancy (less than 12 months) due to non-liver related comorbid conditions.

8. The requested drug correlates with a drug listed within the current KP HCV Treatment Options Table, based on genotype, therapy history and cirrhosis status. (table attached in References section)

If patient meets criteria [#1 and #5-8]: to allow dispense by the Mayo pharmacy in Arizona (post-transplant) - FORCED OVERRIDE REQUIRED
Approve for length of recommended treatment regimen.

- For sofosbuvir/velpatasvir (generic Epclusa) and ledipasvir/sofosbuvir (generic Harvoni), approve at GPID with “Override Force Flag” in the “Override Restriction” field [the force will override the 'must be dispensed by a KP pharmacy restriction'].
- For Vosevi and Sovaldi, approve at GPID level with “Override Force Flag” in the “Override Restriction” field
- For Mavyret, Zepatier, and Viekira, approve at GPID level with “Override Force Flag” in the “Override Restriction” field, and add a formulary override

If patient meets criteria [#2-4 and #5-8]:
Approve for length of recommended treatment regimen.

- For sofosbuvir/velpatasvir (generic Epclusa) and ledipasvir/sofosbuvir (generic Harvoni), approve at GPID with “Override YES Flag” in the “Override Restriction” field
- For Vosevi and Sovaldi, approve at GPID level with “Override YES Flag” in the “Override Restriction” field
- For Mavyret, Zepatier, and Viekira, approve at GPID level with “Override YES Flag” in the “Override Restriction” field, and add a formulary override

If patient does not meet above criteria as outlined, do not approve^

Note: Only if patient is out of state at a Mayo Clinic and just received an HCV+ liver transplant may you place a force override to allow the Hep C drug to be dispensed by a non-KP pharmacy. Very rare!! ONLY if immediate post transplant and out of state.
Note: There are no renewal criteria as reviews using above criteria apply for a one-time treatment regimen.

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HEPATITIS C MEDICATIONS: DIRECT ACTING ANTIVIRALS

RATIONALE

* clinically significant is defined as an interaction that is moderate to severe and cannot be mitigated easily
^ if prescriber questions the accuracy of the HCV Treatment Options Table, please check the hcvguidelines.org website and contact one of the Clinical Pharmacy Specialists

FDA APPROVED INDICATIONS

Hepatitis C

REFERENCES

Note: Special Populations are listed on pages 2-3, including impaired renal function (eGFR <30 or end-stage renal disease), decompensated cirrhosis, post-transplant and pediatrics.

Clinical Pharmacy Services owns the HCV Treatment Options Table maintenance

HCV Treatment Options Table_Feb 2

HCV Treatment Options Table.docx

Clinical Pharmacy Specialists, Erin Stone and Emily Imsirovic, are subject matter experts in the KPCO Region if questions and they maintain the HCV Treatment Options Table

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Reviewed date: 04/2023
Revised date: 03/2023

ADALIMUMAB

Generic	Brand	HICL	GCN	Exception/Other
ADALIMUMAB	HUMIRA	24800		
ADALIMUMAB	HUMIRA (CF)	24800		
ADALIMUMAB-ATTO	AMJEVITA	43886	42592, 42637, 42639, 54007, 54647, 54649, 54648, 54651	
ADALIMUMAB-ADBM	CYLTEZO	44481	53841, 53842, 43789, 54205	Interchangeable biosimilar
ADALIMUMAB-ADAZ	HYRIMOZ	45444	53884, 53875, 53885, 53883, 53891, 53899, 53875, 53887, 53878	
ADALIMUMAB-BWWD	HADLIMA	45894	46718, 46717, 53846, 53848	
ADALIMUMAB-AFZB	ABRILADA			
ADALIMUMAB-FKJP	HULIO	46685	48318, 48336, 48317	
ADALIMUMAB-AQVH	YUSIMRY	47742	53867	
ADALIMUMAB-AACF	IDACIO	48528	53387	
ADALIMUMAB-AATY	YUFLEYMA	48955	54213	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO with the past 90 days, is currently stable on an adalimumab product, medication is not being used in combination with another biologic for the same indication, and has one of the following indications managed by the appropriate specialist as noted below:
   1. Patient has a diagnosis of Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis or subtype, or Polyarticular Juvenile Idiopathic Arthritis and is being managed by a CPMG or affiliated rheumatologist.
   2. The patient has a diagnosis of Ulcerative Colitis and age > or equal to 18 or Crohn's Disease at any age and is being managed by a CPMG or affiliated gastroenterology specialist.
   3. The patient has a diagnosis of Psoriasis or Hidradenitis Suppurativa and age > or equal to 18 and is being managed by a CPMG or affiliated dermatology specialist.

If any product other than Amjevita is requested and criteria are met, approve x1 at GPID, max 2 pens/syringes per 28 days **AND** approve Amjevita indefinitely at HICL max 2 pens/syringes per 28 days [MDD 0.06].
If Amjevita is requested and criteria are met, approve indefinitely at HICL, max 2 pens/syringes per 28 days [MDD 0.06].
If not met, use Initial Criteria for review.

4. The patient has a diagnosis of Uveitis and age > or equal to 18 and is being managed by a CPMG or affiliated rheumatologist or ophthalmologist.

   If any product other than Amjevita is requested and criteria are met, approve x1 at GPID, max 4 pens/syringes per 28 days **AND** approve Amjevita indefinitely at HICL max 4 pens/syringes per 28 days [MDD 0.12].
   If Amjevita is requested and criteria are met, approve indefinitely at HICL, max 4 pens/syringes per 28 days [MDD 0.12].
   If not met, use Initial Criteria for review.

5. The patient has a diagnosis of Ulcerative Colitis and age < 18 and is being managed by a CPMG or affiliated gastroenterology specialist.
6. The patient has a diagnosis of Hidradenitis Suppurativa and age <18 and is being managed by a CPMG or affiliated dermatology specialist.
7. The patient has a diagnosis of Uveitis and age <18 and is being managed by a CPMG or affiliated rheumatologist or ophthalmologist.

   If Humira is requested and criteria are met, approve Humira at HICL until the patient turns 18 years of age, and approve Amjevita at HICL indefinitely.
   If criteria are not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Rheumatoid Arthritis (RA)
B. Psoriatic Arthritis (PsA)
C. Ankylosing Spondylitis or subtype
D. Uveitis
E. Ulcerative Colitis (UC) or Crohn's Disease
F. Psoriasis
G. Hidradenitis Suppurativa (HS)
H. Juvenile Idiopathic Arthritis (JIA)

A. RHEUMATOID ARTHRITIS (RA): All the following must be met:
   1. Patient has a diagnosis of RA, and medication is prescribed by a CPMG or affiliated rheumatologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the

same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
a. at least 2 DMARDs (including methotrexate)
b. Amjevita

If criteria are met, approve at HICL indefinitely, max 2 pens/syringes per 28 days [MDD 0.06].
If criteria are not met, do not approve.

B. PSORIATIC ARTHRITIS (PsA): All the following must be met:
1. Patient has a diagnosis of PsA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. at least two DMARDs (including methotrexate), or the patient has high disease activity in which traditional DMARDs would not be suitable treatment.
   b. Amjevita

If criteria are met, approve at HICL indefinitely, max 2 pens/syringes per 28 days [MDD 0.06].
If criteria are not met, do not approve.

C. ANKYLOSING SPONDYLITIS:
1. Medication must be prescribed by a CPMG or affiliated rheumatologist, and the patient has a diagnosis of ankylosing spondylitis or one of the following subtype diagnoses: spondyloarthritis (SpA), axial SpA, nonradiographic axial SpA, radiographic axial SpA, sacroiliitis, undifferentiated spondyloarthropathy, spondyloarthropathy, or enteropathic arthropathy.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to Amjevita, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria are met, approve at HICL indefinitely, max 2 pens/syringes per 28 days [MDD 0.06].
If criteria are not met, do not approve.

D. UVEITIS: All the following must be met:
1. Patient has a diagnosis of Uveitis, and medication is prescribed by a CPMG or affiliated rheumatologist or ophthalmologist.
2. Medication is not being used in combination with another biologic for the same indication.

3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. at least 1 DMARD, or the patient has documented high disease activity in which traditional DMARDs would not be suitable treatment
    b. Amjevita

If criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.12].
If criteria are not met, do not approve.

E. ULCERATIVE COLITIS AND CROHN'S DISEASE: All the following must be met:
1. Patient has a diagnosis of ulcerative colitis, Crohn's disease, or indeterminant colitis, and the medication is prescribed by, a CPMG or affiliated gastroenterologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Must meet the following based on age and indication, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Patients age 18 years or older with Crohn's disease, indeterminant colitis, or ulcerative colitis: Request must be for Amjevita, or the patient has a documented allergic reaction (excludes injection site reaction) to Amjevita.

       If criteria are met, approve at HICL x1 month, max 6 pens/syringes per 28 days (loading dose) [max qty 6; min ds 28], followed by 2 pens/syringes per 28 days indefinitely [MDD 0.06].
       If criteria are not met, do not approve.

    b. Patients between the age of 13 and 18 years of age with Crohn's disease or indeterminant colitis: Review based on medication requested:
        i. The request is for Amjevita: No additional criteria.

           If criteria are met, approve Amjevita indefinitely at HICL.
           If criteria are not met, do not approve.

        ii. The request is for a biosimilar other than Amjevita: do not approve.

        iii. The request is for Humira: Must meet one of the following:
            1. The patient has not received a full loading dose with adalimumab

               If criteria are met, approve Humira at HICL x 1 month, and Amjevita at HICL indefinitely.

If criteria are not met, do not approve.

2. The patient has a documented allergic reaction (excludes injection site reaction) to Amjevita.

If criteria are met, approve Humira indefinitely at HICL.
If criteria are not met, do not approve.

c. Patients under 13 years of age with Crohn's or indeterminant colitis: Review based on medication requested:
   i. The request is for Amjevita: No additional criteria.

   If criteria are met, approve Amjevita indefinitely at HICL.
   If criteria are not met, do not approve.

   ii. The request is for a biosimilar other than Amjevita: do not approve.

   iii. The request is for Humira: Must meet one of the following:
      1. The patient has not received a full loading dose with adalimumab

      If criteria are met, approve Humira at HICL x 1 month, and Amjevita at HICL indefinitely.
      If criteria are not met, do not approve.

      2. The patient requires maintenance dosing of 80mg weekly:

      If criteria are met, approve Humira at HICL until patient turns 13 years of age, and Amjevita at HICL indefinitely.
      If criteria are not met, do not approve.

      3. The patient has a documented allergic reaction (excludes injection site reaction) to Amjevita.

      If criteria are met, approve Humira indefinitely at HICL.
      If criteria are not met, do not approve.

d. Patients under 18 years of age with Ulcerative Colitis: No additional criteria.

   If criteria are met, approve Humira at HICL until the patient turns 18 years of age, and approve Amjevita at HICL indefinitely.
   If criteria are not met, do not approve.

F. PSORIASIS: All the following must be met:
   2. Patient has a diagnosis of moderate to severe psoriasis, and the medication is prescribed by a dermatology provider.
   3. Medication is not being used in combination with another biologic for the same indication.
   4. Patient with inadequate response (after at least two months of therapy), intolerance, or has a contraindication to, all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical

characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

a. One topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus). [If the patient is reported as having very high disease activity (ex: > 50% BSA, erythrodermic, pustular psoriasis) or disease affecting critical areas (ex: genitals, face), or prior biologic therapy within the past 4 months --skip and proceed to step 3c]
b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the below pre-biologic therapies: Acitretin, Cyclosporine, Methotrexate, Apremilast (Otezla), Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
c. Amjevita

If criteria are met, approve at HICL x1 month, max 4 pens/syringes per 28 days (loading dose) [max qty 4; min ds 28], then 2 pens/syringes per 28 days (maintenance dose) indefinitely [MDD 0.06].
If criteria are not met, do not approve.

G. HIDRADENITIS SUPPURATIVA (HS): All the following must be met:
1. Patient has a diagnosis of moderate to severe HS (Hurley stage II-III), and medication is prescribed by a CPMG or affiliated dermatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with inadequate response, intolerance, or contraindication to all of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. At least 3 of the following [medication trials can be within the same drug category], unless the patient is noted as Hurley Stage III, in which these therapies would not be suitable treatment:
      i. Oral antibiotic (8-week trial unless intolerance is documented)
      ii. Topical antibiotic (ex: clindamycin)
      iii. Oral retinoid (isotretinoin, acitretin)
      iv. Intralesional steroid
      v. Hormonal agent (ex: metformin, spironolactone, oral contraceptive for women)
      vi. Laser hair removal
      vii. Infliximab (Inflectra, Remicade, or other biosimilar) infusion
   b. Amjevita

      If criteria are met, approve at HICL x1 month, max 6 syringes/pens per 28 days (loading dose) [max qty 6; min ds 28], then 4 syringes/pens per 28 days indefinitely [MDD 0.12].
      If criteria are not met, do not approve.

H. Juvenile Idiopathic Arthritis (JIA): All the following must be met:

1. Patient has a diagnosis of JIA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. at least 1 DMARD
   b. Amjevita

If criteria are met, then approve at HICL indefinitely, max 2 pens/syringes per 28 days [MDD 0.06].
If criteria are not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member or Initial PA Criteria prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval.

A. Rheumatoid Arthritis (RA) or Psoriatic Arthritis (PsA)
B. Ulcerative Colitis (UC) or Crohn's Disease
C. Psoriasis
D. Hidradenitis Suppurativa (HS)

A. Patient diagnosis of RA or PsA:
   1. For requests to start on escalated doses (more than 2 pens/syringes per 28 days): Patient must have been on standard maintenance dose of 2 pens/syringes per 28 days for at least 3 months, and provider notes that drug effectiveness lasts only 7-14 days

      If met, approve max 4 pens/syringes per 28 days x1 year [MDD 0.12]
      If not met, deny and offer maximum 2 pens/syringes per 28 days indefinitely [MDD 0.06]

   2. For requests to continue escalated doses (more than 2 pens/syringes per 28 days): Patient must have been assessed by a rheumatologist in the last 1 year, and the rheumatologist evaluated if the dose can be de-escalated and determined that the escalated dose continues to be medically necessary

      If met, approve max 4 pens/syringes per 28 days x2 years [MDD 0.12]
      If not met, deny and offer maximum 2 pens/syringes per 28 days indefinitely [MDD 0.06]

B. Patient diagnosis of Ulcerative Colitis or Crohn's disease
   1. Documentation by gastroenterology provider of the patient resuming therapy after a gap 3 months or longer in treatment (to reload)

      If met, approve at HICL x 1 month, max 6 pens/syringes (loading dose) per 28 days, then 2 pens/syringes per 28 days indefinitely [MDD 0.06]
      If not met, deny and offer maximum 2 pens/syringes per 28 days indefinitely [MDD 0.06]

2. For requests to start on escalated doses (more than 2 pens/syringes per 28 days): Patient must have been on standard maintenance dose of 2 pens/syringes per 28 days with inadequate drug level (less than 12 mcg/mL).

   If met, approve at HICL x1 year, max 4 pens/syringes per 28 days [MDD 0.12]
   If not met, deny and offer maximum 2 pens/syringes per 28 days indefinitely [MDD 0.06]

3. For requests to continue escalated doses (more than 2 pens/syringes per 28 days): Patient must have been assessed by a gastroenterologist in the last 1 year, and the gastroenterologist evaluated if the dose can be de-escalated and determined that the escalated dose continues to be medically necessary

   If met, approve at HICL x2 years, max 4 pens/syringes per 28 days [MDD 0.12]
   If not met, deny and offer maximum 2 pens/syringes per 28 days indefinitely [MDD 0.06]

C. Patient diagnosis of Psoriasis:
   1. Documentation by dermatology provider of the patient resuming therapy after a gap 3 months or longer in treatment (to reload)

      If criteria are met, approve at HICL x1 month, max 4 pens/syringes per 28 days (loading dose), then 2 pens/syringes per 28 days (maintenance dose) indefinitely [MDD 0.06]
      If not met, deny and offer maximum 2 pens/syringes per 28 days indefinitely [MDD 0.06]

D. Patient diagnosis of Hidradenitis Suppurativa (HS):
   1. Documentation by dermatology provider of the patient resuming therapy after a gap 3 months or longer in treatment (to reload)

      If criteria are met, approve at HICL x1 month, max 6 syringes/pens per 28 days (loading dose), then 4 syringes/pens per 28 days (maintenance dose) indefinitely [MDD 0.12]
      If not met, deny and offer maximum 4 pens/syringes per 28 days indefinitely [MDD 0.12]

RATIONALE:
Compared with a reference product, biosimilars:
- Are made with the same types of living sources
- Are given to the patient in the same way
- Have the same strength, dosage, potential treatment benefits, and potential side effects

REGARDING STEP THERAPY:
Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

Step Therapy through preferred adalimumab product, Amjevita is based on interpretation of CO Revised Statute 10-16-145:

(5) THIS SECTION DOES NOT PROHIBIT:
(a) A CARRIER, AN ORGANIZATION, OR A PBM FROM REQUIRING A COVERED PERSON TO TRY A GENERIC EQUIVALENT DRUG, A BIOSIMILAR DRUG, OR AN INTERCHAGEABLE BIOLOGICAL PRODUCT AS DEFINED BY 42 U.S.C.SEC.262(i)(3), UNLESS THE COVERED PERSON OR COVERED PERSON'S PRESCRIBEING PROVIDER HAS REQUESTED A STEP-

THERAPY EXCEPTION AND THE PRESCIBED CRUG MEETS THE CRITERIA FOR A STEP-THERAPY EXCEPTION SPECIFIED IN SUBSECTION (4)(a) OF THIS SECTION;

When the brand and biosimilar do not share the same indication for pediatric patients [at time of writing: Uveitis, HS, and UC], if the provider requests brand, noting the formulary preferred biosimilar Amjevita does not have indication, criteria defined by "the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug" shall be considered met for coverage authorization.

FDA INDICATIONS:
Crohn disease, moderate to severe, induction and maintenance of remission (Humira and adalimumab biosimilars): Treatment of moderately to severely active Crohn disease in adults and pediatric patients ≥6 years of age.

Hidradenitis suppurativa, moderate to severe, refractory: Treatment of moderate to severe hidradenitis suppurativa in adults (Humira and adalimumab biosimilars [except Idacio]) and pediatric patients ≥12 years of age (Humira only).

Juvenile idiopathic arthritis (Humira and adalimumab biosimilars): Treatment (to reduce signs/symptoms) of active polyarticular juvenile idiopathic arthritis (moderate to severe) in pediatric patients ≥2 years of age; may be used alone or in combination with methotrexate.

Plaque psoriasis, moderate to severe (Humira and adalimumab biosimilars): Treatment of chronic plaque psoriasis (moderate to severe) in adults who are candidates for systemic therapy or phototherapy, and when other systemic therapies are less appropriate (with close monitoring and regular follow-up).

Rheumatoid arthritis (Humira and adalimumab biosimilars): Treatment (to reduce signs/symptoms, induce major clinical response, inhibit progression of structural damage, and improve physical function) of active rheumatoid arthritis (moderate to severe) in adults; may be used alone or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs).

Spondyloarthritis (Humira and adalimumab biosimilars):

> Axial spondyloarthritis (eg, ankylosing spondylitis): Treatment (to reduce signs/symptoms) of active ankylosing spondylitis in adults. May also be used off label for nonradiographic axial spondyloarthritis (ACR [Ward 2019]).
>
> Psoriatic arthritis: Treatment (to reduce signs/symptoms, inhibit progression of structural damage, and improve physical function) of psoriatic arthritis (a form of peripheral spondyloarthritis) in adults; may be used alone or in combination with nonbiologic DMARDs. May also be used off label for nonpsoriatic peripheral spondyloarthritis (eg, reactive arthritis, arthritis associated with inflammatory bowel disease) (Mease 2015; Paramarta 2013).

Ulcerative colitis, moderate to severe, induction and maintenance of remission: Treatment of moderately to severely active ulcerative colitis in adults (Humira and adalimumab biosimilars) and pediatric patients ≥5 years of age (Humira only). Note: Efficacy in patients intolerant of or no longer responsive to other tumor necrosis factor blockers has not been established.

Uveitis, noninfectious: Treatment of noninfectious intermediate, posterior, and panuveitis in adults (Humira and adalimumab biosimilars [except Idacio and Yuflyma]) and children ≥2 years of age (Humira only).

References:

1. Currently stable on medication means patient is tolerating well, appears to be effective and provider wishes to continue.
2. Biosimilars. Overview for Health Care Professionals. https://www.fda.gov/drugs/biosimilars/overview-health-care-professionals. Published 12/31/2022. Accessed 2/3/2023.

Treatment	Relative Contraindications in Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (ex: systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for psoriasis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Caution in women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*

Created: 01/2021
Effective: 04/2024
Reviewed: 11/2023
Revised: 11/2023

IBRUTINIB (IMBRUVICA)

Generic	Brand	HICL	GCN	Exception/Other
IBRUTINIB	IMBRUVICA 70MG, 140MG CAPSULES	40745	44475, 35599	Formulary
IBRUTINIB	IMBRUVICA TABLETS 420MG, 560MG	40745	44467, 44468	Formulary
IBRUTINIB	IMBRUVICA TABLETS 140MG, 280MG	40745	44465, 44466	Nonformulary
IBRUTINIB	IMBRUVICA ORAL SUSPENSION 70MG/ML	40745	52826	Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is a new member to KPCO within the past 90 days
2. Medication is prescribed by a CPMG or affiliated Oncologist
3. Request is for a formulary ibrutinib strength/formulation
4. Patient is stable on ibrutinib (Imbruvica) for treatment of one of the following indications: primary central nervous system (CNS) lymphoma, chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL), non-germinal center B cell (GCB) diffuse large B-cell lymphoma (DLBCL), hairy cell leukemia, or Waldenstrom macroglobulinemia

If New Member criteria are met, approve indefinitely at GPID only.
If New Member criteria are not met, review by Pediatric or Adult Initial Criteria based on patient age.

PEDIATRIC INITIAL CRITERIA: Must meet all the following:
1. Patient must be less than 18 years of age
2. Must be prescribed by a CPMG or affiliated Oncologist
3. Request must be for a formulary ibrutinib strength/formulation

If initial criteria are met, approve indefinitely at GPID.
If initial criteria are not met, do not approve.
- [If criteria are failed only because a non-formulary formulation/strength was requested, deny and proactively approve a formulary product in equivalent dosing as the alternative.]

ADULT INITIAL CRITERIA: Must meet all the following:
1. Patient must be age 18 or older
2. Must be prescribed by a CPMG or affiliated Oncologist
3. Request must be for a formulary ibrutinib strength/formulation
4. Must have one of the following indications:
   a. Patient has primary CNS lymphoma and has undergone at least 1 prior line of treatment
   b. Patient has chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL), or Waldenstrom macroglobulinemia and has CNS involvement of their disease
   c. Patient has a diagnosis of chronic graft versus host disease (GVHD) following allogeneic hematopoietic stem cell transplant (HSCT) and meets all the following:
      i. GVHD is not responsive to systemic corticosteroid treatment, or the patient is unable to taper systemic corticosteroids due to GVHD flares
      ii. Patient has tried and failed or did not tolerate ruxolitinib (Jakafi)
   d. Patient has diagnosis of non-germinal center B cell (GCB) diffuse large B-cell lymphoma (DLBCL), is not a transplant candidate, and has undergone at least 1 prior line of treatment

e. Patient has diagnosis of hairy cell leukemia and has undergone at least 2 prior lines of treatment

If initial criteria are met, approve indefinitely at GPID only.
If initial criteria are not met, do not approve.

- [If criteria are failed only because a non-formulary formulation/strength was requested, deny and proactively approve a formulary product in equivalent dosing as the alternative.]
- [If other criteria are not met, do not approve. Alternatives for GVHD include ruxolitinib (Jakafi), formulary steroids, formulary calcineurin inhibitors, imatinib (Gleevec), or formulary mycophenolate. Alternatives for CLL/SLL, or Waldenstrom macroglobulinemia include zanubrutinib (Brukinsa) or acalabrutinib (Calquence).]

RATIONALE
To promote evidence-based, cost-conscious use of oral BTK inhibitor therapy

Commercial formulary strengths/formulations:
Ibrutinib 70 mg capsules, 140 mg capsules, 420 mg tablets, 560 mg tablets

Commercial non-formulary strengths/formulations:
Ibrutinib 140 mg tablets, 280 mg tablets, Ibrutinib 70 mg/mL suspension

FDA APPROVED INDICATIONS
Ibrutinib: CLL/SLL, CLL/SLL with 17p deletion, WM, chronic GVHD after failure of one or more lines of systemic therapy

REFERENCES
1. NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers v.2.2021
2. NCCN Clinical Practice Guidelines in Oncology B-Cell Lymphomas v.4.2021
3. NCCN Clinical Practice Guidelines in Oncology Hairy Cell Leukemia v.1.2022
4. Imbruvica prescribing information. Pharmacyclics LLC. Sunnyvale, CA. 06/2023

Creation Date: 03/2022
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

ILOPERIDONE (FANAPT)

Generic	Brand	HICL	GCN/GPID	Exception/Other
ILOPERIDONE TABLET	FANAPT	36778		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO within the past 90 days and is stable on therapy.

If met, approve indefinitely at HICL.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient is at least 18 years of age and has a diagnosis of schizophrenia.
2. Documented contraindication, intolerance, or treatment failure to at least 1 antipsychotic, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If criteria are met, approve indefinitely, at HICL.
If criteria are not met, do not approve.

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ePA Questions
1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

FDA APPROVED INDICATIONS
Iloperidone (Fanapt)
- **Schizophrenia:** Treatment of adults with schizophrenia

APPENDIX A. Formulary antipsychotics

First-generation antipsychotics	Second-generation antipsychotics

Chlorpromazine	Aripiprazole
Fluphenazine	Clozapine
Haloperidol	Lurasidone
Loxapine	Olanzapine
Molindone	Quetiapine
Perphenazine	Risperidone
Pimozide	Ziprasidone
Thioridazine	
Thiothixene	
Trifluoperazine	

HOW SUPPLIED:
Iloperidone (Fanapt) tablet: 1 MG, 2 MG, 4 MG, 6 MG 8 MG, 10 MG AND 12 MG

REFERENCES
American Psychiatric Association. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. 3rd ed. Washington, DC: American Psychiatric Association; 2021.

Fanapt. Package insert. Vanda Pharmaceuticals, Inc.; September 9, 2021.

Creation Date: 3/2023
Effective Date: 4/2024
Reviewed Date: 3/2024
Revised Date: 3/2024

IMMUNE GLOBULIN (HUMAN)/HYALURONIDASE SUBCUTANEOUS

Generic	Brand	HICL	GCN	Exception/Other
IMMUNE GLOBULIN (HUMAN)/HYALURONIDASE SUBCUTANEOUS	HYQVIA	41391		

GUIDELINES FOR USE

Must meet ALL the following:
1. Must not be administered in a medical office or infusion center
2. Must be self-administered within a home setting
3. Patient must have trial and failure of, intolerance, or contraindication to Hizentra

If the above are met then approve x 1 year.
If the above are not met, do not approve.

RATIONALE
Per Health Plan.

FDA APPROVED INDICATIONS
Treatment of primary humoral immunodeficiency syndromes (congenital agammaglobulinemia, severe combined immunodeficiency syndromes [SCIDS], common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome)

REFERENCES
Per Health Plan.

Creation date: 09/2018
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

INHALED CORTICOSTEROID (ICS) INHALERS
BECLOMETHASONE REDIHALER

Generic name	Brand name	HICL	GPID	Comments
BECLOMETHASONE DIPROPIONATE	QVAR REDIHALER		43724, 43725	

GUIDELINES FOR COVERAGE

A. Criteria for patients 5 years of age or older
B. Criteria for patients under 5 years of age

A. Medication is requested for the maintenance treatment of patient 5 years of age or older with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Alvesco HFA, and/or Asmanex, and/or Pulmicort Flexhaler.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

B. Medication is requested for the maintenance treatment of patient under 5 years of age with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Flovent HFA 44 mcg and/or Asmanex HFA or Twisthaler.

If criteria are met, approve at HICL until the patient turns 5 years of age.
If criteria are not met, do not approve.

RATIONALE

Although the ICSs exert their therapeutic effects through identical mechanisms of action, they differ in their potency, dosing schedules, and dosage form availability. Numerous placebo controlled trials have demonstrated the efficacy of ICS agents in the treatment of asthma, and these agents are considered the most effective agents in the long-term management of the disease. The results of head-to-head trials directly comparing the ICS products have not demonstrated one agent to be significantly more effective than another, regardless of the potency or dosage form of the ICS agent used.

Alvesco (ciclesonide) HFA (1st line) and Asmanex (mometasone) HFA (2nd line step-therapy criteria) are KPCO formulary ICS inhalers for age 5 years and older. Although FDA approved for age 12 years and older, use of Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference. Flovent HFA 44 mcg inhaler and budesonide nebulized solution are formulary for age < 5 years of age.

FDA APPROVED INDICATIONS
All ICS inhalers are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone (QVAR®) and fluticasone propionate (Flovent Diskus®, Flovent HFA®) are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.

GENERIC NAME	BRAND NAME	FORMULARY	FDA APPROVED AGE
ciclesonide	Alvesco HFA	F	12 years and older*
mometasone furoate	Asmanex HFA	F with step-therapy	5 years and older
fluticasone propionate	Flovent HFA 44 mcg	F (age restriction^: < 5 years older)	4 years and older
mometasone furoate	Asmanex Twisthaler	F with PA	4 years and older
budesonide	Pulmicort Flexhaler	NF with PA	6 years and older
fluticasone propionate	Flovent HFA 110 mcg and 220 mcg	NF with PA	12 years and older
fluticasone propionate	Flovent Diskus	NF with PA	4 years and older
fluticasone propionate	ArmonAir Digihaler	NF with PA	12 years and older
fluticasone furoate	Arnuity Ellipta	NF with PA	5 years and older
beclomethasone dipropionate	Qvar Redihaler	NF with PA	4 years and older
*Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference ^Flovent HFA 44 mcg inhaler has age-restriction criteria and adjudicates for benefit for patients < 5 years of age only.			

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INHALED CORTICOSTEROID (ICS) INHALERS
BUDESONIDE FLEXHALER

Generic name	Brand name	HICL	GPID	Comments
BUDESONIDE	PULMICORT FLEXHALER		98024, 98025	

GUIDELINES FOR COVERAGE

A. Medication is requested for the maintenance treatment of patient 5 years of age or older with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Alvesco HFA and/or Asmanex.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Although the ICSs exert their therapeutic effects through identical mechanisms of action, they differ in their potency, dosing schedules, and dosage form availability. Numerous placebo controlled trials have demonstrated the efficacy of ICS agents in the treatment of asthma, and these agents are considered the most effective agents in the long-term management of the disease. The results of head-to-head trials directly comparing the ICS products have not demonstrated one agent to be significantly more effective than another, regardless of the potency or dosage form of the ICS agent used.

Alvesco (ciclesonide) HFA (1st line) and Asmanex (mometasone) HFA (2nd line step-therapy criteria) are KPCO formulary ICS inhalers for age 5 years and older. Although FDA approved for age 12 years and older, use of Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference. Flovent HFA 44 mcg inhaler and budesonide nebulized solution are formulary for age < 5 years of age.

FDA APPROVED INDICATIONS
All ICS inhalers are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone (QVAR®) and fluticasone propionate (Flovent Diskus®, Flovent HFA®) are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.

GENERIC NAME	BRAND NAME	FORMULARY	FDA APPROVED AGE
ciclesonide	Alvesco HFA	F	12 years and older*
mometasone furoate	Asmanex HFA	F with step-therapy	5 years and older

fluticasone propionate	Flovent HFA 44 mcg	F (age restriction^: < 5 years older)	4 years and older
mometasone furoate	Asmanex Twisthaler	F with PA	4 years and older
budesonide	Pulmicort Flexhaler	NF with PA	6 years and older
fluticasone propionate	Flovent HFA 110 mcg and 220 mcg	NF with PA	12 years and older
fluticasone propionate	Flovent Diskus	NF with PA	4 years and older
fluticasone propionate	ArmonAir Digihaler	NF with PA	12 years and older
fluticasone furoate	Arnuity Ellipta	NF with PA	5 years and older
beclomethasone dipropionate	Qvar Redihaler	NF with PA	4 years and older
*Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference ^Flovent HFA 44 mcg inhaler has age-restriction criteria and adjudicates for benefit for patients < 5 years of age only.			

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INHALED CORTICOSTEROID (ICS) INHALERS
FLUTICASONE DIGIHALER

Generic name	Brand name	HICL	GPID	Comments
FLUTICASONE PROPIONATE	ARMONAIR DIGIHALER		48602, 48604, 48615	

GUIDELINES FOR COVERAGE

A. Medication is requested for the maintenance treatment of patient 5 years of age or older with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Alvesco HFA, and/or Asmanex, and/or Pulmicort Flexhaler.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Although the ICSs exert their therapeutic effects through identical mechanisms of action, they differ in their potency, dosing schedules, and dosage form availability. Numerous placebo controlled trials have demonstrated the efficacy of ICS agents in the treatment of asthma, and these agents are considered the most effective agents in the long-term management of the disease. The results of head-to-head trials directly comparing the ICS products have not demonstrated one agent to be significantly more effective than another, regardless of the potency or dosage form of the ICS agent used.

Alvesco (ciclesonide) HFA (1st line) and Asmanex (mometasone) HFA (2nd line step-therapy criteria) are KPCO formulary ICS inhalers for age 5 years and older. Although FDA approved for age 12 years and older, use of Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference. Flovent HFA 44 mcg inhaler and budesonide nebulized solution are formulary for age < 5 years of age.

FDA APPROVED INDICATIONS
All ICS inhalers are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone (QVAR®) and fluticasone propionate (Flovent Diskus®, Flovent HFA®) are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.

GENERIC NAME	BRAND NAME	FORMULARY	FDA APPROVED AGE
ciclesonide	Alvesco HFA	F	12 years and older*
mometasone furoate	Asmanex HFA	F with step-therapy	5 years and older

fluticasone propionate	Flovent HFA 44 mcg	F (age restriction^: < 5 years older)	4 years and older
mometasone furoate	Asmanex Twisthaler	F with PA	4 years and older
budesonide	Pulmicort Flexhaler	NF with PA	6 years and older
fluticasone propionate	Flovent HFA 110 mcg and 220 mcg	NF with PA	12 years and older
fluticasone propionate	Flovent Diskus	NF with PA	4 years and older
fluticasone propionate	ArmonAir Digihaler	NF with PA	12 years and older
fluticasone furoate	Arnuity Ellipta	NF with PA	5 years and older
beclomethasone dipropionate	Qvar Redihaler	NF with PA	4 years and older
*Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference ^Flovent HFA 44 mcg inhaler has age-restriction criteria and adjudicates for benefit for patients < 5 years of age only.			

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INHALED CORTICOSTEROID (ICS) INHALERS
FLUTICASONE DISKUS

Generic name	Brand name	HICL	GPID	Comments
FLUTICASONE PROPIONATE	FLOVENT DISKUS		53633, 53634, 53635	

GUIDELINES FOR COVERAGE

A. Criteria for patients 5 years of age or older
B. Criteria for patients under 5 years of age

A. Medication is requested for the maintenance treatment of patient 5 years of age or older with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Alvesco HFA, and/or Asmanex, and/or Pulmicort Flexhaler.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

B. Medication is requested for the maintenance treatment of patient under 5 years of age with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Flovent HFA 44 mcg and/or Asmanex HFA or Twisthaler.

If criteria are met, approve at HICL until the patient turns 5 years of age.
If criteria are not met, do not approve.

RATIONALE

Although the ICSs exert their therapeutic effects through identical mechanisms of action, they differ in their potency, dosing schedules, and dosage form availability. Numerous placebo controlled trials have demonstrated the efficacy of ICS agents in the treatment of asthma, and these agents are considered the most effective agents in the long-term management of the disease. The results of head-to-head

trials directly comparing the ICS products have not demonstrated one agent to be significantly more effective than another, regardless of the potency or dosage form of the ICS agent used.

Alvesco (ciclesonide) HFA (1st line) and Asmanex (mometasone) HFA (2nd line step-therapy criteria) are KPCO formulary ICS inhalers for age 5 years and older. Although FDA approved for age 12 years and older, use of Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference. Flovent HFA 44 mcg inhaler and budesonide nebulized solution are formulary for age < 5 years of age.

FDA APPROVED INDICATIONS
All ICS inhalers are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone (QVAR®) and fluticasone propionate (Flovent Diskus®, Flovent HFA®) are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.

GENERIC NAME	BRAND NAME	FORMULARY	FDA APPROVED AGE
ciclesonide	Alvesco HFA	F	12 years and older*
mometasone furoate	Asmanex HFA	F with step-therapy	5 years and older
fluticasone propionate	Flovent HFA 44 mcg	F (age restriction^: < 5 years older)	4 years and older
mometasone furoate	Asmanex Twisthaler	F with PA	4 years and older
budesonide	Pulmicort Flexhaler	NF with PA	6 years and older
fluticasone propionate	Flovent HFA 110 mcg and 220 mcg	NF with PA	12 years and older
fluticasone propionate	Flovent Diskus	NF with PA	4 years and older
fluticasone propionate	ArmonAir Digihaler	NF with PA	12 years and older
fluticasone furoate	Arnuity Ellipta	NF with PA	5 years and older
beclomethasone dipropionate	Qvar Redihaler	NF with PA	4 years and older
*Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference ^Flovent HFA 44 mcg inhaler has age-restriction criteria and adjudicates for benefit for patients < 5 years of age only.			

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INHALED CORTICOSTEROID (ICS) INHALERS
FLUTICASONE FUROATE ELLIPTA

Generic name	Brand name	HICL	GPID	Comments
FLUTICASONE FUROATE	ARNUITY ELLIPTA		37007, 37008, 44783	

GUIDELINES FOR COVERAGE

A. Medication is requested for the maintenance treatment of patient 5 years of age or older with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Alvesco HFA, and/or Asmanex, and/or Pulmicort Flexhaler.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Although the ICSs exert their therapeutic effects through identical mechanisms of action, they differ in their potency, dosing schedules, and dosage form availability. Numerous placebo controlled trials have demonstrated the efficacy of ICS agents in the treatment of asthma, and these agents are considered the most effective agents in the long-term management of the disease. The results of head-to-head trials directly comparing the ICS products have not demonstrated one agent to be significantly more effective than another, regardless of the potency or dosage form of the ICS agent used.

Alvesco (ciclesonide) HFA (1st line) and Asmanex (mometasone) HFA (2nd line step-therapy criteria) are KPCO formulary ICS inhalers for age 5 years and older. Although FDA approved for age 12 years and older, use of Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference. Flovent HFA 44 mcg inhaler and budesonide nebulized solution are formulary for age < 5 years of age.

FDA APPROVED INDICATIONS
All ICS inhalers are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone (QVAR®) and fluticasone propionate (Flovent Diskus®, Flovent HFA®) are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.

GENERIC NAME	BRAND NAME	FORMULARY	FDA APPROVED AGE
ciclesonide	Alvesco HFA	F	12 years and older*
mometasone furoate	Asmanex HFA	F with step-therapy	5 years and older

fluticasone propionate	Flovent HFA 44 mcg	F (age restriction^: < 5 years older)	4 years and older
mometasone furoate	Asmanex Twisthaler	F with PA	4 years and older
budesonide	Pulmicort Flexhaler	NF with PA	6 years and older
fluticasone propionate	Flovent HFA 110 mcg and 220 mcg	NF with PA	12 years and older
fluticasone propionate	Flovent Diskus	NF with PA	4 years and older
fluticasone propionate	ArmonAir Digihaler	NF with PA	12 years and older
fluticasone furoate	Arnuity Ellipta	NF with PA	5 years and older
beclomethasone dipropionate	Qvar Redihaler	NF with PA	4 years and older
*Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference ^Flovent HFA 44 mcg inhaler has age-restriction criteria and adjudicates for benefit for patients < 5 years of age only.			

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INHALED CORTICOSTEROID (ICS) INHALERS
FLUTICASONE HFA

Generic name	Brand name	HICL	GPID	Comments
FLUTICASONE PROPIONATE	FLOVENT HFA (110 MCG AND 220 MCG ONLY)		53636, 53639	44 mcg formulary for age < 5 years

GUIDELINES FOR COVERAGE

A. Criteria for patients 5 years of age or older
B. Criteria for patients under 5 years of age

A. Medication is requested for the maintenance treatment of patient 5 years of age or older with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Alvesco HFA, and/or Asmanex, and/or Pulmicort Flexhaler.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

B. Medication is requested for the maintenance treatment of patient under 5 years of age with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Request is for Flovent HFA 110 mcg or 220 mcg: Patient has tried and failed, or has an intolerance or a contraindication to, Flovent HFA 44 mcg

If criteria are met, approve at HICL until the patient turns 5 years of age.
If criteria are not met, do not approve.

RATIONALE

Although the ICSs exert their therapeutic effects through identical mechanisms of action, they differ in their potency, dosing schedules, and dosage form availability. Numerous placebo controlled trials have demonstrated the efficacy of ICS agents in the treatment of asthma, and these agents are considered the most effective agents in the long-term management of the disease. The results of head-to-head

trials directly comparing the ICS products have not demonstrated one agent to be significantly more effective than another, regardless of the potency or dosage form of the ICS agent used.

Alvesco (ciclesonide) HFA (1st line) and Asmanex (mometasone) HFA (2nd line step-therapy criteria) are KPCO formulary ICS inhalers for age 5 years and older. Although FDA approved for age 12 years and older, use of Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference. Flovent HFA 44 mcg inhaler and budesonide nebulized solution are formulary for age < 5 years of age.

FDA APPROVED INDICATIONS
All ICS inhalers are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone (QVAR®) and fluticasone propionate (Flovent Diskus®, Flovent HFA®) are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.

GENERIC NAME	BRAND NAME	FORMULARY	FDA APPROVED AGE
ciclesonide	Alvesco HFA	F	12 years and older*
mometasone furoate	Asmanex HFA	F with step-therapy	5 years and older
fluticasone propionate	Flovent HFA 44 mcg	F (age restriction^: < 5 years older)	4 years and older
mometasone furoate	Asmanex Twisthaler	F with PA	4 years and older
budesonide	Pulmicort Flexhaler	NF with PA	6 years and older
fluticasone propionate	Flovent HFA 110 mcg and 220 mcg	NF with PA	12 years and older
fluticasone propionate	Flovent Diskus	NF with PA	4 years and older
fluticasone propionate	ArmonAir Digihaler	NF with PA	12 years and older
fluticasone furoate	Arnuity Ellipta	NF with PA	5 years and older
beclomethasone dipropionate	Qvar Redihaler	NF with PA	4 years and older
*Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference ^Flovent HFA 44 mcg inhaler has age-restriction criteria and adjudicates for benefit for patients < 5 years of age only.			

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INHALED CORTICOSTEROID (ICS) INHALERS
MOMETASONE HFA

Generic name	Brand name	HICL	GPID	Comments
MOMETASONE FUROATE	ASMANEX HFA		37566, 37565, 47599	

GUIDELINES FOR COVERAGE

A. Criteria for patients 5 years of age or older
B. Criteria for patients under 5 years of age

A. Medication is requested for the maintenance treatment of patient 5 years of age or older with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient has tried and failed, or has an intolerance or a contraindication to, Alvesco HFA

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

B. Medication is requested for the maintenance treatment of patient under 5 years of age with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient has tried and failed, or has an intolerance or a contraindication to, Flovent HFA 44 mcg

If criteria are met, approve at HICL until the patient turns 5 years of age.
If criteria are not met, do not approve.

RATIONALE

Although the ICSs exert their therapeutic effects through identical mechanisms of action, they differ in their potency, dosing schedules, and dosage form availability. Numerous placebo controlled trials have demonstrated the efficacy of ICS agents in the treatment of asthma, and these agents are considered the most effective agents in the long-term management of the disease. The results of head-to-head trials directly comparing the ICS products have not demonstrated one agent to be significantly more effective than another, regardless of the potency or dosage form of the ICS agent used.

Alvesco (ciclesonide) HFA (1st line) and Asmanex (mometasone) HFA (2nd line step-therapy criteria) are KPCO formulary ICS inhalers for age 5 years and older. Although FDA approved for age 12 years and older, use of Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference. Flovent HFA 44 mcg inhaler and budesonide nebulized solution are formulary for age < 5 years of age.

FDA APPROVED INDICATIONS
All ICS inhalers are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone (QVAR®) and fluticasone propionate (Flovent Diskus®, Flovent HFA®) are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.

GENERIC NAME	BRAND NAME	FORMULARY	FDA APPROVED AGE
ciclesonide	Alvesco HFA	F	12 years and older*
mometasone furoate	Asmanex HFA	F with step-therapy	5 years and older
fluticasone propionate	Flovent HFA 44 mcg	F (age restriction^: < 5 years older)	4 years and older
mometasone furoate	Asmanex Twisthaler	F with PA	4 years and older
budesonide	Pulmicort Flexhaler	NF with PA	6 years and older
fluticasone propionate	Flovent HFA 110 mcg and 220 mcg	NF with PA	12 years and older
fluticasone propionate	Flovent Diskus	NF with PA	4 years and older
fluticasone propionate	ArmonAir Digihaler	NF with PA	12 years and older
fluticasone furoate	Arnuity Ellipta	NF with PA	5 years and older
beclomethasone dipropionate	Qvar Redihaler	NF with PA	4 years and older
*Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference ^Flovent HFA 44 mcg inhaler has age-restriction criteria and adjudicates for benefit for patients < 5 years of age only.			

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INHALED CORTICOSTEROID (ICS) INHALERS
MOMETASONE TWISTHALER

Generic name	Brand name	HICL	GPID	Comments
MOMETASONE FUROATE	ASMANEX TWISTHALER		99721, 18987, 24928, 24929	Formulary

GUIDELINES FOR COVERAGE

A. Criteria for patients 5 years of age or older
B. Criteria for patients under 5 years of age

A. Medication is requested for the maintenance treatment of patient 5 years of age or older with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient must have tried and failed, or has an intolerance or a contraindication to, Alvesco HFA and/or Asmanex HFA.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

B. Medication is requested for the maintenance treatment of patient under 5 years of age with asthma or other indication(s) supported in the CMS approved compendia and meets the following medication-specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug:
    1. Patient has tried and failed, or has an intolerance or a contraindication to, Flovent HFA 44 mcg

If criteria are met, approve at HICL until the patient turns 5 years of age.
If criteria are not met, do not approve.

RATIONALE

Although the ICSs exert their therapeutic effects through identical mechanisms of action, they differ in their potency, dosing schedules, and dosage form availability. Numerous placebo controlled trials have demonstrated the efficacy of ICS agents in the treatment of asthma, and these agents are considered the most effective agents in the long-term management of the disease. The results of head-to-head

trials directly comparing the ICS products have not demonstrated one agent to be significantly more effective than another, regardless of the potency or dosage form of the ICS agent used.

Alvesco (ciclesonide) HFA (1st line) and Asmanex (mometasone) HFA (2nd line step-therapy criteria) are KPCO formulary ICS inhalers for age 5 years and older. Although FDA approved for age 12 years and older, use of Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference. Flovent HFA 44 mcg inhaler and budesonide nebulized solution are formulary for age < 5 years of age.

FDA APPROVED INDICATIONS
All ICS inhalers are FDA approved for the maintenance treatment of asthma as prophylactic therapy. Beclomethasone (QVAR®) and fluticasone propionate (Flovent Diskus®, Flovent HFA®) are also indicated for use in asthma patients who require systemic corticosteroid therapy when the addition of an ICS could reduce or eliminate the need for systemic corticosteroids.

GENERIC NAME	BRAND NAME	FORMULARY	FDA APPROVED AGE
ciclesonide	Alvesco HFA	F	12 years and older*
mometasone furoate	Asmanex HFA	F with step-therapy	5 years and older
fluticasone propionate	Flovent HFA 44 mcg	F (age restriction^: < 5 years older)	4 years and older
mometasone furoate	Asmanex Twisthaler	F with PA	4 years and older
budesonide	Pulmicort Flexhaler	NF with PA	6 years and older
fluticasone propionate	Flovent HFA 110 mcg and 220 mcg	NF with PA	12 years and older
fluticasone propionate	Flovent Diskus	NF with PA	4 years and older
fluticasone propionate	ArmonAir Digihaler	NF with PA	12 years and older
fluticasone furoate	Arnuity Ellipta	NF with PA	5 years and older
beclomethasone dipropionate	Qvar Redihaler	NF with PA	4 years and older
*Alvesco HFA in pediatric patients, age 5 to 11 years of age, is strongly supported by evidence from clinical trials; and it is recommended by both the GINA asthma guidelines and the 2012 NAEPP Asthma Care Quick Reference ^Flovent HFA 44 mcg inhaler has age-restriction criteria and adjudicates for benefit for patients < 5 years of age only.			

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INPEN SMART INSULIN PEN DEVICE

Generic	Brand	HICL	GPID	Comments
INSULIN ADMINISTRATION DEVICE	INPEN SMART INSULIN PEN	20334	94200	

GUIDELINES FOR COVERAGE

Must meet all the following criteria:
1. Patient has a diagnosis of type 1 diabetes.
2. Must be prescribed by an Endocrinologist.
3. Prescriber has documented a need for detailed electronic monitoring of the patient's insulin dose administered and time of administration.
4. The patient will be using InPen with Humalog, Novolog, or Fiasp U-100 insulin only.

If all criteria above are met, approve at NDC-9 level indefinitely, maximum quantity of 1 per 365 days.
If criteria are not met, do not approve.

RATIONALE

InPen is the only FDA-cleared smart insulin pen system that combines a reusable Bluetooth-enabled insulin pen and mobile app. InPen is a prescription-only product that records insulin injections and recommends doses based on current blood glucose, insulin dose, and current active insulin. The pen injector is compatible with Lily Humalog U-100 3 mL cartridges (KP preferred), Novo Nordisk U-100 3 mL cartridges, and Novo Nordisk Fiasp U-100 3 mL cartridges. The pen injector allows the user to dial the desired dose from 0.5 to 30 units in one-half unit increments. The InPen system is not intended for anyone unable or unwilling to test blood glucose (BG) levels as recommended by a healthcare provider, maintain sufficient diabetes self-care skills, or visit a healthcare provider regularly. InPen is not recommended for the blind or visually impaired without the assistance of a sighted individual with appropriate training.

Creation Date: 05/2021
Effective Date: 12/2023
Reviewed Date: 11/2023
Revised Date: 11/2023

INSULIN DEGLUDEC

Generic	Brand	HICL	GCN	Exception/Other
INSULIN DEGLUDEC	TRESIBA U-100 VIALS TRESIBA FLEXTOUCH U-100 TRESIBA FLEXTOUCH U-200	40844	42785, 35836, 35837	
INSULIN DEGLUDEC	INSULIN DEGLUDEC U-100 VIALS INSULIN DEGLUDEC U-100 PEN INSULIN DEGLUDEC U-200 PEN	40844	42785, 35836, 35837	73070040011 73070040315 73070050315

GUIDELINES FOR COVERAGE

A) To Treat DIABETES TYPE 1: Must meet below criteria based on requested dosage form:

1. U-100 VIALS: Patient has failed glargine U-100 due to adverse drug reaction/intolerance that is not expected to occur with the requested agent or due to significant hypoglycemia (fingerstick < 70 ml/dL) despite appropriate insulin management (i.e., basal insulin, bolus/mealtime insulin, hypoglycemia management), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If met, approve generic degludec vials at NDC-9 (73070040011) indefinitely.
   If criteria are not met, do not approve.

2. U-100 PENS: Must meet a or b, plus c:
   a) Prescription is written by an Endocrinology specialist
   b) Either the patient is under 18 years of age, or the patient is 18 years or older and unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination
   c) Patient has failed glargine U-100 due to adverse drug reaction/intolerance that is not expected to occur with the requested agent or due to significant hypoglycemia (fingerstick < 70 ml/dL) despite appropriate insulin management (i.e., basal insulin, bolus/mealtime insulin, hypoglycemia management), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve generic degludec pen at NDC-9 (73070040315) indefinitely.
      If criteria are not met, do not approve.

3. U-200 PENS: Must meet the following criteria:

a) Patient's long-acting insulin (including NPH) dose is 100 units/day or more, but their total daily dose of insulin (basal + bolus) does NOT exceed 200 units/day or 2 units/kg/day

If met, approve generic degludec U-200 pen at NDC-9 (73070050315) for 2 years.
If not met, do not approve.

B) To Treat DIABETES TYPE 2: Must meet below criteria based on requested dosage form:

1. U-100 VIALS: Must meet the following criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a) Patient has failed NPH due to adverse drug reaction/intolerance that is not expected to occur with the requested agent or significant hypoglycemia (fingerstick < 70 ml/dL) despite appropriate insulin management (i.e., basal insulin, bolus/mealtime insulin, hypoglycemia management)
   b) Patient has failed glargine U-100 due to adverse drug reaction/intolerance that is not expected to occur with the requested agent or significant hypoglycemia (fingerstick < 70 ml/dL) despite appropriate insulin management (i.e., basal insulin, bolus/mealtime insulin, hypoglycemia management)

   If criteria are met, approve generic degludec vials at NDC-9 (73070040011) indefinitely.
   If criteria are not met, do not approve.

2. U-100 PENS: Must meet a or b, plus step-therapy criteria from both c and d unless the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:::
   a) Prescription is written by an Endocrinology specialist
   b) Either the patient is under 18 years of age, or the patient is 18 years or older and unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination
   c) Patient must fail NPH due to adverse drug reaction/intolerance that is not expected to occur with the requested agent or significant hypoglycemia (fingerstick < 70 ml/dL) despite appropriate insulin management (i.e., basal insulin, bolus/mealtime insulin, hypoglycemia management)
   d) Patient has failed glargine U-100 due to adverse drug reaction/intolerance that is not expected to occur with the requested agent or significant hypoglycemia (fingerstick < 70 ml/dL) despite appropriate insulin management (i.e., basal insulin, bolus/mealtime insulin, hypoglycemia management)

   If criteria are met, approve generic degludec pen at NDC-9 (73070040315) indefinitely.
   If criteria are not met, do not approve.

3. U-200 PENS: Must meet the following criteria:
   a) Patient's long-acting insulin (including NPH) dose is 100 units/day or more, but their total daily dose of insulin (basal + bolus) does NOT exceed 200 units/day or 2 units/kg/day

      If met, approve generic degludec U-200 pen at NDC-9 (73070050315) for 2 years.
      If not met, do not approve.

RENEWAL CRITERIA
Request for U-200 pens: Patient's long-acting insulin dose exceeds 100 units/day but their total daily dose of insulin (basal + bolus) does NOT exceed 200 units/day or 2 units/kg/day

If met, approve generic degludec at NDC-9 (73070050315) for 2 years.
If not met, do not approve.

RATIONALE
Insulin degludec is an ultra-long acting insulin available in 2 concentrations (U-100 and U-200) and 2 dosage forms (vials and pens). Degludec vial is available only in U-100 concentration. Single-patient-use FlexTouch pens are available in 2 concentrations. FlexTouch U-100 pen contains 300 units, delivers doses in 1 unit increments and can deliver up to 80 units in a single injection**.** FlexTouch U-200 pen contains 600 units, delivers doses in 2 unit increments and can deliver up to 160 units in a single injection. Brand insulin degludec (Tresiba) is excluded from coverage and only unbranded insulin degludec is available for coverage. Unbranded biologic products are identical, including inactive ingredients, to the branded drug product and are packaged and marketed by the brand manufacturer but without the brand name on the label/package.

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. NPH and insulin glargine are preferred based on their efficacy and safety profiles, as well as their competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for patients age < 18 years and patients with physical and/or cognitive impairment.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

INSULIN DETEMIR

Generic	Brand	HICL	GCN	Exception/Other
INSULIN DETEMIR	LEVEMIR VIAL		25305	
INSULIN DETEMIR	LEVEMIR FLEXTOUCH PEN		22836	

GUIDELINES FOR COVERAGE

A) To Treat DIABETES TYPE 1: Must meet criteria based on requested dosage form:
1. VIALS: Patient has failed glargine U-100 due to adverse drug reaction/intolerance that is not expected to occur with the requested agent, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If met, approve detemir vials at GPID indefinitely.
   If above criteria are not met, do not approve.

2. PENS: Must meet a or b, plus step-therapy criteria in c:
   a) Prescription is written by an Endocrinology specialist
   b) Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination
   c) Patient has failed glargine U-100 due to adverse drug reaction/intolerance that is not expected to occur with the requested agent, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If above criteria are met, approve detemir pen at GPID indefinitely.
   If above criteria are not met, do not approve.

B) To Treat DIABETES TYPE 2: Must meet below criteria based on requested dosage form:
1. VIALS: Must meet all the following criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

a) Patient has failed NPH either due to adverse drug reaction/intolerance that is not expected to occur with the requested agent or significant hypoglycemia (fingerstick < 70 ml/dL) despite appropriate insulin management (i.e., basal insulin, bolus/mealtime insulin, hypoglycemia management)
b) Patient has failed glargine U-100 due to adverse drug reaction/intolerance that is not expected to occur with the requested agent

If above criteria are met, approve detemir vials at GPID indefinitely.
If above criteria are not met, do not approve.

2. PENS: Must meet either a or b, plus step-therapy criteria from c and d unless the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a) Prescription is written by an Endocrinology specialist
   b) Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination
   c) Patient has failed NPH either due to adverse drug reaction/intolerance that is not expected to occur with the requested agent or significant hypoglycemia (fingerstick < 70 ml/dL) despite appropriate insulin management (i.e., basal insulin, bolus/mealtime insulin, hypoglycemia management)
   d) Patient has failed glargine U-100 due to adverse drug reaction/intolerance that is not expected to occur with the requested agent

   If above criteria are met, approve detemir pen at GPID indefinitely.
   If above criteria are not met, do not approve.

RATIONALE
There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. NPH insulin and insulin glargine are preferred over detemir based on their efficacy and safety profiles, as well as their competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for patients age < 18 years and patients with physical and/or cognitive impairment.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 7/2021
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

INSULIN GLARGINE 100u/ml PEN

Generic	Brand	HICL	GCN	Other
INSULIN GLARGINE	LANTUS SOLOSTAR, BASAGLAR KWIKPEN, BASAGLAR TEMPO PEN		98637	NF

GUIDELINES FOR COVERAGE

INITIAL CRITERIA

A. To Treat DIABETES TYPE 1: Must meet below criteria based on requested dosage form and/or brand:

1. PENS

    a) Must meet i AND either ii or iii, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        i. Patient has documented allergic reaction or injection site reaction to insulin glargine-yfgn
        ii. Prescription is written by an Endocrinology specialist
        iii. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination.

    If above initial criteria are met, then approve indefinitely.
    If above initial criteria are not met, do not approve.
    [NOTE: Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable, and biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente.]

B. To Treat DIABETES TYPE 2: Must meet below criteria based on requested dosage form and/or brand:

1. PENS

    a) Must meet i AND either ii or iii, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        i. Patient has documented allergic reaction or injection site reaction to insulin glargine-yfgn
        ii. Prescription is written by an Endocrinology specialist

iii. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination

If above initial criteria are met, approve indefinitely.
If above initial criteria are not met, do not approve.
[NOTE: Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente.]

RATIONALE
There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin glargine-yfgn is preferred (vial - formulary without PA) based on its efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for patients with physical and/or cognitive impairment.

Toujeo is a unique concentrated insulin glargine, available in a single concentration of 300 units/ml. It comes in 2 single-patient-use prefilled Solostar pens: 1.5-mL pen (450 units/1.5 mL) which can deliver up to 80 units per injection, and a 3-mL Max pen (900 units/3 mL)) which can deliver up to 160 units per injection. Toujeo Solostar pen is an option for patients requiring insulin doses between 100 and 200 units/day.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation Date: 2016-2017
Effective Date: 01/01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INSULIN GLARGINE 300u/ml PEN

Generic	Brand	HICL	GCN	Other
INSULIN GLARGINE	TOUJEO SOLOSTAR PEN U-300		37988	NF
INSULIN GLARGINE	TOUJEO MAX SOLOSTAR PEN U-300		44561	NF

GUIDELINES FOR COVERAGE

INITIAL CRITERIA

A. To Treat DIABETES TYPE 1: Must meet below criteria based on requested dosage form and/or brand:

1. PENS

   a) Must meet the following criteria:
      i. Patient's long-acting insulin dose is 100 units/day or more, but their total daily dose of insulin (basal + bolus) does NOT exceed 200 units/day or 2 units/kg/day
      ii. Patient must have tried and failed, have a contraindication to or an intolerance to insulin degludec U-200 [unbranded insulin degludec is preferred NF, PA]

   If above initial criteria are met, approve at GPID for 2 years.
   If above initial criteria are not met, do not approve.

B. To Treat DIABETES TYPE 2: Must meet below criteria based on requested dosage form and/or brand:

1. PENS

   a) Must meet the following criteria:
      i. Patient's long-acting insulin dose is 100 units/day or more (including NPH), but their total daily dose of insulin (basal + bolus) does NOT exceed 200 units/day or 2 units/kg/day
      ii. Patient must have tried and failed, have a contraindication to or an intolerance to insulin degludec U-200 [unbranded insulin degludec is preferred NF, PA]

   If above initial criteria are met, approve at GPID for 2 years.
   If above initial criteria are not met, do not approve.

RENEWAL CRITERIA

A. Request for Toujeo Solostar or MAX Solostar Pen: Patient's long-acting insulin dose exceeds 100 units/day but their total daily dose of insulin (basal + bolus) does NOT exceed 200 units/day or 2 units/kg/day

   If above renewal criteria are met, approve at GPID for 2 years.
   If above renewal criteria are not met, do not approve.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin glargine-yfgn is

preferred (vial - formulary without PA) based on its efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for patients with physical and/or cognitive impairment.

Toujeo is a unique concentrated insulin glargine, available in a single concentration of 300 units/ml. It comes in 2 single-patient-use prefilled Solostar pens: 1.5-mL pen (450 units/1.5 mL) which can deliver up to 80 units per injection, and a 3-mL Max pen (900 units/3 mL)) which can deliver up to 160 units per injection. Toujeo Solostar pen is an option for patients requiring insulin doses between 100 and 200 units/day.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation Date: 2016-2017
Effective Date: 01/01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INSULIN GLARGINE-AGLR PEN

Generic	Brand	HICL	GCN	Other
INSULIN GLARGINE-AGLR	REZVOGLAR KWIKPEN	47733		

GUIDELINES FOR COVERAGE

INITIAL CRITERIA

A. To Treat DIABETES TYPE 1: Must meet below criteria based on requested dosage form and/or brand:

1. PENS

    a) Request for Rezvoglar: Must meet i AND either ii or iii, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        i. Patient has documented allergic reaction or injection site reaction to insulin glargine-yfgn
        ii. Prescription is written by an Endocrinology specialist
        iii. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination.

    If above initial criteria are met, then approve indefinitely.
    If above initial criteria are not met, do not approve.
    [NOTE: Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable, and biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente.]

B. To Treat DIABETES TYPE 2: Must meet below criteria based on requested dosage form and/or brand:

1. PENS

    a) Request for Rezvoglar: Must meet i AND either ii or iii, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        i. Patient has documented allergic reaction or injection site reaction to insulin glargine-yfgn
        ii. Prescription is written by an Endocrinology specialist

iii. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination

If above initial criteria are met, approve indefinitely.
If above initial criteria are not met, do not approve.
[NOTE: Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente.]

RATIONALE
There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin glargine-yfgn is preferred (vial - formulary without PA) based on its efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for patients with physical and/or cognitive impairment.

Toujeo is a unique concentrated insulin glargine, available in a single concentration of 300 units/ml. It comes in 2 single-patient-use prefilled Solostar pens: 1.5-mL pen (450 units/1.5 mL) which can deliver up to 80 units per injection, and a 3-mL Max pen (900 units/3 mL)) which can deliver up to 160 units per injection. Toujeo Solostar pen is an option for patients requiring insulin doses between 100 and 200 units/day.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation Date: 2016-2017
Effective Date: 01/01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INSULIN GLARGINE-YFGN PEN

Generic	Brand	HICL	GCN	Other
INSULIN GLARGINE-YFGN	SEMGLEE PEN		49993	Insulin glargine-yfgn (unbranded Semglee) - F Semglee - excluded

GUIDELINES FOR COVERAGE

INITIAL CRITERIA

A. To Treat DIABETES TYPE 1: Must meet below criteria based on requested dosage form and/or brand:

1. PENS

    a) Request for insulin glargine-yfgn (unbranded Semglee): Must meet one of the following:
        i. Prescription is written by an Endocrinology specialist
        ii. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination.

    If above initial criteria are met, then approve indefinitely at GPID.
    If above initial criteria are not met, do not approve.
    [NOTE: Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente.]

B. To Treat DIABETES TYPE 2: Must meet below criteria based on requested dosage form and/or brand:

1. PENS

    a) Request for insulin glargine-yfgn (unbranded Semglee): Must meet one of the following:
        i. Prescription is written by an Endocrinology specialist
        ii. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination.

    If above initial criteria are met, then approve indefinitely at GPID.
    If above initial criteria are not met, do not approve.
    [NOTE: Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente.]

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin glargine-yfgn (unbranded Semglee) is an FDA approved, interchangeable biosimilar of Lantus (insulin glargine) and is the preferred product at Kaiser Permanente. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin glargine-yfgn is preferred (vial - formulary without PA) based on its efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for patients with physical and/or cognitive impairment.

Toujeo is a unique concentrated insulin glargine, available in a single concentration of 300 units/ml. It comes in 2 single-patient-use prefilled Solostar pens: 1.5-mL pen (450 units/1.5 mL) which can deliver up to 80 units per injection, and a 3-mL Max pen (900 units/3 mL)) which can deliver up to 160 units per injection. Toujeo Solostar pen is an option for patients requiring insulin doses between 100 and 200 units/day.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation Date: 2016-2017
Effective Date: 03/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

INTERFERON BETA-1A (AVONEX)

Generic	Brand	HICL	GCN	Exception/Other
INTERFERON BETA-1A	AVONEX	11253		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
1. Patient is new to KPCO within the past 90 days and stable on requested therapy

If met, approve x3 months, then must meet Initial Criteria.
If not met, use Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by a CPMG or affiliated neurologist
2. Patient has a diagnosis of a relapsing or active form of multiple sclerosis (This does not include non-active secondary-progressive MS or primary-progressive MS)
3. The patient has tried and failed, or has intolerance or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Extavia or Betaseron
    b. Glatiramer
    c. Dimethyl fumarate

If initial criteria are met, then approve x1 year at HICL.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Requesting physician is a CPMG or affiliated neurologist
2. Patient has a diagnosis of a relapsing or active form of multiple sclerosis (This does not include non-active secondary-progressive MS or primary-progressive MS)

If renewal criteria are met, then approve x1 year at HICL.
If renewal criteria are not met, do not approve.

CONTINUED ON NEXT PAGE

INTERFERON BETA-1A (AVONEX)

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ/IM injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	P
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	P
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	NP
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand - NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Siponimod	Mayzent	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	NP
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

Off-label disease modifying therapy for MS

RATIONALE:
The above guideline was developed by combining individual agent guidelines into one (5/2021)

The armamentarium of options for disease management of MS continues to expand and now includes agents with multiple differing methods of administration including injectables, infused as well as oral agents.

Interferon beta-1a products are injectables FDA approved in the treatment of relapsing forms of MS. The remaining injectables are another IFN beta-1a (Rebif), IFN beta-1b (Extavia and Betaseron), and glatiramer acetate (Copaxone and Glatopa). Comparisons across placebo-controlled trials for these

injectables have found similar effects in reducing relapse frequency of relapses, reducing burden of disease and activity on the MRI in comparison to placebo.

There have been 10 non-randomized, uncontrolled head-to-head trials of interferons that have found no difference between efficacy and safety, although there are two randomized, controlled large head-to-head comparison trials suggesting a dose-related improvement in efficacy. The two trials are the Evidence for Interferon Dose-Effect: European-North American Comparative Efficacy (EVIDENCE) trial and the Independent Comparison of Interferon (INCOMIN) trial. The EVIDENCE trial compared the efficacy of 30 micrograms (mcg) of IM IFN-beta-1a weekly with 44 mcg of SC IFN-beta-1a injected 3 times weekly. After 48 weeks of treatment, the relapse rate and MRI measures were significantly better with the higher dose regimen. However, the difference was primarily seen early in the study, during the first 24 weeks, whereas during the subsequent 24 weeks, the relapse rate was similar for the 2 groups. Additionally, the disability measures were not different at the end of the 1-year study period. The INCOMIN showed greater efficacy of IFN-beta-1b given every other day vs IFN-beta-1a given once weekly on relapse rate, MRI measures, and disability progression during the 2-year study. Unfortunately, the study had design limitations, including unblinded patients and examiners, limiting the conclusions that can be drawn. There are no head-to-head comparison trials assessing differences between Rebif and beta interferon 1b.

Comparisons across placebo-controlled trials for glatiramer acetate (GA) and beta - interferons have found similar effects in reducing relapse frequency of relapses, reducing burden of disease and activity on the MRI in comparison to placebo.

There are no current published consensus guidelines for the treatment of RRMS to guide on the roles in therapy for the injectables or the newer agents such as the infused drugs (i.e., Tysabri) or the orals (ie Aubagio, Gilenya, or Tecfidera). However, the trends and evidence for treatment suggest a two-pronged approach: induction and escalation. Induction treatment with a second- or third- line treatment like Tysabri or Gilenya is reserved for those patients with more aggressive disease requiring a more aggressive drug therapy approach at initiation. Whereas escalation is reserved for those patients with nonaggressive disease, in which safety and quality of life are the most significant considerations. First line treatment with injectables such as the beta-interferons may provide full “efficacy” but at a lower level of risk.

Neither of the injectables has any proven efficacy in those patients demonstrating nonrelapsing progressive disease such as those with secondary progressive MS or primary progressive MS. The main differences between the injectables are routes and frequency of administration as well as side effect profile. Additionally, beta - interferons are associated with the development of neutralizing antibodies in a small percentage of patients which may impact efficacy of drugs requiring change in therapy. Though not an absolute contraindication, untreated severe depression may pose a risk with the use beta – interferons in comparison to GA, thus careful selection of treatments is necessary. Similar caution must be used in patients who develop severe infusion reactions with the interferons or severe skin reactions with either of the injectables including GA.

Given no difference in efficacy or long-term safety outcomes between injectable therapies, choice of agent may reflect patient specific outcomes as well as cost-effectiveness of therapy.

FDA APPROVED INDICATIONS
Treatment of relapsing forms of MS

REFERENCES

1. Shilpa and Nikki Hahn, CPS
2. Avonex® [package insert]. Cambridge, MA: Biogen Idec Inc.; November 2021.
3. Plegridy [package insert]. Cambridge, MA: Biogen Idec Inc.; March 2022.
4. Rebif [package insert]. Rockland, MA: EMD Serono, Inc.; November 2021.
5. Clinical bulletin. Information for health professionals. Overview of multiple sclerosis. National Multiple Sclerosis Society. Available at http://www.nationalmssociety.org/for-professionals/healthcareprofessionals/publications/clinical-bulletins/index.aspx. Accessed on: October 23, 2013.
6. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis. Reports of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology. 2002;58:169-178.
7. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. N Engl J Med. 2002;343:938-952.
8. Expert Opinion Paper by the National Clinical Advisory Board for the National Multiple Sclerosis Society. Treatment recommendations for physicians. Disease management consensus statement. Available at http://www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinionpapers/download.aspx?id=8. Accessed on: October 23, 2013.
9. Gever J. MedPage Today. Two MS Drugs No Better Than One. April 27, 2012. Available at http://www.medpagetoday.com/meetingcoverage/aan/32400. Accessed on: October 23, 2013.
10. Mikol DD, Barkhof F, Chang P, et al. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REbif vs Glatiramer Acetate in Relapsing MS Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. Lancet Neurol. 2008;7(10):903–14.
11. McGraw CA, Lublin FD. Interferon beta and glatiramer acetate therapy. Neurotherapeutics. 2013;10:2–18.
12. Stuve O, Bennett JL, Hemmer B, et al. Pharmacological treatment of early multiple sclerosis. Drugs. 2008;68(1):73–83.
13. Lipsy RJ, Schapiro RT, Prostko CR. Current and future directions of MS management: key considerations for managed care pharmacists. J Manag Care Pharm. 2009;15(9 Suppl a):S2–15.
14. Coyle PK. Early treatment of multiple sclerosis to prevent neurologic damage. Neurol. 2008;71(24 Suppl 3):S3–7.
15. Association of British Neurologists. Association of British Neurologists: revised (2009) guidelines for prescribing in multiple sclerosis. 2009. http://www.theabn.org/abn/userfiles/file/abn_ms_guidelines_2009_final.pdf. Accessed October 23, 2013.
16. Panitch H, Goodin DS, Francis G, et al. Randomized, comparative study of interferon beta-1a treatment regimens in MS: the EVIDENCE trial. Neurology. 2002;59:1496-1506.
17. Durelli L, Verdun E, Barbero P, et al. Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: results of a 2-year prospective randomised multicentre study (INCOMIN). Lancet. 2002;359:1453-1460.

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Revised Date: 05/2023

INTERFERON BETA-1A (REBIF)

Generic	Brand	HICL	GCN	Exception/Other
INTERFERON BETA-1A	REBIF	23353		Nonformulary, least preferred

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
1. Patient is new to KPCO within the past 90 days and stable on requested therapy

If met, approve x3 months, then must meet Initial Criteria.
If not met, use Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by a CPMG or affiliated neurologist
2. Patient has a diagnosis of a relapsing or active form of multiple sclerosis (This does not include non-active secondary-progressive MS or primary-progressive MS)
3. The patient has tried and failed, or has intolerance or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Extavia or Betaseron
    b. Glatiramer
    c. Dimethyl fumarate

If initial criteria are met, then approve x1 year at HICL.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Requesting physician is a CPMG or affiliated neurologist
2. Patient has a diagnosis of a relapsing or active form of multiple sclerosis (This does not include non-active secondary-progressive MS or primary-progressive MS)

If renewal criteria are met, then approve x1 year at HICL.
If renewal criteria are not met, do not approve.

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INTERFERON BETA-1A (REBIF)

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ/IM injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	P
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	P
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	NP
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand - NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Siponimod	Mayzent	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	NP
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

Off-label disease modifying therapy for MS

RATIONALE:
The above guideline was developed by combining individual agent guidelines into one (5/2021)

The armamentarium of options for disease management of MS continues to expand and now includes agents with multiple differing methods of administration including injectables, infused as well as oral agents.

Interferon beta-1a products are injectables FDA approved in the treatment of relapsing forms of MS. The remaining injectables are another IFN beta-1a (Rebif), IFN beta-1b (Extavia and Betaseron), and glatiramer acetate (Copaxone and Glatopa). Comparisons across placebo-controlled trials for these

injectables have found similar effects in reducing relapse frequency of relapses, reducing burden of disease and activity on the MRI in comparison to placebo.

There have been 10 non-randomized, uncontrolled head-to-head trials of interferons that have found no difference between efficacy and safety, although there are two randomized, controlled large head-to-head comparison trials suggesting a dose-related improvement in efficacy. The two trials are the Evidence for Interferon Dose-Effect: European-North American Comparative Efficacy (EVIDENCE) trial and the Independent Comparison of Interferon (INCOMIN) trial. The EVIDENCE trial compared the efficacy of 30 micrograms (mcg) of IM IFN-beta-1a weekly with 44 mcg of SC IFN-beta-1a injected 3 times weekly. After 48 weeks of treatment, the relapse rate and MRI measures were significantly better with the higher dose regimen. However, the difference was primarily seen early in the study, during the first 24 weeks, whereas during the subsequent 24 weeks, the relapse rate was similar for the 2 groups. Additionally, the disability measures were not different at the end of the 1-year study period. The INCOMIN showed greater efficacy of IFN-beta-1b given every other day vs IFN-beta-1a given once weekly on relapse rate, MRI measures, and disability progression during the 2-year study. Unfortunately, the study had design limitations, including unblinded patients and examiners, limiting the conclusions that can be drawn. There are no head-to-head comparison trials assessing differences between Rebif and beta interferon 1b.

Comparisons across placebo-controlled trials for glatiramer acetate (GA) and beta - interferons have found similar effects in reducing relapse frequency of relapses, reducing burden of disease and activity on the MRI in comparison to placebo.

There are no current published consensus guidelines for the treatment of RRMS to guide on the roles in therapy for the injectables or the newer agents such as the infused drugs (i.e., Tysabri) or the orals (ie Aubagio, Gilenya, or Tecfidera). However, the trends and evidence for treatment suggest a two-pronged approach: induction and escalation. Induction treatment with a second- or third- line treatment like Tysabri or Gilenya is reserved for those patients with more aggressive disease requiring a more aggressive drug therapy approach at initiation. Whereas escalation is reserved for those patients with nonaggressive disease, in which safety and quality of life are the most significant considerations. First line treatment with injectables such as the beta-interferons may provide full “efficacy” but at a lower level of risk.

Neither of the injectables has any proven efficacy in those patients demonstrating nonrelapsing progressive disease such as those with secondary progressive MS or primary progressive MS. The main differences between the injectables are routes and frequency of administration as well as side effect profile. Additionally, beta - interferons are associated with the development of neutralizing antibodies in a small percentage of patients which may impact efficacy of drugs requiring change in therapy. Though not an absolute contraindication, untreated severe depression may pose a risk with the use beta – interferons in comparison to GA, thus careful selection of treatments is necessary. Similar caution must be used in patients who develop severe infusion reactions with the interferons or severe skin reactions with either of the injectables including GA.

Given no difference in efficacy or long-term safety outcomes between injectable therapies, choice of agent may reflect patient specific outcomes as well as cost-effectiveness of therapy.

FDA APPROVED INDICATIONS
Treatment of relapsing forms of MS

REFERENCES

1. Shilpa and Nikki Hahn, CPS
2. Avonex® [package insert]. Cambridge, MA: Biogen Idec Inc.; November 2021.
3. Plegridy [package insert]. Cambridge, MA: Biogen Idec Inc.; March 2022.
4. Rebif [package insert]. Rockland, MA: EMD Serono, Inc.; November 2021.
5. Clinical bulletin. Information for health professionals. Overview of multiple sclerosis. National Multiple Sclerosis Society. Available at http://www.nationalmssociety.org/for-professionals/healthcareprofessionals/publications/clinical-bulletins/index.aspx. Accessed on: October 23, 2013.
6. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis. Reports of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology. 2002;58:169-178.
7. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. N Engl J Med. 2002;343:938-952.
8. Expert Opinion Paper by the National Clinical Advisory Board for the National Multiple Sclerosis Society. Treatment recommendations for physicians. Disease management consensus statement. Available at http://www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinionpapers/download.aspx?id=8. Accessed on: October 23, 2013.
9. Gever J. MedPage Today. Two MS Drugs No Better Than One. April 27, 2012. Available at http://www.medpagetoday.com/meetingcoverage/aan/32400. Accessed on: October 23, 2013.
10. Mikol DD, Barkhof F, Chang P, et al. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REbif vs Glatiramer Acetate in Relapsing MS Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. Lancet Neurol. 2008;7(10):903–14.
11. McGraw CA, Lublin FD. Interferon beta and glatiramer acetate therapy. Neurotherapeutics. 2013;10:2–18.
12. Stuve O, Bennett JL, Hemmer B, et al. Pharmacological treatment of early multiple sclerosis. Drugs. 2008;68(1):73–83.
13. Lipsy RJ, Schapiro RT, Prostko CR. Current and future directions of MS management: key considerations for managed care pharmacists. J Manag Care Pharm. 2009;15(9 Suppl a):S2–15.
14. Coyle PK. Early treatment of multiple sclerosis to prevent neurologic damage. Neurol. 2008;71(24 Suppl 3):S3–7.
15. Association of British Neurologists. Association of British Neurologists: revised (2009) guidelines for prescribing in multiple sclerosis. 2009. http://www.theabn.org/abn/userfiles/file/abn_ms_guidelines_2009_final.pdf. Accessed October 23, 2013.
16. Panitch H, Goodin DS, Francis G, et al. Randomized, comparative study of interferon beta-1a treatment regimens in MS: the EVIDENCE trial. Neurology. 2002;59:1496-1506.
17. Durelli L, Verdun E, Barbero P, et al. Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: results of a 2-year prospective randomised multicentre study (INCOMIN). Lancet. 2002;359:1453-1460.

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Revised Date: 05/2023

PEGINTERFERON BETA-1A (PLEGRIDY)

Generic	Brand	HICL	GCN	Exception/Other
PEGINTERFERON BETA-1A	PLEGRIDY	41331		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
1. Patient is new to KPCO within the past 90 days and stable on requested therapy

If met, approve x3 months, then must meet Initial Criteria.
If not met, use Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by a CPMG or affiliated neurologist
2. Patient has a diagnosis of a relapsing or active form of multiple sclerosis (This does not include non-active secondary-progressive MS or primary-progressive MS)
3. The patient has tried and failed, or has intolerance or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Extavia or Betaseron
    b. Glatiramer
    c. Dimethyl fumarate

If initial criteria are met, then approve x1 year at HICL.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Requesting physician is a CPMG or affiliated neurologist
2. Patient has a diagnosis of a relapsing or active form of multiple sclerosis (This does not include non-active secondary-progressive MS or primary-progressive MS)

If renewal criteria are met, then approve x1 year at HICL.
If renewal criteria are not met, do not approve.

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PEGINTERFERON BETA-1A (PLEGRIDY)

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ/IM injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	P
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	P
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	NP
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand - NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Siponimod	Mayzent	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	NP
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

Off-label disease modifying therapy for MS

RATIONALE:
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injectables have found similar effects in reducing relapse frequency of relapses, reducing burden of disease and activity on the MRI in comparison to placebo.

There have been 10 non-randomized, uncontrolled head-to-head trials of interferons that have found no difference between efficacy and safety, although there are two randomized, controlled large head-to-head comparison trials suggesting a dose-related improvement in efficacy. The two trials are the Evidence for Interferon Dose-Effect: European-North American Comparative Efficacy (EVIDENCE) trial and the Independent Comparison of Interferon (INCOMIN) trial. The EVIDENCE trial compared the efficacy of 30 micrograms (mcg) of IM IFN-beta-1a weekly with 44 mcg of SC IFN-beta-1a injected 3 times weekly. After 48 weeks of treatment, the relapse rate and MRI measures were significantly better with the higher dose regimen. However, the difference was primarily seen early in the study, during the first 24 weeks, whereas during the subsequent 24 weeks, the relapse rate was similar for the 2 groups. Additionally, the disability measures were not different at the end of the 1-year study period. The INCOMIN showed greater efficacy of IFN-beta-1b given every other day vs IFN-beta-1a given once weekly on relapse rate, MRI measures, and disability progression during the 2-year study. Unfortunately, the study had design limitations, including unblinded patients and examiners, limiting the conclusions that can be drawn. There are no head-to-head comparison trials assessing differences between Rebif and beta interferon 1b.

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Neither of the injectables has any proven efficacy in those patients demonstrating nonrelapsing progressive disease such as those with secondary progressive MS or primary progressive MS. The main differences between the injectables are routes and frequency of administration as well as side effect profile. Additionally, beta - interferons are associated with the development of neutralizing antibodies in a small percentage of patients which may impact efficacy of drugs requiring change in therapy. Though not an absolute contraindication, untreated severe depression may pose a risk with the use beta – interferons in comparison to GA, thus careful selection of treatments is necessary. Similar caution must be used in patients who develop severe infusion reactions with the interferons or severe skin reactions with either of the injectables including GA.

Given no difference in efficacy or long-term safety outcomes between injectable therapies, choice of agent may reflect patient specific outcomes as well as cost-effectiveness of therapy.

FDA APPROVED INDICATIONS
Treatment of relapsing forms of MS

REFERENCES

1. Shilpa and Nikki Hahn, CPS
2. Avonex® [package insert]. Cambridge, MA: Biogen Idec Inc.; November 2021.
3. Plegridy [package insert]. Cambridge, MA: Biogen Idec Inc.; March 2022.
4. Rebif [package insert]. Rockland, MA: EMD Serono, Inc.; November 2021.
5. Clinical bulletin. Information for health professionals. Overview of multiple sclerosis. National Multiple Sclerosis Society. Available at http://www.nationalmssociety.org/for-professionals/healthcareprofessionals/publications/clinical-bulletins/index.aspx. Accessed on: October 23, 2013.
6. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis. Reports of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology. 2002;58:169-178.
7. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. N Engl J Med. 2002;343:938-952.
8. Expert Opinion Paper by the National Clinical Advisory Board for the National Multiple Sclerosis Society. Treatment recommendations for physicians. Disease management consensus statement. Available at http://www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinionpapers/download.aspx?id=8. Accessed on: October 23, 2013.
9. Gever J. MedPage Today. Two MS Drugs No Better Than One. April 27, 2012. Available at http://www.medpagetoday.com/meetingcoverage/aan/32400. Accessed on: October 23, 2013.
10. Mikol DD, Barkhof F, Chang P, et al. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REbif vs Glatiramer Acetate in Relapsing MS Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. Lancet Neurol. 2008;7(10):903–14.
11. McGraw CA, Lublin FD. Interferon beta and glatiramer acetate therapy. Neurotherapeutics. 2013;10:2–18.
12. Stuve O, Bennett JL, Hemmer B, et al. Pharmacological treatment of early multiple sclerosis. Drugs. 2008;68(1):73–83.
13. Lipsy RJ, Schapiro RT, Prostko CR. Current and future directions of MS management: key considerations for managed care pharmacists. J Manag Care Pharm. 2009;15(9 Suppl a):S2–15.
14. Coyle PK. Early treatment of multiple sclerosis to prevent neurologic damage. Neurol. 2008;71(24 Suppl 3):S3–7.
15. Association of British Neurologists. Association of British Neurologists: revised (2009) guidelines for prescribing in multiple sclerosis. 2009. http://www.theabn.org/abn/userfiles/file/abn_ms_guidelines_2009_final.pdf. Accessed October 23, 2013.
16. Panitch H, Goodin DS, Francis G, et al. Randomized, comparative study of interferon beta-1a treatment regimens in MS: the EVIDENCE trial. Neurology. 2002;59:1496-1506.
17. Durelli L, Verdun E, Barbero P, et al. Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: results of a 2-year prospective randomised multicentre study (INCOMIN). Lancet. 2002;359:1453-1460.

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INTRANASAL DIAZEPAM (VALTOCO)

Generic	Brand	HICL	GCN	Exception/Other
DIAZEPAM	VALTOCO		47548, 47549, 47551, 47552	Formulary

GUIDELINES FOR COVERAGE

Must meet all the following:

1. The requesting provider is a CPMG or affiliated network neurologist or epileptologist.
2. Diagnosis of generalized and/or focal (partial) epilepsy and on a stable regimen of antiseizure medicine.
3. Patient is experiencing seizure activity that necessitates acute treatment and is different from the patient's usual epilepsy pattern. At least one of the following diagnoses must be present:
    a. Acute repetitive seizures
    b. Intermittent seizure episodes
    c. Seizure clusters
    d. Prolonged convulsive seizures (at least 3 min or longer)
4. Patient is 6 years of age or older
5. Stereotypic episodes of frequent or prolonged seizure activity occurring with a frequency of no more than one episode every FIVE days and no more than 5 episodes per month

If initial criteria above are met, approve at HICL indefinitely, max 5 boxes per 30 days
If criteria are not met, do not approve.

NOTE: Valtoco should NOT be used in combination with another benzodiazepine nasal spray (e.g. injectable midazolam for intranasal use, Valtoco, Nayzilam)

RATIONALE

The class of medicines used for the treatment of acute repetitive seizures or clusters has expanded in recent years. The first treatment to be FDA-approved was Diazepam rectal (Diastat®) in 2005 and is indicated for the management of select, refractory participants 2 years of age or older with epilepsy on stable regimens of antiepileptic drugs, who require intermittent use of diazepam to control episodes of increased seizure activity. Diazepam intranasal (Valtoco®) is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from usual seizure pattern in epilepsy participants 6 years of age or older. Lastly, midazolam intranasal (Nayzilam®) is indicated for acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from usual seizure pattern in epilepsy participants 12 years of age or older. All three agents carry the same contraindication of acute narrow-angle glaucoma. Clinical guidelines from both the American Epilepsy Society and Neurocritical Care Society recommend diazepam rectal and midazolam intranasal (off-label) for acute convulsive seizure management when parenteral benzodiazepines are not available. These guidelines were also published prior to the approval of midazolam and diazepam intranasal therapies and did not specifically identify rescue use and non-hospital settings. As of this writing, the Epilepsy Foundation of America is actively working to develop consensus on best practices for rescue therapies.

FDA APPROVED INDICATIONS

1. **Valtoco:** Indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older

	Ages for use	Formulary	Dosage Strengths	Supplied and packaged in doses of
Diazepam (Valtoco)	6yrs and older	Formulary	5mg, 7.5mg, 10mg in 0.1mL	2 individual blister packs: - 5mg carton: one 5mg nasal spray devise - 10mg carton: one 10mg nasal spray devise - 15mg carton: TWO 7.5mg nasal spray devises - 20mg carton TWO 10mg nasal spray devises
Diazepam (Diastat) Diazepam (Diastat Acudial)	2yrs and older	Formulary	5mg/mL	Prefilled, unit dose, rectal delivery system: - 10mg system (doses are 5mg, 7.5mg, 10mg) - 20mg system (doses are 12.5mg, 15mg, 17.5mg 20mg)
Midazolam (Nayzilam)	12yrs and older	Formulary	5mg/0.1mL	Each box contains 2 Single-dose nasal spray units containing 5mg/0.1mL
Midazolam, injectable for use as intranasal	n/a	Formulary	5mg vial	Kit dispensed by KPCO pharmacies

REFERENCES

1. Valtoco [package insert]. San Diego, CA: Neurelis, Inc.; 2023.
2. Nayzilam [package insert]. Smyrna, GA: UCB, Inc.; 2023.
3. Diastat [package insert]. Bridgewater, NJ: Bausch Health US LLC; 2023.
4. Gidal B, Klein P, Hirsch LJ. Seizure clusters, rescue treatments, seizure action plans: Unmet needs and emerging formulations. Epilepsy & Behavior 2020;112:1-10.

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Revised Date: 07/2023

INTRANASAL MIDAZOLAM (NAYZILAM)

Generic	Brand	HICL	GCN	Exception/Other
MIDAZOLAM	NAYZILAM		46309	Formulary

GUIDELINES FOR COVERAGE

Must meet all the following:

1. The requesting provider is a CPMG or affiliated network neurologist or epileptologist.
2. Diagnosis of generalized and/or focal (partial) epilepsy and on a stable regimen of antiseizure medicine.
3. Patient is experiencing seizure activity that necessitates acute treatment and is different from the patient's usual epilepsy pattern. At least one of the following diagnoses must be present:
    a. Acute repetitive seizures
    b. Intermittent seizure episodes
    c. Seizure clusters
    d. Prolonged convulsive seizures (at least 3 min or longer)
4. Patient is 12 years of age or older
5. Stereotypic episodes of frequent or prolonged seizure activity occurring with a frequency of no more than one episode every THREE days and no more than 5 episodes per month

If initial criteria above are met, approve indefinitely at HICL, max 5 boxes per 30 days.
If criteria are not met, do not approve.

NOTE: Nayzilam should NOT be used in combination with another benzodiazepine nasal spray (e.g. injectable midazolam for intranasal use, Valtoco, Nayzilam)

RATIONALE

The class of medicines used for the treatment of acute repetitive seizures or clusters has expanded in recent years. The first treatment to be FDA-approved was Diazepam rectal (Diastat®) in 2005 and is indicated for the management of select, refractory participants 2 years of age or older with epilepsy on stable regimens of antiepileptic drugs, who require intermittent use of diazepam to control episodes of increased seizure activity. Diazepam intranasal (Valtoco®) is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from usual seizure pattern in epilepsy participants 6 years of age or older. Lastly, midazolam intranasal (Nayzilam®) is indicated for acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from usual seizure pattern in epilepsy participants 12 years of age or older. All three agents carry the same contraindication of acute narrow-angle glaucoma. Clinical guidelines from both the American Epilepsy Society and Neurocritical Care Society recommend diazepam rectal and midazolam intranasal (off-label) for acute convulsive seizure management when parenteral benzodiazepines are not available. These guidelines were also published prior to the approval of midazolam and diazepam intranasal therapies and did not specifically identify rescue use and non-hospital settings. As of this writing, the Epilepsy Foundation of America is actively working to develop consensus on best practices for rescue therapies.

FDA APPROVED INDICATIONS

1. **Nayzilam:** Indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy (ages 12 years and older)

	Ages for use	Formulary	Dosage Strengths	Supplied and packaged in doses of
Diazepam (Valtoco)	6yrs and older	Formulary	5mg, 7.5mg, 10mg in 0.1mL	2 individual blister packs: - 5mg carton: one 5mg nasal spray devise - 10mg carton: one 10mg nasal spray devise - 15mg carton: TWO 7.5mg nasal spray devises - 20mg carton TWO 10mg nasal spray devises
Diazepam (Diastat) Diazepam (Diastat Acudial)	2yrs and older	Formulary	5mg/mL	Prefilled, unit dose, rectal delivery system: - 10mg system (doses are 5mg, 7.5mg, 10mg) - 20mg system (doses are 12.5mg, 15mg, 17.5mg 20mg)
Midazolam (Nayzilam)	12yrs and older	Formulary	5mg/0.1mL	Each box contains 2 Single-dose nasal spray units containing 5mg/0.1mL
Midazolam, injectable for use as intranasal	n/a	Formulary	5mg vial	Kit dispensed by KPCO pharmacies

REFERENCES

1. Valtoco [package insert]. San Diego, CA: Neurelis, Inc.; 2023.
2. Nayzilam [package insert]. Smyrna, GA: UCB, Inc.; 2023.
3. Diastat [package insert]. Bridgewater, NJ: Bausch Health US LLC; 2023.
4. Gidal B, Klein P, Hirsch LJ. Seizure clusters, rescue treatments, seizure action plans: Unmet needs and emerging formulations. Epilepsy & Behavior 2020;112:1-10.

Creation Date: 06/2021
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

IPRATROPIUM NASAL SPRAY STEP THERAPY

Generic	Brand	HICL	GCN	Exception/Other
IPRATROPIUM NASAL 0.03% & 0.06%	IPRATROPIUM NASAL		42238, 42239	Formulary w/MD Spec and Step through azelastine

Step Therapy Criteria

Either step 1 or step 2 must be met for approval:

- **Step 1 -** prescribed by an Allergy, Ear/Nose/Throat, Otolaryngology specialist or a prescriber in Head & Neck Surgery specialty department
  OR
- **Step 2 -**
  - Patient has tried and failed, or had an intolerance/allergy to azelastine nasal spray, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If met, approve indefinitely.
If not met, do not approve.

RATIONALE

Per Allergy, Head & Neck Surgery and Health Plan.
The KPCO preferred nasal spray is azelastine and ipratropium nasal should be reserved for failures on azelastine.

Creation date: 09/2020
Effective date: 01/2024
Reviewed date: 09/2023
Revised date: 09/2023

IVACAFTOR (KALYDECO)

Generic	Brand	HICL	GCN	Exception/Other
IVACAFTOR	KALYDECO	38461		

GUIDELINES FOR USE

Requests for IVACAFTOR will be approved if ALL the following are met:

1. Prescribed by a pulmonologist
2. Patient has a diagnosis of cystic fibrosis (CF) with documentation of at least one mutation in the CFTR gene that is responsive to ivacaftor [Consult Kalydeco website to check for eligible mutations: https://www.kalydeco.com/who-kalydeco#table]
3. Patient is **NOT** homozygous for the F508del-CFTR mutation
4. Patient is 1 month and older

If all above criteria are met, approve indefinitely, max #2/day.
If above criteria are not met, do not approve.

RATIONALE

Per plan

FDA APPROVED INDICATIONS

Kalydeco is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 1 month and older who have one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data.

REFERENCES

Kalydeco [package insert]. Boston, MA: Vertex Pharmaceuticals Incorporated; 2020.
2020 PDR online revised 12/2018

Creation date: 07/25/2018
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

IXEKIZUMAB (TALTZ)

Generic	Brand	HICL	GCN	Exception/Other
IXEKIZUMAB	TALTZ	43193		Non-formulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on therapy, Medication is not being used in combination with another biologic for the same indication, and meets all indication-specific criteria below:
   1. Patient has a diagnosis of Psoriatic Arthritis (PsA) or Ankylosing Spondylitis or Nonradiographic Axial Spondyloarthritis, is being prescribed by a CPMG or affiliated rheumatologist
   2. Patient has a diagnosis of Psoriasis and is being prescribed by a CPMG or affiliated dermatologist

If met, then approve at HICL indefinitely with the following quantity limit of 1 pen/syringe per 28 days [MDD 0.04].
If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Psoriatic Arthritis
B. Ankylosing Spondylitis or Nonradiographic Axial Spondyloarthritis
C. Psoriasis

A. Psoriatic Arthritis: All the following must be met:
   1. Patient has a diagnosis of Psoriatic Arthritis
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least 2 of the following medications, or the patient has documented high disease activity in which these medications would not be suitable treatment: methotrexate, leflunomide, sulfasalazine
      b. at least 1 TNF inhibitor (e.g., adalimumab-atto (Amjevita)-preferred [F, PA], infliximab-dyyb (Inflectra)-preferred [F], etanercept (Enbrel) [F, PA])
      c. secukinumab (Cosentyx) [F]
      d. guselkumab (Tremfya) [NF, PA]
      e. at least 1 JAK inhibitor [e.g. tofacitinib (Xeljanz)-preferred]

If criteria are met, approve at HICL, max #2 per 28 days [MDD 0.08] x1 month (loading dose), then #1 per 28 days [MDD 0.04] indefinitely.
If criteria are not met, do not approve.

B. Ankylosing Spondylitis or Nonradiographic Axial Spondyloarthritis: All the following must be met:
   1. Patient has a diagnosis of Ankylosing Spondylitis or Nonradiographic Axial Spondyloarthritis.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response, intolerance, or has a contraindication to, all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Methotrexate or sulfasalazine, or the patient has documented high disease activity in which these medications would not be suitable treatment
      b. Cosentyx [F]
      c. at least 1 TNF inhibitor (e.g., adalimumab-atto (Amjevita)-preferred [F, PA], infliximab-dyyb (Inflectra)-preferred [F], etanercept (Enbrel) [F, PA])

If criteria are met, approve at HICL with the quantity limits below based on indication:
- Ankylosing Spondylitis: max #2 per 28 days [MDD 0.08] x1 month (loading dose), then #1 per 28 days [MDD 0.04] (maintenance) indefinitely.
- Nonradiographic Axial Spondyloarthritis: max #1 per 28 days [MDD 0.04] indefinitely.

If criteria are not met, do not approve.

B. Psoriasis: All the following must be met:
   1. Patient has a diagnosis of moderate to severe psoriasis and the medication is prescribed by a dermatology provider.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response (after at least two months of therapy), intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. A topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus), or the patient is reported as having very high disease activity (ex: > 50% BSA, erythrodermic, pustular psoriasis), disease affecting critical areas (ex: genitals, face), or prior biologic therapy within the past 4 months, skip and proceed to step 4c
      b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Acitretin, Cyclosporine, Methotrexate, Apremilast (Otezla), Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
      c. At least one TNF inhibitor (adalimumab (Amjevita) - preferred [F, PA], infliximab (Inflectra) - preferred [F], etanercept (Enbrel) [F, PA]) - unless the patient has failed an IL-17 inhibitor
      d. At least one IL-17 inhibitor (secukinumab (Cosentyx) - preferred [F])
      e. For patients 18 years of age or older, at least one IL-23 inhibitor: guselkumab (Tremfya) - preferred [NF, PA], risankizumab-rzaa (Skyrizi) [NF, PA]

If criteria are met, approve at HICL with quantity limits of: max 3 syringes/pens per 28 days [MDD 0.11] x 1 month (loading dose), then max 2 syringes/pens per 28 days [MDD 0.08] for the next two months (loading dose), then max 1 syringe/pen per 28 days [MDD 0.04] (maintenance dose after 12-week load) indefinitely.
If above criteria are not met, do not approve.

RENEWAL CRITERIA:
1. The diagnosis for which the patient was originally authorized medication coverage, has been assessed by the applicable specialist in the past two years.
2. Medication is not being used in combination with another biologic for the same indication.

If met, then approve at HICL indefinitely with a quantity limit of 1 pen/syringe per 28 days [MDD 0.04].
If not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member, Initial, or Renewal PA Criteria prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval.

A. Patient diagnosis of PsA or Ankylosing Spondylitis:
   1. Documentation by rheumatology provider of the patient resuming therapy after a gap 3 months or longer in treatment (to reload)

If above criteria are met, approve Ixekizumab (Taltz) at HICL, max #2 per 28 days [MDD 0.08] x1 month (loading dose), then #1 per 28 days [MDD 0.04] (maintenance) indefinitely.
If above criteria are not met, deny and offer Ixekizumab (Taltz) maximum 1 pen/syringe per 28 days [MDD 0.04] indefinitely.

B. Patient diagnosis of Psoriasis:
   1. Documentation by dermatology provider of the patient resuming therapy after a gap 3 months or longer in treatment (to reload)

If above criteria are met, then approve at HICL with the following quantity limits of max 3 syringes/pens per 28 days [MDD 0.11] x 1 month (loading dose), then max 2 syringes/pens per 28 days [MDD 0.08] for the next two months (loading dose), then max 1 syringe/pen per 28 days [MDD 0.04] (maintenance dose after 12-week load) indefinitely.
If above criteria are not met, deny and offer indefinite approvals of Ixekizumab (Taltz): 1 pen/syringe per 28 days [MDD 0.04].

RATIONALE
Per Health Plan - CPS in Derm, CPS in Rheum

FDA APPROVED INDICATIONS
1. Taltz: Treatment for the following indications
   a. Moderate to severe plaque psoriasis in patients 6 years of age and older
   b. Ankylosing Spondylitis (Taltz) in adults
   c. Psoriatic arthritis (Taltz) in adults

REFERENCES

"Currently stable on medication," means patient is tolerating well, medication appears to be effective, and provider wishes to continue therapy.

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (e.g., systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for psoriasis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*

Creation Date: 11/2019
Effective Date: 01/2024
Reviewed Date: 11/2023
Revised Date: 11/2023

KETOCONAZOLE (ORAL)

Generic	Brand	HICL	GCN	Exception/Other
KETOCONAZOLE	NIZORAL		42590	

GUIDELINES FOR COVERAGE: All the following must be met:
1. Medication is NOT being used to treat a skin and/or nail fungal infection.
2. Medication is being used to treat a systemic fungal infection or Cushing's disease.
3. Medication is being prescribed by an infectious disease, oncology, or endocrinology specialist.

If criteria are met, approve indefinitely.
If criteria are not met, do not approve.

RATIONALE
Ketoconazole should only be used when other effective antifungal therapy is not available or tolerated and the potential benefits outweigh the potential risks. Ketoconazole tablets are not indicated for the treatment of onychomycosis, cutaneous dermatophyte infections, or Candida infections.

FDA APPROVED INDICATIONS
Treatment of susceptible systemic fungal infections, including blastomycosis, histoplasmosis, paracoccidioidomycosis, coccidioidomycosis, and chromomycosis in patients who have failed or who are intolerant to other antifungal therapies.

REFERENCES
Lexicomp

Creation date: 07/25/2018
Effective date: 12/2023
Reviewed date: 11/2023
Revised date: 11/2023

LAROTRECTINIB (VITRAKVI)

Generic	Brand	HICL	GCN	Exception/Other
LAROTRECTINIB SULFATE	VITRAKVI	45494		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
1. Patient is new to KPCO within the past 90 days and is stable on therapy.

   If met, approve indefinitely.
   If not met, do not approve.

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by an oncology specialist
2. Must have a solid tumor
3. Must have a confirmed neurotrophic receptor tyrosine kinase (NTRK) gene fusion
4. Must not have a known acquired resistance mutation
5. Must have metastatic disease or non-metastatic disease that cannot be surgically resected without likely resulting in severe morbidity
6. Must have no satisfactory alternative treatment options or must have progressed following alternative treatment
7. Must not have progressed through entrectinib
8. Must have an intolerance or contraindication to entrectinib, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

   If above initial criteria are met, approve indefinitely.
   If criteria are not met, do not approve; recommend entrectinib if patient has not progressed through, and does not have an intolerance or contraindication to entrectinib.

RENEWAL CRITERIA:
1. Patient's disease has not progressed since initiation of medication, or the treating provider believes patient is deriving significant clinical benefit to justify treatment continuation

   If met, approve indefinitely.
   If not met, do not approve.

CONTINUED ON NEXT PAGE

LAROTRECTINIB (VITRAKVI)

RATIONALE
Ensure appropriate use consistent with FDA indication
Steer use toward KP preferred alternative entrectinib when appropriate

FDA APPROVED INDICATIONS
Treatment of solid tumors (in adult and pediatric patients) that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation; are metastatic or where surgical resection is likely to result in severe morbidity; and have no satisfactory alternative treatments or that have progressed following treatment.

REFERENCES
1. Larotrectinib [Package Insert], Stamford, CT: Loxo Oncology, Inc: 2018.

Creation Date: 12/31/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

LEMBOREXANT (DAYVIGO)

Generic Name	Brand Name	HICL	GPID	Comments
LEMBOREXANT	DAYVIGO	46275		Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all General Criteria and all Age Criteria in applicable age section

A. **General Criteria for All Requests:** Must meet all the following:
1. Medication is prescribed by Behavioral Health or Sleep Medicine provider
2. Patient must be age 18 or older
3. Diagnosis of insomnia characterized by difficulties with sleep onset and/or sleep maintenance
4. Potential factors contributing to sleep disturbances have been addressed (e.g., inappropriate sleep hygiene, sleep environment issues and co-morbid conditions contributing to insomnia)
5. Patient has no history of substance abuse
6. Patient has no history of narcolepsy

B. **Age 65 Years or Older:** Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
1. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to trazodone
2. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to ramelteon or OTC melatonin

If initial criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.
If initial criteria are not met, do not approve.

C. **Age Less Than 65 Years:** Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
1. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to trazodone
2. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to ramelteon or OTC melatonin
3. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to at least ONE of the following sedative-hypnotic alternatives: zolpidem (F), zaleplon (NF), eszopiclone (NF)

If initial criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.

If initial criteria are not met, do not approve.

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ePA Questions

1. Have factors that could contribute to sleep disturbances been addressed (e.g., inappropriate sleep hygiene, sleep environment issues and co-morbid conditions contributing to insomnia)?
2. Does the patient have history of substance abuse?
3. Does the patient have history of narcolepsy?
4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
5. Is there reasoning why alternatives (OTC melatonin, trazodone, zolpidem IR tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

FDA APPROVED INDICATIONS

Dayvigo (lemborexant) and Belsomra (suvorexant), and Quviviq (daridorexant) are indicated for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.

REFERENCES

Per Health Plan

Creation Date: 03/2021
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

LHRH ANTAGONIST ORGOVYX PA CRITERIA

Generic	Brand	HICL	GCN	Exception/Other
RELUGOLIX	ORGOVYX	47035	49005	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:

1. Patient must be age 18 or older
2. Must be prescribed by a CPMG or affiliated Oncologist or Urologist
3. Must have biopsy-confirmed prostate adenocarcinoma
4. Serum PSA level at diagnosis is greater than 2ng/mL
5. Must have metastatic disease or biochemical recurrence
6. Must be castration-sensitive (no history of progression or PSA rise on any androgen deprivation therapy [leuprolide (Eligard, Lupron), goserelin (Zoladex), triptorelin (Trelstar, Triptodur), histrelin (Supprelin, Vantas), degarelix (Firmagon), bilateral orchiectomy)
7. No active uncontrolled Crohn's disease or active peptic ulcer disease or history of gastric bypass surgery or gastrectomy
8. Serum testosterone level at diagnosis is at least 150ng/dL prior to beginning androgen deprivation therapy
9. Patient is unable to use leuprolide (Eligard, Lupron) due to one of the following clinical features, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Patient has a history of a major cardiovascular event (myocardial infarction, angina, symptomatic ischemic heart disease, CHF, ventricular arrhythmias, 2nd degree heart block, stroke, history of CABG and/or cardiac stents)
   b. Patient is at immediate risk of serious complications due to their prostate cancer (e.g., spinal cord compression, severe bone pain, risk of bone fracture due to metastases)
   c. Patient is intolerant to 2 androgen blockers (bicalutamide, flutamide or nilutamide) and newly beginning androgen deprivation therapy (ADT) [i.e., unable to prevent tumor flare when starting leuprolide]
10. Patient has an intolerance or contraindication to degarelix (Firmagon), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
To promote cost-conscious, evidence-based use of the medication

FDA APPROVED INDICATIONS
Advanced prostate cancer

REFERENCES

Creation Date: 3/2021
Effective Date: 01/01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

LINACLOTIDE (LINZESS)

Generic	Brand	HICL	GCN	Exception/Other
LINACLOTIDE	LINZESS	39583	42975, 33187, 33188	Nonformulary

GUIDELINES FOR COVERAGE
Must meet one of the following indications and meet all indication-specific criteria:

A. Irritable Bowel Syndrome with Constipation (IBS-C) or Chronic Idiopathic Constipation (CIC)
B. Pediatric Functional Constipation

A. Irritable Bowel Syndrome with Constipation (IBS-C) or Chronic Idiopathic Constipation (CIC)
   1. The patient is 18 years of age or older with a diagnosis of IBS-C or CIC
   2. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least one bulk-forming laxative (a bulk forming laxative contains psyllium, methylcellulose, or polycarbophil and examples may include Metamucil, Citrucel, FiberCon)
      b. at least one osmotic laxative (an osmotic laxative contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)
      c. lubiprostone
      d. Trulance

If criteria are met, approve indefinitely at HICL, max 1 tablet per day.
If criteria are not met, do not approve.

B. Pediatric Functional Constipation
   1. The request is for Linzess 72mcg capsules
   2. The patient is 6-17 years old with a diagnosis of pediatric functional constipation
   3. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least one bulk-forming laxative (a bulk forming laxative contains psyllium, methylcellulose, or polycarbophil and examples may include Metamucil, Citrucel, FiberCon)
      b. at least one osmotic laxative (an osmotic laxative contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)

If criteria are met, approve indefinitely at GPID, max 1 capsule per day.
If criteria are not met, do not approve.

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ePA Questions

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (bulk-forming laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Plan.

REFERENCES

Per Plan.

Creation date: 3/15/2017
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

LISDEXAMFETAMINE (VYVANSE)

Generic	Brand	HICL	GCN	Exception/Other
LISDEXAMFETAMINE	VYVANSE	34486		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:

A. Patient is new to KPCO within the past 90 days and stable on lisdexamfetamine therapy and has ONE of the following diagnoses [for patients with BED and ADHD/ADD, must meet criteria for either diagnosis]:
   1. Requested medication is prescribed for the treatment of Binge Eating Disorder (BED)
   2. Requested medication is prescribed for treatment of attention-deficit/hyperactivity disorder (ADHD) or attention deficit disorder (ADD), and the patient meets the following age criteria:
      a. The patient is 18 years old or younger
      b. The patient is 19 years or older and has failed an adequate trial* of, experienced adverse events with, or has an allergy or contraindication to an amphetamine product** regardless of dosage form, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If met, approve indefinitely at HICL.
   If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following diagnoses and meet all associated criteria [for patients with BED and ADHD/ADD, must meet criteria for either diagnosis], or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

A. Patient has a diagnosis of Binge Eating Disorder with adequate trial* (6 weeks) and failure of, or intolerance to at least one formulary selective serotonin reuptake inhibitor (SSRI)
B. Patient has a diagnosis of ADHD or attention deficit disorder (ADD) and meets the following criteria based on age:
   1. Patient is 6 to 18 years old with a previous adequate trial* (7 days) and therapeutic failure or adverse event with a long-acting amphetamine product that is not resolved by adjusting the dose or frequency
   2. Patient is 19 years of age or older and meets both of the following:
      a. Prior adequate trial* (7 days) and failure, or has a contraindication, or allergy to methylphenidate OR dexmethylphenidate regardless of dosage form
      b. Prior adequate trial* (7 days) and failure, or has a contraindication, or allergy to an amphetamine product regardless of dosage form

If initial criteria are met, approve indefinitely at HICL.
If initial criteria are not met, do not approve.

RATIONALE
To provide guidelines for consistent non-formulary review of the non-formulary medication.

FDA APPROVED INDICATIONS
Lisdexamfetamine is FDA approved for the treatment of attention-deficit/hyperactive disorder (ADHD) in adults and pediatric patients ≥ 6 years of age. It is also FDA approved for treatment of binge eating disorder in adults

REFERENCES
***** Adequate trial of a long-acting agent is further defined as wearing off that is not resolved by increasing the dose AND adding a short-acting agent OR increasing frequency to twice daily OR clinically significant side effects related to the dosage form that cannot be resolved by adjusting the dose or timing.

** Amphetamine products may include any of the following:

Drug	Initial suggested SIGs
Amphetamine mixed salts (Adderall XR capsule)	10 mg Daily
Amphetamine mixed salts (Adderall IR tablet)	5 mg BID
Dextroamphetamine ER (Dexedrine SR Spansules)	10 mg Daily
Dextroamphetamine IR (Dexedrine IR tablet)	5 mg BID

Creation Date: 07/2022
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

LOKELMA MD RESTRICTION

Generic	Brand	HICL	GCN/GPID	Other
SODIUM ZIRCONIUM CYCLOSILICATE	LOKELMA	44935	44774, 44775	Formulary

GUIDELINES FOR COVERAGE: Must meet the following:

1. Is the requesting provider a CPMG or an affiliated network nephrologist, nephrology specialist, or transplant hepatologist with appropriate referral, if needed?

   If yes, **approve the MD restriction at HICL x 1 year.**
   If no, do not approve.

RATIONALE
Lokelma is formulary, however it should only be prescribed by appropriate specialists. There are other formulary alternatives available for other prescribers.

FDA APPROVED INDICATIONS

REFERENCES

Creation Date: 03/2021
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

LONG-ACTING BETA AGONIST (LABA) CLASS
FORMOTEROL FUMARATE (PERFOROMIST)

Generic name	Brand name	HICL	GPID	Comments
FORMOTEROL FUMARATE	PERFOROMIST		98776	Nebulized inhalation solution

GUIDELINES FOR COVERAGE: Must have one of the following indications and meet all criteria associated with that diagnosis:

A. For the maintenance treatment of chronic obstructive pulmonary disease (COPD):
   1. Patient must be age 18 years or older
   2. Must meet all the following medication specific criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has tried and failed, or has an intolerance or a contraindication to, all the following: Striverdi Respimat, Spiriva Respimat, Stiolto Respimat, and arformoterol (Brovana)

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Striverdi Respimat (olodaterol) is KPCO preferred long-acting beta agonist (LABA) inhaler on the formulary. Non-preferred agents should be reserved after Striverdi and more established treatments for COPD such as long-acting muscarinic antagonist (LAMA). Either LABA or LAMA are acceptable for patients with group B COPD but LAMA generally preferred over LABA in COPD as it is recommended for group C and D in COPD.

LABA should not be used as monotherapy in patients with asthma. Use of more established therapies, such as inhaled corticosteroid (ICS) and ICS/LABA combination agents, are preferred over LABA in asthma.

FDA APPROVED INDICATIONS
All LABAs are indicated for the maintenance treatment of bronchospasm associated with COPD. In addition, Serevent Diskus (salmeterol) is also indicated for the treatment of asthma in patients aged 4 years and older with an ICS and prevention of exercise-induced bronchospasm (EIB) in patients aged 4 years and older.

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

LONG-ACTING BETA AGONIST (LABA) CLASS
SALMETEROL XINAFOATE (SEREVENT DISKUS)

Generic name	Brand name	HICL	GPID	Comments
SALMETEROL XINAFOATE	SEREVENT DISKUS		64012	Dry powder inhaler

GUIDELINES FOR COVERAGE: Must have one of the following indications and meet all criteria associated with that diagnosis:

A. Chronic Obstructive Pulmonary Disease (COPD) indication
B. Asthma indication

A. For the maintenance treatment of chronic obstructive pulmonary disease (COPD):
   1. Patient must be age 18 years or older
   2. Must meet all the following medication specific criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      b. Patient has tried and failed, or has an intolerance or a contraindication to, all the following: Striverdi Respimat, Spiriva Respimat, and Stiolto Respimat

B. For the treatment of asthma:
   1. Patient must be age 4 years or older
   2. Requested medication is Serevent Diskus
   3. Patient is not using as monotherapy for maintenance treatment of asthma
   4. Must meet all the following medication specific criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has tried and failed, or has intolerance or contraindication to, one inhaled corticosteroid [formulary agents: Alvesco HFA, Asmanex HFA] and at least one inhaled corticosteroid/long-acting beta agonist combination product [formulary agents: Wixela Inhub, Breyna HFA (generic Symbicort)].

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE

Striverdi Respimat (olodaterol) is KPCO preferred long-acting beta agonist (LABA) inhaler on the formulary. Non-preferred agents should be reserved after Striverdi and more established treatments for COPD such as long-acting muscarinic antagonist (LAMA). Either LABA or LAMA are acceptable for

patients with group B COPD but LAMA generally preferred over LABA in COPD as it is recommended for group C and D in COPD.

LABA should not be used as monotherapy in patients with asthma. Use of more established therapies, such as inhaled corticosteroid (ICS) and ICS/LABA combination agents, are preferred over LABA in asthma.

FDA APPROVED INDICATIONS
All LABAs are indicated for the maintenance treatment of bronchospasm associated with COPD. In addition, Serevent Diskus (salmeterol) is also indicated for the treatment of asthma in patients aged 4 years and older with an ICS and prevention of exercise-induced bronchospasm (EIB) in patients aged 4 years and older.

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

LONG-ACTING MUSCARINIC ANTAGONIST (LAMA) CLASS
ACLIDINIUM (TUDORZA PRESSAIR)

Generic name	Brand name	HICL	GPID	Comments
ACLIDINIUM BROMIDE	TUDORZA PRESSAIR		33084	Dry powder inhaler

GUIDELINES FOR COVERAGE

Must have one of the following indications and meets all criteria associated with that diagnosis, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

A. Medication is requested for the maintenance treatment of chronic obstructive pulmonary disease (COPD) and meets all the following:
   1. Patient must be age 18 years or older.
   2. Patient must have tried and failed, or has an intolerance or a contraindication to Spiriva Respimat 2.5 mcg/actuation and/or Incruse Ellipta

If all criteria are met, approve at HICL indefinitely.
If all criteria are not met, do not approve.

RATIONALE

Spiriva Respimat (tiotropium) is the preferred LAMA therapy based on cost-effectiveness of reducing COPD exacerbations and is the only LAMA with an indication for the management of asthma. Spiriva Respimat 1.25 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for asthma and 2.5 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for COPD. However, the 2.5 mcg/actuation inhaler (sig: 1 or 2 inhalations once daily) can be used off-label for asthma [5 mcg once daily has been recommended for patients with insufficient response to inhaled corticosteroid plus long-acting beta agonist (GINA 2020) with efficacy found in adults with severe asthma (ERS/ATS, Holguin 2019)]. All other LAMAs, including Spiriva Handihaler, are indicated for COPD only.

FDA APPROVED INDICATIONS

Anticholinergic bronchodilators are indicated for the long-term maintenance treatment of COPD. Spiriva (tiotropium) is also indicated for reducing COPD exacerbations and management of asthma (Respimat device only for asthma).

REFERENCES

Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 5/2023
Revised Date: 5/2023

LONG-ACTING MUSCARINIC ANTAGONIST (LAMA) CLASS
REVEFENACIN (YUPELRI)

Generic name	Brand name	HICL	GPID	Comments
REVEFENACIN	YUPELRI		45742	Nebulized solution

GUIDELINES FOR COVERAGE

Must have one of the following indications and meets all criteria associated with that diagnosis, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

A. Medication is requested for the maintenance treatment of chronic obstructive pulmonary disease (COPD) and meets all the following:
   1. Patient must be age 18 years or older.
   2. Patient must have tried and failed, or has an intolerance or a contraindication to Spiriva Respimat 2.5 mcg/actuation, and/or Incruse Ellipta, and/or Tudorza Pressair

If all criteria are met, approve at HICL indefinitely.
If all criteria are not met, do not approve.

RATIONALE

Spiriva Respimat (tiotropium) is the preferred LAMA therapy based on cost-effectiveness of reducing COPD exacerbations and is the only LAMA with an indication for the management of asthma. Spiriva Respimat 1.25 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for asthma and 2.5 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for COPD. However, the 2.5 mcg/actuation inhaler (sig: 1 or 2 inhalations once daily) can be used off-label for asthma [5 mcg once daily has been recommended for patients with insufficient response to inhaled corticosteroid plus long-acting beta agonist (GINA 2020) with efficacy found in adults with severe asthma (ERS/ATS, Holguin 2019)]. All other LAMAs, including Spiriva Handihaler, are indicated for COPD only.

FDA APPROVED INDICATIONS

Anticholinergic bronchodilators are indicated for the long-term maintenance treatment of COPD. Spiriva (tiotropium) is also indicated for reducing COPD exacerbations and management of asthma (Respimat device only for asthma).

REFERENCES

Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 5/2023
Revised Date: 5/2023

LONG-ACTING MUSCARINIC ANTAGONIST (LAMA) CLASS
TIOTROPIUM BROMIDE (SPIRIVA HANDIHALER)

Generic name	Brand name	HICL	GPID	Comments
TIOTROPIUM BROMIDE	SPIRIVA HANDIHALER		17853	Respimat 2.5 mcg/actuation formulary preferred

GUIDELINES FOR COVERAGE

Must have one of the following indications and meets all criteria associated with that diagnosis, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

A. Medication is requested for the maintenance treatment of chronic obstructive pulmonary disease (COPD) and meets all the following:
   1. Patient must be age 18 years or older.
   2. Patient must have tried and failed, or has an intolerance or a contraindication to Spiriva Respimat 2.5 mcg/actuation.

If all criteria are met, approve at HICL indefinitely.
If all criteria are not met, do not approve.

RATIONALE

Spiriva Respimat (tiotropium) is the preferred LAMA therapy based on cost-effectiveness of reducing COPD exacerbations and is the only LAMA with an indication for the management of asthma. Spiriva Respimat 1.25 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for asthma and 2.5 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for COPD. However, the 2.5 mcg/actuation inhaler (sig: 1 or 2 inhalations once daily) can be used off-label for asthma [5 mcg once daily has been recommended for patients with insufficient response to inhaled corticosteroid plus long-acting beta agonist (GINA 2020) with efficacy found in adults with severe asthma (ERS/ATS, Holguin 2019)]. All other LAMAs, including Spiriva Handihaler, are indicated for COPD only.

FDA APPROVED INDICATIONS

Anticholinergic bronchodilators are indicated for the long-term maintenance treatment of COPD. Spiriva (tiotropium) is also indicated for reducing COPD exacerbations and management of asthma (Respimat device only for asthma).

REFERENCES

Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 5/2023
Revised Date: 5/2023

LONG-ACTING MUSCARINIC ANTAGONIST (LAMA) CLASS
TIOTROPIUM BROMIDE (SPIRIVA RESPIMAT 1.25MG)

Generic name	Brand name	HICL	GPID	Comments
TIOTROPIUM BROMIDE	SPIRIVA RESPIMAT 1.25 MCG/ACTUATION		39587	Respimat 2.5 mcg/actuation formulary preferred

GUIDELINES FOR COVERAGE

Must have one of the following indications and meets all criteria associated with that diagnosis, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

A. Medication requested is Spiriva 1.25 mcg for the maintenance treatment of asthma and meets all the following:
   1. Patient must be age 6 years or older.
   2. Persistent symptoms and/or asthma exacerbation despite combination medium-to-high dose ICS/LABA therapy.
   3. Patient has tried and failed or has an intolerance or a contraindication to Spiriva Respimat 2.5 mcg/actuation.

If all criteria are met, approve indefinitely.
If all criteria are not met, do not approve.

RATIONALE

Spiriva Respimat (tiotropium) is the preferred LAMA therapy based on cost-effectiveness of reducing COPD exacerbations and is the only LAMA with an indication for the management of asthma. Spiriva Respimat 1.25 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for asthma and 2.5 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for COPD. However, the 2.5 mcg/actuation inhaler (sig: 1 or 2 inhalations once daily) can be used off-label for asthma [5 mcg once daily has been recommended for patients with insufficient response to inhaled corticosteroid plus long-acting beta agonist (GINA 2020) with efficacy found in adults with severe asthma (ERS/ATS, Holguin 2019)]. All other LAMAs, including Spiriva Handihaler, are indicated for COPD only.

FDA APPROVED INDICATIONS

Anticholinergic bronchodilators are indicated for the long-term maintenance treatment of COPD. Spiriva (tiotropium) is also indicated for reducing COPD exacerbations and management of asthma (Respimat device only for asthma).

REFERENCES

Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 5/2023
Revised Date: 5/2023

LONG-ACTING MUSCARINIC ANTAGONIST (LAMA) CLASS
UMECLIDINIUM BROMIDE (INCRUSE ELLIPTA)

Generic name	Brand name	HICL	GPID	Comments
UMECLIDINIUM BROMIDE	INCRUSE ELLIPTA		36574	Dry powder inhaler

GUIDELINES FOR COVERAGE

Must have one of the following indications and meets all criteria associated with that diagnosis, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

A. Medication is requested for the maintenance treatment of chronic obstructive pulmonary disease (COPD) and meets all the following:
   1. Patient must be age 18 years or older.
   2. Patient has tried and failed, or has an intolerance or a contraindication to Spiriva Respimat 2.5 mcg/actuation.

If all criteria are met, approve at HICL indefinitely.
If all criteria are not met, do not approve.

RATIONALE

Spiriva Respimat (tiotropium) is the preferred LAMA therapy based on cost-effectiveness of reducing COPD exacerbations and is the only LAMA with an indication for the management of asthma. Spiriva Respimat 1.25 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for asthma and 2.5 mcg/actuation inhaler (sig: 2 inhalations once daily) is FDA labeled for COPD. However, the 2.5 mcg/actuation inhaler (sig: 1 or 2 inhalations once daily) can be used off-label for asthma [5 mcg once daily has been recommended for patients with insufficient response to inhaled corticosteroid plus long-acting beta agonist (GINA 2020) with efficacy found in adults with severe asthma (ERS/ATS, Holguin 2019)]. All other LAMAs, including Spiriva Handihaler, are indicated for COPD only.

FDA APPROVED INDICATIONS

Anticholinergic bronchodilators are indicated for the long-term maintenance treatment of COPD. Spiriva (tiotropium) is also indicated for reducing COPD exacerbations and management of asthma (Respimat device only for asthma).

REFERENCES

Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 5/2023
Revised Date: 5/2023

LONG-ACTING MUSCARINIC ANTAGONIST/LONG-ACTING BETA AGONIST (LAMA/LABA) ANORO ELLIPTA

Generic name	Brand name	HICL	GPID	Comments
UMECLIDINIUM/VILANTEROL	ANORO ELLIPTA		35903	

GUIDELINES FOR COVERAGE: Must meet all the following:

1. Patient has a diagnosis of COPD
2. Patient must be age 18 or older
3. Must meet medication specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Patient has tried and failed, or has an intolerance or a contraindication to, Stiolto Respimat (tiotropium/olodaterol)

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Stiolto Respimat (tiotropium/olodaterol) is the most cost-effective LAMA/LABA inhaler with no significant difference in safety or efficacy among the different LAMA/LABA inhalers.

FDA APPROVED INDICATIONS
Combination LAMA/LABA inhalers are FDA approved for the maintenance treatment of patients with COPD.

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

LONG-ACTING MUSCARINIC ANTAGONIST/LONG-ACTING BETA AGONIST (LAMA/LABA)
BEVESPI AEROSPHERE

Generic name	Brand name	HICL	GPID	Comments
GLYCOPYRROLATE/ FORMOTEROL	BEVESPI AEROSPHERE		41199	

GUIDELINES FOR COVERAGE: Must meet all the following:

1. Patient has a diagnosis of COPD
2. Patient must be age 18 or older
3. Must meet medication specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Patient must have tried and failed, or has an intolerance or a contraindication to, Stiolto Respimat (tiotropium/olodaterol) and/or Anoro Ellipta.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Stiolto Respimat (tiotropium/olodaterol) is the most cost-effective LAMA/LABA inhaler with no significant difference in safety or efficacy among the different LAMA/LABA inhalers.

FDA APPROVED INDICATIONS
Combination LAMA/LABA inhalers are FDA approved for the maintenance treatment of patients with COPD.

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

LONG-ACTING MUSCARINIC ANTAGONIST/LONG-ACTING BETA AGONIST (LAMA/LABA)
DUAKLIR PRESSAIR

Generic name	Brand name	HICL	GPID	Comments
ACLIDINIUM/FORMOTEROL	DUAKLIR PRESSAIR		37735	

GUIDELINES FOR COVERAGE: Must meet all the following:

1. Patient has a diagnosis of COPD
2. Patient must be age 18 or older
3. Must meet medication specific criteria (medications listed in preferred order of use below), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   b. Patient must have tried and failed, or has an intolerance or a contraindication to, Stiolto Respimat (tiotropium/olodaterol), and/or Anoro Ellipta, and/or Bevespi Aerosphere.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE

Stiolto Respimat (tiotropium/olodaterol) is the most cost-effective LAMA/LABA inhaler with no significant difference in safety or efficacy among the different LAMA/LABA inhalers.

FDA APPROVED INDICATIONS

Combination LAMA/LABA inhalers are FDA approved for the maintenance treatment of patients with COPD.

REFERENCES

Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

LUBIPROSTONE (AMITIZA)

Generic	Brand	HICL	GCN	Exception/Other
LUBIPROSTONE	AMITIZA	33451	99658, 26473	Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must have one of the following indications, and meet all indication-specific criteria below:

A. Irritable Bowel Syndrome with Constipation (IBS-C) or Chronic Idiopathic Constipation (CIC)
B. Opioid Induced Constipation (OIC)

A. The patient has a diagnosis of irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC) and meets all the following:
   1. The patient must be 18 years of age or older
   2. The patient tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least one bulk-forming laxative (contains psyllium, methylcellulose, or polycarbophil and examples may include Metamucil, Citrucel, FiberCon)
      b. at least one osmotic laxative (contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)

If criteria are met, approve indefinitely at HICL, max 2 caps per day.
If criteria are not met, do not approve.

B. The patient has a diagnosis of opioid induced constipation (OIC) with an active opioid prescription and meets all the following:
   1. The patient must be 18 years of age or older
   2. The patient currently uses opioids chronically
   3. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. one stimulant laxative (contains sennosides or bisacodyl and examples may include Senokot, Ex-Lax, and Dulcolax)
      b. one osmotic laxative (contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)

If criteria are met, approve indefinitely at HICL, max 2 caps per day.
If criteria are not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet Initial PA Criteria prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval. Escalation review does not change the duration of the PA Approval.

1. For requests to start on escalated doses of #2 capsules of 8 mcg twice daily: Patient must have tried and failed standard maintenance dose of one 8 mcg capsule twice daily due to lack of efficacy, and the 24mcg twice daily dose due to intolerability.
2. For requests to continue escalated doses (more than 2 capsules/day): Patient must have been assessed by a gastroenterologist in the last 1 year, and the gastroenterologist evaluated if the dose can be de-escalated and determined that the escalated dose continues to be medically necessary.

If met, approve the 8mcg capsule, max 4 per day x1 year.
If not met, deny and offer maximum 2 capsules/day.

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ePA Questions

1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Irritable Bowel Syndrome with Constipation (IBS-C) or Chronic Idiopathic Constipation (CIC); Opioid Induced Constipation (OIC)]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Irritable Bowel Syndrome with Constipation (IBS-C) or Chronic Idiopathic Constipation (CIC)

   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (bulk-forming laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Opioid Induced Constipation (OIC)

   8. Is the patient currently using opioids chronically?
   9. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   10. Is there reasoning why alternatives (stimulant laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Plan.

Creation date: 3/15/2017
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

LUMACAFTOR/IVACAFTOR (ORKAMBI)

Generic	Brand	HICL	GCN	Exception/Other
LUMACAFTOR/IVACAFTOR	ORKAMBI	42235		

GUIDELINES FOR COVERAGE

Requests for LUMACAFTOR/IVACAFTOR will be approved if ALL the following are met:
1. Prescribed by a pulmonologist
2. Patient has a diagnosis of cystic fibrosis (CF) and is homozygous for the F508del mutation (verified by testing)
3. Patient is at least 1 year old

If all above criteria are met, approve indefinitely, max #4 tablets/day or #2 packets/day.
If criteria are not met, do not approve.

RATIONALE
Per Health Plan.

FDA APPROVED INDICATIONS
Treatment of cystic fibrosis (CF) in patients 1 year and older who are homozygous for the F508del mutation in the CFTR gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene.

Limitations of use: Efficacy and safety have not been established in patients with CF other than those homozygous for the F508del mutation.

REFERENCES
1. Per Health Plan.
2. Orkambi [package insert]. Boston, MA: Vertex Pharmaceuticals Incorporated; 2019

Creation date: 07/2018
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

LUMATEPERONE (CAPLYTA)

Generic	Brand	HICL	GCN/GPID	Exception/Other
LUMATEPERONE CAPSULE	CAPLYTA	46280		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO within the past 90 days and is stable on therapy.

If met, approve indefinitely at HICL.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following diagnoses and meet all related criteria below:

A. Bipolar depression
B. Schizophrenia

A. Bipolar Depression
   1. Patient is at least 18 years of age
   2. Documented contraindication, intolerance, or treatment failure to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
      a. Lurasidone (Latuda)
      b. One mood stabilizer: lamotrigine, lithium, valproic acid and derivatives

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

B. Schizophrenia
   1. Patient is at least 18 years of age
   2. Documented contraindication, intolerance, or treatment failure to at least 1 antipsychotic, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

ePA Questions

1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Bipolar Depression; Schizophrenia]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Bipolar Depression

   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules; Lithium capsules, as carbonate: 150 mg, 300 mg; Lithium tablets, as carbonate: 300 mg; Lithium CR tablets, as carbonate (Eskalith CR): 450 mg; Lithium SR tablets, as carbonate (Lithobid): 300 mg; Lamotrigine tablets; Divalproex sodium DR (12 hr) or ER (24 hr) tablets, valproic acid capsules (250 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Schizophrenia

   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Regarding bipolar depression criteria, cariprazine (Vraylar), lumateperone (Caplyta), and lurasidone all have low risk of metabolic side effects. Lurasidone is the only formulary antipsychotic option that has both low risk of metabolic side effects and a labeled FDA indication for treatment of bipolar depression as quetiapine and olanzapine have moderate and high metabolic risk, respectively. As such, if patient has trialed formulary lurasidone, one formulary mood stabilizer, nonformulary criteria will be met for bipolar depression treatment.

Carbamazepine, divalproex, and lithium are teratogenic so avoiding use in women of reproductive potential is not unreasonable (and highly recommended for divalproex). Unfortunately, most of the non-formulary antipsychotics lack reassuring data and absence of evidence of risk is not the same as absence of risk. Lithium may still be continued or started in women that are pregnant as the benefits of use are often considered to outweigh the small absolute risk of cardiac malformation (1-2 extra cases per 100 live births with first trimester in utero exposure compared with no lithium exposure).

FDA APPROVED INDICATIONS

Lumateperone (Caplyta)

- **Bipolar disorder:** As monotherapy or as an adjunct to lithium or valproate for treatment of depressive episodes associated with bipolar disorder I or II in adults.
- **Schizophrenia:** Treatment of schizophrenia in adults.

APPENDIX A. Formulary antipsychotics

First-generation antipsychotics	Second-generation antipsychotics
Chlorpromazine	Aripiprazole
Fluphenazine	Clozapine
Haloperidol	Lurasidone
Loxapine	Olanzapine
Molindone	Quetiapine
Perphenazine	Risperidone
Pimozide	Ziprasidone
Thioridazine	
Thiothixene	
Trifluoperazine	

HOW SUPPLIED:
Lumateperone (Caplyta): 42 MG

REFERENCES
American Psychiatric Association. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. 3rd ed. Washington, DC: American Psychiatric Association; 2021.

Caplyta. Package insert. Intra-Cellular Therapies, Inc.; June 29, 2023.

Patorno E, Huybrechts KF, Bateman BT, et al. Lithium use in pregnancy and the risk of cardiac malformations. N Engl J Med. 2017;376:23.

Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord 2018;20:97-170.

Creation Date: 3/2023
Effective Date: 4/2024
Reviewed Date: 3/2024
Revised Date: 3/2024

LUPKYNIS (VOCLOSPORIN)

Generic	Brand	HICL	GCN	Exception/Other
VOCLOSPORIN	LUPKYNIS	47077	49037	Nonformulary

GUIDELINES FOR COVERAGE:

INITIAL CRITERIA: Must meet all the following:
1. Patient must be age 18 or older
2. Have a diagnosis of lupus nephritis (LN)
3. Must be prescribed by CPMG or affiliated Rheumatologist or Nephrologist

AND must meet either #4 or #5 below:

4. Patient has a diagnosis of LN and is currently stable on voclosporin (Lupkynis) in combination with a background immunosuppressive therapy regimen (e.g., mycophenolate mofetil (Cellcept) or mycophenolic acid (Myfortic) and systemic corticosteroids)
   OR
5. Patient has tried and failed, or has an intolerance or contraindication to all of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   i. Mycophenolate mofetil (Cellcept) or mycophenolic acid (Myfortic) or cyclophosphamide (Cytoxan) (PO or IV) **AND**
   ii. Combination treatment with mycophenolate mofetil (Cellcept) or mycophenolic acid (Myfortic) and tacrolimus **AND**
   iii. Combination treatment with either mycophenolate mofetil (Cellcept), or mycophenolic acid (Myfortic) or cyclophosphamide (Cytoxan PO or IV) and belimumab (Benlysta SQ or IV)

If initial criteria above are met, approve x6 months, max #168 capsules per 28 days.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Patients' Lupus Nephritis has been assessed by Rheumatologist and/or Nephrologist in the past year
2. Voclosporin (Lupkynis) is being used in combination with a background immunosuppressive therapy regimen [e.g., mycophenolate mofetil (Cellcept) or mycophenolic acid (Myfortic) and systemic corticosteroids]
3. Documentation of a positive clinical response to therapy, i.e., patient has shown improvement in renal response from baseline laboratory values (eGFR) or proteinuria (urine protein: creatinine ratio) and/or clinical parameters (such as fluid retention, use of rescue drug, glucocorticoid use)

If renewal criteria are met, approve x6 months, max #168 capsules per 28 days.
If renewal criteria are not met, do not approve.

LUPKYNIS (VOCLOSPORIN)

FDA APPROVED INDICATIONS

Voclosporin (Lupkynis) is a calcineurin-inhibitor immunosuppressant indicated in combination with a background immunosuppressive therapy regimen for the treatment of adult patients with active lupus nephritis.

REFERENCES

Currently stable on medication means patient is tolerating well, appears to be effective and provider wishes to continue

Creation Date: 9/2021
Effective Date: 01/2024
Reviewed Date: 9/2023
Revised Date: 9/2022

MAVACAMTEN (CAMZYOS)

Generic	Brand	HICL	GCN	Exception/Other
MAVACAMTEN	CAMZYOS	47972		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Camzyos (mavacamten)

If met, approve indefinitely.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient must be age 18 years or older
2. Symptomatic obstructive hypertrophic cardiomyopathy (oHCM, HOCM) demonstrated by both of the following:
    a. Peak LVOT gradient ≥50 mm Hg
    b. NYHA class II to III symptoms
3. Left ventricular ejection fraction (LVEF) ≥55%
4. No history of syncope or sustained ventricular tachycardia in previous 6 months
5. QTc interval ≤ 500 ms
6. Patient has not had successful treatment with septal reduction therapy in the previous 6 months
7. Therapeutic failure of (e.g. still symptomatic), failure to tolerate, or contraindication to a beta blocker and/or a nondihydropyridine calcium channel blocker, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If all the above are met, approve indefinitely at HICL.
If any of the above are not met, do not approve.

RATIONALE
KP Interregional Practice Recommendations for Mavacamten (Camzyos) 5/15/2022

FDA APPROVED INDICATIONS
Treatment of adults with symptomatic NYHA class II-III obstructive hypertrophic cardiomyopathy

REFERENCES

- KP Interregional Practice Recommendations for Mavacamten (Camzyos) 5/15/2022
- Olivotto I, Oreziak A, Barriales-Villa R, et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2020; 396:759-69.
- Camzyos [package insert]. Brisban, CA: MyoKardia, Inc, a wholly-owned subsidiary of Bristol Myers Squibb; 2022

Creation Date: 07/2022
Effective Date: 01/2024
Reviewed Date: 08/2023
Revised Date: 08/2023

METHYLNALTREXONE (RELISTOR) - INJECTABLE FORMS

Generic	Brand	HICL	GPID	Exception/Other
METHYLNALTREXONE	RELISTOR	35611	99722, 31278, 31279	Available as oral and injectable forms. This criteria specific to injections.

GUIDELINES FOR COVERAGE
Must meet all the following:

1. The patient is 18 years of age or older
2. The patient uses opioids chronically and has a diagnosis of opioid induced constipation (OIC)
3. The patient is unable to take oral medications or unable to use any oral laxatives through feeding tube
4. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. one stimulant laxative (contains sennosides or bisacodyl and examples may include Senokot, Ex-Lax, and Dulcolax)
    b. one osmotic laxative (contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)
    c. lubiprostone
    d. Movantik, Symproic, and/or oral Relistor

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

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ePA Questions

1. Is the patient currently using opioids chronically?
2. Is the patient unable to take medications orally or through feeding tube?
3. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
4. Is there reasoning why alternatives (stimulant laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Plan.

NOTE: KPCO Palliative Care department is now the KPCO Supportive Care department, if looking through KPHC you may find notes from Supportive Care which is the same as palliative care.

Creation date: 4/6/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

METHYLNALTREXONE (RELISTOR) - ORAL

Generic	Brand	HICL	GPID	Exception/Other
METHYLNALTREXONE	RELISTOR	35611	41923	Available as oral form injectable forms. This criteria specific to oral form.

GUIDELINES FOR COVERAGE
Must meet all the following:

1. The patient is 18 years of age or older
2. The patient uses opioids chronically and has a diagnosis of opioid induced constipation (OIC)
3. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. one stimulant laxative (contains sennosides or bisacodyl and examples may include Senokot, Ex-Lax, and Dulcolax)
    b. one osmotic laxative (contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)
    c. lubiprostone
    d. Movantik and/or Symproic

If criteria are met, approve indefinitely at GPID, max 1 tablet per day.
If criteria are not met, do not approve.

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ePA

1. Is the patient currently using opioids chronically?
2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
3. Is there reasoning why alternatives (stimulant laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Plan.

NOTE: KPCO Palliative Care department is now the KPCO Supportive Care department, if looking through KPHC you may find notes from Supportive Care which is the same as palliative care

REFERENCES
Per Plan.

Creation date: 4/6/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

MIFEPRISTONE (KORLYM)

Generic	Brand	HICL	GCN	Exception/Other
MIFEPRISTONE 300MG	KORLYM		31485	

NOTE: only the 300mg strength follows this guideline

GUIDELINES FOR COVERAGE

All the following must be met:

1. Must be prescribed by an Endocrinologist
2. Patient has diagnosis of endogenous Cushing's syndrome with type 2 diabetes or glucose intolerance
3. Patient has tried and failed or has a contraindication to oral ketoconazole, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
4. Patient has tried and failed, is not a candidate for, or is awaiting surgical/radiologic interventions

If criteria are met, approve indefinitely, at GPID, max daily dose of 4 tablets.
If crteria are not met, do not approve.

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ePA Questions

4. Does the patient have endogenous Cushing's syndrome, with type 2 diabetes or glucose intolerance?
5. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
6. Is there reasoning why alternatives (ketoconazole tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
7. Regarding surgical/radiologic intervention, please check the box that most accurately describes this patient:
   a. The patient is not a candidate for surgical/radiologic intervention
   b. The patient is awaiting surgical/radiologic intervention
   c. The patient has failed surgical/radiologic intervention

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RATIONALE

To ensure appropriate use of Korlym.

FDA APPROVED INDICATIONS

• Korlym is a cortisol receptor antagonist indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing’s syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery
• Korlym should not be used for the treatment of diabetes type 2 unrelated to endogenous Cushing’s syndrome.

REFERENCES

1. Korlym [Prescribing Information]. Menlo Park, CA: Corcept Therapeutics; March 2012.
2. Hamrahian, AH et al. AACE/ACE diiseasse state clinical review: medical management of Cushing's disease. Endo Practice. 20(7); July 7, 2014.

Creation date: 11/28/2016
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

MIGLUSTAT (ZAVESCA)

Generic	Brand	HICL	GCN/GPID	Other
MIGLUSTAT	ZAVESCA	25098		Specialty Non-formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:

A. Must be prescribed by, or in consultation with a specialist in the area of the patient's diagnosis (e.g., endocrinologist, hematologist or geneticist).
B. Must be prescribed as monotherapy and is not given in combination with other SRT agents or enzyme replacement therapies [velaglucerase (Vpriv), imiglucerase (Cerezyme), or taliglucerase (Elelyso)].
C. Must have one of the following diagnoses and meet the disease specific criteria below:
   1. **Gaucher Disease Type 1.** Must meet all the following:
      a. Patient must be age 18 or older
      b. Prior to any treatment for the intended diagnosis, patient has had at least ONE of the following clinical presentations:
         - Anemia (Hgb <13 g/dL in men, <12 g/dL in women)
         - Thrombocytopenia (platelet count <100,000/µL)
         - Hepatomegaly
         - Splenomegaly
         - Growth failure
         - Evidence of bone disease not due to other causes
      c. Must meet the drug specific criteria below:
         - Patient has documented mild-to-moderate Type 1 Gaucher disease
           AND
         - In whom enzyme replacement therapy [Elelyso (taliglucerase alfa) is KP preferred] is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If initial criteria are met, approve x12 months at HICL/GPID.
   If initial criteria are not met, do not approve.

   2. **Niemann-Pick disease Type C.** Must meet all the following
      a. Patient must be age 4 or older
      b. Documented mild-to-moderate neurologic manifestations (e.g., ataxia, vertical supranuclear gaze palsy), psychiatric manifestations (e.g., psychosis), or cognitive manifestations.

   If initial criteria are met, approve x12 months at HICL/GPID.
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following disease specific criteria:

1. Gaucher Disease Type 1: Patient has demonstrated clinical symptom improvement or stability since starting on the drug, and no new contraindications to use, to at least one of the following:
   a. Hemoglobin level
   b. Platelet count
   c. Liver volume
   d. Spleen volume
   e. Growth
   f. Bone pain or crisis
2. Niemann-Pick disease Type C
   a. Patient has demonstrated clinical improvement or stability in neurologic, psychiatric, or cognitive symptoms since starting on the drug and has no new contraindications to use.

   If renewal criteria are met, approve x 1 year at HICL/GPID .
   If renewal criteria are not met, do not approve.

RATIONALE

Cerdelga (eliglustat) has been shown to be non-inferior to enzyme replacement therapy (ERT) and is a first-line option for Gaucher Disease. Zavesca (miglustat) is a second-line alternative to ERT.

Per the 2018 consensus guidelines for Niemann-Pick Disease Type C (NPC), miglustat is the only disease modifying medication that may be used in the treatment of neurological manifestations of NPC. Miglustat may halt or attenuate disease progression in some patients. Miglustat is currently used off-label in treatment of NPC in the United States.

FDA APPROVED INDICATIONS

Cerdelga (eliglustat): Treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers, intermediate metabolizers, or poor metabolizers.

Zavesca (miglustat): Treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (eg, due to allergy, hypersensitivity, or poor venous access).

REFERENCES

1. Bennett LL, Fellner C. Pharmacotherapy of Gaucher Disease: Current and Future Options. *P T*. 2018;43(5):274-309.
2. Rosenbloom BE, Cox TM, Drelichman GI, et al. Encore - a randomized, controlled, open-label non-inferiority study comparing ELIGLUSTAT to imiglucerase in Gaucher disease type 1 patients stabilized on enzyme replacement therapy: 24-month results. *Blood*. 2014;124(21):1406-1406. doi:10.1182/blood.v124.21.1406.1406
3. Geberhiwot T, Moro A, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. Orphanet J Rare Dis. 2018;13(1):50. Published 2018 Apr 6. doi:10.1186/s13023-018-0785-7

Creation Date: 07/2022
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

MILNACIPRAN

Generic	Brand	HICL	GCN	Other
MILNACIPRAN	SAVELLA	21229		Formulary

GUIDELINES FOR COVERAGE

Must meet all the following:
1. Patient is 18 years of age or older.
2. Patient has a diagnosis of fibromyalgia.
3. Patient has tried and failed or has an intolerance or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. At least one TCA or cyclobenzaprine (IF < 65 years of age)
    b. At least one SNRI
    c. gabapentin or pregabalin

If the above criteria are met, approve indefinitely with a max daily dose of 2 tablets.
If the above criteria are not met, do not approve.

RATIONALE
Ensure appropriate utilization of preferred drug therapies

FDA APPROVED INDICATIONS
Fibromyalgia in adults.

REFERENCES
1. KPHC Fibromyalgia SmartRx
2. Pregabalin Drug Use Guidelines: https://cl.kp.org/natl/home/refcontainerpage.dam.html?damrefpath=/content/dam/clinicallibrary/co/operations/department/pharmacy/PriorAuth/lyrica.pdf

Creation Date: 09/2020
Effective Date: 12/2023
Reviewed Date: 11/2023
Revised Date: 11/2023

MIRABEGRON (MYRBETRIQ)

Generic	Brand	HICL	GCN	Exception/Other
MIRABEGRON	MYRBETRIQ TABLETS AND GRANULES (8MG/ML SUS ER REC)	39357	32766, 32767, 49454	Nonformulary with max daily dose of 1/day

GUIDELINES FOR COVERAGE

Review based on diagnoses noted in section A, B, or C:

A. PATIENTS WITH A DIAGNOSIS OF OVERACTIVE BLADDER AND MYASTHENIA GRAVIS: Must meet all of the following criteria:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm.
   2. Patient has a diagnosis of myasthenia gravis.

   If criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.
   If criteria are not met, do not approve.

B. PATIENTS WITH A DIAGNOSIS OF OVERACTIVE BLADDER WITHOUT A DIAGNOSIS OF MYASTHENIA GRAVIS: Must meet all the following criteria:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm.
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to at least one of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed in preferential order]: oxybutynin IR/ER, solifenacin, trospium IR and tolterodine IR/ER.

   If criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.
   If criteria are not met, do not approve.

C. PEDIATRIC PATIENTS WITH A DIAGNOSIS OF NEUROGENIC DETRUSOR OVERACTIVITY: Must meet all the following criteria:
   1. Patient has a diagnosis of neurogenic detrusor overactivity.
   2. Request is for mirabegron (Myrbetriq) granules (8 mg/ml susp).
   3. Patient is between the ages of 3 and 17 years, and meets the following based on age:
      a. Patients 5 to 17 years of age: Trial/failure of, intolerance or contraindication to oxybutynin (ER or syrup preferred) and/or solifenacin (if able to swallow tablets and dose amenable with current tablet strength), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was

discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

b. Patients 3 to 4 years of age: no additional requirements

If criteria above are met, approve mirabegron at HICL level indefinitely.
If criteria are not met, do not approve.

RATIONALE

Per Health Plan.

- An adequate response is defined as one less episode of frequency or incontinence per day after an adequate trial of 4-6 weeks. Patients with a diagnosis of myasthenia gravis should avoid the use of anticholinergic agents.
- Preferred formulary agents, in order: oxybutynin ER, oxybutynin IR, solifenacin, trospium IR and oxybutynin syrup.
- Oral oxybutynin is not preferred in patients with dementia or cognitive impairment. Darifenacin is a preferred non-formulary option for patients with history of cognitive issues after solifenacin and trospium IR.
- Preferred nonformulary agents in order: tolterodine IR, tolterodine ER, darifenacin, fesoterodine, trospium ER, mirabegron and vibegron, Oxybutynin gel (Gelnique) and oxybutynin patch (Oxytrol) are excluded from coverage.
- Mirabegron granules are FDA approved for pediatric patients 3 to 17 years of age for neurogenic detrusor overactivity. Both oxybutynin (ER formulation) and solifenacin are FDA approved for neurogenic detrusor overactivity.

FDA APPROVED INDICATIONS

See individual medication.

REFERENCES

Creation Date: 9/26/2019
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

MS DRUGS - FUMARIC ACID DERIVATIVES
BAFIERTAM

Generic	Brand	HICL	GCN	Exception/Other
MONOMETHYL FUMARATE	BAFIERTAM	46576	48156	NF, specialty tier, least preferred

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
1. The member is new to KPCO within the past 90 days, stable on therapy with Bafiertam

If met, approve x3 months [max 4 capsules per day], then must meet initial criteria.
If not met, review by initial criteria.

INITIAL CRITERIA: Must meet all the following:
1. The requesting provider is a CPMG or affiliated network neurologist
2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active Secondary-Progressive MS or Primary-Progressive MS)
3. The patient has tried and failed, or has an intolerance or allergy to dimethyl fumarate, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve at HICL x2 years, max 4 capsules per day.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: All the following must be met:
1. The requesting provider is a CPMG or affiliated network neurologist
2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active Secondary-Progressive MS or Primary-Progressive MS)

If renewal criteria are met, approve at HICL x2 years, max 4 capsules per day.
If renewal criteria are not met, do not approve.

Quantity and PA Approval Limits

Medication	Dosage Strength	Dosage Regimen	Typical Quantity dispensed	Duration of Approval
Vumerity	231 mg capsules	7-day titration: 231 mg BID	#14 capsules (for 7-day titration)	**Initial:** Approve x 90 days **Renewal:** 2 years
	231 mg capsules	Maintenance: 462 mg BID	#120 capsules	

Bafiertam	95 mg capsules	7-day titration: 95 mg BID	#14 capsules (for 7-day titration)	**Initial:** Approve x 90 days **Renewal:** 2 years
	95 mg capsules	Maintenance: 190 mg BID	#120 capsules	

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegidy	SQ/IM injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	NP
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	P
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	NP
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand - NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Ponesimod	Ponvory	Oral	NP
	Siponimod	Mayzent	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	NP
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP

Off-label disease modifying therapy for MS

RATIONALE

Per Plan.

FDA APPROVED INDICATIONS

Treatment of patients with relapsing forms of multiple sclerosis

REFERENCES

Creation date: 07/2020
Effective date: 01/01/2024
Reviewed date: 05/2023
Revised date: 05/2023

MS DRUGS - FUMARIC ACID DERIVATIVES
VUMERITY

Generic	Brand	HICL	GCN	Exception/Other
DIROXIMEL FUMARATE	VUMERITY	46164	47209	NF, specialty tier, preferred after dimethyl fumarate

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
1. The member is new to KPCO within the past 90 days, stable on therapy with Vumerity

If met, approve x3 months [max 4 capsules per day], then must meet initial criteria.
If not met, review by initial criteria.

INITIAL CRITERIA: Must meet all the following:
1. The requesting provider is a CPMG or affiliated network neurologist
2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active Secondary-Progressive MS or Primary-Progressive MS)
3. The patient has tried and failed, or has an intolerance or allergy to dimethyl fumarate, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve at HICL x2 years, max 4 capsules per day.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: All the following must be met:
1. The requesting provider is a CPMG or affiliated network neurologist
2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active Secondary-Progressive MS or Primary-Progressive MS)

If renewal criteria are met, approve at HICL x2 years, max 4 capsules per day.
If renewal criteria are not met, do not approve.

Quantity and PA Approval Limits

Medication	Dosage Strength	Dosage Regimen	Typical Quantity dispensed	Duration of Approval
Vumerity	231 mg capsules	7-day titration: 231 mg BID	#14 capsules (for 7-day titration)	**Initial:** Approve x 90 days **Renewal:** 2 years
	231 mg capsules	Maintenance: 462 mg BID	#120 capsules	

Bafiertam	95 mg capsules	7-day titration: 95 mg BID	#14 capsules (for 7-day titration)	**Initial:** Approve x 90 days **Renewal:** 2 years
	95 mg capsules	Maintenance: 190 mg BID	#120 capsules	

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegidy	SQ/IM injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	NP
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	P
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	NP
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand - NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Ponesimod	Ponvory	Oral	NP
	Siponimod	Mayzent	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	NP
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP

Off-label disease modifying therapy for MS

RATIONALE

Per Plan.

FDA APPROVED INDICATIONS
Treatment of patients with relapsing forms of multiple sclerosis

REFERENCES

Creation date: 07/2020
Effective date: 01/01/2024
Reviewed date: 05/2023
Revised date: 05/2023

MYFEMBREE

Generic	Brand	HICL	GCN/GPID	Exception/Other
RELUGOLIX, ESTRADIOL, NORETHINDRONE ACETATE	MYFEMBREE	47392	49699	Specialty tier

****Length of approval applies to Federal Group**

GUIDELINES FOR COVERAGE

Must have one of the following indications and meet indication specific criteria as follows:

A. **Premenopausal, fibroid induced, heavy menstrual bleeding [NEW MEMBER CRITERIA, INITIAL CRITERIA, RENEWAL CRITERIA]**
B. **Premenopausal endometriosis with moderate to severe pain [NEW MEMBER CRITERIA, INITIAL CRITERIA, RENEWAL CRITERIA]**

A. To treat premenopausal, fibroid induced, heavy menstrual bleeding
NEW MEMBER CRITERIA: Must meet the following:

1. Patient is new to KPCO within the past 90 days and is stable on therapy with relugolix +E2NETA (Myfembree)
2. Patient has not been on relugolix +E2NETA (Myfembree) for 24 months or more
3. Patient meets one of the following:
   a. Patient is currently taking relugolix +E2NETA (Myfembree) and has a history of blood transfusion to treat heavy menstrual bleeding
   b. Patient has experienced a clinically significant improvement in fibroid-induced heavy menstrual bleeding, defined as at least 50% reduction in menstrual blood loss from baseline to the final month (6 months) of treatment with relugolix +E2NETA (Myfembree)

If met, then approve x1 fill, to allow time to be evaluated by Ob/Gyn [**Use for Federal Group]. If not met, review by applicable indication-specific Initial Criteria below.

INITIAL CRITERIA: Must meet all the following criteria:

1. Patient is a female at least 18 years of age
2. Medication is prescribed by an OB/GYN (with an appropriate referral, if required)
3. Patient is premenopausal with a diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids)
4. Patient has tried and failed, has an intolerance to, or has a contraindication to each of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Combined Oral Contraceptive Pill (OCP) - Note: cannot take concurrently with Myfembree
   b. Levonorgestrel-releasing intrauterine device (LNG IUD), Depot Medroxyprogesterone or Nora-Be
   c. GnRH (leuprolide)
5. Patient must not have previously completed 24 months of treatment with elagolix +E2/NETA (Oriahnn), relugolix +E2NETA (Myfembree), or elagolix monotherapy (Orilissa)

6. Patient must not be on an organic anion transporting polypeptide (OATP)1B1 inhibitor[b] (most common: cyclosporine, gemfibrozil; see comprehensive list in footnote)

   If initial criteria are met, then approve up to 6 months, but no more than maximum of 24 total months of therapy [**Use for FEDERAL Group].
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
1. Patient has not been on relugolix +E2NETA (Myfembree) for 24 months or more
2. Patient meets one of the following:
   a. Patient is currently taking relugolix +E2NETA (Myfembree) and has a history of blood transfusion to treat heavy menstrual bleeding
   b. Patient has experienced a clinically significant improvement in fibroid-induced heavy menstrual bleeding, defined as at least 50% reduction in menstrual blood loss from baseline to the final month (6 months) of treatment with relugolix +E2NETA (Myfembree)

   If met, then approve for the number of months to meet the maximum of 24 total months of therapy. [**Use for Federal Group].
   If not met, do not approve.

B. To treat moderate to severe pain associated with endometriosis in premenopausal patients:
NEW MEMBER CRITERIA: Must meet the following:
1. Patient new to KCPO within the past 90 days and is stable on treatment with relugolix +E2NETA (Myfembree)
2. Patient has not been on relugolix +E2NETA (Myfembree) for 24 months or more
3. Patient has had at least a 50% improvement in symptoms of pain since starting treatment with relugolix +E2NETA (Myfembree)

   If met, approve x1 fill, to allow time to be evaluated by Ob/Gyn [**Use for Federal Group].
   If not met, review by applicable indication-specific Initial Criteria below.

INITIAL CRITERIA: Must meet all of the following:
1. Patient is a female and at least 18 years of age
2. Medication is prescribed by an OB/GYN (with an appropriate referral, if required)
3. Patient is premenopausal with a diagnosis of moderate to severe pain associated with endometriosis
4. Patient has tried and failed, has an intolerance to, or has a contraindication to each of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. At least one NSAID
   b. At least two estrogen-progestin combination contraceptives (pills, patch, or ring) taken in a continuous fashion (skipping placebo tablets) with different progestins - Note: cannot take concurrent with Myfembree

c. Norethindrone acetate oral, Depot medroxyprogesterone acetate injection, medroxyprogesterone acetate oral, levonorgestrel intrauterine device, or etonorgestrel implant
d. GnRH (nafarelin, leuprolide, goserelin or triptorelin) with add-back hormonal therapy (norethindrone [to counteract estrogen suppression effect of GnRH agonist])

5. Patient must not have previously completed 24 months of treatment with elagolix +E2/NETA (Oriahnn), relugolix +E2NETA (Myfembree), or elagolix monotherapy (Orilissa)
6. Patient must not be on organic anion transporting polypeptide (OATP)1B1 inhibitor [b] (most common: cyclosporine, gemfibrozil; see comprehensive list in footnote)

If initial criteria are met, then approve up to 6 months, but no more than maximum of 24 total months of therapy [**Use for FEDERAL Group].
If initial criteria are met, do not approve.

RENEWAL CRITERIA: Must meet the following:

1. Has not been on relugolix +E2NETA (Myfembree) for 24 months or more
2. Patient has experienced a 50% improvement in pain since starting treatment with relugolix +E2NETA (Myfembree)

If met, approve for the number of months to meet the maximum of 24 total months of therapy. [**Use for Federal Group].
If not met, do not approve.

RATIONALE- per OB/GYN

FDA APPROVED INDICATIONS
Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women and management of moderate to severe pain associated with endometriosis in premenopausal patients.

REFERENCES
package insert
[a](including women >35 years of age who smoke, current or history of deep vein thrombosis or pulmonary embolism, vascular disease (e.g., cerebrovascular disease, coronary artery disease, peripheral vascular disease), thrombogenic valvular or thrombogenic rhythm diseases of the heart (e.g., subacute bacterial endocarditis with valvular disease, atrial fibrillation), inherited or acquired hypercoagulopathies, uncontrolled hypertension, or headaches with focal neurological symptoms or have migraine headaches with aura if >35 years of age.)
[b](atazanavir, clarithromycin, cobicistat, cyclosporine, daclatasvir, darolutamide, elbasvir, eltrombopag, eluxadoline, gemfibrozil, grazoprevir, ledipasvir, leflunomide, letermovir, lopinavir, simeprevir, teriflunomide, velpatasvir, voxilaprevir. Additional category X interactions are those with CYP3A4 metabolism (fusidic acid, idelalisib), and drugs reliant on PGP. The concentrations of these may be increased to toxic levels if administered with PGP inhibitor elagolix: pazopanib, IV topotecan, vincristine (liposomal).)

Management of Symptomatic Uterine Leiomyomas VOL. 137, NO. 6, JUNE 2021 OBSTETRICS & GYNECOLOGY
Myfembree PACKAGE INESERT

Creation Date: 12/2020

Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

NALDEMEDINE (SYMPROIC)

Generic	Brand	HICL	GCN	Exception/Other
NALDEMEDINE	SYMPROIC	44176		

GUIDELINES FOR COVERAGE
Must meet all the following:
1. The patient is 18 years of age or older
2. The patient uses opioids chronically and has a diagnosis of opioid induced constipation (OIC)
3. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. one stimulant laxative (contains sennosides or bisacodyl and examples may include Senokot, Ex-Lax, and Dulcolax)
    b. one osmotic laxative (contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)
    c. lubiprostone
    d. Movantik

If criteria are met, approve indefinitely at HICL, max 1 tablet per day.
If criteria are not met, do not approve.

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ePA Questions
1. Is the patient currently using opioids chronically?
2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
3. Is there reasoning why alternatives (stimulant laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Plan.

NOTE: KPCO Palliative Care department is now the KPCO Supportive Care department, if looking through KPHC you may find notes from Supportive Care which is the same as palliative care

Creation date: 4/6/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

NALOXEGOL (MOVANTIK)

Generic	Brand	HICL	GCN	Exception/Other
NALOXEGOL	MOVANTIK	41686		

GUIDELINES FOR COVERAGE
Must meet all the following:
1. The patient is 18 years of age or older
2. The patient uses opioids chronically and has a diagnosis of opioid induced constipation (OIC)
3. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. one stimulant laxative (contains sennosides or bisacodyl and examples may include Senokot, Ex-Lax, and Dulcolax)
    b. one osmotic laxative (contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)
    c. lubiprostone

If criteria are met, approve indefinitely at HICL, max 1 tablet per day.
If criteria are not met, do not approve.

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ePA Questions
1. Is the patient currently using opioids chronically?
2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
3. Is there reasoning why alternatives (stimulant laxatives, osmotic laxatives) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Plan.

NOTE: KPCO Palliative Care department is now the KPCO Supportive Care department, if looking through KPHC you may find notes from Supportive Care which is the same as palliative care

Creation date: 4/6/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

NILOTINIB

Generic	Brand	HICL	GCN/GPID	Other
NILOTINIB	TASIGNA	35149		Formulary, 2nd Generation TKI

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

A. Patient is new to KPCO within the past 90 days, and the medication has been prescribed by an Oncologist

If met, approve x 2 years.
If not met, then use Initial Criteria.

INITIAL CRITERIA: Must meet the following criteria based on drug and diagnosis below:

A. Nilotinib (Tasigna) for Chronic Myeloid Leukemia (CML)
B. Nilotinib (Tasigna) for Acute Lymphoblastic Leukemia (ALL)
C. Nilotinib (Tasigna) for Gastrointestinal Stromal Tumor (GIST)
D. All other indications

A. **Nilotinib (Tasigna) for CML (any phase): Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Patient must not have any of the following BCR-ABL1 mutations: T315I, Y253H, E255K/V or F359V/C/I
   3. Patient must have Philadelphia Chromosome (aka BCR-ABL) and one of a through d below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has tried and failed imatinib (Gleevec, if chronic phase CML) and/or dasatinib (Sprycel) with an inadequate response that is not due to patient nonadherence
      b. Patient must have a documented intolerance to dasatinib (Sprycel) not alleviated by dose reductions (≤70 mg/day [adults]; for peds use below weight-based dosing)

Weight	Dose of dasatinib (Sprycel) which must be tried and failed before deeming patient "intolerant"
10 to <20kg	20mg
20 to <30kg	20mg
30 to <45kg	50mg
45kg+	Use adult dose cutoff

      c. Patient developed pulmonary arterial hypertension (PAH) during treatment with dasatinib (Sprycel) (at any dose)
      d. Patient must have one of the following BCR-ABL1 mutations: F317L/V/I/C, T315A, or V299L

If criteria are met, approve x 2 years.
If criteria are not met, do not approve [direct to dasatinib (Sprycel) (if meets that criteria) or imatinib (Gleevec) as appropriate].

B. **Nilotinib (Tasigna) for Acute Lymphoblastic Leukemia (ALL): Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Patient must have Philadelphia Chromosome (aka BCR-ABL) and one of a through c below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient must have a documented intolerance to dasatinib (Sprycel) not alleviated by dose reductions (≤70 mg/day [adults]; for peds use below weight-based dosing)

Weight	Dose of dasatinib (Sprycel) which must be tried and failed before deeming patient "intolerant"
10 to <20kg	20mg
20 to <30kg	20mg
30 to <45kg	50mg
45kg+	Use adult dose cutoff

      b. Patient developed pulmonary arterial hypertension (PAH) during treatment with dasatinib (Sprycel) (at any dose)
      c. Patient must not have any of the following BCR-ABL1 mutations: T315I, Y253H, E255K/V, F359V/C/I or G250E

If criteria are met, approve indefinitely.
If criteria are not met, do not approve [direct to dasatinib (Sprycel) (if meets that criteria) or imatinib (Gleevec) as appropriate].

C. **Nilotinib (Tasigna) for Gastrointestinal Stromal Tumor (GIST): Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Patient must have metastatic or unresectable GIST
   3. Patient has had disease progression, documented intolerance, or contraindications to all of the following medications in a through d below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a) imatinib (Gleevec)
      b) sunitinib (Sutent)
      c) regorafenib (Stivarga)
      d) ripretinib (Qinlock)

If criteria are met, approve indefinitely.
If criteria are not met, do not approve.

D. **If for any other diagnosis (e.g., hypereosinophilic syndrome, eosinophilic leukemia, dermatofibrosarcoma, chordoma): Must meet all the following:**
   1. Prescribed by an oncology specialist
   2. Use must meet the Medicare Compendia criteria as detailed in the following policy: Medicare Benefit Policy Manual Chapter 15 - Covered Medical and Other Health Services Section 50.4.5 - Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

If criteria are met, approve x 1 year.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
A. Patient has been on the TKI for greater than 3 months and one of the following criteria:
   1. Disease progression or relapse are not noted in the chart
   2. Patient has experienced improvement in disease symptoms since starting the medication

If criteria are met, approve x 2 years.
If criteria are not met, do not approve.

RATIONALE

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology Chronic Myeloid Leukemia v.2.2023 www.nccn.org
2. NCCN Clinical Practice Guidelines in Oncology Acute Lymphoblastic Leukemia v.1.2022 www.nccn.org
3. NCCN Clinical Practice Guidelines in Oncology Gastrointestinal Stromal Tumors (GISTs) v.1.2023 www.nccn.org

Creation Date: 11/2019
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

NITAZOXANIDE (ALINIA)

Generic	Brand	HICL	GPID	Comments
NITAZOXANIDE	ALINIA	13845	42761, 42763	Specialty tier

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must have one of the diagnoses and meet the specific criteria noted below:

A) Cryptosporidiosis: Must meet one of the following:
   1. Patient is severely immunocompromised (e.g. uncontrolled HIV infection but is receiving antiretroviral therapy [ART], solid organ transplant)
   2. Patient is immunocompetent but either has severe disease or continued symptoms 2 weeks after symptom onset

   If all criteria are met, approve x1 fill, max 14-day supply.

B) Cystoisosporiasis: Must meet all the following:
   1. HIV positive
   2. Trial and failure of, or intolerance to each of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. trimethoprim/sulfamethoxazole DS
      b. ciprofloxacin

   If all criteria are met, approve x1 fill, max 3-day supply.

C) Microsporidiosis: E. bieneusi GI disease
   1. Diagnosis of E. bieneusi strain specifically
   2. Immunocompromised (e.g. uncontrolled HIV infection but is receiving ART, solid organ transplant)
   3. Trial and failure of, or intolerance to albendazole, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If all criteria are met, approve x2 months.

D) Giardiasis: Must meet the following:
   1. Trial and failure of, or intolerance to metronidazole (F) or tinidazole (NF), or the provider has submitted justification and supporting clinical documentation that states one of the following: i)

the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If met, approve x1 fill, max 3-day supply.

E) H. pylori: Must meet all the following:
1. 18 years or older
2. Trial and failure of, intolerance/allergy to, or drug resistance to regimens containing the following therapies, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Clarithromycin
    b. Amoxicillin
    c. Metronidazole

If all criteria are met, approve x1 fill, max 10-day supply.

F) Ascariasis: Must meet the following:
1. Trial and failure of, or intolerance to each of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. albendazole (F)
    b. ivermectin (F)
    c. pyrantel pamoate (NF)

If all criteria are met, approve x1 fill, max 3-day supply.

G) Balantidiasis: Must meet the following:
1. Trial and failure of, or intolerance to each of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

a. a tetracycline antibiotic
b. metronidazole (F) or tinidazole (NF)

If all criteria are met, approve x1 fill, max 3-day supply.

H) Blastocystosis: Must meet all the following:
1. Severe or prolonged (2 weeks of symptoms) disease
2. Trial and failure of, or intolerance to each of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. metronidazole (F) or tinidazole (NF)
    b. trimethoprim/sulfamethoxazole DS

If all criteria are met, approve x1 fill, max 3-day supply.

I) Hymenolepiasis (Hymenolepis nana) dwarf tapeworm: Must meet all the following:
1. Trial and failure of, or intolerance to praziquantel, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
2. At least 11 kg in weight

If all criteria are met, approve x1 fill, max 7-day supply.

J) Fascioliasis (Fasciola hepatica): Must meet the following:
1. Trial and failure of, or intolerance to triclabendazole (NF), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If all criteria are met, approve x1 fill, max 7-day supply.

CONTINUED ON NEXT PAGE

NITAZOXANIDE (ALINIA)

RENEWAL CRITERIA: Must meet both of the following criteria:
1. Minimal to no improvement in symptoms after completion of treatment
2. Confirmation of diagnosis after treatment completion

If both criteria are met, approve x1 additional fill.

RATIONALE
Alinia is used to treat many parasitic infections; however, it is costly and may not be the most appropriate first option. This is in place to ensure appropriate use for uncommon infections.

FDA APPROVED INDICATIONS
Infectious Diarrhea
- Cryptosporidiosis
- Giardiasis

REFERENCES
1. CDC - Fasciola - resources for Health Professionals. Centers for Disease Control and Prevention. https://www.cdc.gov/parasites/fasciola/health_professionals/index.html#:~:text=Triclabendazole%2C%20a%20benzimidazole%20compound%20active,least%206%20years%20of%20age%20. Published September 16, 2020. Accessed October 20, 2021.
2. CDC - Hymenolepis - resources for Health Professionals. Centers for Disease Control and Prevention. https://www.cdc.gov/parasites/hymenolepis/health_professionals/index.html. Published May 22, 2020. Accessed October 20, 2021.
3. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2021. Record No. *T116444*, *Ascariasis*; [updated *2018 Nov 30*, cited **2021 Oct 20**]. Available from https://www.dynamed.com/topics/dmp~AN~*T116444*. Registration and login required.
4. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2021. Record No. *T1604504933105*, *Cryptosporidiosis*; [updated *2020 Jun 3*, cited **2021 Oct 20**]. Available from https://www.dynamed.com/topics/dmp~AN~*T1604504933105*. Registration and login required.
5. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2021. Record No. *T115636*, *Cystoisosporiasis*; [updated *2018 Nov 30*, cited **2021 Oct 20**]. Available from https://www.dynamed.com/topics/dmp~AN~*T115636*. Registration and login required.
6. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2021. Record No. *T1598386231998*, *Balantidium coli*; [updated *2020 Nov 11*, cited **2021 Oct 20**]. Available from https://www.dynamed.com/topics/dmp~AN~*T1598386231998*. Registration and login required.
7. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 -2021. Record No. *T1597688374547*, *Blastocystosis*; [updated *2020 Aug 28*, cited **2021 Oct 20**]. Available from https://www.dynamed.com/topics/dmp~AN~*T1597688374547*. Registration and login required.
8. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 -2021. Record No. *T113949*, *Giardiasis*; [updated *2018 Nov 30*, cited 2021 Oct 20]. Available from https://www.dynamed.com/topics/dmp~AN~*T113949*. Registration and login required.
9. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 -2021. Record No. *T114484*, *Helicobacter pylori Infection*; [updated *2018 Dec 04*, cited **2021 Oct 20**]. Available from https://www.dynamed.com/topics/dmp~AN~*T114484*. Registration and login required.
10. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2021. Record No. *T1621883489380*, *Microsporidiosis*; [updated *2021 Sep 8*, cited 2021 **Oct 20**]. Available from https://www.dynamed.com/topics/dmp~AN~*T1621883489380*. Registration and login required.

11. Nitazoxanide. Clinical Pharmacology https://www-clinicalkey-com.dml.regis.edu/pharmacology/monograph/767. Updated 2021 June, 23. Accessed 2021 Oct 20.
12. Shrivastava AK, Kumar S, Smith WA, Sahu PS. Revisiting the global problem of cryptosporidiosis and recommendations. *Trop Parasitol*. 2017;7(1):8-17. doi:10.4103/2229-5070.202290

Creation Date: 01/2022
Effective Date: 12/2023
Reviewed Date: 11/2023
Revised Date: 11/2023

NONFORMULARY MEDICATIONS

GUIDELINES FOR USE OF NONFORMULARY MEDICATIONS (EXCLUDING BRANDS WHEN A GENERIC IS AVAILABLE)

NONFORMULARY USE GUIDELINE FOR Commercial Members:
Nonformulary medications, when not excluded from benefit coverage, will be approved when all the following criteria are met:

1) Formulary medications treating the same indication have been tried at adequate dosage, taken for an adequate duration, and have been documented as failed, and/or would have adverse effects and/or would be contraindicated, based on individual needs and circumstances, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
2) The use of the drug must be evidence-based, and either be for an FDA-approved indication or have supporting evidence in CMS approved compendia.

NONFORMULARY USE GUIDELINE FOR Federal Group Members (Group 600):
Nonformulary medications, when not excluded from benefit coverage, will be approved when all the following criteria are met:

1) Formulary medications treating the same indication have been tried at adequate dosage, taken for an adequate duration, and have been documented as failed, and/or would have adverse effects and/or would be contraindicated, based on individual needs and circumstances, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
2) The use of the drug must be evidence-based, and either be for an FDA-approved indication or if off-label its use is supported by the clinical evidence from established compendia or peer-reviewed literature and is consistent with generally accepted medical practice. Per OPM Carrier Letter No 2021-02, February 9, 2021, page 4

CONTRACEPTIVE PRODUCT NONFORMULARY USE GUIDELINE FOR Commercial non-grandfathered plans:
Per Emergency Regulation 23-E-07, Contraceptive Benefit Requirements for Health Benefit Plans, effective 1/1/2024:

- All requests for nonformulary contraceptives are considered to be EXPEDITED
- Carriers must cover all FDA-approved contraceptive products, regardless of OTC or Rx status, without cost sharing.
- If the prescriber determines the contraceptive to be medically necessary, that determination shall be final

- We may outreach the prescriber and ask if they would consider changing to one of our formulary alternatives
- Nonformulary requests for contraceptives cannot be denied

RATIONALE
Per KPCO Health Plan, Pharmacy Benefits Department

Created: 1/2019
Reviewed: 11/2022
Revised: 11/2023

NON GLP-1 WEIGHT LOSS MEDICATIONS
NALTREXONE-BUPROPION (CONTRAVE)

Generic	Brand	HICL	GPID	Other
NALTREXONE - BUPROPION	CONTRAVE	41389	37096	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA

A. Must meet all the following:
   1. Patient must have benefit plan with coverage for weight loss medications.
   2. Patient must have an initial body mass index (BMI) greater than or equal to 30 kg/m2, OR an initial BMI greater than or equal to 27 kg/m2 with at least one weight-related comorbid condition, such as hypertension, dyslipidemia, or type 2 diabetes.
   3. Provider attests to patient being on a reduced calorie diet with increased physical activity.
   4. Meets medication specific criteria below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

      a. Patient has tried and failed or has a contraindication* to either phentermine or diethylpropion, and Qsymia.

      If initial criteria are met, approve at HICL x 4 months.
      If initial criteria are not met, do not approve.

RENEWAL CRITERIA

1. Patient must have achieved and maintained at least a 5% weight loss from baseline (objectively measured with in-office weight checks).

   If met, approve x 1 year at HICL.
   If not met, do not approve.

RATIONALE

*Phentermine and diethylpropion have similar efficacy and side effects. In addition, both medications have some chemical and pharmacologic similarities to amphetamines and therefore should not be used in combination with other stimulants as this would lead to pharmacologic duplication and additive side effects.

Setmelanotide (Imcivree) is considered experimental, investigation or unproven for ANY other use including the following (this may not be all inclusive):
* Other Genetic Obesity Syndromes (examples: Prader-Willi syndrome, Alstrom syndrome)
* General Obesity

REFERENCES

Phentermine (phentermine hydrochloride) [package insert]. Epic Pharma, LLC. Revised 11.2019
Diethylpropion (diethylpropion hydrochloride immediate release, diethylpropion hydrochloride controlled release) [package insert]. Ketlman Pharmaceuticals Inc. Revised 6.2010

Setmelanotide (Imcivree) for Rare Genetic Disorders of Obesity – Interregional Practice Recommendations
https://cl.kp.org/co/home/refcontainerpage.html/content/clinicallibrary/natl/cmi/interregional/genetic_obesity/imcivree.nohf.ref.html?q=imcivree&context=shareform

Creation Date: 3/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

NON GLP-1 WEIGHT LOSS MEDICATIONS
SETMELANOTIDE (IMCIVREE)

Generic	Brand	HICL	GPID	Other
SETMELANOTIDE	IMCIVREE	47002	48922	Nonformulary Specialty tier

GUIDELINES FOR COVERAGE

INITIAL CRITERIA

A. Must meet all the following:
   1. Prescribed by an endocrinologist, a geneticist, or a board-certified obesity medicine specialist.
   2. Patient has at least one FDA approved indication:
      a. Obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by:
         i. Genetic testing demonstrating variants in POMC, PCSK1 or LEPR genes
         ii. The genetic variant is interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS)
      b. Bardet-Biedl Syndrome (BBS) confirmed by generic testing or highly suspected BBS based on review and evaluation by specialist
   3. Patient meets one of the following criteria (a or b):
      a. Patient is 18 years of age or older with a body mass index (BMI) greater than or equal to 30 kg/m2
      b. Patient is 6 to 17 years of age with a BMI above the 95th percentile for age and gender

      If initial criteria are met, approve based on patient age:
      - 18 years of age or older: x4 months at HICL.
      - Under 18 years of age: x12 months at HICL.

      If initial criteria are not met, do not approve.

RENEWAL CRITERIA

A. Must meet all the following:
   1. Prescribed by an endocrinologist, a geneticist, or a board-certified obesity medicine specialist.
   2. Patient must have achieved and maintained at least a 5% weight loss from baseline, or 5% of baseline BMI (objectively measured with in-office weight checks).

      If met, approve x 1 year at HICL.
      If not met, do not approve.

RATIONALE

*Phentermine and diethylpropion have similar efficacy and side effects. In addition, both medications have some chemical and pharmacologic similarities to amphetamines and therefore should not be used in combination with other stimulants as this would lead to pharmacologic duplication and additive side effects.

Setmelanotide (Imcivree) is considered experimental, investigation or unproven for ANY other use including the following (this may not be all inclusive):
* Other Genetic Obesity Syndromes (examples: Prader-Willi syndrome, Alstrom syndrome)
* General Obesity

REFERENCES

Phentermine (phentermine hydrochloride) [package insert]. Epic Pharma, LLC. Revised 11.2019
Diethylpropion (diethylpropion hydrochloride immediate release, diethylpropion hydrochloride controlled release) [package insert]. Ketlman Pharmaceuticals Inc. Revised 6.2010

Setmelanotide (Imcivree) for Rare Genetic Disorders of Obesity – Interregional Practice Recommendations
https://cl.kp.org/co/home/refcontainerpage.html/content/clinicallibrary/natl/cmi/interregional/genetic_obesity/imcivree.nohf.ref.html?q=imcivree&context=shareform

Creation Date: 3/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

NON GLP-1 WEIGHT LOSS MEDICATIONS
PHENTERMINE-TOPIRAMATE (QSYMIA)

Generic	Brand	HICL	GPID	Other
PHENTERMINE - TOPIRAMATE	QSYMIA	39347	32744, 32745, 32746, 32515	Formulary w/PA

GUIDELINES FOR COVERAGE

INITIAL CRITERIA

A. Must meet all the following:
   1. Patient must have benefit plan with coverage for weight loss medications.
   2. Patient must have an initial body mass index (BMI) greater than or equal to 30 kg/m2, OR an initial BMI greater than or equal to 27 kg/m2 with at least one weight-related comorbid condition, such as hypertension, dyslipidemia, or type 2 diabetes.
   3. Provider attests to patient being on a reduced calorie diet with increased physical activity.
   4. Meets medication specific criteria below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

      a. Patient has tried and failed or has a contraindication* to phentermine or diethylpropion.

         If initial criteria are met, approve at HICL x 4 months.
         If initial criteria are not met, do not approve.

RENEWAL CRITERIA

1. Patient must have achieved and maintained at least a 5% weight loss from baseline (objectively measured with in-office weight checks).

   If met, approve x 1 year at HICL.
   If not met, do not approve.

RATIONALE

*Phentermine and diethylpropion have similar efficacy and side effects. In addition, both medications have some chemical and pharmacologic similarities to amphetamines and therefore should not be used in combination with other stimulants as this would lead to pharmacologic duplication and additive side effects.

Setmelanotide (Imcivree) is considered experimental, investigation or unproven for ANY other use including the following (this may not be all inclusive):
* Other Genetic Obesity Syndromes (examples: Prader-Willi syndrome, Alstrom syndrome)
* General Obesity

REFERENCES

Phentermine (phentermine hydrochloride) [package insert]. Epic Pharma, LLC. Revised 11.2019
Diethylpropion (diethylpropion hydrochloride immediate release, diethylpropion hydrochloride controlled release) [package insert]. Ketlman Pharmaceuticals Inc. Revised 6.2010

Setmelanotide (Imcivree) for Rare Genetic Disorders of Obesity – Interregional Practice Recommendations
https://cl.kp.org/co/home/refcontainerpage.html/content/clinicallibrary/natl/cmi/interregional/genetic_obesity/imcivree.nohf.ref.html?q=imcivree&context=shareform

Creation Date: 3/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

NON-PREFERRED JAK INHIBITORS
CIBINQO

Generic	Brand	Tablet Strength	HICL	GCN	Exception/Other
ABROCITINIB	CIBINQO	50 MG, 100 MG, 200 MG	47767	51825, 51827, 51828	Nonformulary Specialty tier

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on therapy, Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine), and has one of the following indications managed by the appropriate specialist as noted below:
   1. The patient has a diagnosis of Atopic Dermatitis and requested medication is prescribed by a CPMG or affiliated dermatology specialist.

      If met, approve indefinitely.
      If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Atopic Dermatitis:
   1. The patient has a diagnosis of moderate to severe atopic dermatitis, and the medication requested is prescribed by a CPMG or affiliated dermatology provider.
   2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, methotrexate, cyclosporine)
   3. Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Inadequate response (after at least 2 months) or intolerance to at least one topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus). [If the patient has been on biologic therapy within the past 4 months, skip and proceed to step 3c.]
      b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy, Azathioprine, Cyclosporine, Methotrexate, Mycophenolate
      c. Inadequate response (after at least 2 months), intolerance, or relative contraindication to dupilumab (Dupixent) or tralokinumab (Adbry).

      If criteria are met, approve indefinitely with max daily dose of 1 tablet per day.
      If criteria are not met, do not approve.

RATIONALE:
Per Health Plan

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

Note: A Health Plan cannot deny based on patients' ability to cut tablets, so if qualifies for the drug and cannot cut tablets, must approve the 5mg or 11mg strength as applicable. However, please inform the provider/patient that the 10mg strength is a formulary brand tier medication and the 5mg and 11mg strengths are specialty tier medications.

In alopecia areata, time to initial hair growth with JAK inhibitors does not appear for at least several months.

FDA APPROVED INDICATIONS
Ulcerative colitis
Crohn's disease (Rinvoq only)
Rheumatoid arthritis
Psoriatic arthritis
Atopic dermatitis
Polyarticular course juvenile idiopathic arthritis
Alopecia Areata

REFERENCES
Per Health Plan.

30-DAY QUANTITY LIMITS:

Brand Name	Dosage Form	Strength(s)	# units per day supply or dispense
Xeljanz	Tablet	5 mg	2 per day
Xeljanz XR	Tablet	11 mg, 22 mg	1 per day
Xeljanz	Solution	1 mg/ml	Max 10 mg (10 ml) per day
Olumiant	Tablet	1 mg, 2 mg, 4 mg	1 per day
Rinvoq	Tablet	15 mg, 30 mg, 45 mg	1 per day
Cibinqo	Tablet	50 mg, 100 mg, 200 mg	1 per day

Creation date: 03/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

NON-PREFERRED JAK INHIBITORS
LITFULO

Generic	Brand	Tablet Strength	HICL	GCN	Exception/Other
RITLECITINIB	LITFULO	50 MG	49026	54429	Nonformulary Specialty tier

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on therapy, Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine), and has one of the following indications managed by the appropriate specialist as noted below:
   1. The patient has a diagnosis of severe Alopecia Areata (AA) and requested medication is prescribed by a CPMG or affiliated dermatologist.

      If met, approve indefinitely.
      If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Alopecia Areata:
   1. Patient is 12 years of age or older and has a diagnosis of severe alopecia areata with 50% or more scalp hair loss, and the medication requested is prescribed by a CPMG or affiliated dermatologist.
   2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, methotrexate, cyclosporine)
   3. Patient with inadequate response (after at least 4 months), intolerance, or contraindication to methotrexate or oral tofacitinib (Xeljanz), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
   4. And must meet ONE of the following:
      a. Patient with inadequate response (after at least 4 months), intolerance, or relative contraindication to baricitinib (Olumiant), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
      b. Patient is under 18 years of age

If criteria are met, approve ritlecitinib (Litfulo) indefinitely, max 1 capsule per day.
If criteria are not met, do not approve.

RATIONALE:
Per Health Plan

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

Note: A Health Plan cannot deny based on patients' ability to cut tablets, so if qualifies for the drug and cannot cut tablets, must approve the 5mg or 11mg strength as applicable. However, please inform the provider/patient that the 10mg strength is a formulary brand tier medication and the 5mg and 11mg strengths are specialty tier medications.

In alopecia areata, time to initial hair growth with JAK inhibitors does not appear for at least several months.

FDA APPROVED INDICATIONS
Ulcerative colitis
Crohn's disease (Rinvoq only)
Rheumatoid arthritis
Psoriatic arthritis
Atopic dermatitis
Polyarticular course juvenile idiopathic arthritis
Alopecia Areata

REFERENCES
Per Health Plan.

30-DAY QUANTITY LIMITS:

Brand Name	Dosage Form	Strength(s)	# units per day supply or dispense
Xeljanz	Tablet	5 mg	2 per day
Xeljanz XR	Tablet	11 mg, 22 mg	1 per day
Xeljanz	Solution	1 mg/ml	Max 10 mg (10 ml) per day
Olumiant	Tablet	1 mg, 2 mg, 4 mg	1 per day
Rinvoq	Tablet	15 mg, 30 mg, 45 mg	1 per day
Cibinqo	Tablet	50 mg, 100 mg, 200 mg	1 per day

Creation date: 03/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

NON-PREFERRED JAK INHIBITORS
OLUMIANT

Generic	Brand	Tablet Strength	HICL	GCN	Exception/Other
BARICITINIB	OLUMIANT	1 MG 2 MG 4 MG	44296	47205, 43468, 43469	Nonformulary Specialty tier

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on therapy, Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine), and has one of the following indications managed by the appropriate specialist as noted below:
   1. Patient has a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Ankylosing Spondylitis, Nonradiographic Axial Spondyloarthritis, or Polyarticular Juvenile Idiopathic Arthritis (JIA) and requested medication is prescribed by a CPMG or affiliated rheumatologist.
   2. The patient has a diagnosis of severe Alopecia Areata (AA) and requested medication is prescribed by a CPMG or affiliated dermatologist.

      If met, approve indefinitely.
      If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Rheumatoid Arthritis
B. Alopecia Areata (severe)

B. Rheumatoid Arthritis:
   1. Patient is 18 years of age or older, has a diagnosis of RA, and medication is prescribed by a CPMG or affiliated rheumatologist.
   2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine)
   3. Patient with failure or intolerance to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. At least 2 DMARDs including methotrexate, hydroxychloroquine, sulfasalazine, or leflunomide
      b. At least 1 TNFi (e.g. infliximab-dyyb-preferred [F], adalimumab-atto-preferred [F, PA])
   4. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug;

iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

a. Olumiant 1 mg or 2 mg: Patient with failure, intolerance, or contraindication to Xeljanz

If criteria are met, approve indefinitely, max 1 per day.
If criteria are not met, do not approve.

C. Alopecia Areata:
1. Patient is 12 years of age or older and has a diagnosis of severe alopecia areata with 50% or more scalp hair loss, and the medication requested is prescribed by a CPMG or affiliated dermatologist.
2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, methotrexate, cyclosporine)
3. Patient with inadequate response (after at least 4 months), intolerance, or contraindication to methotrexate or oral tofacitinib (Xeljanz), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If criteria are met, approve baricitinib (Olumiant) indefinitely, max 1 tablet per day.
If criteria are not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member or Initial prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval.

- Patient with diagnosis of alopecia areata and must be for 2 mg baricitinib tablets only, 2 total tablets per day:
1. Provider states patient is experiencing worsening or no improvement of alopecia areata on baricitinib (Olumiant) 2mg per day dosing after at least 4 months

If criteria are met, approve baricitinib (Olumiant) 2mg tablets, max 2 tablets per day.
If criteria are not met, do not approve.

RATIONALE:
Per Health Plan

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

Note: A Health Plan cannot deny based on patients' ability to cut tablets, so if qualifies for the drug and cannot cut tablets, must approve the 5mg or 11mg strength as applicable. However, please inform the provider/patient that the 10mg strength is a formulary brand tier medication and the 5mg and 11mg strengths are specialty tier medications.

In alopecia areata, time to initial hair growth with JAK inhibitors does not appear for at least several months.

FDA APPROVED INDICATIONS
Ulcerative colitis
Crohn's disease (Rinvoq only)
Rheumatoid arthritis
Psoriatic arthritis
Atopic dermatitis
Polyarticular course juvenile idiopathic arthritis
Alopecia Areata

REFERENCES
Per Health Plan.

30-DAY QUANTITY LIMITS:

Brand Name	Dosage Form	Strength(s)	# units per day supply or dispense
Xeljanz	Tablet	5 mg	2 per day
Xeljanz XR	Tablet	11 mg, 22 mg	1 per day
Xeljanz	Solution	1 mg/ml	Max 10 mg (10 ml) per day
Olumiant	Tablet	1 mg, 2 mg, 4 mg	1 per day
Rinvoq	Tablet	15 mg, 30 mg, 45 mg	1 per day
Cibinqo	Tablet	50 mg, 100 mg, 200 mg	1 per day

Creation date: 03/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

NON-PREFERRED JAK INHIBITORS
RINVOQ

Generic	Brand	Tablet Strength	HICL	GCN	Exception/Other
UPADACITINIB	RINVOQ	15 MG 30 MG 45 MG	45955	46822, 51719, 52085	Nonformulary Specialty tier

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on therapy, Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine), and has one of the following indications managed by the appropriate specialist as noted below:
   1. Patient has a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Ankylosing Spondylitis, Nonradiographic Axial Spondyloarthritis, or Polyarticular Juvenile Idiopathic Arthritis (JIA) and requested medication is prescribed by a CPMG or affiliated rheumatologist.
   2. Patient has a diagnosis of Ulcerative Colitis, Crohn's Disease, or Inflammatory Bowel Disease-Unspecified/Indeterminate Colitis (IBD-U) and requested medication is prescribed by a CPMG or affiliated gastroenterology specialist.
   3. Patient has a diagnosis of Atopic Dermatitis and requested medication is prescribed by a CPMG or affiliated dermatology specialist.

   If met, approve indefinitely.
   If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Rheumatoid Arthritis
B. Psoriatic Arthritis (PsA)
C. Ankylosing Spondylitis, Nonradiographic Axial Spondyloarthritis
D. Ulcerative Colitis (UC), Crohn’s Disease (CD) or Inflammatory Bowel Disease-Unspecified/Indeterminate Colitis (IBD-U)
E. Atopic Dermatitis

A. Rheumatoid Arthritis:
   1. Patient is 18 years of age or older, has a diagnosis of RA, and medication is prescribed by a CPMG or affiliated rheumatologist.
   2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine)
   3. Patient with failure or intolerance to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

   a. At least 2 DMARDs including methotrexate, hydroxychloroquine, sulfasalazine, or leflunomide
   b. At least 1 TNFi (e.g. infliximab-dyyb-preferred [F], adalimumab-atto-preferred [F, PA])
4. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Rinvoq 15 mg: Patient with failure, intolerance, or contraindication to Xeljanz and/or Olumiant

      If criteria are met, approve at GPID indefinitely, max 1 per day.
      If criteria are not met, do not approve.

B. Psoriatic Arthritis (PsA):
1. Patient is 18 years of age or older, has a diagnosis of PsA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine)
3. Patient with failure or intolerance to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. At least 2 DMARDs including methotrexate, hydroxychloroquine, sulfasalazine, or leflunomide
   b. At least 1 TNFi (e.g. infliximab-dyyb-preferred [F], adalimumab-atto-preferred [F, PA])
4. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Rinvoq 15 mg: Patient with failure, intolerance, or contraindication to Xeljanz

      If criteria are met, approve at GPID indefinitely, max 1 per day.
      If criteria are not met, do not approve.

C. Ankylosing Spondylitis or Nonradiographic Axial Spondyloarthritis:

1. Patient is 18 years of age or older, has a diagnosis of either Ankylosing Spondylitis or Nonradiographic Axial Spondyloarthritis, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine)
3. Patient with failure or intolerance to at least 1 TNFi (e.g. infliximab-dyyb-preferred [F], adalimumab-atto-preferred [F, PA]), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
4. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Rinvoq 15 mg: Patient with failure, intolerance, or contraindication to Xeljanz

       If criteria are met, approve at GPID indefinitely, max 1 per day.
       If criteria are not met, do not approve.

D. Ulcerative Colitis (UC), Crohn's Disease (CD) or Inflammatory Bowel Disease-Unspecified/Indeterminate Colitis (IBD-U):
    1. Patient is 18 years of age or older, has a diagnosis of UC, CD, or IBD-U, and medication is prescribed by a CPMG or affiliated gastroenterologist.
    2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitors, azathioprine, cyclosporine)
    3. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        a. Rinvoq: Patient has experienced an inadequate response, intolerance, or has a contraindication to at least 1 TNF inhibitor (ex: infliximab [F], adalimumab [F, PA], golimumab [NF, PA] or certolizumab [NF, PA])

       If criteria are met, approve as follows:

- FIRST APPROVAL: Approve Rinvoq 45 mg at GPID x 12 weeks with a quantity limit of #1 tablet per day.
- SECOND and THIRD APPROVALS: Approve Rinvoq 15 mg and 30 mg, each at GPID, indefinitely with a quantity limit of #1 tablet per day. (Please enter start date of 1 week BEFORE the END date of first approval.)

If criteria are not met, do not approve.

E. Atopic Dermatitis:
1. The patient has a diagnosis of moderate to severe atopic dermatitis, and the medication requested is prescribed by a CPMG or affiliated dermatology provider.
2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, methotrexate, cyclosporine)
3. Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Inadequate response (after at least 2 months) or intolerance to at least one topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus). [If the patient has been on biologic therapy within the past 4 months, skip and proceed to step 3c.]
   b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy, Azathioprine, Cyclosporine, Methotrexate, Mycophenolate
   c. Inadequate response (after at least 2 months), intolerance, or relative contraindication to dupilumab (Dupixent) or tralokinumab (Adbry).

   If criteria are met, approve indefinitely with max daily dose of 1 tablet per day.
   If criteria are not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member or Initial prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval.

- Patient with diagnosis of Ulcerative Colitis, Crohn's Disease, or Inflammatory Bowel Disease-Unspecified/Indeterminate Colitis (IBD-U) for whom provider is requesting continuation of Rinvoq 45 mg beyond the initial 12-week approval:
  1. Provider states patient has had no significant clinical response. Patient should have objective signs of ongoing disease activity as demonstrated on colonoscopy or with elevated inflammatory markers (fecal calprotectin or C-reactive protein).

     If criteria are met, approve x additional 12 weeks with a quantity limit of #1 tablet per day.
     If criteria are not met, do not approve. Patient should proceed with maintenance dosing of 15 mg or 30 mg tablets.

RATIONALE
Per Health Plan

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

Note: A Health Plan cannot deny based on patients' ability to cut tablets, so if qualifies for the drug and cannot cut tablets, must approve the 5mg or 11mg strength as applicable. However, please inform the provider/patient that the 10mg strength is a formulary brand tier medication and the 5mg and 11mg strengths are specialty tier medications.

In alopecia areata, time to initial hair growth with JAK inhibitors does not appear for at least several months.

FDA APPROVED INDICATIONS
Ulcerative colitis
Crohn's disease (Rinvoq only)
Rheumatoid arthritis
Psoriatic arthritis
Atopic dermatitis
Polyarticular course juvenile idiopathic arthritis
Alopecia Areata

REFERENCES
Per Health Plan.

30-DAY QUANTITY LIMITS:

Brand Name	Dosage Form	Strength(s)	# units per day supply or dispense
Xeljanz	Tablet	5 mg	2 per day
Xeljanz XR	Tablet	11 mg, 22 mg	1 per day
Xeljanz	Solution	1 mg/ml	Max 10 mg (10 ml) per day
Olumiant	Tablet	1 mg, 2 mg, 4 mg	1 per day
Rinvoq	Tablet	15 mg, 30 mg, 45 mg	1 per day
Cibinqo	Tablet	50 mg, 100 mg, 200 mg	1 per day

Creation date: 03/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

NON-PREFERRED JAK INHIBITORS
XELJANZ

Generic	Brand	Tablet Strength	HICL	GCN	Exception/Other
TOFACITINIB CITRATE	XELJANZ, XELJANZ XR	5 MG, 11 MG XR 22 MG XR 1 MG/ML		33617, 38086, 47546, 48684	Xeljanz 10mg tablets are Preferred Formulary and NOT Specialty tier

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Rheumatoid Arthritis
B. Psoriatic Arthritis (PsA)
C. Ankylosing Spondylitis, Nonradiographic Axial Spondyloarthritis
D. Polyarticular Juvenile Idiopathic Arthritis (PJIA)
E. Ulcerative Colitis (UC), Crohn's Disease (CD) or Inflammatory Bowel Disease-Unspecified/Indeterminate Colitis (IBD-U)

A. Rheumatoid Arthritis:
   1. Patient is 18 years of age or older, has a diagnosis of RA, and medication is prescribed by a CPMG or affiliated rheumatologist.
   2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine)
   3. Patient with failure or intolerance to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. At least 2 DMARDs including methotrexate, hydroxychloroquine, sulfasalazine, or leflunomide
      b. At least 1 TNFi (e.g. infliximab-dyyb-preferred [F], adalimumab-atto-preferred [F, PA])
   4. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Xeljanz 5 mg or 11 mg XR: Patient is unable to use 10 mg tablets, one-half tablet 2 times a day, due to a clinical/physical/medical reason (i.e., dexterity or vision issues)

         If criteria are met, approve indefinitely, max 2 per day for 5mg or 1 per day for the XR.

If criteria are not met, do not approve.

B. Psoriatic Arthritis (PsA):
1. Patient is 18 years of age or older, has a diagnosis of PsA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine)
3. Patient with failure or intolerance to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. At least 2 DMARDs including methotrexate, hydroxychloroquine, sulfasalazine, or leflunomide
   b. At least 1 TNFi (e.g. infliximab-dyyb-preferred [F], adalimumab-atto-preferred [F, PA])
4. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Xeljanz 5 mg or 11 mg XR: Patient is unable to use 10 mg tablets, one-half tablet 2 times a day, due to a clinical/physical/medical reason (i.e., dexterity or vision issues)

      If criteria are met, approve indefinitely, max 2 per day for 5mg or 1 per day for the XR.
      If criteria are not met, do not approve.

C. Ankylosing Spondylitis or Nonradiographic Axial Spondyloarthritis:
1. Patient is 18 years of age or older, has a diagnosis of either Ankylosing Spondylitis or Nonradiographic Axial Spondyloarthritis, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine)
3. Patient with failure or intolerance to at least 1 TNFi (e.g. infliximab-dyyb-preferred [F], adalimumab-atto-preferred [F, PA]), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

4. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Xeljanz 5 mg or 11 mg XR: Patient is unable to use 10 mg tablets, one-half 2 times a day, due to clinical/physical/medical reason (i.e., dexterity or vision issues)

      If criteria are met, approve Xeljanz 5 mg or 11 mg XR indefinitely, max 2 per day for 5mg or 1 per day for the XR.
      If criteria are not met, do not approve.

D. Polyarticular Juvenile Idiopathic Arthritis (PJIA):
   1. Patient is 2 years of age or older, has a diagnosis of JIA, and medication is prescribed by a CPMG or affiliated rheumatologist.
   2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitor, azathioprine, cyclosporine)
   3. Patient with failure or intolerance to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. At least 1 DMARD
      b. at least 1 TNFi (e.g. adalimumab-atto (Amjevita)-preferred [F, PA])
   4. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Xeljanz 1 mg/ml solution: Patient body weight is less than 40 kg, or the patient is unable to swallow tablets
      b. Xeljanz 5 mg: Patient body weight is 40 kg or more and the patient is unable to use the 10 mg tablets, one-half tablet 2 times a day, due to a clinical/physical/medical reason (i.e., dexterity or vision issues)

      If criteria are met, approve indefinitely.
      If criteria are not met, do not approve.

E. Ulcerative Colitis (UC), Crohn's Disease (CD) or Inflammatory Bowel Disease-Unspecified/Indeterminate Colitis (IBD-U):
   1. Patient is 18 years of age or older, has a diagnosis of UC, CD, or IBD-U, and medication is prescribed by a CPMG or affiliated gastroenterologist.
   2. Medication is not being used in combination with another biologic or relevant immunosuppressive therapy for the same indication (TNFi, IL 12/23i, IL 17i, alpha4beta7 Integrin-inhibitors, azathioprine, cyclosporine)
   3. Medication requested is one of the following and all medication-specific criteria below are met, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Xeljanz 5 mg or 11 mg XR: Patient has UC or IBD-U. Patient stepped down from 10 mg 2 times a day to 5 mg 2 times a day, and is unable to use 10 mg tablets, one-half tablet 2 times a day, due to a clinical/physical/medical reason (i.e., dexterity or vision issues)
      b. Xeljanz 22 mg XR: Patient has UC or IBD-U and is unable to use 10 mg tablets, one tablet 2 times a day, due to clinical/physical/medical reason (i.e., dexterity or vision issues)

      If criteria are met, approve indefinitely, max 2 per day for 5 mg or 1 per day for XR.
      If criteria are not met, do not approve.

RATIONALE:
Per Health Plan

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

Note: A Health Plan cannot deny based on patients' ability to cut tablets, so if qualifies for the drug and cannot cut tablets, must approve the 5mg or 11mg strength as applicable. However, please inform the provider/patient that the 10mg strength is a formulary brand tier medication and the 5mg and 11mg strengths are specialty tier medications.

In alopecia areata, time to initial hair growth with JAK inhibitors does not appear for at least several months.

FDA APPROVED INDICATIONS
Ulcerative colitis
Crohn's disease (Rinvoq only)
Rheumatoid arthritis
Psoriatic arthritis
Atopic dermatitis
Polyarticular course juvenile idiopathic arthritis
Alopecia Areata

REFERENCES

Per Health Plan.

30-DAY QUANTITY LIMITS:

Brand Name	Dosage Form	Strength(s)	# units per day supply or dispense
Xeljanz	Tablet	5 mg	2 per day
Xeljanz XR	Tablet	11 mg, 22 mg	1 per day
Xeljanz	Solution	1 mg/ml	Max 10 mg (10 ml) per day
Olumiant	Tablet	1 mg, 2 mg, 4 mg	1 per day
Rinvoq	Tablet	15 mg, 30 mg, 45 mg	1 per day
Cibinqo	Tablet	50 mg, 100 mg, 200 mg	1 per day

Creation date: 03/2020
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

NOVEL MIGRAINE MEDICATIONS
ATOGEPANT (QULIPTA)

Generic	Brand	HICL	GCN/GPID	Exception/Other
ATOGEPANT	QULIPTA	47599	51231, 51232, 51236	Oral CGRP antagonist; "Gepant" for preventive tx

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:

A. Patient is new to KPCO within the past 90 days
B. Patient is stable on atogepant (Qulipta) for preventive migraine treatment

If above are met, then approve x 3 months (to allow time for consideration of formulary preferred alternatives) at HICL with a maximum 1 tablet per day.

(Then must meet Initial Criteria for ongoing coverage).
If New Member criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the following:

A. Patient must be age 18 or older
B. Must be prescribed by a Neurologist, Pain Specialist, or Headache Specialist
C. Must meet diagnosis and medication specific criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Must meet the following:
    a. Request is for atogepant (Qulipta) daily for the preventive treatment of migraine
    b. Patient is not taking another CGRP-directed medication for migraine prevention
    c. Prescriber attests that patient is decreasing or stopping medications causing medication overuse headaches (MOH), if MOH is noted or apparent
    d. Patient is not taking an opiate (including tramadol) or barbiturate (including butalbital-containing product) for the treatment of headache for more than 4 days per month, including in the month prior to this request
    e. Patient has completed a Migraine Disability Assessment (MIDAS) or has documentation of headache days per month for at least one month in the past three months
    f. Patient with failure of (after at least 6-8 weeks at maximally tolerated dose), intolerance to, or contraindication to, at least one medication from each of the three migraine preventive classes:
        i. Anticonvulsants: divalproex, valproate, topiramate
        ii. Beta blockers: atenolol, metoprolol, nadolol, propranolol, timolol
        iii. Antidepressants: amitriptyline, nortriptyline, venlafaxine, duloxetine
    g. Patient with failure of (after at least two monthly doses), intolerance to, or contraindication to, at least 1 CGRP-mAb [erenumab (Aimovig), eptinezumab (Vyepti), fremanezumab (Ajovy), galcanezumab (Emgality)] for migraine prevention

If initial criteria are met, then approve x3 months at HICL with a quantity limit of maximum 1 tablet per day.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following criteria:
A. Request is for atogepant (Qulipta) daily for preventive treatment of migraine
B. Patient has experienced improvement after at least 3 months of starting atogepant (Qulipta) for migraine prevention, as demonstrated by one of the following:
   1. At least 30% reduction in migraine days per month
   2. A decrease in MIDAS score by 8 or more points

If renewal criteria are met, then approve indefinitely at HICL with a quantity limit of maximum 1 tablet per day.
If renewal criteria are not met, do not approve.

Available triptan/ergotamine options:

Generic	Brand	Formulations available
Almotriptan	Axert	Tablet
Eletriptan	Relpax	Tablet
Frovatriptan	Frova	Tablet
Naratriptan	Amerge	Tablet
Rizatriptan	Maxalt/Maxalt MLT	Tablet, ODT
Sumatriptan	Imitrex, Sumavel, Onzetra, Zembrace	Tablet, nasal spray, injection
Zolmitriptan	Zomig/Zomig ZMT	Tablet, ODT, nasal spray
Ergotamine	Ergomar	Sublingual
Ergotamine/caffeine	Cafergot	Tablet, suppository
Dihydroergotamine	Migranal, Trudhesa D.H.E.	Nasal spray, injection

ODT=orally disintegrating tablet

True contraindications to triptan class
- Ischemic coronary artery disease including angina pectoris, history of myocardial infarction, documented silent ischemia, coronary artery vasospasm (including Prinzmetal's angina)
- History of stroke or transient ischemic attack
- Peripheral vascular disease
- Ischemic bowel disease
- Uncontrolled hypertension
- Hemiplegic or basilar migraine
- Wolff-Parkinson-White syndrome

Quantity Limits for Acute Migraine Treatment

Medication	Dosage Strength	Maximum quantity limit for 30 days	Notes
Acute migraine indication			
Ubrogepant (Ubrelvy)	50 mg, 100 mg	10	Tablet splitting of the 100 mg tablet has been approved and

			should be recommended for all patients prescribed to take a dose of 50 mg at onset of migraine
Rimegepant (Nurtec ODT)	75 mg	8	Tablet splitting n/a
Zavegepant (Zavzpret)	10 mg	6	Available as a ready-to-use, unit-dose disposable nasal spray device that contains 10 mg of zavegepant. Each carton contains 6 nasal spray units.
Lasmiditan (Reyvow)	50 mg	4	Tablet splitting NOT approved Approved doses to take at onset of migraine are 50 mg, 100 mg, or 200 mg, however, only 50 mg and 100 mg tablet strengths are available
	100 mg	8	
Preventive migraine indication			
Atogepant (Qulipta)	10 mg, 30 mg, 60 mg	30	Tablet splitting of the 60 mg tablet has been approved and should be recommended for all patients prescribed 30 mg daily
Rimegepant (Nurtec ODT)	75 mg	15	Tablet splitting n/a

CGRP-Directed Migraine Medications

Generic (Brand)	Route CGRP "class"	Acute Migraine Approval	Preventive Migraine Approval
Eptinezumab (Vyepti)	IV, CGRP-mAb	X	100 mg or 300 mg Q 3 mo
Erenumab (Aimovig)	SC, CGRP-mAb	X	70 mg or 140 mg Q mo
Fremanezumab (Ajovy)	SC, CGRP-mAb	X	225 mg Q mo, OR 675 mg Q 3 mo
Galcanezumab (Emgality)	SC, CGRP-mAb	X	240 mg loading dose, then 120 mg Q mo
Atogepant (Qulipta)	Oral, CGRP antagonist "gepant"	X	10 mg, 30 mg or 60 mg daily
Rimegepant (Nurtec ODT)	Orally disintegrating tablet, CGRP antagonist "gepant"	75 mg at onset do NOT repeat dose	75 mg every OTHER day
Ubrogepant (Ubrelvy)	Oral, CGRP antagonist "gepant"	50 mg or 100 mg at onset, may repeat in 2 hours	X
Zavegepant (Zavzpret)	Intranasal, CGRP antagonist "gepant"	10 mg at onset do NOT repeat dose	X

RATIONALE

Acute migraine indication

At this time, there is a lack of compelling data for ubrogepant, rimegepant, or lasmiditan to replace triptans as the gold standard for acute migraine treatment, considering cost and familiarity [1]. The 2019 AHS update briefly mentions role of emerging acute therapies as these options were not approved until about one year after its publication AHS [2]. Reiterated is the role for these novel treatment options, which do not result in constriction of blood vessels, for patients with vascular-related contraindications to triptans. Also acknowledged is the higher cost of these new agents compared to the generic availability of oral triptans and recommendation for ubrogepant, rimegepant, or lasmiditan to be used only in patients who have contraindications to triptans or who have failed to respond or tolerate at least two oral triptans. Patients should treat at least 2 migraine attacks before a provider makes a determination on efficacy and tolerability.

A comparative analysis of ubrogepant, lasmiditan, and rimegepant was performed by the Institute of Clinical and Economic Review (ICER) to assess the effectiveness and safety of these medications. [3] In comparison to placebo, ubrogepant [odds ratio (OR) 2.12], rimegepant [OR 2.11], and lasmiditan [OR 3.01] showed higher odds of achieving pain freedom at 2 hours. The analysis did not demonstrate statistically significant differences among the medications in pain freedom at two hours, absence of the most bothersome symptoms at two hours, and no disability at two hours in comparison to one another. On the other hand, in comparing triptans and ubrogepant, sumatriptan [OR 4.09] and eletriptan [OR 5.6] have shown to have higher odds of pain freedom at two hours than ubrogepant.

With regards to safety, nausea was the most common adverse effect seen with the use of ubrogepant. For single migraine attacks, ubrogepant and rimegepant had similar odds of experiencing any adverse event compared to triptans and placebo, but ubrogepant [OR 5.10] had lower odds for treatment-emergent adverse events compared to lasmiditan. Also, the risk of medication overuse headaches, which is present with triptans, is unknown with repeated use of ubrogepant and rimegepant.

In terms of cost per quality-adjusted life year (QALY) gained threshold, ubrogepant is considered cost effective at $40,000 per QALY gained. Ubrogepant has similar QALY values compared to rimegepant. Comparing ubrogepant and triptans, the cost of ubrogepant is substantially greater than triptans and has less QALYs than sumatriptan and eletriptan.

If choosing one of these new acute medication options, pharmacokinetics and characteristics of a patient's migraine attacks should be kept in mind. Lasmiditan has pharmacokinetic characteristic similar to faster-acting triptans and most closely similar to almotriptan and eletriptan in regard to onset of action, time to maximum concentration, and half-life. Ubrogepant and rimegepant have slower onsets of action but longer half-lives which may be helpful for patients experiencing migraine recurrence. Dosing recommendations should also be considered when using these new medications including if a dose can be repeated in 2 hours, dose adjustments with other disease states, and potential for drug interactions (Table 1).

As the only gepant medication supplied in a non-oral formulation, zavegepant 10 mg nasal spray could be particularly useful in patients with characteristics associated with guideline-based recommendations for non-oral therapies, including headache attacks with severe nausea or vomiting or rapidly escalating headache pain, as well as for patients in whom oral forms are associated with inadequate response, slow onset of action, or poor tolerability. Additional trials are needed to provide evidence for the long-term safety and consistency of effect over time.

Using triptans as part of a combination therapy regimen can be useful (although possibly underutilized in clinical practice) and careful selection of agents to combine can achieve synergistic pharmacokinetic effects. For example, in patients needing a quick onset of action to relieve the migraine pain but also a longer duration to avoid migraine recurrence, a fast acting triptan (e.g. nasal spray, injectable, or faster-acting oral) can be combined with a long-acting NSAID. Effectiveness and safety of combining gepants or lasmiditan with other acute therapies is less defined. Pertaining to other acute migraine medications that could be utilized, study protocols for phase 3 clinical trials differed slightly, but all included specific recommendations for what patients could or could not take within 24 hours or 48 hours after the initial dose of the study medication. Due to the potential for duplicating mechanisms, it appears logical to avoid the combination of lasmiditan with a triptan, but there may be a role for combining lasmiditan with an analgesic and/or antiemetic if needed. While gepants and triptans do not appear to directly have overlapping mechanisms, they do both target the trigeminovascular system, and thus the utility in combining a gepant with a triptan remains unclear. Given the slower onset of gepants, there may be clinical situations where combining a gepant with a faster acting NSAID could be beneficial. Overall, more data is needed.

More real-world utilization and long-term safety and efficacy data is needed for these new acute medication options, but the development of these therapy options fills a long-standing gap in therapy for patients with multiple trials and failures of triptans or those with contraindications to this class.

Preventive migraine indication
Rimegepant was the first oral gepant approved for preventive treatment of migraine and this expanded indication came after rimegepant had already been approved for acute treatment of migraine. Atogepant is the second oral gepant approved for the preventive treatment of migraine and this is the only indication for which it is approved for (unlike rimegepant, atogepant does not have an indication for acute migraine treatment).

Preventive indication approvals for both rimegepant and atogepant came after injectable/infused CGRP-mAbs (erenumab, eptinezumab, fremanezumab, galcanezumab). There are no head-to-head clinical trials comparing oral and injectable/infused CGRP directed medications.

FDA APPROVED INDICATIONS
Ubrogepant: Acute treatment of migraine with or without aura in adults
Lasmiditan: Acute treatment of migraine with or without aura in adults
Zavegepant: Acute treatment of migraine with or without aura in adults
Rimegepant: Acute treatment of migraine with or without aura in adults AND preventive treatment for episodic migraine
Atogepant: Preventive treatment of migraine in adults

REFERENCES
1. Moreno-Ajona D, Pérez-Rodríguez A, Goadsby PJ. Gepants, calcitonin-gene-related peptide receptor antagonists: what could be their role in migraine treatment? Curr Opin Neurol. 2020;33(3):309-315.
2. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019;59(1):1-18.
3. Atlas S, Touchette D, Agboola F, et al. Acute Treatments for Migraine: Effectiveness and Value. Institute for Clinical and Economic Review. February 25, 2020. Available at: icer-review.org/wp-content/uploads/2019/06/ICER_Acute-Migraine_Final-Evidence-Report_updated_030320.pdf. Accessed August 27, 2020.
4. Ashina M. Migraine. N Engl J Med 2020;383:1866-76.

5. Yang CP, Liang CS, Chang CM, et al. Comparison of new pharmacologic agents with triptans for treatment of migraine: a systematic review and meta-analysis. JAMA Netw Open. 2021;4(10):e2128544.

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Revised Date: 01/2024

NOVEL MIGRAINE MEDICATIONS
LASMIDITAN (REYVOW)

Generic	Brand	HICL	GCN/GPID	Exception/Other
LASMIDITAN	REYVOW	46082	47084, 47083	Oral selective 5HT1f agonist; "Ditan" for acute tx

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:

A. Patient is new to KPCO within the past 90 days
B. Patient is stable on lasmiditan (Reyvow) for acute migraine treatment

If above are met, then approve x 3 months (to allow time for consideration of formulary preferred alternatives) at HICL with quantity limits, maximum 4 of the 50mg tablets [max qty: 4, min ds: 30] or 8 of the 100mg tablets per 30 days [max qty: 8, min ds: 30].

(Then must meet Initial Criteria for ongoing coverage).
If New Member criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the following:

A. Patient must be age 18 or older
B. Must be prescribed by a Neurologist, Pain Specialist, or Headache Specialist
C. Must meet diagnosis and medication specific criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Must meet all the following:
   a. Prescribed for acute treatment of migraine with or without aura
   b. Patient with failure of (after at least one month of therapy), intolerance to, or contraindication to, at least one triptan
   c. Patient with failure of (after at least one month of therapy), intolerance to, or contraindication to, a gepant.

   If criteria are met, approve indefinitely at HICL, max 4 tablets per 30 days for 50 mg requests [max qty: 4, min ds: 30], max 8 tablets per 30 days for 100 mg requests [max qty: 8, min ds: 30].
   If criteria are not met, do not approve.

Available triptan/ergotamine options:

Generic	Brand	Formulations available
Almotriptan	Axert	Tablet
Eletriptan	Relpax	Tablet
Frovatriptan	Frova	Tablet
Naratriptan	Amerge	Tablet
Rizatriptan	Maxalt/Maxalt MLT	Tablet, ODT

Sumatriptan	Imitrex, Sumavel, Onzetra, Zembrace	Tablet, nasal spray, injection
Zolmitriptan	Zomig/Zomig ZMT	Tablet, ODT, nasal spray
Ergotamine	Ergomar	Sublingual
Ergotamine/caffeine	Cafergot	Tablet, suppository
Dihydroergotamine	Migranal, Trudhesa D.H.E.	Nasal spray, injection

ODT=orally disintegrating tablet

True contraindications to triptan class

- Ischemic coronary artery disease including angina pectoris, history of myocardial infarction, documented silent ischemia, coronary artery vasospasm (including Prinzmetal's angina)
- History of stroke or transient ischemic attack
- Peripheral vascular disease
- Ischemic bowel disease
- Uncontrolled hypertension
- Hemiplegic or basilar migraine
- Wolff-Parkinson-White syndrome

Quantity Limits for Acute Migraine Treatment

Medication	Dosage Strength	Maximum quantity limit for 30 days	Notes
Acute migraine indication			
Ubrogepant (Ubrelvy)	50 mg, 100 mg	10	Tablet splitting of the 100 mg tablet has been approved and should be recommended for all patients prescribed to take a dose of 50 mg at onset of migraine
Rimegepant (Nurtec ODT)	75 mg	8	Tablet splitting n/a
Zavegepant (Zavzpret)	10 mg	6	Available as a ready-to-use, unit-dose disposable nasal spray device that contains 10 mg of zavegepant. Each carton contains 6 nasal spray units.
Lasmiditan (Reyvow)	50 mg	4	Tablet splitting NOT approved Approved doses to take at onset of migraine are 50 mg, 100 mg, or 200 mg, however, only 50 mg and 100 mg tablet strengths are available
	100 mg	8	
Preventive migraine indication			
Atogepant (Qulipta)	10 mg, 30 mg, 60 mg	30	Tablet splitting of the 60 mg tablet has been approved and should be recommended for all patients prescribed 30 mg daily

Rimegepant (Nurtec ODT)	75 mg	15	Tablet splitting n/a

CGRP-Directed Migraine Medications

Generic (Brand)	Route CGRP "class"	Acute Migraine Approval	Preventive Migraine Approval
Eptinezumab (Vyepti)	IV, CGRP-mAb	X	100 mg or 300 mg Q 3 mo
Erenumab (Aimovig)	SC, CGRP-mAb	X	70 mg or 140 mg Q mo
Fremanezumab (Ajovy)	SC, CGRP-mAb	X	225 mg Q mo, OR 675 mg Q 3 mo
Galcanezumab (Emgality)	SC, CGRP-mAb	X	240 mg loading dose, then 120 mg Q mo
Atogepant (Qulipta)	Oral, CGRP antagonist "gepant"	X	10 mg, 30 mg or 60 mg daily
Rimegepant (Nurtec ODT)	Orally disintegrating tablet, CGRP antagonist "gepant"	75 mg at onset do NOT repeat dose	75 mg every OTHER day
Ubrogepant (Ubrelvy)	Oral, CGRP antagonist "gepant"	50 mg or 100 mg at onset, may repeat in 2 hours	X
Zavegepant (Zavzpret)	Intranasal, CGRP antagonist "gepant"	10 mg at onset do NOT repeat dose	X

RATIONALE

Acute migraine indication

At this time, there is a lack of compelling data for ubrogepant, rimegepant, or lasmiditan to replace triptans as the gold standard for acute migraine treatment, considering cost and familiarity [1]. The 2019 AHS update briefly mentions role of emerging acute therapies as these options were not approved until about one year after its publication AHS [2]. Reiterated is the role for these novel treatment options, which do not result in constriction of blood vessels, for patients with vascular-related contraindications to triptans. Also acknowledged is the higher cost of these new agents compared to the generic availability of oral triptans and recommendation for ubrogepant, rimegepant, or lasmiditan to be used only in patients who have contraindications to triptans or who have failed to respond or tolerate at least two oral triptans. Patients should treat at least 2 migraine attacks before a provider makes a determination on efficacy and tolerability.

A comparative analysis of ubrogepant, lasmiditan, and rimegepant was performed by the Institute of Clinical and Economic Review (ICER) to assess the effectiveness and safety of these medications. [3] In comparison to placebo, ubrogepant [odds ratio (OR) 2.12], rimegepant [OR 2.11], and lasmiditan [OR 3.01] showed higher odds of achieving pain freedom at 2 hours. The analysis did not demonstrate statistically significant differences among the medications in pain freedom at two hours, absence of the most bothersome symptoms at two hours, and no disability at two hours in comparison to one another. On the other hand, in comparing triptans and ubrogepant, sumatriptan [OR 4.09] and eletriptan [OR 5.6] have shown to have higher odds of pain freedom at two hours than ubrogepant.

With regards to safety, nausea was the most common adverse effect seen with the use of ubrogepant. For single migraine attacks, ubrogepant and rimegepant had similar odds of experiencing any adverse event compared to triptans and placebo, but ubrogepant [OR 5.10] had lower odds for treatment-

emergent adverse events compared to lasmiditan. Also, the risk of medication overuse headaches, which is present with triptans, is unknown with repeated use of ubrogepant and rimegepant.

In terms of cost per quality-adjusted life year (QALY) gained threshold, ubrogepant is considered cost effective at $40,000 per QALY gained. Ubrogepant has similar QALY values compared to rimegepant. Comparing ubrogepant and triptans, the cost of ubrogepant is substantially greater than triptans and has less QALYs than sumatriptan and eletriptan.

If choosing one of these new acute medication options, pharmacokinetics and characteristics of a patient's migraine attacks should be kept in mind. Lasmiditan has pharmacokinetic characteristic similar to faster-acting triptans and most closely similar to almotriptan and eletriptan in regard to onset of action, time to maximum concentration, and half-life. Ubrogepant and rimegepant have slower onsets of action but longer half-lives which may be helpful for patients experiencing migraine recurrence. Dosing recommendations should also be considered when using these new medications including if a dose can be repeated in 2 hours, dose adjustments with other disease states, and potential for drug interactions (Table 1).

As the only gepant medication supplied in a non-oral formulation, zavegepant 10 mg nasal spray could be particularly useful in patients with characteristics associated with guideline-based recommendations for non-oral therapies, including headache attacks with severe nausea or vomiting or rapidly escalating headache pain, as well as for patients in whom oral forms are associated with inadequate response, slow onset of action, or poor tolerability. Additional trials are needed to provide evidence for the long-term safety and consistency of effect over time.

Using triptans as part of a combination therapy regimen can be useful (although possibly underutilized in clinical practice) and careful selection of agents to combine can achieve synergistic pharmacokinetic effects. For example, in patients needing a quick onset of action to relieve the migraine pain but also a longer duration to avoid migraine recurrence, a fast acting triptan (e.g. nasal spray, injectable, or faster-acting oral) can be combined with a long-acting NSAID. Effectiveness and safety of combining gepants or lasmiditan with other acute therapies is less defined. Pertaining to other acute migraine medications that could be utilized, study protocols for phase 3 clinical trials differed slightly, but all included specific recommendations for what patients could or could not take within 24 hours or 48 hours after the initial dose of the study medication. Due to the potential for duplicating mechanisms, it appears logical to avoid the combination of lasmiditan with a triptan, but there may be a role for combining lasmiditan with an analgesic and/or antiemetic if needed. While gepants and triptans do not appear to directly have overlapping mechanisms, they do both target the trigeminovascular system, and thus the utility in combining a gepant with a triptan remains unclear. Given the slower onset of gepants, there may be clinical situations where combining a gepant with a faster acting NSAID could be beneficial. Overall, more data is needed.

More real-world utilization and long-term safety and efficacy data is needed for these new acute medication options, but the development of these therapy options fills a long-standing gap in therapy for patients with multiple trials and failures of triptans or those with contraindications to this class.

Preventive migraine indication
Rimegepant was the first oral gepant approved for preventive treatment of migraine and this expanded indication came after rimegepant had already been approved for acute treatment of migraine. Atogepant is the second oral gepant approved for the preventive treatment of migraine and this is the only indication for which it is approved for (unlike rimegepant, atogepant does not have an indication for acute migraine treatment).

Preventive indication approvals for both rimegepant and atogepant came after injectable/infused CGRP-mAbs (erenumab, eptinezumab, fremanezumab, galcanezumab). There are no head-to-head clinical trials comparing oral and injectable/infused CGRP directed medications.

FDA APPROVED INDICATIONS

Ubrogepant: Acute treatment of migraine with or without aura in adults
Lasmiditan: Acute treatment of migraine with or without aura in adults
Zavegepant: Acute treatment of migraine with or without aura in adults
Rimegepant: Acute treatment of migraine with or without aura in adults AND preventive treatment for episodic migraine
Atogepant: Preventive treatment of migraine in adults

REFERENCES

1. Moreno-Ajona D, Pérez-Rodríguez A, Goadsby PJ. Gepants, calcitonin-gene-related peptide receptor antagonists: what could be their role in migraine treatment? Curr Opin Neurol. 2020;33(3):309-315.
2. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019;59(1):1-18.
3. Atlas S, Touchette D, Agboola F, et al. Acute Treatments for Migraine: Effectiveness and Value. Institute for Clinical and Economic Review. February 25, 2020. Available at: icer-review.org/wp-content/uploads/2019/06/ICER_Acute-Migraine_Final-Evidence-Report_updated_030320.pdf. Accessed August 27, 2020.
4. Ashina M. Migraine. N Engl J Med 2020;383:1866-76.
5. Yang CP, Liang CS, Chang CM, et al. Comparison of new pharmacologic agents with triptans for treatment of migraine: a systematic review and meta-analysis. JAMA Netw Open. 2021;4(10):e2128544.

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NOVEL MIGRAINE MEDICATIONS
RIMEGEPANT (NURTEC ODT)

Generic	Brand	HICL	GCN/GPID	Exception/Other
RIMEGEPANT	NURTEC ODT	46383	47762	Oral CGRP antagonist; "Gepant" for acute and preventive tx

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:

A. Patient is new to KPCO within the past 90 days
B. Patient is stable on rimegepant (Nurtec) for acute migraine treatment or for preventive migraine treatment

If above are met, then approve x 3 months (to allow time for consideration of formulary preferred alternatives) at HICL with quantity limits as follows:

- For migraine treatment:
  - Rimegepant (Nurtec): maximum 8 tablets per 30 days [max qty: 8, min ds: 30].
- For migraine prevention:
  - Rimegepant (Nurtec): maximum 1 tablet every other day [max daily dose 0.5].

(Then must meet Initial Criteria for ongoing coverage).
If New Member criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the following:

A. Patient must be age 18 or older
B. Must be prescribed by a Neurologist, Pain Specialist, or Headache Specialist
C. Must meet diagnosis and medication specific criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Acute Migraine Treatment: Must meet all the following:
   a. Prescribed for acute treatment of migraine with or without aura
   b. Patient with failure of (after at least one month of therapy), intolerance to, or contraindication to, at least one triptan
   c. Meets specific medication criteria below:
      i. Patient with failure of (after at least one month of therapy), intolerance to, or contraindication to, ubrogepant (Ubrelvy)
      ii. Patient has significant nausea and/or vomiting with migraine attacks that require an orally disintegrating tablet (ODT) option

   If criteria are met, approve indefinitely at HICL, max 8 tablets per 30 days [max qty: 8, min ds: 30].
   If criteria are not met, do not approve.

2. Preventive Migraine Treatment: Must meet the following:
   a. Request is for rimegepant (Nurtec) every other day for the preventive treatment of migraine
   b. Patient is not taking another CGRP-directed medication for migraine prevention
   c. Prescriber attests that patient is decreasing or stopping medications causing medication overuse headaches (MOH), if MOH is noted or apparent
   d. Patient is not taking an opiate (including tramadol) or barbiturate (including butalbital-containing product) for the treatment of headache for more than 4 days per month, including in the month prior to this request
   e. Patient has completed a Migraine Disability Assessment (MIDAS) or has documentation of headache days per month for at least one month in the past three months
   f. Patient with failure of (after at least 6-8 weeks at maximally tolerated dose), intolerance to, or contraindication to, at least one medication from each of the three migraine preventive classes:
      i. Anticonvulsants: divalproex, valproate, topiramate
      ii. Beta blockers: atenolol, metoprolol, nadolol, propranolol, timolol
      iii. Antidepressants: amitriptyline, nortriptyline, venlafaxine, duloxetine
   g. Patient with failure of (after at least two monthly doses), intolerance to, or contraindication to, at least 1 CGRP-mAb [erenumab (Aimovig), eptinezumab (Vyepti), fremanezumab (Ajovy), galcanezumab (Emgality)] for migraine prevention
   h. Patient must have tried and failed or have contraindication to Qulipta for migraine prevention

   If initial criteria are met, then approve x3 months at HICL with quantity limit of a maximum 1 tablet every other day [max daily dose 0.5].
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following criteria:
A. Request is for rimegepant (Nurtec) every other day for the preventive treatment of migraine
B. Patient has experienced improvement after at least 3 months of starting rimegepant (Nurtec) for migraine prevention, as demonstrated by one of the following:
   1. At least 30% reduction in migraine days per month
   2. A decrease in MIDAS score by 8 or more points

   If renewal criteria are met, then approve indefinitely at HICL with quantity limit of a maximum 1 tablet every other day [max daily dose 0.5].
   If renewal criteria are not met, do not approve.

Available triptan/ergotamine options:

Generic	Brand	Formulations available
Almotriptan	Axert	Tablet
Eletriptan	Relpax	Tablet
Frovatriptan	Frova	Tablet
Naratriptan	Amerge	Tablet
Rizatriptan	Maxalt/Maxalt MLT	Tablet, ODT
Sumatriptan	Imitrex, Sumavel, Onzetra, Zembrace	Tablet, nasal spray, injection
Zolmitriptan	Zomig/Zomig ZMT	Tablet, ODT, nasal spray
Ergotamine	Ergomar	Sublingual
Ergotamine/caffeine	Cafergot	Tablet, suppository
Dihydroergotamine	Migranal, Trudhesa D.H.E.	Nasal spray, injection

ODT=orally disintegrating tablet

True contraindications to triptan class

- Ischemic coronary artery disease including angina pectoris, history of myocardial infarction, documented silent ischemia, coronary artery vasospasm (including Prinzmetal's angina)
- History of stroke or transient ischemic attack
- Peripheral vascular disease
- Ischemic bowel disease
- Uncontrolled hypertension
- Hemiplegic or basilar migraine
- Wolff-Parkinson-White syndrome

Quantity Limits for Acute Migraine Treatment

Medication	Dosage Strength	Maximum quantity limit for 30 days	Notes
Acute migraine indication			
Ubrogepant (Ubrelvy)	50 mg, 100 mg	10	Tablet splitting of the 100 mg tablet has been approved and should be recommended for all patients prescribed to take a dose of 50 mg at onset of migraine
Rimegepant (Nurtec ODT)	75 mg	8	Tablet splitting n/a
Zavegepant (Zavzpret)	10 mg	6	Available as a ready-to-use, unit-dose disposable nasal spray device that contains 10 mg of zavegepant. Each carton contains 6 nasal spray units.
Lasmiditan (Reyvow)	50 mg	4	Tablet splitting NOT approved Approved doses to take at onset of migraine are 50 mg, 100 mg, or 200 mg, however, only 50 mg and 100 mg tablet strengths are available
	100 mg	8	
Preventive migraine indication			
Atogepant (Qulipta)	10 mg, 30 mg, 60 mg	30	Tablet splitting of the 60 mg tablet has been approved and should be recommended for all patients prescribed 30 mg daily
Rimegepant (Nurtec ODT)	75 mg	15	Tablet splitting n/a

CGRP-Directed Migraine Medications

Generic (Brand)	Route CGRP "class"	Acute Migraine Approval	Preventive Migraine Approval
Eptinezumab (Vyepti)	IV, CGRP-mAb	X	100 mg or 300 mg Q 3 mo

Erenumab (Aimovig)	SC, CGRP-mAb	X	70 mg or 140 mg Q mo
Fremanezumab (Ajovy)	SC, CGRP-mAb	X	225 mg Q mo, OR 675 mg Q 3 mo
Galcanezumab (Emgality)	SC, CGRP-mAb	X	240 mg loading dose, then 120 mg Q mo
Atogepant (Qulipta)	Oral, CGRP antagonist "gepant"	X	10 mg, 30 mg or 60 mg daily
Rimegepant (Nurtec ODT)	Orally disintegrating tablet, CGRP antagonist "gepant"	75 mg at onset do NOT repeat dose	75 mg every OTHER day
Ubrogepant (Ubrelvy)	Oral, CGRP antagonist "gepant"	50 mg or 100 mg at onset, may repeat in 2 hours	X
Zavegepant (Zavzpret)	Intranasal, CGRP antagonist "gepant"	10 mg at onset do NOT repeat dose	X

RATIONALE

Acute migraine indication

At this time, there is a lack of compelling data for ubrogepant, rimegepant, or lasmiditan to replace triptans as the gold standard for acute migraine treatment, considering cost and familiarity [1]. The 2019 AHS update briefly mentions role of emerging acute therapies as these options were not approved until about one year after its publication AHS [2]. Reiterated is the role for these novel treatment options, which do not result in constriction of blood vessels, for patients with vascular-related contraindications to triptans. Also acknowledged is the higher cost of these new agents compared to the generic availability of oral triptans and recommendation for ubrogepant, rimegepant, or lasmiditan to be used only in patients who have contraindications to triptans or who have failed to respond or tolerate at least two oral triptans. Patients should treat at least 2 migraine attacks before a provider makes a determination on efficacy and tolerability.

A comparative analysis of ubrogepant, lasmiditan, and rimegepant was performed by the Institute of Clinical and Economic Review (ICER) to assess the effectiveness and safety of these medications. [3] In comparison to placebo, ubrogepant [odds ratio (OR) 2.12], rimegepant [OR 2.11], and lasmiditan [OR 3.01] showed higher odds of achieving pain freedom at 2 hours. The analysis did not demonstrate statistically significant differences among the medications in pain freedom at two hours, absence of the most bothersome symptoms at two hours, and no disability at two hours in comparison to one another. On the other hand, in comparing triptans and ubrogepant, sumatriptan [OR 4.09] and eletriptan [OR 5.6] have shown to have higher odds of pain freedom at two hours than ubrogepant.

With regards to safety, nausea was the most common adverse effect seen with the use of ubrogepant. For single migraine attacks, ubrogepant and rimegepant had similar odds of experiencing any adverse event compared to triptans and placebo, but ubrogepant [OR 5.10] had lower odds for treatment-emergent adverse events compared to lasmiditan. Also, the risk of medication overuse headaches, which is present with triptans, is unknown with repeated use of ubrogepant and rimegepant.

In terms of cost per quality-adjusted life year (QALY) gained threshold, ubrogepant is considered cost effective at $40,000 per QALY gained. Ubrogepant has similar QALY values compared to rimegepant. Comparing ubrogepant and triptans, the cost of ubrogepant is substantially greater than triptans and has less QALYs than sumatriptan and eletriptan.

If choosing one of these new acute medication options, pharmacokinetics and characteristics of a patient's migraine attacks should be kept in mind. Lasmiditan has pharmacokinetic characteristic similar to faster-acting triptans and most closely similar to almotriptan and eletriptan in regard to onset of action, time to maximum concentration, and half-life. Ubrogepant and rimegepant have slower onsets of action but longer half-lives which may be helpful for patients experiencing migraine recurrence. Dosing recommendations should also be considered when using these new medications including if a dose can be repeated in 2 hours, dose adjustments with other disease states, and potential for drug interactions (Table 1).

As the only gepant medication supplied in a non-oral formulation, zavegepant 10 mg nasal spray could be particularly useful in patients with characteristics associated with guideline-based recommendations for non-oral therapies, including headache attacks with severe nausea or vomiting or rapidly escalating headache pain, as well as for patients in whom oral forms are associated with inadequate response, slow onset of action, or poor tolerability. Additional trials are needed to provide evidence for the long-term safety and consistency of effect over time.

Using triptans as part of a combination therapy regimen can be useful (although possibly underutilized in clinical practice) and careful selection of agents to combine can achieve synergistic pharmacokinetic effects. For example, in patients needing a quick onset of action to relieve the migraine pain but also a longer duration to avoid migraine recurrence, a fast acting triptan (e.g. nasal spray, injectable, or faster-acting oral) can be combined with a long-acting NSAID. Effectiveness and safety of combining gepants or lasmiditan with other acute therapies is less defined. Pertaining to other acute migraine medications that could be utilized, study protocols for phase 3 clinical trials differed slightly, but all included specific recommendations for what patients could or could not take within 24 hours or 48 hours after the initial dose of the study medication. Due to the potential for duplicating mechanisms, it appears logical to avoid the combination of lasmiditan with a triptan, but there may be a role for combining lasmiditan with an analgesic and/or antiemetic if needed. While gepants and triptans do not appear to directly have overlapping mechanisms, they do both target the trigeminovascular system, and thus the utility in combining a gepant with a triptan remains unclear. Given the slower onset of gepants, there may be clinical situations where combining a gepant with a faster acting NSAID could be beneficial. Overall, more data is needed.

More real-world utilization and long-term safety and efficacy data is needed for these new acute medication options, but the development of these therapy options fills a long-standing gap in therapy for patients with multiple trials and failures of triptans or those with contraindications to this class.

Preventive migraine indication
Rimegepant was the first oral gepant approved for preventive treatment of migraine and this expanded indication came after rimegepant had already been approved for acute treatment of migraine. Atogepant is the second oral gepant approved for the preventive treatment of migraine and this is the only indication for which it is approved for (unlike rimegepant, atogepant does not have an indication for acute migraine treatment).

Preventive indication approvals for both rimegepant and atogepant came after injectable/infused CGRP-mAbs (erenumab, eptinezumab, fremanezumab, galcanezumab). There are no head-to-head clinical trials comparing oral and injectable/infused CGRP directed medications.

FDA APPROVED INDICATIONS
Ubrogepant: Acute treatment of migraine with or without aura in adults
Lasmiditan: Acute treatment of migraine with or without aura in adults

Zavegepant: Acute treatment of migraine with or without aura in adults
Rimegepant: Acute treatment of migraine with or without aura in adults AND preventive treatment for episodic migraine
Atogepant: Preventive treatment of migraine in adults

REFERENCES

1. Moreno-Ajona D, Pérez-Rodríguez A, Goadsby PJ. Gepants, calcitonin-gene-related peptide receptor antagonists: what could be their role in migraine treatment? Curr Opin Neurol. 2020;33(3):309-315.
2. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019;59(1):1-18.
3. Atlas S, Touchette D, Agboola F, et al. Acute Treatments for Migraine: Effectiveness and Value. Institute for Clinical and Economic Review. February 25, 2020. Available at: icer-review.org/wp-content/uploads/2019/06/ICER_Acute-Migraine_Final-Evidence-Report_updated_030320.pdf. Accessed August 27, 2020.
4. Ashina M. Migraine. N Engl J Med 2020;383:1866-76.
5. Yang CP, Liang CS, Chang CM, et al. Comparison of new pharmacologic agents with triptans for treatment of migraine: a systematic review and meta-analysis. JAMA Netw Open. 2021;4(10):e2128544.

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NOVEL MIGRAINE MEDICATIONS
UBROGEPANT (UBRELVY)

Generic	Brand	HICL	GCN/GPID	Exception/Other
UBROGEPANT	UBRELVY	46273	47477, 47478	Oral CGRP antagonist; "Gepant" for acute tx

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:

A. Patient is new to KPCO within the past 90 days
B. Patient is stable on ubrogepant (Ubrelvy) for acute migraine treatment

If above are met, then approve x 3 months (to allow time for consideration of formulary preferred alternatives) at HICL with quantity limit maximum 10 tablets per 30 days [max qty: 10, min ds: 30].

(Then must meet Initial Criteria for ongoing coverage).
If New Member criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the following:

A. Patient must be age 18 or older
B. Must be prescribed by a Neurologist, Pain Specialist, or Headache Specialist
C. Must meet diagnosis and medication specific criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Must meet all the following:
   a. Prescribed for acute treatment of migraine with or without aura
   b. Patient with failure of (after at least one month of therapy), intolerance to, or contraindication to, at least one triptan

   If criteria are met, approve indefinitely at HICL, max 10 tablets per 30 days [max qty: 10, min ds: 30].
   If criteria are not met, do not approve.

Available triptan/ergotamine options:

Generic	Brand	Formulations available
Almotriptan	Axert	Tablet
Eletriptan	Relpax	Tablet
Frovatriptan	Frova	Tablet
Naratriptan	Amerge	Tablet
Rizatriptan	Maxalt/Maxalt MLT	Tablet, ODT
Sumatriptan	Imitrex, Sumavel, Onzetra, Zembrace	Tablet, nasal spray, injection
Zolmitriptan	Zomig/Zomig ZMT	Tablet, ODT, nasal spray

Ergotamine	Ergomar	Sublingual
Ergotamine/caffeine	Cafergot	Tablet, suppository
Dihydroergotamine	Migranal, Trudhesa D.H.E.	Nasal spray, injection

ODT=orally disintegrating tablet

True contraindications to triptan class

- Ischemic coronary artery disease including angina pectoris, history of myocardial infarction, documented silent ischemia, coronary artery vasospasm (including Prinzmetal's angina)
- History of stroke or transient ischemic attack
- Peripheral vascular disease
- Ischemic bowel disease
- Uncontrolled hypertension
- Hemiplegic or basilar migraine
- Wolff-Parkinson-White syndrome

Quantity Limits for Acute Migraine Treatment

Medication	Dosage Strength	Maximum quantity limit for 30 days	Notes
Acute migraine indication			
Ubrogepant (Ubrelvy)	50 mg, 100 mg	10	Tablet splitting of the 100 mg tablet has been approved and should be recommended for all patients prescribed to take a dose of 50 mg at onset of migraine
Rimegepant (Nurtec ODT)	75 mg	8	Tablet splitting n/a
Zavegepant (Zavzpret)	10 mg	6	Available as a ready-to-use, unit-dose disposable nasal spray device that contains 10 mg of zavegepant. Each carton contains 6 nasal spray units.
Lasmiditan (Reyvow)	50 mg	4	Tablet splitting NOT approved Approved doses to take at onset of migraine are 50 mg, 100 mg, or 200 mg, however, only 50 mg and 100 mg tablet strengths are available
	100 mg	8	
Preventive migraine indication			
Atogepant (Qulipta)	10 mg, 30 mg, 60 mg	30	Tablet splitting of the 60 mg tablet has been approved and should be recommended for all patients prescribed 30 mg daily
Rimegepant (Nurtec ODT)	75 mg	15	Tablet splitting n/a

CGRP-Directed Migraine Medications

Generic (Brand)	Route CGRP "class"	Acute Migraine Approval	Preventive Migraine Approval
Eptinezumab (Vyepti)	IV, CGRP-mAb	X	100 mg or 300 mg Q 3 mo
Erenumab (Aimovig)	SC, CGRP-mAb	X	70 mg or 140 mg Q mo
Fremanezumab (Ajovy)	SC, CGRP-mAb	X	225 mg Q mo, OR 675 mg Q 3 mo
Galcanezumab (Emgality)	SC, CGRP-mAb	X	240 mg loading dose, then 120 mg Q mo
Atogepant (Qulipta)	Oral, CGRP antagonist "gepant"	X	10 mg, 30 mg or 60 mg daily
Rimegepant (Nurtec ODT)	Orally disintegrating tablet, CGRP antagonist "gepant"	75 mg at onset do NOT repeat dose	75 mg every OTHER day
Ubrogepant (Ubrelvy)	Oral, CGRP antagonist "gepant"	50 mg or 100 mg at onset, may repeat in 2 hours	X
Zavegepant (Zavzpret)	Intranasal, CGRP antagonist "gepant"	10 mg at onset do NOT repeat dose	X

RATIONALE

Acute migraine indication

At this time, there is a lack of compelling data for ubrogepant, rimegepant, or lasmiditan to replace triptans as the gold standard for acute migraine treatment, considering cost and familiarity [1]. The 2019 AHS update briefly mentions role of emerging acute therapies as these options were not approved until about one year after its publication AHS [2]. Reiterated is the role for these novel treatment options, which do not result in constriction of blood vessels, for patients with vascular-related contraindications to triptans. Also acknowledged is the higher cost of these new agents compared to the generic availability of oral triptans and recommendation for ubrogepant, rimegepant, or lasmiditan to be used only in patients who have contraindications to triptans or who have failed to respond or tolerate at least two oral triptans. Patients should treat at least 2 migraine attacks before a provider makes a determination on efficacy and tolerability.

A comparative analysis of ubrogepant, lasmiditan, and rimegepant was performed by the Institute of Clinical and Economic Review (ICER) to assess the effectiveness and safety of these medications. [3] In comparison to placebo, ubrogepant [odds ratio (OR) 2.12], rimegepant [OR 2.11], and lasmiditan [OR 3.01] showed higher odds of achieving pain freedom at 2 hours. The analysis did not demonstrate statistically significant differences among the medications in pain freedom at two hours, absence of the most bothersome symptoms at two hours, and no disability at two hours in comparison to one another. On the other hand, in comparing triptans and ubrogepant, sumatriptan [OR 4.09] and eletriptan [OR 5.6] have shown to have higher odds of pain freedom at two hours than ubrogepant.

With regards to safety, nausea was the most common adverse effect seen with the use of ubrogepant. For single migraine attacks, ubrogepant and rimegepant had similar odds of experiencing any adverse event compared to triptans and placebo, but ubrogepant [OR 5.10] had lower odds for treatment-emergent adverse events compared to lasmiditan. Also, the risk of medication overuse headaches, which is present with triptans, is unknown with repeated use of ubrogepant and rimegepant.

In terms of cost per quality-adjusted life year (QALY) gained threshold, ubrogepant is considered cost effective at $40,000 per QALY gained. Ubrogepant has similar QALY values compared to rimegepant. Comparing ubrogepant and triptans, the cost of ubrogepant is substantially greater than triptans and has less QALYs than sumatriptan and eletriptan.

If choosing one of these new acute medication options, pharmacokinetics and characteristics of a patient's migraine attacks should be kept in mind. Lasmiditan has pharmacokinetic characteristic similar to faster-acting triptans and most closely similar to almotriptan and eletriptan in regard to onset of action, time to maximum concentration, and half-life. Ubrogepant and rimegepant have slower onsets of action but longer half-lives which may be helpful for patients experiencing migraine recurrence. Dosing recommendations should also be considered when using these new medications including if a dose can be repeated in 2 hours, dose adjustments with other disease states, and potential for drug interactions (Table 1).

As the only gepant medication supplied in a non-oral formulation, zavegepant 10 mg nasal spray could be particularly useful in patients with characteristics associated with guideline-based recommendations for non-oral therapies, including headache attacks with severe nausea or vomiting or rapidly escalating headache pain, as well as for patients in whom oral forms are associated with inadequate response, slow onset of action, or poor tolerability. Additional trials are needed to provide evidence for the long-term safety and consistency of effect over time.

Using triptans as part of a combination therapy regimen can be useful (although possibly underutilized in clinical practice) and careful selection of agents to combine can achieve synergistic pharmacokinetic effects. For example, in patients needing a quick onset of action to relieve the migraine pain but also a longer duration to avoid migraine recurrence, a fast acting triptan (e.g. nasal spray, injectable, or faster-acting oral) can be combined with a long-acting NSAID. Effectiveness and safety of combining gepants or lasmiditan with other acute therapies is less defined. Pertaining to other acute migraine medications that could be utilized, study protocols for phase 3 clinical trials differed slightly, but all included specific recommendations for what patients could or could not take within 24 hours or 48 hours after the initial dose of the study medication. Due to the potential for duplicating mechanisms, it appears logical to avoid the combination of lasmiditan with a triptan, but there may be a role for combining lasmiditan with an analgesic and/or antiemetic if needed. While gepants and triptans do not appear to directly have overlapping mechanisms, they do both target the trigeminovascular system, and thus the utility in combining a gepant with a triptan remains unclear. Given the slower onset of gepants, there may be clinical situations where combining a gepant with a faster acting NSAID could be beneficial. Overall, more data is needed.

More real-world utilization and long-term safety and efficacy data is needed for these new acute medication options, but the development of these therapy options fills a long-standing gap in therapy for patients with multiple trials and failures of triptans or those with contraindications to this class.

Preventive migraine indication
Rimegepant was the first oral gepant approved for preventive treatment of migraine and this expanded indication came after rimegepant had already been approved for acute treatment of migraine. Atogepant is the second oral gepant approved for the preventive treatment of migraine and this is the only indication for which it is approved for (unlike rimegepant, atogepant does not have an indication for acute migraine treatment).

Preventive indication approvals for both rimegepant and atogepant came after injectable/infused CGRP-mAbs (erenumab, eptinezumab, fremanezumab, galcanezumab). There are no head-to-head clinical trials comparing oral and injectable/infused CGRP directed medications.

FDA APPROVED INDICATIONS

Ubrogepant: Acute treatment of migraine with or without aura in adults
Lasmiditan: Acute treatment of migraine with or without aura in adults
Zavegepant: Acute treatment of migraine with or without aura in adults
Rimegepant: Acute treatment of migraine with or without aura in adults AND preventive treatment for episodic migraine
Atogepant: Preventive treatment of migraine in adults

REFERENCES

1. Moreno-Ajona D, Pérez-Rodríguez A, Goadsby PJ. Gepants, calcitonin-gene-related peptide receptor antagonists: what could be their role in migraine treatment? Curr Opin Neurol. 2020;33(3):309-315.
2. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019;59(1):1-18.
3. Atlas S, Touchette D, Agboola F, et al. Acute Treatments for Migraine: Effectiveness and Value. Institute for Clinical and Economic Review. February 25, 2020. Available at: icer-review.org/wp-content/uploads/2019/06/ICER_Acute-Migraine_Final-Evidence-Report_updated_030320.pdf. Accessed August 27, 2020.
4. Ashina M. Migraine. N Engl J Med 2020;383:1866-76.
5. Yang CP, Liang CS, Chang CM, et al. Comparison of new pharmacologic agents with triptans for treatment of migraine: a systematic review and meta-analysis. JAMA Netw Open. 2021;4(10):e2128544.

Creation Date: 08/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

NOVEL MIGRAINE MEDICATIONS
ZAVEGEPANT (ZAVZPRET)

Generic	Brand	HICL	GCN/GPID	Exception/Other
ZAVEGEPANT	ZAVZPRET	48771	53837	Intranasal CGRP antagonist; "Gepant" for acute tx

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
A. Patient is new to KPCO within the past 90 days
B. Patient is stable on zavegepant (Zavzpret) for acute migraine treatment

If above are met, then approve x 3 months (to allow time for consideration of formulary preferred alternatives) at HICL with quantity limit of a maximum 1 carton containing 6 single use nasal spray units per 30 days [max qty: 6, min ds: 30].

(Then must meet Initial Criteria for ongoing coverage).
If New Member criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the following:
A. Patient must be age 18 or older
B. Must be prescribed by a Neurologist, Pain Specialist, or Headache Specialist
C. Must meet diagnosis and medication specific criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Must meet all the following:
   a. Prescribed for acute treatment of migraine with or without aura
   b. Patient with failure of (after at least one month of therapy), intolerance to, or contraindication to, at least one triptan
   c. Patient with failure of (after at least one month of therapy), intolerance to, or contraindication to, dihydroergotamine nasal spray (Migranal preferred)
   d. Patient with failure of (after at least one month of therapy), intolerance to, or contraindication to, ubrogepant (Ubrelvy) and/or Rimegepant (Nurtec ODT)

   If criteria are met, approve indefinitely at HICL, max 1 carton containing 6 single use nasal spray units per 30 days [max qty: 6, min ds: 30].
   If criteria are not met, do not approve.

Available triptan/ergotamine options:

Generic	Brand	Formulations available
Almotriptan	Axert	Tablet
Eletriptan	Relpax	Tablet
Frovatriptan	Frova	Tablet

Naratriptan	Amerge	Tablet
Rizatriptan	Maxalt/Maxalt MLT	Tablet, ODT
Sumatriptan	Imitrex, Sumavel, Onzetra, Zembrace	Tablet, nasal spray, injection
Zolmitriptan	Zomig/Zomig ZMT	Tablet, ODT, nasal spray
Ergotamine	Ergomar	Sublingual
Ergotamine/caffeine	Cafergot	Tablet, suppository
Dihydroergotamine	Migranal, Trudhesa D.H.E.	Nasal spray, injection

ODT=orally disintegrating tablet

True contraindications to triptan class

- Ischemic coronary artery disease including angina pectoris, history of myocardial infarction, documented silent ischemia, coronary artery vasospasm (including Prinzmetal's angina)
- History of stroke or transient ischemic attack
- Peripheral vascular disease
- Ischemic bowel disease
- Uncontrolled hypertension
- Hemiplegic or basilar migraine
- Wolff-Parkinson-White syndrome

Quantity Limits for Acute Migraine Treatment

Medication	Dosage Strength	Maximum quantity limit for 30 days	Notes
Acute migraine indication			
Ubrogepant (Ubrelvy)	50 mg, 100 mg	10	Tablet splitting of the 100 mg tablet has been approved and should be recommended for all patients prescribed to take a dose of 50 mg at onset of migraine
Rimegepant (Nurtec ODT)	75 mg	8	Tablet splitting n/a
Zavegepant (Zavzpret)	10 mg	6	Available as a ready-to-use, unit-dose disposable nasal spray device that contains 10 mg of zavegepant. Each carton contains 6 nasal spray units.
Lasmiditan (Reyvow)	50 mg	4	Tablet splitting NOT approved Approved doses to take at onset of migraine are 50 mg, 100 mg, or 200 mg, however, only 50 mg and 100 mg tablet strengths are available
	100 mg	8	
Preventive migraine indication			
Atogepant (Qulipta)	10 mg, 30 mg, 60 mg	30	Tablet splitting of the 60 mg tablet has been approved and should be recommended for all

			patients prescribed 30 mg daily
Rimegepant (Nurtec ODT)	75 mg	15	Tablet splitting n/a

CGRP-Directed Migraine Medications

Generic (Brand)	Route CGRP "class"	Acute Migraine Approval	Preventive Migraine Approval
Eptinezumab (Vyepti)	IV, CGRP-mAb	X	100 mg or 300 mg Q 3 mo
Erenumab (Aimovig)	SC, CGRP-mAb	X	70 mg or 140 mg Q mo
Fremanezumab (Ajovy)	SC, CGRP-mAb	X	225 mg Q mo, OR 675 mg Q 3 mo
Galcanezumab (Emgality)	SC, CGRP-mAb	X	240 mg loading dose, then 120 mg Q mo
Atogepant (Qulipta)	Oral, CGRP antagonist "gepant"	X	10 mg, 30 mg or 60 mg daily
Rimegepant (Nurtec ODT)	Orally disintegrating tablet, CGRP antagonist "gepant"	75 mg at onset do NOT repeat dose	75 mg every OTHER day
Ubrogepant (Ubrelvy)	Oral, CGRP antagonist "gepant"	50 mg or 100 mg at onset, may repeat in 2 hours	X
Zavegepant (Zavzpret)	Intranasal, CGRP antagonist "gepant"	10 mg at onset do NOT repeat dose	X

RATIONALE

Acute migraine indication

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With regards to safety, nausea was the most common adverse effect seen with the use of ubrogepant. For single migraine attacks, ubrogepant and rimegepant had similar odds of experiencing any adverse event compared to triptans and placebo, but ubrogepant [OR 5.10] had lower odds for treatment-emergent adverse events compared to lasmiditan. Also, the risk of medication overuse headaches, which is present with triptans, is unknown with repeated use of ubrogepant and rimegepant.

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Preventive migraine indication
Rimegepant was the first oral gepant approved for preventive treatment of migraine and this expanded indication came after rimegepant had already been approved for acute treatment of migraine.

Atogepant is the second oral gepant approved for the preventive treatment of migraine and this is the only indication for which it is approved for (unlike rimegepant, atogepant does not have an indication for acute migraine treatment).

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FDA APPROVED INDICATIONS

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Atogepant: Preventive treatment of migraine in adults

REFERENCES

1. Moreno-Ajona D, Pérez-Rodríguez A, Goadsby PJ. Gepants, calcitonin-gene-related peptide receptor antagonists: what could be their role in migraine treatment? Curr Opin Neurol. 2020;33(3):309-315.
2. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019;59(1):1-18.
3. Atlas S, Touchette D, Agboola F, et al. Acute Treatments for Migraine: Effectiveness and Value. Institute for Clinical and Economic Review. February 25, 2020. Available at: icer-review.org/wp-content/uploads/2019/06/ICER_Acute-Migraine_Final-Evidence-Report_updated_030320.pdf. Accessed August 27, 2020.
4. Ashina M. Migraine. N Engl J Med 2020;383:1866-76.
5. Yang CP, Liang CS, Chang CM, et al. Comparison of new pharmacologic agents with triptans for treatment of migraine: a systematic review and meta-analysis. JAMA Netw Open. 2021;4(10):e2128544.

Creation Date: 08/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

NPH INSULIN PENS

Generic	Brand	HICL	GCN	Exception/Other
INSULIN NPH HUMAN ISOPHANE	HUMULIN N KWIKPEN		18488	

GUIDELINES FOR COVERAGE

Must meet ONE of the below criteria:
1. Prescription is written by an Endocrinology specialist
2. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination

   If met, approve indefinitely.
   If above criteria are not met, do not approve.

RATIONALE
The use of insulin pens at KPCO is reserved for patients with physical and cognitive impairment.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

NUCALA (MEPOLIZUMAB) - COGS

Generic	Brand	HICL	GCN	Exception/Other
MEPOLIZUMAB	NUCALA	42775	46413, 46414	Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

1. Medication is prescribed by an Allergist, Pulmonologist, or ENT Specialist
2. Medication is not being used in combination with another biologic for the same indication
3. Patient is new to KPCO within the past 90 days, noted as stable on therapy with Nucala, and meets one of the following indication-specific criteria:
    a. Patient has a diagnosis of EGPA (Churg-Strauss syndrome)
    b. Patient has a diagnosis of Chronic rhinosinusitis with nasal polyposis (CRSwNP) and has failed therapy with, or has contraindications to Dupixent
    c. Patient has a diagnosis of asthma and has failed therapy with, or has contraindications to Fasenra

If above criteria are met, approve indefinitely, max 1mL per 28 days.
If above criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the diagnosis-specific criteria below:

A. Eosinophilic granulomatosis with polyangiitis (EGPA - i.e. Churg-Strauss syndrome): Must meet all the following:
    1. Must be prescribed by an Allergist or Pulmonologist
    2. Medication is not being used in combination with another biologic for the same indication

If initial criteria above are met, then approve indefinitely, max 1 per 28 days.
If initial criteria are not met, do not approve.

B. Chronic rhinosinusitis with nasal polyposis (CRSwNP): Must meet all the following:
    1. Must be prescribed by an Allergist, Pulmonologist, or ENT specialist
    2. Medication is not being used in combination with another biologic for the same indication
    3. Must have persistent rhinosinusitis symptoms (lasting longer than 12 weeks) with severe nasal obstruction and rhinorrhea or reduced sense of smell
    4. Patient has had sinus surgery
    5. Failure of normalization of mucosa after sinus surgery and despite medical management (e.g., nasal saline irrigation, intranasal corticosteroids [e.g., fluticasone, mometasone, etc.], antileukotriene antagonists [e.g., montelukast, zafirlukast, zileuton])
    6. Received two or more courses of oral corticosteroids in the past year
    7. Must have trial and failure of, intolerance to, or contraindication to dupilumab (Dupixent)

If initial criteria above are met, then approve indefinitely, max 1 per 28 days.
If initial criteria are not met, do not approve.

C. Asthma (moderate / severe): Must meet all the following:
    1. Must be prescribed by an Allergist or Pulmonologist
    2. Medication is not being used in combination with another biologic for the same indication
    3. Must have uncontrolled asthma as evidenced by ANY one of the following:

- Two or more asthma exacerbations requiring systemic corticosteroids (≥3 days each) in the past 12 months
- one asthma-related hospitalization in the past 12 months
- Asthma Control Test (ACT) consistently <20

4. Adherent (>75% proportion of days covered) to optimized drug therapy (triple drug therapy with high-dose ICS-LABA plus tiotropium (Spiriva Respimat)) for the previous 6 months, OR has contraindications or intolerance to ICS/LABA/tiotropium
5. Must have trial and failure of, intolerance to, or contraindication to benralizumab (Fasenra)

If initial criteria above are met, then approve indefinitely, max 1 per 28 days.
If initial criteria are not met, do not approve.

D. Hematologic hypereosinophilic syndromes: Must meet all the following:
   1. Must be prescribed by a hematologist
   2. Medication is not being used in combination with another biologic for the same indication
   3. Absolute eosinophil count of >1.5 on 2 occasions >1 month apart or tissue showing 20% involvement on bone marrow or other tissue infiltration
   4. Documented end organ dysfunction caused by this syndrome
   5. FIP1L1-PDGFRA mut negative
   6. Diagnosed at least 6 months prior
   7. Disease relapse after at least 2 previous trials of systemic corticosteroids in conjunction with hydroxyurea

If initial criteria above are met, then approve x8 months, max 3 per 28 days.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:

1. Patient previously authorized for coverage of Nucala for the treatment of asthma or CRSwNP

If met, approve indefinitely, max 1 per 28 days.
If renewal criteria are not met, do not approve.
[Nucala for the treatment of hematologic hyper-eosinophilic syndromes is not designed as an open-ended intervention.]

RATIONALE
Per Health Plan and current treatment guidelines.

Although other agents may also be effective for EGPA and are reasonable, mepolizumab generally has the largest body of evidence to support its use.

New member criteria notes: Patients coming into KPCO stable on therapy with Nucala for any indication other than EGPA could/should be considered for transition to KPCO's more preferred therapies as outlined in Initial Criteria.

FDA APPROVED INDICATIONS
Asthma
Chronic rhinosinusitis with nasal polyposis

REFERENCES

Table 1: High-dose ICS and High-dose ICS plus LABA combinations for Age ≥12 years

fluticasone/salmeterol DPI (Advair Diskus) 500/50 mcg, 1 inh twice daily
fluticasone/salmeterol MDI (Advair HFA) 230/21 mcg, 2 puffs twice daily
mometasone/formoterol MDI (Dulera) 200/5 mcg, 2 puffs twice daily
ciclesonide MDI (Alvesco) 160 mcg, 2 puffs twice daily
fluticasone MDI (Flovent HFA) 220 mcg, 2 puffs twice daily
Budesonide DPI (Pulmicort Flexhaler) 180 mcg, 4 inh twice daily
Mometasone MDI (Asmanex HFA) 200 mcg, 2 puffs twice daily
Mometasone DPI (Asmanex Twisthaler) 220 mcg, 2 inh twice daily

Creation Date: 10/2021
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

OBETICHOLIC ACID

Generic	Brand	HICL	GCN	Exception/Other
OBETICHOLIC ACID	OCALIVA	43438		

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Patient has a diagnosis of primary biliary cholangitis
2. Patient is at least 18 years of age and older
3. Patient does not have cirrhosis OR has compensated cirrhosis with no evidence of portal hypertension
4. Prescribed by a gastroenterologist or hepatologist
5. The requested agent will be used in combination with ursodeoxycholic acid (e.g., Ursodiol, Urso 250, Urso Forte) in adults with an inadequate response to ursodeoxycholic acid at a dosage of 13-15mg/kg/day for at least 1 year, OR as monotherapy in adults unable to tolerate ursodeoxycholic acid
6. Patient does not have complete biliary obstruction

If met, approve for 12 months at HICL with a quantity limit of #1 per day.
If not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Patient has a diagnosis of primary biliary cholangitis
2. Patient's alkaline phosphatase levels are less than 1.67-times the upper limit of normal OR have decreased by at least 15% from baseline while on treatment with obeticholic acid
3. The patient has not developed complete biliary obstruction

If met, approve indefinitely at HICL with a quantity limit of #1 per day.
If not met, do not approve.

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Ocaliva.

REFERENCES
Ocaliva [Prescribing Information]. New York, NY: Intercept Pharmaceuticals, Inc. May 2021.

Creation date: 07/2022
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

OCTREOTIDE ACETATE CAPSULES (MYCAPSSA)

Generic Name	Brand Name	HICL	GPID	Comments
OCTREOTIDE ACETATE	MYCAPSSA	02826	48334	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by an endocrinology specialist
2. Patient must be age 18 years or older
3. Patient must have a diagnosis of acromegaly
4. Patient has had inadequate response to surgery or radiation, or surgery or radiation are not medically appropriate per provider documentation
5. The patient is currently stable (defined as currently receiving a stable dose for at least the previous 3 months) on an injectable somatostatin analog therapy (e.g., octreotide, lanreotide, pasireotide)
6. Patient has experienced severe injection site pain or reaction using injectable somatostatin analog therapy for long-term maintenance treatment, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception. [Documentation of needle phobia or unwillingness to receive injections does not qualify as medical necessity or contraindication to injectable products.]

If initial criteria are met, approve x 3 months, max daily dose 4 capsules.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:
1. Individual's condition responded while on therapy defined as meeting all the following criteria:
    a. Achieved and maintains both:
        i. GH levels are < 1 µg/L within 2-hours after 75 g of oral glucose
        ii. IGF-1 levels are less than or equal to the upper limit of normal for the patient's age and gender
    b. No evidence of disease progression

If criteria are met, approve x 12 months, max daily dose 4 capsules.
If criteria are not met, do not approve.

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ePA Questions
Initial Review Questions
1. Is the patient stable (defined as currently receiving a stable dose for at least the previous 3 months) on an injectable somatostatin analog therapy (e.g., octreotide, lanreotide, pasireotide)?
2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
3. Is there reasoning why alternatives (injectable somatostatin analogs) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

4. Regarding surgical/radiologic intervention, please check the box that most accurately describes this patient:
    a. The patient is not a candidate for surgery or radiation. (Please provide details in Provider Comment section or attach applicable chart notes with rationale.)
    b. The patient has inadequate response to surgery or radiation.

Renewal Review Questions

1. Is there evidence of disease progression in this patient since starting Mycapssa?
2. Current GH level drawn within 2-hours after 75 g of oral glucose (µg/L):
3. Date of GH after glucose lab (MMDDYY):
4. Current IGF-1 level:
5. Date of IGF-1 lab (MMDDYY):

FDA APPROVED INDICATIONS

Octreotide acetate capsules (Mycapssa) are indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

REFERENCES

Per Health Plan.
Preference is for continued use of injectable over oral formulation.

Creation Date: 01/05/2021
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

ODEVIXIBAT

Generic	Brand	HICL	GCN	Exception/Other
ODEVIXIBAT	BYLVAY	47501		Specialty tier

GUIDELINES FOR COVERAGE

Must meet all the following:

1. Patient is 3 months of age or older.
2. Must be prescribed by a GI or Hepatology specialist.
3. Patient has pruritus due to progressive familial intrahepatic cholestasis (PFIC: an inherited liver condition).
4. Patient has had an inadequate response to at least two other conventional treatments for the symptomatic relief of pruritus (cholestyramine or other bile acid sequestrant, naltrexone, rifampin, ursodeoxycholic acid), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria met, approve indefinitely at HICL.
If criteria not met, do not approve.

RATIONALE

REFERENCES

Creation date: 09/2022
Effective date: 01/2024
Reviewed date: 9/2023
Revised date: 9/2023

KESIMPTA

Generic	Brand	HICL	GCN	Exception/Other
OFATUMUMAB	KESIMPTA	36708	48513	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
1. New member to KPCO within the past 90 days stable on therapy.

If met, approve x 3 months at HICL/GPID.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Requesting provider is a CPMG or affiliated neurologist
2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active secondary progressive MS or primary progressive MS)
3. Patient has tried an infused rituximab product (brand or biosimilar) and with the infusion, experienced a severe Grade 3 or Grade 4 infusion reaction, or the provider submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
    a. Severe Grade 3 infusion reaction:
        i. prolonged reaction that is NOT rapidly responsive to symptomatic medication and/or brief interruption of infusion, or
        ii. hospitalization for clinical sequelae directly related to infusion of medication, or
        iii. severe infusion reaction that does not improve with subsequent infusion despite highly effective home PO premedications in the days prior to the infusion, day of infusion IV premedications, and slow infusion rate
    b. Severe Grade 4 infusion reaction: life-threatening reaction requiring urgent intervention

If initial criteria are met, approve x 1 year at HICL/GPID.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
1. Requesting provider is a CPMG or affiliated neurologist
2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active secondary progressive MS or primary progressive MS)

If renewal criteria are met, approve x 2 years at HICL/GPID.
If renewal criteria are not met, do not approve.

RATIONALE

Ofatumumab (Kesimpta) is the second anti-CD20 monoclonal antibody FDA-approved for the treatment of relapsing forms of MS, but the first that is given through subcutaneous injection. Ocrelizumab (Ocrevus) was the first anti-CD20 approved, is given through intravenous (IV) infusion, and rituximab (Rituxan, Truxima, Ruxience), also IV, has long been used off-label for the treatment of MS.[1-3]

Although ofatumumab may have more clinical trial data to support its use, rituximab has more real-world experience at KP. The KP Interregional guideline recommends the use of rituximab as the preferred highly-effective disease modifying therapy (DMT), over both ocrelizumab and ofatumumab.[4] Long-term safety data with ofatumumab is also unknown.

Ofatumumab was studied compared to teriflunomide, a modestly-effective DMT, in the ASCLEPIOS I and II phase 3 clinical trials.[5] There are no head-to-head trials with ofatumumab and other highly-effective DMTs.

- Ocrelizumab, ofatumumab, rituximab and ublituximab are part of the Anti-CD20 monoclonal antibody class of drugs. For the most part these agents in the class are molecularly similar and mechanistically the same.
- Off-label, non-oncologic use of rituximab is supported by a CMS-approved Compendia resource.
    - Micromedex categorizes off-label use of rituximab for Multiple Sclerosis; Strength of recommendation, Adult, Class IIb. Strength of evidence, Adult, Category B
- Additional supporting national standard treatment guidelines, peer-reviewed medical literature and/or recognized standards of care includes the following:
    - In June 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS. Rituximab is listed among various options, involving different mechanisms of action and modes of administration, which have shown benefits in patients with MS.
    - In 2018, the American Academy of Neurology has practice guidelines regarding disease modifying therapies for adults with MS. The guidelines mention rituximab for use in MS.
    - The recent 2021 update of the KP Inter-regional MS Treatment Practice Recommendations continues to recommend the utilization of our preferred drug in the Anti-CD20 mAB class, rituximab or its biosimilar.
    - There are no head-to-head evidence shows that either ocrelizumab or ublituximab are superior to rituximab products.
    - Use of rituximab products in MS is backed by real-world, published clinical experience at KP. Long-term ocrelizumab and ublituximab safety is less understood than that of rituximab
    - A network meta-analysis found that there was no significant difference between ocrelizumab and ofatumumab in terms of annualized relapse rate and time to confirmed disability worsening at three or six months.[6] Of note, rituximab was not included in this meta-analysis. There is no data to show that ofatumumab is superior to rituximab for the treatment of MS.

Ofatumumab may be appropriate for patients who are unable to tolerate rituximab, rituximab-abbs, or ocrelizumab due to Grade 3 or Grade 4 infusion-related reactions despite aggressive pre-medication regimens. One example of an aggressive pre-medication regimen for an IV anti-CD20 is cetirizine/loratadine 10 mg twice daily + famotidine 20 mg twice daily +/- dexamethasone 4-8 mg daily for 3 days before each infusion.

FDA APPROVED INDICATIONS
Treatment of relapsing forms of multiple sclerosis.

[a]Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	NP
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone;	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	P
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide[c] (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	P
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand – NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Siponimod	Mayzent	Oral	NP
	Ponesimod	Ponvory	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	P
B-cell Depleting Antibodies	Rituximab-abbs[c]	Biosimilar: Truxima,	Infusion	P
	Rituximab-arrx[c]	Biosimilar: Riabni	Infusion	NP
	Rituximab[c]	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

[c]*Off-label as a disease modifying treatment for MS*

[b]**High risk features defined as meeting at least 1 of the following criteria** (MRI obtained within past 12months):

a. Incomplete recovery defined as an attack that lasts ≥ 30 days and has significant functional limitations with the exception of ongoing sensory symptoms
b. Relapse w sphincter dysfunction, including urinary urgency or hesitancy

c. Motor relapse
d. Cerebellar relapse
e. 3 or more relapses in the first 2 years after diagnosis
f. After at least 6 months of therapy, a relapse in the next 6 months
g. Annualized relapse rate of ≥1
h. After 1yr of therapy, ≥ 3 new or enlarging T2, gadolinium-enhancing lesions, or diffusion-weighted imaging lesions
i. ≥ 1 cord lesion on imaging

REFERENCES

1. Ineichen BV, Moridi T, Granberg T, Piehl F. Rituximab treatment for multiple sclerosis. Mult Scler. 2020 Feb;26(2):137-152.
2. Zecca C, Bovis F, Novi G, et al. Treatment of multiple sclerosis with rituximab: A multicentric Italian-Swiss experience. Mult Scler. 2020 Oct;26(12):1519-1531.
3. Torgauten HM, Myhr KM, Wergeland S, et al. Safety and efficacy of rituximab as first- and second line treatment in multiple sclerosis - A cohort study. Mult Scler J Exp Transl Clin. 2021 Jan 31;7(1):2055217320973049.
4. Kaiser Permanente Interregional MS Leaders Workgroup. The KP Interregional Treatment Algorithm: Disease Modifying Therapies (DMTs) for Relapsing Forms of Multiple Sclerosis. Last updated November 2021. Available at: Multiple Sclerosis (MS) Treatment Algorithm - Disease Modifying Therapies (DMTs) for Relapsing Forms: Inter-Regional Consensus | CO Clinical Library (kp.org)
5. Hauser SL, Bar-Or A, Cohen JA, et al. Ofatumumab versus Teriflunomide in Multiple Sclerosis. *N Engl J Med*. 2020 Aug 6;383(6):546-557.
6. Samjoo IA, Worthington E, Drudge C, et al. Comparison of ofatumumab and other disease-modifying therapies for relapsing multiple sclerosis: a network meta-analysis. J Comp Eff Res. 2020 Dec;9(18): 1255-1274.

Creation Date: 05/2022
Effective Date: 01/01/2024
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Revised Date: 05/2023

OMALIZUMAB (XOLAIR)

Generic	Brand	HICL	GCN	Comments
OMALIZUMAB SYRINGE	XOLAIR SYRINGE	25399		COGS - labeled as self-injectable with MD discretion

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

1. Patient is new to KPCO within the past 90 days and noted as stable on Xolair for the treatment of Chronic Idiopathic Urticaria (CIU), Asthma, and/or Chronic rhinosinusitis with nasal polyposis (CRSwNP)
2. Medication is prescribed by an Allergist, Pulmonologist, or ENT specialist
3. Medication is not being used in combination with another biologic for the same indication

If above criteria are met, approve indefinitely.
If above criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet the diagnosis-specific criteria below:

A - Ages 18 and older with Chronic Idiopathic Urticaria (CIU)
B - Ages 12 through 17 with Chronic Idiopathic Urticaria (CIU)
C - Asthma
D - Chronic rhinosinusitis with nasal polyposis (CRSwNP)

A. Chronic idiopathic urticaria, ages 18 and older (CIU): Must meet all the following:
   1. Medication is prescribed by an Allergist
   2. Medication is not being used in combination with another biologic for the same indication
   3. Patient has received at least 2 doses within a healthcare setting and the provider attests to have performed a careful assessment of risk for anaphylaxis and mitigation strategies, including patient education

   And all the following if KP Colorado did not approve the use of Xolair as a clinic-administered medication, unless the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

   4. Tried and failed higher dose second-generation H1 antihistamine (Table 1) OR two standard dose second-generation H1 antihistamines in combination
   5. Tried and failed second-generation antihistamine in combination with first-generation H1 antihistamine (Table 2) OR H2-antagonist (Table 3) OR leukotriene modifier (montelukast or zafirlukast)

If initial criteria above are met, then approve indefinitely.
If initial criteria above are not met, do not approve.

B. Chronic idiopathic urticaria, ages 12 through 17 (CIU): Must meet all the following:

1. Medication is prescribed by an Allergist
2. Medication is not being used in combination with another biologic for the same indication
3. Patient has received at least 2 doses within a healthcare setting and the provider attests to have performed a careful assessment of risk for anaphylaxis and mitigation strategies, including patient education

And all the following if KP Colorado did not approve the use of Xolair as a clinic-administered medication, unless the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

4. Tried and failed two antihistamines (either first or second-generation H1 antihistamine) OR one course of an antihistamine (either first or second-generation H1 antihistamine) AND one course of doxepin
5. Tried and failed antihistamine (either first or second- generation) in combination with H2-antagonist OR leukotriene modifier (montelukast or zafirlukast)

If initial criteria above are met, then approve indefinitely.
If initial criteria above are not met, do not approve.

C. Asthma: Must meet all the following:
1. Patient is 12 years of age or older
2. Medication is prescribed by an Allergist or Pulmonologist
3. Medication is not being used in combination with another biologic for the same indication
4. Patient has received at least 2 doses within a healthcare setting and the provider attests to have performed a careful assessment of risk for anaphylaxis and mitigation strategies, including patient education

And all the following, if KP Colorado did not approve the use of Xolair as a clinic-administered medication

5. Determination of atopic asthma phenotype by prescribing physician.
6. Moderate-to-severe persistent asthma as evidenced by spirometry (FEV1 ≤80% of predicted and FEV1/forced vital capacity [FVC] reduced by 5% or greater from age appropriate values)
7. Uncontrolled asthma as evidenced by ANY of the following:
   - Two or more asthma exacerbations requiring systemic corticosteroids (≥3 days each) in the past 12 months
   - one asthma-related hospitalization in the past 12 months
   - Asthma Control Test (ACT) consistently <20
8. Adherent (>75% proportion of days covered) to optimized drug therapy (triple drug therapy with high-dose ICS (Table 2) plus LABA combination plus tiotropium (Spiriva Respimat) OR has contraindications or intolerance to above in the previous 6 months, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria above are met, then approve indefinitely.
If initial criteria above are not met, do not approve.

D. Chronic rhinosinusitis with nasal polyposis (CRSwNP): Must meet all the following:
   1. Patient is 18 years of age or older
   2. Must be prescribed by an Allergist or an Ear, Nose & Throat specialist
   3. Medication is not being used in combination with another biologic for the same indication
   4. Patient has received at least 2 doses within a healthcare setting and the provider attests to have performed a careful assessment of risk for anaphylaxis and mitigation strategies, including patient education

   And all the following, if KP Colorado did not approve the use of Xolair as a clinic-administered medication
   5. Persistent rhinosinusitis symptoms (lasting longer than 12 weeks) with severe nasal obstruction and rhinorrhea or reduce sense of smell
   6. Patient has had sinus surgery
   7. Failure of normalization of mucosa after sinus surgery and despite medical management (e.g. nasal saline irrigation, intranasal corticosteroids [e.g. fluticasone, mometasone, etc.], antileukotriene antagonists [e.g. montelukast, zafirlukast, zileuton])
   8. Received two or more courses of oral corticosteroids in the past year
   9. Previous treatment with and failure of, or intolerance to, both dupilumab and mepolizumab, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria above are met, then approve indefinitely.
If initial criteria above are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:
1. Patient previously authorized for coverage of Xolair.

If met, approve indefinitely.

RATIONALE
The primary role of omalizumab is the treatment of refractory chronic idiopathic urticaria (CIU). Omalizumab is generally not as preferred for refractory asthma when compared to dupilumab or benralizumab as they cover more common asthma phenotypes and are generally easier and safer to use.

FDA APPROVED INDICATIONS
Asthma: Treatment of moderate to severe persistent asthma in adults and patients 6 years and older who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. (Limitations of use: Not indicated for acute bronchospasm or status asthmaticus.)

Rhinosinusitis (chronic) with nasal polyps: Add-on maintenance treatment of chronic rhinosinusitis with nasal polyps in adults with inadequate response to nasal corticosteroids.

Urticaria (chronic spontaneous): Treatment of chronic spontaneous urticaria in adults and adolescents 12 years and older who remain symptomatic despite H1 antihistamine treatment. (Limitations of use: Not indicated for other allergic conditions or other forms of urticaria.)

REFERENCES

Table 1: Second-generation H1 antihistamines

Generic name	Standard dose	Higher dose
Cetirizine	10 mg orally once daily	20 mg orally twice daily
Desloratadine	5 mg orally once daily	10 mg orally twice daily
Fexofenadine	180 mg orally once daily	240 mg orally twice daily
Levocetirizine	5 mg orally once daily	10 mg orally twice daily
Loratadine	10 mg orally once daily	20 mg orally twice daily

Table 2: First-generation H1 antihistamines

Generic name
Brompheniramine
Chlorpheniramine
Diphenhydramine
Doxylamine
Triprolidine

Table 3: H2 antihistamines

Cimetidine
Famotidine
Nizatidine
Ranitidine

Table 4: High-dose ICS and High-dose ICS plus LABA combinations for Age >12 years

fluticasone/salmeterol DPI (Advair Diskus) 500/50 mcg, 1 inh twice daily
fluticasone/salmeterol MDI (Advair HFA) 230/21 mcg, 2 puffs twice daily
mometasone/formoterol MDI (Dulera) 200/5 mcg, 2 puffs twice daily
ciclesonide MDI (Alvesco) 160 mcg, 2 puffs twice daily
fluticasone MDI (Flovent HFA) 220 mcg, 2 puffs twice daily
budesonide DPI (Pulmicort Flexhaler) 180 mcg, 4 inh twice daily
mometasone MDI (Asmanex HFA) 200 mcg, 2 puffs twice daily
mometasone DPI (Asmanex Twisthaler) 220 mcg, 2 inh twice daily

Creation Date:07/28/2021
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

OMAVELOXOLONE (SKYCLARYS)

Generic	Brand	HICL	GCN	Exception/Other
OMAVELOXOLONE	SKYCLARYS	48741	53799	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
1. Patient is new to KPCO within the past 90 days and is stable on the requested medication for the treatment of Friedreich's Ataxia.

If New Member Criteria are met, approve x3 months, then use Initial Criteria for full review and future coverage determination.
If New Member Criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient age is between 16 and 40 years.
2. Medication is prescribed by a CPMG or affiliated Neurologist or Geneticist
3. Patient has genetically confirmed Friedreich’s ataxia without pes cavus*
4. Patient has a modified Friedreich's Ataxia Rating Scale (mFARS) score ≥20 and ≤80
5. Patient is ambulatory without assistance

If initial criteria above are met, approve x6 months.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Documentation of improvement on the modified Friedreich's Ataxia Rating Scale (mFARS) score from baseline

If renewal criteria are met, approve indefinitely.
If renewal criteria are not met, do not approve.

*Pes Cavus is a particular type of foot deformity. Clinical trial data did not show benefit of Omaveloxolone in patients with FA and this deformity.

RATIONALE
ETSP guidelines

FDA APPROVED INDICATIONS
Skyclarys is indicated for the treatment of Friedreich’s ataxia (FA) in adults and adolescents aged 16 years and older.

REFERENCES
Skyclarys Prescribing Information. Plano, TX: Reata Pharmaceuticals, Inc.; February 2023. https://www.skyclarys.com/docs/skyclarys_us_prescribing_information/

Creation Date: 07/2023
Effective Date: 01/2024
Reviewed Date:
Revised Date:

OPIOID CUMULATIVE DOSING OVERRIDE

Generic	Brand	HICL	GCN	Exception/Other
OPIOIDS	OPIOIDS			

GUIDELINES FOR USE

1. Is the request for an opioid product equal to or exceeding the soft-stop threshold (90 mg morphine equivalent dose [MED])?

   NOTE: Claims should stop for DUR_MAX_CUMUL_DOSE 2 edit with SOFT_DENY_LIMIT= 90 (i.e., Cumulative morphine equivalent dose of [patient's current MED] = / exceeds threshold of [90 mg MED per day]).

   If yes, continue to #2.
   If no, guideline does not apply.

2. Does the patient have one of the following conditions?
   - Diagnosis of cancer
   - Diagnosis of palliative care
   - Diagnosis of sickle cell disease
   - Patients enrolled in hospice
   - Patient is a resident of a long-term care facility or intermediate care for intellectually disabled

   If yes, **approve as follows:**
   - **Inform the pharmacist to place the appropriate HD (High Dose) DUR code into the claim {see below for listing of OCDP PPS codes}**

   If no, continue to #3.

3. Is the prescriber aware of multiple prescribers for opioid prescriptions?

   If yes, Inform pharmacist to make a clinical judgment about dispensing. Pharmacist may use applicable DUR codes to process the claim, if appropriate. {see below for listing of OCDP PPS codes}

   If no, Inform pharmacist to discuss with the prescribers and make a clinical judgment about dispensing. Pharmacist may use applicable DUR codes to process claim, if appropriate.

Reason for Service Code	Professional Service Code	Result of Service Code	Limits Overridden	Persistence Logic
HD (High Dose)	M0 (Prescriber Consulted)	4C (Hospice)	Soft & Hard Limit	Class Persistent
HD (High Dose)	R0 (RPh Consulted Other Source)	4C (Hospice)	Soft & Hard Limit	Class Persistent
HD (High Dose)	M0 (Prescriber Consulted)	4B (Palliative Care)	Soft & Hard Limit	Class Persistent
HD (High Dose)	R0 (RPh Consulted Other Source)	4B (Palliative Care)	Soft & Hard Limit	Class Persistent
HD (High Dose)	M0 (Prescriber Consulted)	4D (Cancer)	Soft & Hard Limit	Class Persistent
HD (High Dose)	R0 (RPh Consulted Other Source)	4D (Cancer)	Soft & Hard Limit	Class Persistent
HD (High Dose)	MR (Medication Review)	4D (Cancer)	Soft & Hard Limit	Class Persistent
HD (High Dose)	M0 (Prescriber Consulted)	1G (Prescr Approval)	Soft Limit Only	Persistent

CONTINUED ON NEXT PAGE

OPIOID CUMULATIVE DOSING OVERRIDE

RATIONALE

To align with opioid restrictions per CMS 2017 Call Letter. Prior authorization will be required for opioid prescriptions in excess of hard opioid edit. Soft opioid edit thresholds may be overridden by a dispensing pharmacist or provider/patient may request a coverage determination. MedImpact's standard soft opioid edit is set at ⩾ 120 mg morphine equivalent dose (MED). MedImpact's standard hard opioid edit threshold is set at ⩾ 200 mg MED. This requirement should not apply to patients with cancer, hospice patients, or patients approved by case management or retrospective DUR Programming. Additional payment determination is required for patients identified as hospice. Soft-thresholds may also be override by the pharmacy via DUR PPS codes or as part of coverage determination process. Hard-thresholds are only overridable as part of the coverage determination process. The cumulative opioid edit minimizes false positives by accounting for known exceptions: 1) patients on hospice, have certain cancer diagnosis 2) overlapping dispensing dates for Rx refills and new Rx orders for continuing fills 3) high-dose opioid usage previously determined to be medically necessary (approved PAs, previous coverage determinations, case management) 4) no consecutive high-MED days criterion as it would not prevent beneficiaries from reaching high opioid doses.

REFERENCES

- Announcement of Calendar Year (CY) 2017 Medicare Advantage Capitation Rates and Medicare Advantage and Part D Payment Policies and Final Call Letter.
- Ballas SK. Pain Management of Sickle Cell Disease, 2005. Hematol Oncol Clin N Am 19 (2005) 785-802.
- Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016; 65(No. RR-1):1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1.Available at http://www.cdc.gov/drugoverdose/prescribing/guideline.html. [Assessed August 11, 2016].
- Washington State Interagency Guideline on Prescribing Opioids for Pain. June 2015. Available at http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf [Accessed August 11, 2016].
- CMS Medicare Benefit Policy Manual Chapter 9 – Coverage of Hospice Services Under Hospital Insurance. Available at https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/bp102c09.pdf [Accessed January 2, 2017].

Created: 12/18
Effective: 03/05/21 Client Approval: 02/26/21

OPSUMIT (MACITENTAN)

Generic	Brand	HICL	GCN	Exception/Other
MACITENTAN	OPSUMIT	40677	35443	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Opsumit

If met, approve indefinitely.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Prescriber must be either a pulmonologist or a cardiologist
2. Patient has a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) verified by right heart catheterization
3. Patient currently has WHO Functional Class II, III or IV symptoms
4. Patient has tried and failed or has an intolerance to or a contraindication to ambrisentan (Letairis) or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If all the above criteria are met, approve indefinitely.
If criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS
Treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to reduce risks of disease progression and hospitalization

REFERENCES
1. Opsumit (macitentan) [product monograph]. Toronto, Ontario, Canada: Jassen Inc; July 2020.
2. Opsumit (macitentan) [prescribing information]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc; Jan 2021.

Creation Date: 3/25/2021
Effective Date: 01/01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

ORAL CLADRIBINE (MAVENCLAD)

Generic	Brand	HICL	GCN	Exception/Other
CLADRIBINE	MAVENCLAD	07840	44338	Oral formulation

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past year
2. Medication is prescribed by a CPMG or affiliated neurologist
3. Must have had at least one and no more than one treatment course (consisting of 2 treatment cycles) of cladribine, with last dose at least 43 weeks prior (if no prior treatment course, use initial criteria)

If above criteria are met, approve x1 year, max 2 fills, max qty 10 tablets.
If above criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: All the following must be met:
1. Medication is prescribed by a CPMG or affiliated neurologist
2. Patient is 18 years or older
3. Patient is diagnosed with a relapsing or active form of multiple sclerosis, but NOT clinically isolated syndrome (CIS) (this does not include non-active secondary-progressive MS or primary-progressive MS)
4. The patient must have high-risk features** for early progression to non-relapsing progressive MS, or any of these high-risk features while on disease modifying treatment
5. Patient has never taken more than two treatment courses (consisting of 2 treatment cycles each) of cladribine, and the patient has not taken cladribine within the past 43 weeks. [FDA states treatment beyond 2 years/courses may further increase the risk of malignancy.]
6. The patient has had a trial and inadequate response or intolerance to at least 2 alternative drugs indicated for the treatment of multiple sclerosis, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Rituximab or its biosimilar (Anti-CD20)
    b. Ocrelizumab (Anti-CD20)
    c. Ofatumumab (Anti-CD20)
    d. Ublituximab (Anti-CD20)
    e. Natalizumab (if JCV neg) - (alpha-4 integrin inhibitor)
    f. Fingolimod (S1P)
    g. Siponimod (S1P)
    h. Ozanimod (S1P)
    i. Ponesimod (S1P)

If above criteria are met, approve x1 year, max 2 fills, max qty 10 tablets.
If above criteria are not met, do not approve.

RENEWAL CRITERIA: All the following must be met:
1. Medication is prescribed by a CPMG or affiliated neurologist
2. Patient is 18 years or older
3. Patient is diagnosed with a relapsing or active form of multiple sclerosis, but not CIS (this does not include non-active Secondary-Progressive MS or Primary-Progressive MS)
4. Patient must have completed at least one treatment cycle within the past year, but no more than 3 treatment cycles in the course of their lifetime
5. Previous initial treatment course must have been approved by and covered by Kaiser Permanente (if initial course was denied by Kaiser Permanente, second course will not be covered)

If above criteria are met, approve x1 year, max 2 fills, max qty 10 tablets.
If above criteria are not met, do not approve.

REFERENCES:
Treatment course 1:
Cycle 1: start day 0-5
Cycle 2: start on days 23-27 to finish on days 27-32

Wait at least 43 weeks after last dose of Course 1, Cycle 2

Treatment course 2:
Cycle 1: start day 0-5
Cycle 2: start on days 23-27 to finish on days 27-32

* Contraindications & Serious Precautions to Mavenclad:
    1. patients with current malignancy.
    2. pregnant women, and women and men of reproductive potential who do not plan to use effective contraception during MAVENCLAD dosing and for 6 months after the last dose in each treatment course.
    3. HIV infection.
    4. active chronic infections (e.g., hepatitis or tuberculosis).
    5. history of hypersensitivity to cladribine.
    6. women intending to breastfeed on a MAVENCLAD treatment day and for 10 days after the last dose.
    7. lymphopenia (grade 2) at baseline.
    8. liver function abnormality at baseline.

***** High risk features defined as meeting at least 1 of the following criteria (MRI obtained within past 12months):
    a. Incomplete recovery defined as an attack that lasts ≥ 30 days and has significant functional limitations with the exception of ongoing sensory symptoms
    b. Relapse w sphincter dysfunction, including urinary urgency or hesitancy
    c. Motor relapse
    d. Cerebellar relapse
    e. 3 or more relapses in the first 2 years after diagnosis
    f. After at least 6 months of therapy, a relapse in the next 6 months
    g. Annualized relapse rate of ≥1
    h. After 1yr of therapy, ≥ 3 new or enlarging T2, gadolinium-enhancing lesions, or diffusion-weighted imaging lesions
    i. ≥ 1 cord lesion on imaging

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	NP
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone;	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	P
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	NP
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand – NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Ponesimod	Ponvory	Oral	NP
	Siponimod	Mayzent	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	NP
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

Off-label disease modifying therapy for MS

Creation date: 5/2020
Effective date: 01/01/2024
Reviewed date: 05/2023
Revised date: 05/2023

ORENCIA (ABATACEPT)

Generic Name	Brand Name	HICL	GCN/GPID	Exception/Other
ABATACEPT	ORENCIA	37825		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Orencia
2. Medication is not being used in combination with another biologic
3. Patient has a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), or Juvenile Idiopathic Arthritis (JIA) and is being prescribed by a CPMG or affiliated rheumatologist

If met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.15].
If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

A. Rheumatoid Arthritis (RA)
B. Psoriatic Arthritis (PsA)
C. Juvenile Idiopathic Arthritis (JIA)

A. Rheumatoid Arthritis (RA): All the following must be met:
   1. Patient has a diagnosis of RA and medication is prescribed by CPMG or affiliated rheumatologist
   2. Patient with failure, intolerance, or contraindication to at least 2 of the following medications:
      a. Methotrexate
      b. Leflunomide
      c. Hydroxychloroquine
      d. Sulfasalazine
   3. Patient with failure, intolerance, or contraindication to at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred [F] or originator or biosimilar, adalimumab-atto (Amjevita)-preferred [F, PA] or originator or biosimilar)
   4. Medication is not being used in combination with another biologic

If above criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.15].
If above criteria are not met, do not approve.

B. Psoriatic Arthritis (PsA): All the following must be met:
   1. Patient has a diagnosis of PsA, and medication is prescribed by CPMG or affiliated rheumatologist
   2. Patient with failure, intolerance, or contraindication to:

   a. at least 2 of the following medications, or the patient has documented high disease activity in which these medications would not be suitable treatment: methotrexate, leflunomide, sulfasalazine
   b. at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred [F] or originator or biosimilar, adalimumab-atto (Amjevita)-preferred [F, PA] or originator or biosimilar)
   c. secukinumab (Cosentyx) [F]
   d. guselkumab (Tremfya) [NF, PA]
3. Medication is not being used in combination with another biologic

If above criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.15].
If above criteria are not met, do not approve.

C. Juvenile Idiopathic Arthritis (JIA): All the following must be met:
1. Patient has a diagnosis of JIA, and medication is prescribed by CPMG or affiliated rheumatologist
2. Patient with failure, intolerance, or contraindication to at least 1 of the following medications:
   a. Methotrexate
   b. Leflunomide
   c. Hydroxychloroquine
   d. Sulfasalazine
3. Medication is not being used in combination with another biologic

If above criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.15].
If above criteria are not met, do not approve.

RENEWAL CRITERIA
1. Patient has been assessed by a rheumatologist in the past 2 years
2. Medication is not being used in combination with another biologic

If met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.15].
If not met, do not approve.

FDA APPROVED INDICATIONS: Psoriatic arthritis, Rheumatoid arthritis, Juvenile idiopathic arthritis

REFERENCES
Abatacept (Orencia) 50mg/0.4mL, 87.5mg/0.7mL, 125mg/mL

“Currently stable” means patient is tolerating well, medication appears to be effective, and provider wishes to continue therapy.

Creation Date:07/27/21
Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

ORENITRAM (TREPROSTINIL)

Generic	Brand	HICL	GCN	Exception/Other
TREPROSTINIL	ORENITRAM	40827		

GUIDELINES FOR COVERAGE:
NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Orenitram

If met, approve indefinitely at HICL.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Prescriber must be either a pulmonologist or a cardiologist
2. Patient has a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) verified by right heart catheterization
3. Patient currently has WHO Functional Class II, III or IV symptoms
4. Patient has tried and failed or has an intolerance to or a contraindication to all the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. One phosphodiesterase type 5 (PDE5) inhibitor: Sildenafil (Revatio®) or Tadalafil (Adcirca®)
   b. One endothelin receptor antagonist (ERA): Bosentan (Tracleer®), Ambrisentan (Letairis®), or macitentan (Opsumit®)

If all the above are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS
Treatment of pulmonary arterial hypertension (PAH) (WHO Group I) verified by right heart catheterization to reduce risks of disease progression and hospitalization.

REFERENCES
1. Orenitram (treprostinil) [prescribing information]. Research Triangle Park, NC: United Therapeutics Corp; October 2019.

Creation Date: 8/18/2020
Effective Date: 01/01/2024
Reviewed Date: 5/2023
Revised Date: 5/2023

ORIAHNN

Generic	Brand	HICL	GCN	Exception/Other
ELAGOLIX/ ESTRADIOL /NORETHINDRONE (elagolix+E2/NETA)	ORIAHNN	46577	48158	

****Length of approval applies to Federal Group**

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is stable on therapy with elagolix+E2/NETA (Oriahnn)
2. Patient has not been on elagolix+E2/NETA (Oriahnn) for 24 months or more
3. Patient meets one of the following:
   a. Patient is currently taking elagolix+E2/NETA (Oriahnn) and has a history of blood transfusion to treat heavy menstrual bleeding
   b. Patient has experienced a clinically significant improvement in fibroid-induced heavy menstrual bleeding, defined as at least 50% reduction in menstrual blood loss from baseline to the final month (6 months) of treatment with elagolix+E2/NETA (Oriahnn)

   If met, then approve x1 fill, to allow time to be evaluated by Ob/Gyn [**Use for Federal Group].
   If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following criteria:
1. Patient is a female at least 18 years of age
2. Medication is prescribed by an OB/GYN (with an appropriate referral, if required)
3. Patient is premenopausal with a diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids)
4. Patient has tried and failed, has an intolerance to, or has a contraindication to each of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Combined Oral Contraceptive Pill (OCP) - Note: cannot take concurrently with Oriahnn
   b. Levonorgestrel-releasing Intrauterine device (LNG IUD), depot medroxyprogesterone, or Nora-BE
   c. GnRH (leuprolide)
5. Patient must not have previously completed 24 months of treatment with elagolix +E2/NETA (Oriahnn), relugolix + e2NETA (Myfembree), or elagolix monotherapy (Orilissa)
6. Patient must not be on an organic anion transporting polypeptide (OATP)1B1 inhibitor[b] (most common: cyclosporine, gemfibrozil; see comprehensive list in footnote)

   If initial criteria are met, then approve x6 months [**Use for FEDERAL Group].
   If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
1. Patient has not been on elagolix+E2/NETA (Oriahnn) for 24 months or more

2. Patient meets one of the following:
   a. Patient is currently taking elagolix+E2/NETA (Oriahnn) and has a history of blood transfusion to treat heavy menstrual bleeding
   b. Patient has experienced a clinically significant improvement in fibroid-induced heavy menstrual bleeding, defined as at least 50% reduction in menstrual blood loss from baseline to the final month (6 months) of treatment with elagolix+E2/NETA (Oriahnn)

      If met, then approve for the number of months to meet the maximum of 24 total months of therapy. [**Use for Federal Group].
      If not met, do not approve.

RATIONALE- per OB/GYN

FDA APPROVED INDICATIONS Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women

REFERENCES
package insert
[a](including women >35 years of age who smoke, current or history of deep vein thrombosis or pulmonary embolism, vascular disease (eg, cerebrovascular disease, coronary artery disease, peripheral vascular disease), thrombogenic valvular or thrombogenic rhythm diseases of the heart (eg, subacute bacterial endocarditis with valvular disease, atrial fibrillation), inherited or acquired hypercoagulopathies, uncontrolled hypertension, or headaches with focal neurological symptoms or have migraine headaches with aura if >35 years of age.)
[b](atazanavir, clarithromycin, cobicistat, cyclosporine, daclatasvir, darolutamide, elbasvir, eltrombopag, eluxadoline, gemfibrozil, grazoprevir, ledipasvir, leflunomide, letermovir, lopinavir, simeprevir, teriflunomide, velpatasvir, voxilaprevir. Additional category X interactions are those with CYP3A4 metabolism (fusidic acid, idelalisib), and drugs reliant on PGP. The concentrations of these may be increased to toxic levels if administered with PGP inhibitor elagolix: pazopanib, IV topotecan, vincristine (liposomal).)

Management of Symptomatic Uterine Leiomyomas: ACOG Practice Bulletin, Number 228.

Therapeutic management of uterine fibroid tumors: updated French guidelines.

NICE guideline [NG88] Heavy menstrual bleeding: assessment and management. National Institute for Health and Care Excellence. March 2020
https://www.nice.org.uk/guidance/ng88/chapter/Recommendations#management-of-hmb (Accessed on April 01, 2020).

Creation Date: 12/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

OSILODROSTAT (ISTURISA)

Generic Name	Brand Name	HICL	GPID	Comments
OSILODROSTAT	ISTURISA	46396	47793, 47794, 47795	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:

1. Patient must be 18 years of age or older
2. Prescriber must be an Endocrinologist
3. Documented diagnosis of Cushing's disease
4. Documentation of failed pituitary surgery or contraindication to pituitary surgery
5. Must meet diagnosis/drug specific criteria below:
   a. Treatment to inhibit cortisol synthesis (steroidogenesis inhibitors) in Cushings disease: Patient has failed, is intolerant to, or has a contraindication to, all of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      i. Oral ketoconazole
      ii. Oral metyrapone
   b. Treatment to reduce ACTH levels in Cushing's disease related to pituitary tumor: Patient has failed, is intolerant to, or has a contraindication to all of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      i. Oral ketoconazole
      ii. Oral cabergoline
      iii. Injectable pasireotide

      If initial criteria are met, approve at HICL x 3 months, max 6 tablets per day.
      If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:

1. Individual's condition responded while on therapy.
   Response is defined as: Achieved and maintains at least three of the following:
   - A urinary free cortisol (UFC) ≤ the upper limit of normal (ULN)
   - Cortisol levels is within normal limits
   - No symptoms consistent with Cushing's disease
   - No evidence or symptoms of hypercortisolism
   - No evidence of disease progression

If renewal criteria are met, approve at HICL x 1 year, max 6 tablets per day.
If renewal criteria are not met, do not approve.

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ePA Questions
Initial Review Questions

1. Has the patient experienced failed pituitary surgery, or does the patient have a contraindication to pituitary surgery? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
2. Indication associated with this request: [check boxes for all diagnoses listed in criteria: Treatment to inhibit cortisol synthesis (steroidogenesis inhibitors) in Cushing's disease; Treatment to reduce ACTH levels in Cushing's disease related to pituitary tumor]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Treatment to inhibit cortisol synthesis (steroidogenesis inhibitors) in Cushing's disease
   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (ketoconazole tablets, metyrapone tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Treatment to reduce ACTH levels in Cushing's disease related to pituitary tumor
   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (ketoconazole tablets, cabergoline tablets, injectable pasireotide) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Renewal Review Questions

1. Does the patient have any of the following (check any/all applicable boxes): Symptoms associated with Cushing's disease; Evidence or symptoms of hypercortisolism; Evidence of disease progression
2. Current Urinary Free Cortisol (UFC) lab:
3. Date of UFC Lab (MMDDYY):
4. Current Cortisol level:
5. Date of Cortisol lab (MMDDYY):

RATIONALE
To ensure appropriate use of osilodrostat

FDA APPROVED INDICATIONS
Isturisa (osilodrostat) is a cortisol synthesis inhibitor indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative. It inhibits 11beta-hydroxylase (CYP11B1), the enzyme responsible for the final step of cortisol biosynthesis in the adrenal gland, thereby lowering cortisol levels.

REFERENCES
Per Health Plan

Tablet Strength	GPI	Quantity limit per day
1 mg tablet	30022060600320	8 tablets
5 mg tablet	30022060600330	6 tablets

10 mg tablet	30022060600340	6 tablets

Creation Date: 03/2021
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 09/2023

OXYBATE SALTS (SODIUM, CALCIUM, MAG, POT) (XYWAV)

Generic	Brand	HICL	GCN	Exception/Other
OXYBATE SALTS (SODIUM, CALCIUM, MAG, POT)	XYWAV	46743	48419	4th preferred in narcolepsy class

GUIDELINES FOR COVERAGE

CRITERIA FOR ALL PATIENTS CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

1. Medication is prescribed by a Neurology or a Board-Certified Sleep Medicine provider.
2. Medication is being prescribed for Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; or Cataplexy (not excessive daytime sleepiness) due to narcolepsy.
3. Medication requested is not be used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xyrem, Lumryz).
4. Patient must have tried and failed or have intolerance or contraindication to sodium oxybate (generic Xyrem) [Prior Authorization required], or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria are met, approve indefinitely, max 18 mL/day.
If criteria are not met, do not approve.

CRITERIA FOR ANY PATIENT NOT CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

A. Medication is prescribed by Neurology or a Board-Certified Sleep Medicine provider.
B. Medication requested is not be used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xyrem, Lumryz).
C. Patient must have one of the following indications and meet all criteria pertaining to that indication:
    1. Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia: Must meet all the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        a. Patient must have tried and failed or have a contraindication to each of the following: amphetamines, methylphenidate, and either modafinil or armodafinil.
        b. Patient must have tried and failed or have a contraindication to Sunosi, Wakix, and sodium oxybate (generic Xyrem) [Prior Authorization required for all].

    If criteria are met, approve indefinitely, max 18 mL/day.
    If criteria are not met, do not approve.

2. Cataplexy (not excessive daytime sleepiness) due to narcolepsy: Must meet all the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Patient must have tried and failed or have a contraindication to each of the following: a tricyclic antidepressant (TCA), a selective serotonin reuptake inhibitor (SSRI), and a selective serotonin-norepinephrine (SNRI).
    b. Patient must have tried and failed or have a contraindication to Wakix and sodium oxybate (generic Xyrem) [Prior Authorization required for all].

   If critieria are met, approve indefinitely, max 18 mL/day.
   If criteria are not met, do not approve.

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ePA Questions

1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; Cataplexy (not excessive daytime sleepiness) due to narcolepsy]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia

   1. Is the patient stable on therapy with this medication?
   2. For patients noted stable on therapy, start date of therapy (MMDDYY):
   3. Is the medication being used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xyrem, Lumryz)?
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (amphetamines, methylphenidate, modafinil, armodafinil) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Cataplexy (not excessive daytime sleepiness) due to narcolepsy

   1. Is the patient stable on therapy with this medication?
   2. For patients noted stable on therapy, start date of therapy (MMDDYY):
   3. Is the medication being used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xyrem, Lumryz)?
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (amitriptyline tablets, desipramine tablets, nortriptyline capsules; citalopram tablets/solution, escitalopram tablets, fluoxetine capsules/solution, paroxetine IR tablets, sertraline tablets/susp; venlafaxine ER capsules (37.5 mg, 75 mg, 150 mg), duloxetine capsules (20 mg, 30 mg, 60 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Dr. Richey and Health Plan

FDA APPROVED INDICATIONS AND SUPPORTED OFF-LABEL INDICATIONS
Xyrem/Xywav/Lumryz = Cataplexy; Narcolepsy; Idiopathic hypersomnia
Sunosi = Narcolepsy; Idiopathic hypersomnia; Hypersomnia associated with Obstructive sleep apnea
Wakix = Cataplexy; Narcolepsy; Idiopathic hypersomnia

Creation date: 03/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

PALIPERIDONE (INVEGA)

Generic	Brand	HICL	GCN/GPID	Exception/Other
PALIPERIDONE ER TABLET	INVEGA	34343		Quantity limits

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO within the past 90 days and is stable on therapy.

If met, approve indefinitely at HICL, max 1 tab per day.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following diagnoses and meet all related criteria below:

A. Bipolar mania or mixed episodes
B. Schizophrenia / schizoaffective disorder

A. Bipolar Mania or Mixed Episodes
   1. Patient is at least 18 years of age
   2. Documented contraindication, intolerance, or treatment failure to the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Risperidone
      b. One mood stabilizer (e.g. lithium, carbamazepine, valproic acid and derivatives)

If criteria are met, approve indefinitely at HICL, max 1 tab per day.
If criteria are not met, do not approve.

B. Schizophrenia / schizoaffective disorder
   1. Patient is at least 12 years of age
   2. Documented contraindication, intolerance, or treatment failure to risperidone, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If criteria are met, approve indefinitely at HICL, max 1 tab per day.
If criteria are not met, do not approve.

ESCALATION CRITERIA: Must meet one of the following:
1. Daily dose is below or equal to the maximum approved by FDA unless prescribed by psychiatry.
2. Dose is unable to be met within the quantity limit restriction (e.g. paliperidone ER 4.5 mg daily).

If met, then approve indefinitely at HICL without quantity limits.
If not met, deny quantity requested, maintaining original quantity limit approved.

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ePA Questions

2. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Bipolar mania or mixed episodes; Schizophrenia/Schizoaffective disorder]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Bipolar mania or mixed episodes

   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules; Lithium capsules, as carbonate: 150 mg, 300 mg; Lithium tablets, as carbonate: 300 mg; Lithium CR tablets, as carbonate (Eskalith CR): 450 mg; Lithium SR tablets, as carbonate (Lithobid): 300 mg; carbamazepine ER tablets (100 mg, 200 mg, 400 mg), carbamazepine IR tablets (200 mg), carbamazepine chewable tablets (100 mg); Divalproex sodium DR (12 hr) or ER (24 hr) tablets, valproic acid capsules (250 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Schizophrenia/Schizoaffective disorder

   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (i.e. aripiprazole tablets, lurasidone tablets, olanzapine IR tablets, quetiapine IR or ER tablets, risperidone IR tablets, ziprasidone capsules) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Risperidone is metabolized to paliperidone by CYP2D6; approximately 83% of the active moiety is paliperidone. Concomitant use of strong CYP2D6 inhibitor or known CYP2D6 poor metabolizers is not a contraindication to risperidone treatment per FDA labeling. Tolerability is similar though paliperidone does have higher affinity at alpha-1-adrenergic receptors and a slightly higher risk of hyperprolactinemia compared to risperidone. As such, risperidone trials (formulary agent) are recommended prior to paliperidone trials (nonformulary agent). Notably, paliperidone is not FDA approved for bipolar mania/mixed episodes but its parent compound, risperidone, is FDA approved for this indication. Given this, it might be clinically reasonable to use but would first require a risperidone trial.

Carbamazepine, divalproex, and lithium are teratogenic so avoiding use in women of reproductive potential is not unreasonable (and highly recommended for divalproex). Unfortunately, most of the non-formulary antipsychotics lack reassuring data and absence of evidence of risk is not the same as absence of risk. Lithium may still be continued or started in women that are pregnant as the benefits of use are often considered to outweigh the small absolute risk of cardiac malformation (1-2 extra cases per 100 live births with first trimester in utero exposure compared with no lithium exposure).

FDA APPROVED INDICATIONS

Paliperidone

- **Schizophrenia:** Treatment of schizophrenia (max daily dose: 12 mg).
- **Schizoaffective disorder:** Treatment of schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants (max daily dose: 12 mg).

APPENDIX A. Formulary antipsychotics

First-generation antipsychotics	Second-generation antipsychotics
Chlorpromazine	Aripiprazole
Fluphenazine	Clozapine
Haloperidol	Lurasidone
Loxapine	Olanzapine
Molindone	Quetiapine
Perphenazine	Risperidone
Pimozide	Ziprasidone
Thioridazine	
Thiothixene	
Trifluoperazine	

HOW SUPPLIED:

Paliperidone (Invega) ER Tablet: 1.5 MG, 3 MG, 6 MG, 9 MG

REFERENCES

American Psychiatric Association. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. 3rd ed. Washington, DC: American Psychiatric Association; 2021.

Invega. Package insert. Janssen Pharmaceuticals, Inc.; March 31, 2022.

Meyer JM and Stahl SM. Stahl's Handbooks: The clinical use of antipsychotic plasma levels. Cambridge University Press. 2021.

Patorno E, Huybrechts KF, Bateman BT, et al. Lithium use in pregnancy and the risk of cardiac malformations. N Engl J Med. 2017;376:23.

Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord 2018;20:97-170.

Creation Date: 3/2023
Effective Date: 4/2024
Reviewed Date: 3/2024
Revised Date: 3/2024

PATIROMER (VELTASSA) - STEP THERAPY

Generic	Brand	HICL	GCN	Exception/Other
PATIROMER	VELTASSA	42767	40065, 40066, 40067	Nonformulary

Step Therapy Criteria
Must meet the criteria below or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed another drug in the same pharmacological class or with the same mechanism of action as the required drug and the drug was discontinued due to lack of efficacy, diminished effect, or adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Requesting provider is a CPMG or an affiliated network nephrologist.
2. Patient has tried and failed or has contraindications to sodium zirconium cyclosilicate (Lokelma).

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

RATIONALE
Per Health Plan

- Sodium zirconium cyclosilicate (Lokelma) is the first-line KPCO formulary therapy for hyperkalemia. Patiromer (Veltassa) is the second-line KPCO therapy for hyperkalemia and is non-formulary
- Both sodium zirconium cyclosilicate (Lokelma) and patiromer (Veltassa) have quantity limits
    - Lokelma - max of 3 per day to avoid medication overuse, and to account for initial titration.
    - Veltassa - max of 1 per day to avoid medication overuse and doubling of strengths.

REFERENCES

Creation date: 06/2022
Effective date: 01/2024
Reviewed date: 05/2023
Revised date: 05/2023

PEGFILGRASTIM-APGF (NYVEPRIA)

Generic	Brand	HICL	GCN	Exception/Other
PEGFILGRASTIM-APGF 6MG/0.6ML	NYVEPRIA	46612	48222	Biologic - Nonformulary

GUIDELINES FOR COVERAGE

Review based on patient age:

A. ADULT USE (ages 18 years and older): Must meet all the following criteria:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Patient has experienced febrile neutropenia or neutropenia resulting in delay of chemotherapy despite 10 days of Nivestym or other short-acting GCSF, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

B. PEDIATRIC USE (ages 17 years and younger): Must meet all the following:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Must be using GCSF to prevent febrile neutropenia with chemotherapy
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Adult Use: Fulphila is our preferred long-acting GCSF in adults; however, use of a short-acting GCSF is preferred over long-acting unless patient fails short-acting GCSF
Pediatric Use: Fulphila is our preferred GCSF for pediatric patients

FDA APPROVED INDICATIONS
See pegfilgrastim package insert

Creation Date:01/2020
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

PEGFILGRASTIM-BMEZ

Generic	Brand	HICL	GCN	Exception/Other
PEGFILGRASTIM-BMEZ 6MG/0.6ML	ZIEXTENZO	46183	47234	Biologic - Nonformulary

GUIDELINES FOR COVERAGE

Review based on patient age:

A. ADULT USE (ages 18 years and older): Must meet all the following criteria:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Patient has experienced febrile neutropenia or neutropenia resulting in delay of chemotherapy despite 10 days of Nivestym or other short-acting GCSF, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

B. PEDIATRIC USE (ages 17 years and younger): Must meet all the following:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Must be using GCSF to prevent febrile neutropenia with chemotherapy
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Adult Use: Fulphila is our preferred long-acting GCSF in adults; however, use of a short-acting GCSF is preferred over long-acting unless patient fails short-acting GCSF
Pediatric Use: Fulphila is our preferred GCSF for pediatric patients

FDA APPROVED INDICATIONS
See pegfilgrastim package insert

Creation Date:01/2020
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

PEGFILGRASTIM-CBQV

Generic	Brand	HICL	GCN	Exception/Other
PEGFILGRASTIM-CBQV 6MG/0.6ML	UDENYCA	45445	45679	Biologic - Nonformulary - LATEX FREE

GUIDELINES FOR COVERAGE

Review based on patient age:

A. ADULT USE (ages 18 years and older): Must meet all the following criteria:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Patient has experienced febrile neutropenia or neutropenia resulting in delay of chemotherapy despite 10 days of Nivestym or other short-acting GCSF, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

B. PEDIATRIC USE (ages 17 years and younger): Must meet all the following:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Must be using GCSF to prevent febrile neutropenia with chemotherapy
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Adult Use: Fulphila is our preferred long-acting GCSF in adults; however, use of a short-acting GCSF is preferred over long-acting unless patient fails short-acting GCSF

Pediatric Use: Fulphila is our preferred GCSF for pediatric patients

FDA APPROVED INDICATIONS
See pegfilgrastim package insert

Creation Date:01/2020
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

PEGFILGRASTIM-FPGK

Generic	Brand	HICL	GCN	Exception/Other
PEGFILGRASTIM-FPGK 6MG/0.6ML	STIMUFEND	48269	52848	Biologic - Nonformulary

GUIDELINES FOR COVERAGE

Review based on patient age:

A. ADULT USE (ages 18 years and older): Must meet all the following criteria:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Patient has experienced febrile neutropenia or neutropenia resulting in delay of chemotherapy despite 10 days of Nivestym or other short-acting GCSF, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

B. PEDIATRIC USE (ages 17 years and younger): Must meet all the following:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Must be using GCSF to prevent febrile neutropenia with chemotherapy
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Adult Use: Fulphila is our preferred long-acting GCSF in adults; however, use of a short-acting GCSF is preferred over long-acting unless patient fails short-acting GCSF
Pediatric Use: Fulphila is our preferred GCSF for pediatric patients

FDA APPROVED INDICATIONS
See pegfilgrastim package insert

Creation Date:01/2020
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

PEGFILGRASTIM-JMDB

Generic	Brand	HICL	GCN	Exception/Other
PEGFILGRASTIM-JMDB 6MG/0.6ML	FULPHILA	45010	44881	Biologic - Nonformulary - LATEX FREE

GUIDELINES FOR COVERAGE

Review based on patient age:

A. ADULT USE (ages 18 years and older): Must meet all the following criteria:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Patient has experienced febrile neutropenia or neutropenia resulting in delay of chemotherapy despite 10 days of Nivestym or other short-acting GCSF, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve Fulphila indefinitely.
      If criteria are not met, do not approve.

B. PEDIATRIC USE (ages 17 years and younger): Must meet all the following:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Must be using GCSF to prevent febrile neutropenia with chemotherapy

      If criteria are met, approve Fulphila indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Adult Use: Fulphila is our preferred long-acting GCSF in adults; however, use of a short-acting GCSF is preferred over long-acting unless patient fails short-acting GCSF
Pediatric Use: Fulphila is our preferred GCSF for pediatric patients

FDA APPROVED INDICATIONS

See pegfilgrastim package insert

Creation Date:01/2020
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

PEGFILGRASTIM

Generic	Brand	HICL	GCN	Exception/Other
PEGFILGRASTIM 6MG/0.6ML	NEULASTA	23255	15666 / 37706	Nonformulary

GUIDELINES FOR COVERAGE

Review based on patient age:

A. ADULT USE (ages 18 years and older): Must meet all the following criteria:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Patient has experienced febrile neutropenia or neutropenia resulting in delay of chemotherapy despite 10 days of Nivestym or other short-acting GCSF, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

B. PEDIATRIC USE (ages 17 years and younger): Must meet all the following:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Must be using GCSF to prevent febrile neutropenia with chemotherapy
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Adult Use: Fulphila is our preferred long-acting GCSF in adults; however, use of a short-acting GCSF is preferred over long-acting unless patient fails short-acting GCSF
Pediatric Use: Fulphila is our preferred GCSF for pediatric patients

FDA APPROVED INDICATIONS
See pegfilgrastim package insert

Creation Date:01/2020
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

PEGFILGRASTIM ONPRO

Generic	Brand	HICL	GCN	Exception/Other
PEGFILGRASTIM 6MG/0.6ML	NEULASTA ONPRO	23255	37706	Nonformulary

GUIDELINES FOR COVERAGE

Review based on patient age:

A. ADULT USE (ages 18 years and older): Must meet all the following criteria:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Patient has experienced febrile neutropenia or neutropenia resulting in delay of chemotherapy despite 10 days of Nivestym or other short-acting GCSF, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

B. PEDIATRIC USE (ages 17 years and younger): Must meet all the following:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Must be using GCSF to prevent febrile neutropenia with chemotherapy
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Adult Use: Fulphila is our preferred long-acting GCSF in adults; however, use of a short-acting GCSF is preferred over long-acting unless patient fails short-acting GCSF
Pediatric Use: Fulphila is our preferred GCSF for pediatric patients

FDA APPROVED INDICATIONS
See pegfilgrastim package insert

Creation Date:01/2020
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

PEGFILGRASTIM-PBBK

Generic	Brand	HICL	GCN	Exception/Other
PEGFILGRASTIM-PBBK 6MG/0.6ML	FYLNETRA	48035	52395	Biologic - Nonformulary - LATEX FREE

GUIDELINES FOR COVERAGE

Review based on patient age:

A. ADULT USE (ages 18 years and older): Must meet all the following criteria:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Patient has experienced febrile neutropenia or neutropenia resulting in delay of chemotherapy despite 10 days of Nivestym or other short-acting GCSF, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

B. PEDIATRIC USE (ages 17 years and younger): Must meet all the following:
   1. Medication is prescribed by a Hematologist/Oncologist
   2. Must be using GCSF to prevent febrile neutropenia with chemotherapy
   3. Patient has intolerance or contraindication to Fulphila, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve requested product indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Adult Use: Fulphila is our preferred long-acting GCSF in adults; however, use of a short-acting GCSF is preferred over long-acting unless patient fails short-acting GCSF

Pediatric Use: Fulphila is our preferred GCSF for pediatric patients

FDA APPROVED INDICATIONS
See pegfilgrastim package insert

Creation Date:01/2020
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

PEGVISOMANT (SOMAVERT)

Generic	Brand	HICL	GCN	Exception/Other
PEGVISOMANT	SOMAVERT	25062	19372, 19373, 19374, 37056, 37056, 37057	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Medication is prescribed by an endocrinologist
2. Patient has a diagnosis of acromegaly
3. Patient is not a candidate for, or has had an inadequate response to surgery and/or radiotherapy
4. Failure of a somatostatin analog [octreotide (KP preferred) or lanreotide] at maximally indicated dose, unless contraindicated or clinically significant adverse effects are experienced, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If initial criteria are met, approve x 12 months.
If criteria are not met, do not approve.

RENEWAL CRITERIA
1. Patient has had a positive clinical response to therapy (i.e., normalization of IGF-1 levels and/or improvement in symptoms)

If met, approve indefinitely.
If criteria are not met, do not approve.

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ePA Questions
Initial Review Questions
1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (octreotide or lanreotide) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.
3. Regarding surgical/radiologic intervention, please check the box that most accurately describes this patient:
    a. The patient is not a candidate for surgery or radiotherapy. (Please provide details in Provider Comment section or attach applicable chart notes with rationale.)
    b. The patient has inadequate response to surgery or radiotherapy.

Renewal Review Questions
1. Has the patient had a positive clinical response to therapy?

RATIONALE
The Acromegaly Consensus Group suggests use of pegvisomant as a second-line therapy option in patients with persistent, significant disease despite surgical resection and minimal/no response to first-line therapy, either as monotherapy (in patients without concern for tumor growth) or in combination with a somatostatin analog (in patients with concern for tumor growth).

FDA APPROVED INDICATIONS
Somavert, a growth hormone receptor antagonist, is indicated for the treatment of acromegaly in patients who have had inadequate response to surgery and/or radiation therapy and/or other medical therapies, or for whom these therapies are not appropriate. The goal of treatment is to normalize serum insulin-like growth factor-1 levels.

REFERENCES
Per Health Plan.

Creation Date: 03/2022
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 09/2023

FYCOMPA (PERAMPANEL)

Generic	Brand	HICL	GCN	Exception/Other
PERAMPANEL	FYCOMPA	39628	41309, 33271, 33272, 33273, 33274, 33275, 33276	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and is stable on perampanel (Fycompa)
2. Patient has a diagnosis of Partial Onset or Primary Generalized Tonic-Clonic Seizures and is being managed by a CPMG or affiliated neurologist or epileptologist

If New Member Criteria are met, approve x3 months.
If New Member Criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: Review based on diagnosis-specific criteria below:
A. To treat Partial Onset Seizures (also known as focal onset aware or impaired awareness): All the following must be met:
   1. Medication is prescribed by a CMPG or affiliated neurologist or epileptologist
   2. Patient has a diagnosis of partial onset seizures (also known as focal onset aware or impaired awareness)
   3. The patient is stable on perampanel (Fycompa), or the patient has failed at least 2 of the following medications, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a) Brivaracetam [non-formulary]
      b) Carbamazepine [preferred formulary]
      c) Eslicarbazepine [non-formulary]
      d) Felbamate [formulary]
      e) Gabapentin [formulary]
      f) Lacosamide [preferred formulary]
      g) Lamotrigine [preferred formulary]
      h) Levetiracetam [preferred formulary]
      i) Oxcarbazepine [preferred formulary]
      j) Phenobarbital [formulary]
      k) Phenytoin [formulary]
      l) Pregabalin [formulary]
      m) Primidone [formulary]
      n) Tiagabine [non-formulary]
      o) Topiramate [preferred formulary]

p) Valproic acid derivative [formulary]
q) Vigabatrin [non-formulary]
r) Zonisamide [preferred formulary]

4. Dose does not exceed 12 mg per day

If initial criteria are met, approve indefinitely.
If initial criteria are not met, do not approve.

B. To treat Primary Generalized Tonic-Clonic Seizures (also known as generalized onset motor tonic-clonic): All the following must be met:
1. Medication is prescribed by a CMPG or affiliated neurologist or epileptologist
2. Patient has a diagnosis of primary generalized tonic-clonic seizures (also known as generalized onset motor tonic-clonic)
3. The patient is stable on perampanel (Fycompa), or patient has failed least 2 of the following medications, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
a) clobazam [formulary]
b) felbamate [formulary]
c) lacosamide [preferred formulary]
d) lamotrigine [preferred formulary]
e) levetiracetam [preferred formulary]
f) rufinamide [non-formulary]
g) topiramate [preferred formulary]
h) valproic acid derivative [formulary]
i) zonisamide [preferred formulary]
4. This medication will be used as adjunctive therapy with at least one other anti-seizure drug
5. Dose does not exceed 12 mg per day

If initial criteria are met, approve indefinitely.
If initial criteria are not met, do not approve.

FDA APPROVED INDICATIONS

Fycompa is indicated:

- For the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 4 years of age and older.
- For adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients with epilepsy 12 years of age and older.

REFERENCES

1. Fycompa Prescribing Information. Woodcliff Lake, NJ: Eisai Inc.; December 2021. Available at: www.fycompa.com. Accessed May 12, 2022
2. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs II: Treatment resistant epilepsy. Report of the Guideline

Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Epilepsy Curr. Jul-Aug 2018;18(4):269-78.

Creation Date: 07/2023
Effective Date: 01/2024
Reviewed Date:
Revised Date:

PHARMACY DISPENSED CONTINUOUS INSULIN DELIVERY DEVICE PA GUIDELINE OMNIPOD

Generic	Brand	HICL	GCN	Exception/Other
INSULIN PUMP CONTROLLER	OMNIPOD DASH	33823		
INSULIN PUMP CONTROLLER	OMNIPOD DASH PDM KIT	40278		
INSULIN PUMP CARTRIDGE	OMNIPOD 5 G6 PODS	47736		
INSULIN PUMP CONTROLLER	OMNIPOD 5 G6 CONTROLLER	47922		

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following based on type of diabetes:

A – Type 1 Diabetes, Not Currently Using an Insulin Pump
B – Type 1 Diabetes, Currently Using an Insulin Pump
C – Type 2 Diabetes, Not Currently Using an Insulin Pump
D – Gestational Diabetes
E – Type 2 Diabetes, Currently Using an Insulin Pump

A. Type 1 Diabetes, Not Currently Using an Insulin Pump: Must meet all the following:
   1. Patient must have diagnosis of Type 1 Diabetes
   2. The prescriber must be an Endocrinology or Diabetes specialist
   3. Request must be for Omnipod DASH or Omnipod 5
   4. Patient has completed a comprehensive diabetes education program
   5. Patient has been on a program of at least 3 daily injections of insulin with frequent self-adjustments of dose for at least 1 to 2 months prior to this request
   6. Patient has documented frequency of glucose self-testing of at least 3 times per day for 1 to 2 months prior to this request
   7. Meets one or more of the following, while on the multiple injection regimen:
      a. Glycosylated hemoglobin level (HbA1C) greater than 6%
      b. History of recurring hypoglycemia
      c. Wide fluctuations in blood glucose before mealtime
      d. Dawn phenomenon with fasting blood sugars frequently exceeding 200 mg/dl
      e. History of severe glycemic excursions

      If initial criteria are met, approve the PDM kit at HICL x 1 fill only and the DASH or 5 pods at HICL indefinitely.
      If initial criteria are not met, do not approve. The patient does not qualify for a continuous insulin delivery device at this time and may continue other means of insulin administration.

B. Type 1 Diabetes, Currently Using an Insulin Pump: Must meet all the following:
   1. Patient must have diagnosis of Type 1 Diabetes
   2. The prescriber must be an Endocrinology or Diabetes specialist
   3. Request must be for Omnipod DASH or Omnipod 5

      If initial criteria are met, approve the PDM kit at HICL x 1 fill only and the DASH or 5 pods at HICL indefinitely.

If initial criteria are not met, do not approve. The patient does not qualify for a continuous insulin delivery device at this time and may continue other means of insulin administration.

C. Type 2 Diabetes, Not Currently Using an Insulin Pump: Must meet the following based on product requested:
   I. Omnipod DASH: Must meet all the following:
      1. Patient must have diagnosis of Type 2 Diabetes
      2. Prescriber must be an Endocrinology or Diabetes specialist
      3. Patient has completed a comprehensive diabetes education program
      4. Patient monitors blood glucose at least 3-4 times per 24 hours
      5. Patient is currently using at least 3-4 insulin injections per 24 hours
      6. Meets one or more of the following, while on the multiple injection regimen:
         a. Glycosylated hemoglobin level (HbA1C) greater than 6%
         b. History of recurring hypoglycemia
         c. Wide fluctuations in blood glucose before mealtime
         d. Dawn phenomenon with fasting blood sugars frequently exceeding 200 mg/dl
         e. History of severe glycemic excursions
      7. Patient has worked with a Diabetes Care Specialist for at least 6 months on insulin adjustments and the following continue to occur:
         a. At least 2 or more nocturnal hypoglycemia episodes (blood glucose <65mg/dL) in the past month
         b. Use of glucagon in the past 12 months
      8. Patient has been on a program of at least 3 daily injections of insulin with frequent self-adjustments of dose for at least 1 to 2 months prior to this request
      9. Patient has documented frequency of glucose self-testing of at least 3 times per day for 1 to 2 months prior to this request

   If initial criteria are met, approve the PDM kit at HICL x 1 fill only and the DASH or 5 pods at HICL indefinitely.
   If initial criteria are not met, do not approve. The patient does not qualify for a continuous insulin delivery device at this time and may continue other means of insulin administration.

D. Gestational Diabetes: Must meet all the following:
   1. Request must be for Omnipod DASH
   2. Patient must be pregnant and at high risk of developing pregnancy-related complications
   3. Prescriber must be an Endocrinology or Maternal Fetal Medicine provider

   If initial criteria are met, approve the PDM kit at HICL x 1 fill only and the DASH pods at HICL x 1 year.
   If initial criteria are not met, do not approve.

E. Type 2 Diabetes, Currently Using an Insulin Pump: Must meet the following based on product requested:
   I. Omnipod DASH: Must meet all the following:
      1. Patient must have diagnosis of Type 2 Diabetes
      2. The prescriber must be an Endocrinology or Diabetes specialist
      3. Request must be for Omnipod DASH

   If initial criteria are met, approve the PDM kit at HICL x 1 fill only and the DASH pods at HICL indefinitely.

If initial criteria are not met, do not approve. The patient does not qualify for a continuous insulin delivery device at this time and may continue other means of insulin administration

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RATIONALE
KPCO Insulin pump guidelines are included to ensure just and fair reviews between the DME benefit and the Pharmacy benefit.
CMS designated these products as 'disposable insulin delivery devices similar to syringes' therefore are not durable medical equipment and are covered under Part D. KP is following this guidance for the Commercial lines of business as well as Medicare lines.

NOTE: The Freestyle Libre and the Dexcom products are reviewed and approved through the DME process and dispensed through the DME vendor

FDA APPROVED INDICATIONS
Type 1 and Type 2 Diabetes with multiple daily insulin injections - Omnipod Dash
Type 1 Diabetes with multiple daily insulin injections - Omnipod 5 G6
Type 2 Diabetes with multiple daily insulin injections - V-Go

REFERENCES
KPCO Insulin Pump Guidelines 4.8.19
KPCO Endocrinology Dept
Omnipod DASH Insulin Management System with interoperable technology. 2019
https://www.accessdata.fda.gov/cdrh_docs/pdf19/K191679.pdf

Creation date: 10/2019
Effective date: 01/2024
Reviewed date: 11/2023
Revised date: 11/2023

PHARMACY DISPENSED CONTINUOUS INSULIN DELIVERY DEVICE PA GUIDELINE
V-GO

Generic	Brand	HICL	GCN	Exception/Other
SUBCUTANEOUS INSULIN DEVICE 20 UNITS	V-GO 20	38483		
SUBCUTANEOUS INSULIN DEVICE 30 UNITS	V-GO 30	38484		
SUBCUTANEOUS INSULIN DEVICE 40 UNITS	V-GO 40	38486		

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following based on type of diabetes:

A – Type 2 Diabetes, Not Currently Using an Insulin Pump
B – Type 2 Diabetes, Currently Using an Insulin Pump

A. Type 2 Diabetes, Not Currently Using an Insulin Pump: Must meet the following based on product requested:
   I. V-Go: Must meet all the following:
      1. Patient must have diagnosis of Type 2 Diabetes
      2. Prescriber must be an Endocrinology or Diabetes specialist
      3. Patient has completed a comprehensive diabetes education program
      4. Patient monitors blood glucose at least 3-4 times per 24 hrs
      5. Patient is currently using at least 3-4 insulin injections per 24 hrs
      6. Patient is using 40 units or less of basal insulin per day
      7. Meets one or more of the following, while on the multiple injection regimen:
         a. Glycosylated hemoglobin level (HbA1C) greater than 6 %
         b. History of recurring hypoglycemia
         c. Wide fluctuations in blood glucose before mealtime
         d. Dawn phenomenon with fasting blood sugars frequently exceeding 200 mg/dl
         e. History of severe glycemic excursions
      8. Patient has worked with a Diabetes Care Specialist for at least 6 months on insulin adjustments and the following continue to occur:
         a. At least 2 or more nocturnal hypoglycemia episodes (blood glucose <65mg/dL) in the past month
         b. Use of glucagon in the past 12 months
      9. Patient has been on a program of at least 3 daily injections of insulin with frequent self-adjustments of dose for at least 1 to 2 months prior to this request
      10. Patient has documented frequency of glucose self-testing of at least 3 times per day for 1 to 2 months prior to this request

   If initial criteria are met, approve at HICL indefinitely.
   If initial criteria are not met, do not approve. The patient does not qualify for a continuous insulin delivery device at this time and may continue self-administering insulin.

B. Type 2 Diabetes, Currently Using an Insulin Pump: Must meet the following based on product requested:
   I. V-Go: Must meet all the following:
      1. Patient must have diagnosis of Type 2 Diabetes

2. Prescriber must be an Endocrinology or Diabetes specialist
3. Patient is using 40 units or less of basal insulin per day

If initial criteria are met, approve at HICL indefinitely.
If initial criteria are not met, do not approve. The patient does not qualify for a continuous insulin delivery device at this time and may continue other means of insulin administration.

RATIONALE
KPCO Insulin pump guidelines are included to ensure just and fair reviews between the DME benefit and the Pharmacy benefit.
CMS designated these products as 'disposable insulin delivery devices similar to syringes' therefore are not durable medical equipment and are covered under Part D. KP is following this guidance for the Commercial lines of business as well as Medicare lines.

NOTE: The Freestyle Libre and the Dexcom products are reviewed and approved through the DME process and dispensed through the DME vendor

FDA APPROVED INDICATIONS
Type 1 and Type 2 Diabetes with multiple daily insulin injections - Omnipod Dash
Type 1 Diabetes with multiple daily insulin injections - Omnipod 5 G6
Type 2 Diabetes with multiple daily insulin injections - V-Go

REFERENCES
KPCO Insulin Pump Guidelines 4.8.19
KPCO Endocrinology Dept
Omnipod DASH Insulin Management System with interoperable technology. 2019
https://www.accessdata.fda.gov/cdrh_docs/pdf19/K191679.pdf

Creation date: 10/2019
Effective date: 01/2024
Reviewed date: 11/2023
Revised date: 11/2023

PITOLISANT (WAKIX)

Generic	Brand	HICL	GCN	Exception/Other
PITOLISANT HCL	WAKIX	45575	45948, 45949	2nd preferred (after Sunosi)

GUIDELINES FOR COVERAGE

CRITERIA FOR ALL PATIENTS CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

1. Medication is prescribed by a Neurology or a Board-Certified Sleep Medicine provider.
2. Medication is being prescribed for Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; or Cataplexy (not excessive daytime sleepiness) due to narcolepsy.
3. Medication requested is not be used in combination with solriamfetol (Sunosi) or any oxybate product (i.e. Xyrem, Xywav, Lumryz).

If criteria are met, approve indefinitely, max 2 tablets/day.
If criteria are not met, do not approve.

CRITERIA FOR ANY PATIENT NOT CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

A. Medication is prescribed by Neurology or a Board-Certified Sleep Medicine provider.
B. Medication requested is not be used in combination with solriamfetol (Sunosi) or any oxybate product (i.e. Xyrem, Xywav, Lumryz).
C. Patient must have one of the following indications and meet all criteria pertaining to that indication:
    1. Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia: Must meet all the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        a. Patient must have tried and failed or have a contraindication to each of the following: amphetamines, methylphenidate, and either modafinil or armodafinil.
        b. Patient must have tried and failed or have a contraindication to Sunosi [Prior Authorization required].

        If criteria are met, approve indefinitely, max 2 tablets/day.
        If criteria are not met, do not approve.

    2. Cataplexy (not excessive daytime sleepiness) due to narcolepsy: Patient must have tried and failed or have a contraindication to each of the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy

exception: a tricyclic antidepressant (TCA), a selective serotonin reuptake inhibitor (SSRI), and a selective serotonin-norepinephrine (SNRI).

If critieria are met, approve indefinitely, max 2 tablets/day.
If criteria are not met, do not approve.

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ePA Questions

2. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; Cataplexy (not excessive daytime sleepiness) due to narcolepsy]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia

   1. Is the patient stable on therapy with this medication?
   2. For patients noted stable on therapy, start date of therapy (MMDDYY):
   3. Is the medication being used in combination with solriamfetol (Sunosi) or any other oxybate product (i.e. Xywav, Xyrem, Lumryz)?
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (amphetamines, methylphenidate, modafinil, armodafinil) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Cataplexy (not excessive daytime sleepiness) due to narcolepsy

   1. Is the patient stable on therapy with this medication?
   2. For patients noted stable on therapy, start date of therapy (MMDDYY):
   3. Is the medication being used in combination with solriamfetol (Sunosi) or any other oxybate product (i.e. Xywav, Xyrem, Lumryz)?
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (amitriptyline tablets, desipramine tablets, nortriptyline capsules; citalopram tablets/solution, escitalopram tablets, fluoxetine capsules/solution, paroxetine IR tablets, sertraline tablets/susp; venlafaxine ER capsules (37.5 mg, 75 mg, 150 mg), duloxetine capsules (20 mg, 30 mg, 60 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Dr. Richey and Health Plan

FDA APPROVED INDICATIONS AND SUPPORTED OFF-LABEL INDICATIONS

Xyrem/Xywav/Lumryz = Cataplexy; Narcolepsy; Idiopathic hypersomnia
Sunosi = Narcolepsy; Idiopathic hypersomnia; Hypersomnia associated with Obstructive sleep apnea
Wakix = Cataplexy; Narcolepsy; Idiopathic hypersomnia

Creation date: 03/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

PONATINIB

Generic	Brand	HICL	GCN/GPID	Other
PONATINIB	ICLUSIG	39859		Nonformulary, 2nd Generation TKI

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

A. Patient is new to KPCO within the past 90 days, and the medication has been prescribed by an Oncologist

If met, approve x 2 years.
If not met, then use Initial Criteria.

INITIAL CRITERIA: Must meet the following criteria based on drug and diagnosis below:

A. Ponatinib (Iclusig) for All Phases of CML and ALL
B. All other indications

A. **Ponatinib (Iclusig) for CML (any phase) or ALL: Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Patient must have Philadelphia Chromosome (aka BCR-ABL) and one of a through c below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient has tried and failed imatinib (Gleevec, if chronic phase CML), and/or dasatinib (Sprycel), and/or nilotinib (Tasigna), and/or bosutinib (Bosulif) with an inadequate response that is not due to patient nonadherence
      b. Patient must have a documented intolerance to at least one of the following agents not alleviated by dose reductions:
         i. Imatinib (Gleevec): ≤200 mg/day [adult] or 260mg/m^2 [peds; if this calculates to >200mg/day use adult dose cutoff]
         ii. Bosutinib (Bosulif): ≤300mg/day
         iii. Nilotinib (Tasigna): 400mg/day; if peds 230mg/m2 daily
         iv. Dasatinib (Sprycel): 70mg/day [If patient developed pulmonary arterial hypertension [PAH] during treatment with dasatinib (Sprycel) at any dose, patient may be deemed "intolerant"]; for peds use table below:

Weight	Dose of dasatinib (Sprycel) which must be tried and failed before deeming patient "intolerant"
10 to <20kg	20mg
20 to <30kg	20mg
30 to <45kg	50mg
45kg+	Use adult dose cutoff

c. Patient must have one of the following BCR-ABL1 mutations: T315I

If criteria are met, approve indefinitely.
If criteria are not met, do not approve.

B. **If for any other diagnosis (e.g., hypereosinophilic syndrome, eosinophilic leukemia, dermatofibrosarcoma, chordoma): Must meet all the following:**
   1. Prescribed by an oncology specialist
   2. Use must meet the Medicare Compendia criteria as detailed in the following policy: Medicare Benefit Policy Manual Chapter 15 - Covered Medical and Other Health Services Section 50.4.5 - Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

If criteria are met, approve x 1 year.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
A. Patient has been on the TKI for greater than 3 months and one of the following criteria:
   1. Disease progression or relapse are not noted in the chart
   2. Patient has experienced improvement in disease symptoms since starting the medication

If criteria are met, approve x 2 years.
If criteria are not met, do not approve.

RATIONALE

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology Chronic Myeloid Leukemia v.2.2023 www.nccn.org
2. NCCN Clinical Practice Guidelines in Oncology Acute Lymphoblastic Leukemia v.1.2022 www.nccn.org
3. NCCN Clinical Practice Guidelines in Oncology Gastrointestinal Stromal Tumors (GISTs) v.1.2023 www.nccn.org

Creation Date: 11/2019
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

POSACONAZOLE (NOXAFIL)

Generic	Brand	HICL	GCN	Exception/Other
POSACONAZOLE	NOXAFIL	33461		Formulary

GUIDELINES FOR COVERAGE

NEW MEMBER/INITIAL CRITERIA: Must meet ALL the following:

1. Prescriber specializes in Hematology, Oncology, Hematopoietic Stem Cell Transplantation, Solid Organ Transplant or Infectious Disease
2. Patient is at least 13 years of age, OR is at least 2 years of age AND weighs at least 40kg (88 pounds)
3. Posaconazole is being used as treatment or prophylaxis in patients with ONE of the following conditions:
   a. Acute leukemia or myelodysplastic syndrome (MDS) and receiving systemic chemotherapy
   b. Patient is s/p allogeneic hematopoietic stem cell transplant (HCT) and meets ONE of the following conditions:
      i. history of invasive fungal infection
      ii. is 30+days s/p transplant AND ANC remains <1,500
      iii. is 14+days s/p transplant AND ANC remains <500
   c. Graft versus host disease (GVHD) and currently being treated with systemic immunosuppressive therapy
   d. Invasive fungal infection with organism known to be resistant to voriconazole and fluconazole
   e. Invasive fungal infection with documented failure, intolerance or contraindication to fluconazole and/or voriconazole (as appropriate), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
4. If request is for posaconazole suspension, patient must have documented intolerance or contraindication, or inability to swallow to posaconazole tablets.

If Initial Criteria are met, approve x3 months at HICL/GPID.
If Initial Criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet ONE OF the following:

1. If initial approval was for invasive fungal infection, patient has shown improvement of symptoms since starting on the drug.
2. If initial approval was for acute leukemia or MDS, patient continues to receive systemic chemotherapy for their diagnosis.
3. If initial approval was for s/p allogeneic HSCT, patient must continue to be neutropenic.
4. If initial approval was for GVHD, patient must be receiving either high dose corticosteroids OR other systemic anti-GVHD therapies (e.g., tacrolimus, sirolimus, ruxolitinib, ibrutinib, belumosudil, others).

If renewal criteria are met, approve x6 months at HICL/GPID.
If renewal criteria are not met, do not approve.

POSACONAZOLE (NOXAFIL)

RATIONALE
To promote cost-effective, evidence-based use of posaconazole.

FDA APPROVED INDICATIONS
Treatment of fungal infections in adults and children 13 years of age and older
Prevention of fungal infections in adults and children 2 years of age and older who weigh greater than 88 lbs (40kg)

REFERENCES
1. NCCN Guidelines on Prevention and Treatment of Cancer-Related Infections. V.2.2022. www.nccn.org
2. Noxafil Prescribing Information. Merck & Co, Inc. Rahway NJ. Revised 09/2022.

Creation Date: 09/2023
Effective Date: 01/2024
Reviewed Date:
Revised Date:

POTASSIUM CHLORIDE (KCL) SOLUTION - AGE RESTRICTION

Generic	Brand	HICL	GPID	Exception/Other
POTASSIUM CHLORIDE LIQUID 20mEq/15mL			3443	Non-formulary
POTASSIUM CHLORIDE LIQUID 40mEq/15mL			3442	Non-formulary
POTASSIUM CHLORIDE 10 mEq POWDER PACKETS			54758	Non-formulary
POTASSIUM CHLORIDE 20mEq POWDER PACKETS			3404	

GUIDELINES FOR COVERAGE

INITIAL AND RENEWAL CRITERIA: ONE of the following must be met:

1. Patient must be less than or equal to 10 years old
2. Current dosage is greater than 40mEq twice daily
3. Patient is using an alternative administration route, such as a gastrostomy tube
4. Patient has failed therapy using Klor-Con M tablets dissolved in water, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If coverage criteria are met at criterion 1, approve until patient turns the age of 11.
If coverage criteria are met at criterion 2, 3, or 4, approve indefinitely.

Note:
The preferred alternative for patients who do not meet coverage criteria is to disperse the Klor-Con M tablets in water and swallow the slurry per the instructions below.

- Klor-Con M tablet slurry instructions:
  - Dissolve 1 tablet (20mEq) in 120 mL of water over 2 minutes
  - Stir for approximately 30 seconds and consume immediately
  - Add an additional 30mL of water to the container and consume immediately

RATIONALE
Per KPCO UM Team

REFERENCES
Per Health Plan

Creation date: 5/2019
Effective date: 03/2024
Revised date: 12/2023
Reviewed date: 12/2023

RAPID-ACTING INSULIN PENS
ASPART

Generic	Brand	HICL	GCN	Exception/Other
INSULIN ASPART	NOVOLOG FLEXPEN, NOVOLOG RELION PEN		92336	
INSULIN ASPART	NOVOLOG PENFILL CARTRIDGE		92886	For use with NovoPen Echo device for ½ unit dosing

GUIDELINES FOR INITIAL AND CONTINUED USE

Must meet criteria based on requested product:

1. Request for Aspart (Novolog FlexPen, Novolog Flex Touch Pen, Novolog ReliOn Pen, Novolog Cartridge): Must meet a, and either b or c below:
    a. Patient has failed* insulin Lispro (Humalog), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
    b. Prescription is written by an Endocrinology specialist
    c. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination.

    If above criteria are met, approve insulin aspart, generic only, indefinitely.
    If above criteria are not met, do not approve.
    [NOTE: Brand Novolog products are excluded from coverage. Kaiser Permanente will dispense unbranded insulin aspart.]

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin Lispro (Humalog Kwikpen) is preferred based on its efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for children and adults with physical and/or cognitive impairment.

Certain insulin products offer ½ unit dosing such as Lispro (Humalog Junior KwikPen, Humalog Cartridge), Aspart (Novolog Cartridge), and Lispro aabc (Lyumjev Junior KwikPen). Humalog Junior KwikPen or Humalog Cartridge are preferred based on this insulin's efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO.

Two rapid-acting insulin pens are available in a higher concentration such as Lispro (Humalog KwikPen U-200) and Lispro aabc (Lyumjev KwikPen U-200). Humalog KwikPen U-200 is KPCO preferred option for patients requiring insulin doses between 100 and 200 units/day.

Two insulin products are considered ultra-rapid acting insulins due to additives and their ability to speed up absorption by 5-10 minutes. These insulins are Lispro aabc and Aspart with niacinamide. Lispro aabc (Lyumjev) is the first insulin approved as a biologic. It has no clinical advantage over Fiasp but offeres a cost advantage and therefore is the preferred product. All insulins will be approved as biologics from now on.

Tempo pens are personalized diabetes management platform that combines the Tempo prefilled insulin pen, diabetes management devices, and app-driven support to deliver personalized guidance for people with diabetes.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

RAPID-ACTING INSULIN PENS
ASPART NIACINAMIDE

Generic	Brand	HICL	GCN	Exception/Other
INSULIN ASPART (NIACINAMIDE)	FIASP FLEXTOUCH FIASP PENFILL CARTRIDGE		43053	Ultra rapid

GUIDELINES FOR INITIAL AND CONTINUED USE

Must meet criteria based on requested product:

1. Request for Aspart with niacinamide (Fiasp FlexTouchPen or Penfill Cartridges): Must meet a or b, and step-therapy criteria from c, d, and e below unless provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Prescription is written by an Endocrinology specialist
    b. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination
    c. Has failed insulin lispro (Humalog) due to due difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent
    d. Has failed insulin aspart (Novolog) due to difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent
    e. Has failed insulin lispro aabc (Lyumjev) due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent unless request is for Fiasp cartridge (Lyumjev not available in cartridge)

    If above criteria are met, approve indefinitely.
    If above criteria are not met, do not approve.

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin Lispro (Humalog Kwikpen) is preferred based on its efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for children and adults with physical and/or cognitive impairment.

Certain insulin products offer ½ unit dosing such as Lispro (Humalog Junior KwikPen, Humalog Cartridge), Aspart (Novolog Cartridge), and Lispro aabc (Lyumjev Junior KwikPen). Humalog Junior

KwikPen or Humalog Cartridge are preferred based on this insulin's efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO.

Two rapid-acting insulin pens are available in a higher concentration such as Lispro (Humalog KwikPen U-200) and Lispro aabc (Lyumjev KwikPen U-200). Humalog KwikPen U-200 is KPCO preferred option for patients requiring insulin doses between 100 and 200 units/day.

Two insulin products are considered ultra-rapid acting insulins due to additives and their ability to speed up absorption by 5-10 minutes. These insulins are Lispro aabc and Aspart with niacinamide. Lispro aabc (Lyumjev) is the first insulin approved as a biologic. It has no clinical advantage over Fiasp but offeres a cost advantage and therefore is the preferred product. All insulins will be approved as biologics from now on.

Tempo pens are personalized diabetes management platform that combines the Tempo prefilled insulin pen, diabetes management devices, and app-driven support to deliver personalized guidance for people with diabetes.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

RAPID-ACTING INSULIN PENS
GLULISINE

Generic	Brand	HICL	GCN	Exception/Other
INSULIN GLULISINE	APIDRA SOLOSTAR		26508	

GUIDELINES FOR INITIAL AND CONTINUED USE

Must meet criteria based on requested product:

1. Request for Glulisine (Apidra SoloStar): Must meet a, and either b or c below:
    a. Patient has failed* each of the following: Lispro (Humalog KwikPen), Aspart (Novolog FlexPen), and Lispro-aabc (Lyumjev KwikPen, Lyumjev TempoPen), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
    b. Prescription is written by an Endocrinology specialist
    c. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination

    If above criteria are met, approve indefinitely.
    If above criteria are not met, do not approve.

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin Lispro (Humalog Kwikpen) is preferred based on its efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for children and adults with physical and/or cognitive impairment.

Certain insulin products offer ½ unit dosing such as Lispro (Humalog Junior KwikPen, Humalog Cartridge), Aspart (Novolog Cartridge), and Lispro aabc (Lyumjev Junior KwikPen). Humalog Junior KwikPen or Humalog Cartridge are preferred based on this insulin's efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO.

Two rapid-acting insulin pens are available in a higher concentration such as Lispro (Humalog KwikPen U-200) and Lispro aabc (Lyumjev KwikPen U-200). Humalog KwikPen U-200 is KPCO preferred option for patients requiring insulin doses between 100 and 200 units/day.

Two insulin products are considered ultra-rapid acting insulins due to additives and their ability to speed up absorption by 5-10 minutes. These insulins are Lispro aabc and Aspart with niacinamide. Lispro

aabc (Lyumjev) is the first insulin approved as a biologic. It has no clinical advantage over Fiasp but offeres a cost advantage and therefore is the preferred product. All insulins will be approved as biologics from now on.

Tempo pens are personalized diabetes management platform that combines the Tempo prefilled insulin pen, diabetes management devices, and app-driven support to deliver personalized guidance for people with diabetes.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

RAPID-ACTING INSULIN PENS
LISPRO

Generic	Brand	HICL	GCN	Exception/Other
INSULIN LISPRO	HUMALOG KWIKPEN, ADMELOG SOLOSTAR, HUMALOG TEMPO PEN		96719	GSN = 34731 HICL = 11528 Humalog KwikPen - preferred product
INSULIN LISPRO	HUMALOG CARTRIDGE		5678	For use with HumaPen Luxura for ½ unit dosing (device no longer made)
INSULIN LISPRO	HUMALOG JUNIOR KWIKPEN		43753	Preferred product for ½ unit dosing
INSULIN LISPRO	HUMALOG KWIKPEN U-200		37798	

GUIDELINES FOR INITIAL AND CONTINUED USE

Must meet criteria based on requested product:

1. Request for Lispro 100 unit/ml: Must meet ONE of the following:
    a. Prescription is written by an Endocrinology specialist
    b. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination.

    If met, approve indefinitely.
    If above criteria are not met, do not approve.
    [Note: Biosimilars of Humalog are non-preferred. Kaiser Permanente will dispense brand Humalog.]

2. Request for Lispro 200 unit/ml: Must meet the following criteria:
    a. Patient's short-acting insulin dose is 100 units per day or more (including Regular) but their total daily insulin dose (basal + bolus) is less than 200 units/day or 2 units/kg/day

    If above criteria are met, approve x2 years.
    If above criteria are not met, do not approve.

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RENEWAL CRITERIA

Request for U-200: Patient's long-acting insulin dose exceeds 100 units/day but their total daily dose of insulin (basal + bolus) does NOT exceed 200 units/day or 2 units/kg/day.

If above renewal criteria are met, approve at GPID for 2 years.
If above renewal criteria are not met, do not approve.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin Lispro (Humalog Kwikpen) is preferred based on its efficacy and safety profile, as

well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for children and adults with physical and/or cognitive impairment.

Certain insulin products offer ½ unit dosing such as Lispro (Humalog Junior KwikPen, Humalog Cartridge), Aspart (Novolog Cartridge), and Lispro aabc (Lyumjev Junior KwikPen). Humalog Junior KwikPen or Humalog Cartridge are preferred based on this insulin's efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO.

Two rapid-acting insulin pens are available in a higher concentration such as Lispro (Humalog KwikPen U-200) and Lispro aabc (Lyumjev KwikPen U-200). Humalog KwikPen U-200 is KPCO preferred option for patients requiring insulin doses between 100 and 200 units/day.

Two insulin products are considered ultra-rapid acting insulins due to additives and their ability to speed up absorption by 5-10 minutes. These insulins are Lispro aabc and Aspart with niacinamide. Lispro aabc (Lyumjev) is the first insulin approved as a biologic. It has no clinical advantage over Fiasp but offeres a cost advantage and therefore is the preferred product. All insulins will be approved as biologics from now on.

Tempo pens are personalized diabetes management platform that combines the Tempo prefilled insulin pen, diabetes management devices, and app-driven support to deliver personalized guidance for people with diabetes.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

RAPID-ACTING INSULIN PENS
LISPRO AABC

Generic	Brand	GCN	Exception/Other
INSULIN LISPRO-AABC	LYUMJEV U-100 KWIKPEN, LYUMJEV U-100 TEMPO PEN, LYUMJEV U-200 KWIKPEN	48229, 48231	1st insulin approved as a biologic Ultra rapid

GUIDELINES FOR INITIAL AND CONTINUED USE

Must meet criteria based on requested product:

1. Request for Lispro-aabc 100 units/ml: Must meet a, and either b or c below:
    a. Has failed insulin lispro (Humalog) due to difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
    b. Prescription is written by an Endocrinology specialist
    c. Patient is under 18 years of age, or the patient is 18 years of age or older and is unable to use insulin vials and syringes due to cognitive function, difficulties with manual dexterity, visual disturbances, visual impairment, uncorrectable poor injection technique, or compromised fine-motor coordination

    If above criteria are met, approve indefinitely.
    If above criteria are not met, do not approve.

2. Request for Lispro-aabc 200 units/ml: Must meet all the following criteria:
    a. Patient's short-acting insulin dose is 100 units per day or more (including Regular) but their total daily insulin dose (basal + bolus) is less than 200 units/d or 2 units/kg/d
    b. Patient has failed insulin Lispro U-200 (Humalog KwikPen U-200) due to difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

    If above criteria are met, approve x2 years.
    If above criteria are not met, do not approve.

*NOTE: Failure can be defined as an adverse drug reaction or intolerance that is not expected to occur with the requested agent.

RENEWAL CRITERIA
Request for U-200: Patient's long-acting insulin dose exceeds 100 units/day but their total daily dose of insulin (basal + bolus) does NOT exceed 200 units/day or 2 units/kg/day.

If above renewal criteria are met, approve at GPID for 2 years.
If above renewal criteria are not met, do not approve.

RATIONALE
There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Insulin Lispro (Humalog Kwikpen) is preferred based on its efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO. The use of insulin pens at KPCO is reserved for children and adults with physical and/or cognitive impairment.

Certain insulin products offer ½ unit dosing such as Lispro (Humalog Junior KwikPen, Humalog Cartridge), Aspart (Novolog Cartridge), and Lispro aabc (Lyumjev Junior KwikPen). Humalog Junior KwikPen or Humalog Cartridge are preferred based on this insulin's efficacy and safety profile, as well as its competitive cost advantage for patients and KPCO.

Two rapid-acting insulin pens are available in a higher concentration such as Lispro (Humalog KwikPen U-200) and Lispro aabc (Lyumjev KwikPen U-200). Humalog KwikPen U-200 is KPCO preferred option for patients requiring insulin doses between 100 and 200 units/day.

Two insulin products are considered ultra-rapid acting insulins due to additives and their ability to speed up absorption by 5-10 minutes. These insulins are Lispro aabc and Aspart with niacinamide. Lispro aabc (Lyumjev) is the first insulin approved as a biologic. It has no clinical advantage over Fiasp but offeres a cost advantage and therefore is the preferred product. All insulins will be approved as biologics from now on.

Tempo pens are personalized diabetes management platform that combines the Tempo prefilled insulin pen, diabetes management devices, and app-driven support to deliver personalized guidance for people with diabetes.

FDA APPROVED INDICATIONS
Diabetes type 1 and type 2 treatment

REFERENCES
Per Plan

Creation date: 5/4/2017
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

RIFAXIMIN (XIFAXAN)

Generic	Brand	HICL	GCN	Exception/Other
RIFAXIMIN	XIFAXAN	20401	93749, 28530	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis, A-E below:

A. Irritable Bowel Syndrome with Diarrhea (IBS-D)
B. Hepatic Encephalopathy (HE)
C. Small Intestinal Bacterial Overgrowth (SIBO)
D. Clostridium difficile infection (CDI)
E. Traveler's Diarrhea

A. Irritable Bowel Syndrome with Diarrhea (IBS-D): The following must be met: 1-5 below:
   1. Patient is at least 18 years of age
   2. Prescribed by a Gastroenterologist
   3. Failure of dietary modification (low FODMAP)
   4. Failure, contraindication, or intolerance to all of the following: at least one bile acid sequestrant for 2-week trial, at least one antispasmodic (dicyclomine) [if patient less than 65 years of age] for 2-week trial; at least one tricyclic antidepressant [if patient less than 65 years of age] for 6-week trial, and at least one antidiarrheal (loperamide or diphenoxylate-atropine) for 2-week trial, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   5. Request is for 550 mg tablet

      If above criteria are met, then approve 1 fill, max 14-day supply, max 3 tablets daily.
      If above criteria are not met, then do not approve.

B. Hepatic Encephalopathy (HE): The following must be met: 1-4, or 1,2 and 5 below:
   1. Patient is at least 18 years of age
   2. Request is for 550 mg tablet
   3. Prescribed by a Gastroenterologist
   4. Failure, contraindication, or intolerance to lactulose, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   5. Initiated during inpatient admission with diagnosis of hepatic encephalopathy

If above criteria are met, then approve indefinitely, max 2 tablets daily.
If above criteria are not met, then do not approve.

C. Small Intestinal Bacterial Overgrowth (SIBO): The following must be met: 1-4 below:
   1. Prescribed by a Gastroenterologist
   2. Failure of dietary modification (low FODMAP)
   3. Failure, contraindication, or intolerance to at least two of the following antibiotics: amoxicillin-clavulanate, ciprofloxacin, metronidazole, neomycin, doxycycline or tetracycline, or sulfamethoxazole-trimethoprim DS, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   4. Request is for 550 mg tablet

   If above criteria are met, then approve 1 fill, max 14-day supply, max 3 tablets daily.
   If above criteria are not met, then do not approve.

D. Clostridium difficile infection (CDI): The following must be met: 1-3 below:
   1. Patient is at least 18 years of age
   2. Prescribed by a Gastroenterologist or Infectious Disease specialist
   3. Patient is being treated for a second or subsequent recurrence of CDI after completion of 2 full prior treatment courses (unless documented intolerance resulting in early discontinuation)

   If above criteria are met, then approve 1 fill.
   If above criteria are not met, then do not approve.

E. Traveler's Diarrhea: The following must be met: 1-3 below:
   1. Patient is at least 12 years of age
   2. Failure, contraindication, or intolerance to azithromycin and either ciprofloxacin or levofloxacin, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
   3. Request is for 200 mg tablet

   If above criteria are met, then approve 1 fill, max 3-day supply, max 3 tablets daily.
   If above criteria are not met, then do not approve.

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RIFAXIMIN (XIFAXAN)

RENEWAL CRITERIA: Review based on diagnosis, A-B below:

A. Irritable Bowel Syndrome with Diarrhea (IBS-D)
B. Small Intestinal Bacterial Overgrowth (SIBO)

A. Irritable Bowel Syndrome with Diarrhea (IBS-D): The following must be met: 1-3 below:
   1. Patient has recurrence of symptoms after documentation of positive clinical response to prior course(s).
   2. Patient has not received more than 2 prior treatment courses with rifaximin.
   3. Request is for 550 mg tablet

   If above criteria are met, then approve 1 fill, max 14-day supply, max 3 tablets daily. Up to 3 total treatment courses may be approved.
   If above criteria are not met, then do not approve.

B. Small Intestinal Bacterial Overgrowth (SIBO): The following must be met: 1-3 below:
   1. Patient has recurrence of symptoms after documentation of positive clinical response to prior course(s).
   2. Patient has not received more than 1 other treatment course with rifaximin in the past year.
   3. Request is for 550 mg tablet

   If above criteria are met, then approve 1 fill, max 14-day supply, max 3 tablets daily. Up to 2 treatment courses may be approved per year.
   If above criteria are not met, then do not approve.

Created: 02/2022
Effective: 12/2023
Reviewed: 11/2023
Revised: 11/2023

RISDIPLAM (EVRYSDI)

Generic	Brand	HICL	GCN	Exception/Other
RISDIPLAM	EVRYSDI	46765	48456	Survival motor neuron 2 (SMN2)- directed RNA splicing modifier

GUIDELINES FOR COVERAGE

CRITERIA FOR ALL PATIENTS CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING

1. Must be prescribed by a Neurologist
2. LFTs (liver function tests), PT (prothrombin time), and PTT (partial thromboplastin time) labs have been completed in the past year
3. Motor function assessment(s)* has/have been completed in the past year
4. Pulmonary assessment* has been completed in the past year
5. Patient is not, and will not be using this medication with nusinersen (Spinraza)
6. Patient does not require/have permanent invasive ventilation or tracheostomy
7. Patient is not dependent on invasive or non-invasive ventilation during waking hours to control hypercarbia, nor does patient have hypercarbia without ventilatory support
8. Patient has not experienced loss of function or progressive weakness (physical and/or pulmonary) since starting this medication
9. Patient has no prior or planned treatment with onasemnogene abeparvovec or other gene therapy for SMA

If all criteria above are met, approve at HICL (override PA Res and Formulary) x1 year.
Notify neurology clinical pharmacy specialists and CPMG neurologist representative after all approvals and denials^

CRITERIA FOR ANY PATIENT NOT CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

1. Patient must be 25 years of age or younger
2. Medication must be prescribed by a Neurologist
3. Patient has a confirmed diagnosis of 5q-autosomal recessive SMA (biallelic deletions or mutations in the SMN1 gene)
4. Patient has 2-4 copies of SMN2 gene
5. Patient has no prior or planned treatment with onasemnogene abeparvovec or other gene therapy for SMA
6. Patient will not be using this medication with nusinersen (Spinraza)
7. Patient does not require/have permanent invasive ventilation or tracheostomy
8. Patient is not dependent on invasive or non-invasive ventilation during waking hours to control hypercarbia, nor does patient have hypercarbia without ventilatory support
9. Patient has motor function assessment(s) completed within the past three months as appropriate based on age and ambulatory status*
10. Pulmonary assessment(s) have been completed within the past three months as appropriate based on age and ambulatory status*

If criteria are met, approve at HICL (override PA Res and Formulary) x1 year
If criteria are not met, do not approve. For patients less than 2 months of age, recommend onasemnogene abeparvovec-xioi (Zolgensma).

ePA Questions

1. Please select the box that most accurately describes this patient:
    a. Patient is currently taking risdiplam
    b. Patient is not currently taking risdiplam

    PATIENTS CURRENTLY TAKING RISDIPLAM

    1. Have LFTs (liver function tests), PT (prothrombin time), and PTT (partial thromboplastin time) labs been completed in the past year?
    2. Have motor function and pulmonary assessments been completed in the past year?
    3. Will the patient be using this medication with nusinersen (Spinraza)?
    4. Does the patient require/have permanent invasive ventilation or tracheostomy?
    5. Is the patient dependent on invasive or non-invasive ventilation during waking hours to control hypercarbia?
    6. Does the patient have hypercarbia without ventilatory support?
    7. Has the patient experienced loss of function or progressive weakness (physical and/or pulmonary) since starting risdiplam?
    8. Has the patient been, or is the patient planning to be treated with onasemnogene abeparvovec or other gene therapy for SMA?

    PATIENTS NOT CURRENTLY TAKING RISDIPLAM

    1. Does the patient have a confirmed diagnosis of 5q-autosomal recessive SMA (biallelic deletions or mutations in the SMN1 gene)?
    2. Does the patient have 2-4 copies of SMN2 gene?
    3. Has the patient been, or is the patient planning to be treated with onasemnogene abeparvovec or other gene therapy for SMA?
    4. Will the patient be using this medication with nusinersen (Spinraza)?
    5. Does the patient require/have permanent invasive ventilation or tracheostomy?
    6. Is the patient dependent on invasive or non-invasive ventilation during waking hours to control hypercarbia?
    7. Does the patient have hypercarbia without ventilatory support?
    8. Have motor function and pulmonary assessments been completed in the past year?

***Motor function assessments for initial use:**

Age/Ambulatory status	Assessment
Infants (<24 months)	Hammersmith Infant Neurological Examination Section 2 (HINE-2) **OR** Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
Children (≥24 months) **Adolescents** **Adults**	Hammersmith Functional Motor Scale-Expanded Exam (HFMSE) **AND** Revised Upper Limb Module (RULM)
All ambulatory patients	6-minute walk test (6MWT)

***Pulmonary assessments for initial use:**

Age	Assessment
< 6 years	Pulse oximetry and End-Tidal CO2 (ETCO2) measurements

	(Providers may also consider screening sleep studies in non-ambulatory, hypotonic infants and young children)
≥ 6 years	Pulmonary function tests (PFTs)

RATIONALE
Risdiplam, a survival motor neuron 2 (SMN2)-directed RNA splicing modifier, is the first oral therapy to be FDA approved for spinal muscular atrophy (SMA). It was approved in 2020 for the treatment of SMA in patients 2 months of age and older. FDA approval was based on data from two unpublished studies. One study, a Phase 2/3 open-label trial in symptomatic infants aged 1 to 7 months, demonstrated motor function ability after 12 months of treatment and 81% survival without permanent ventilation after at least 23 months of treatment, both of which are not expected with typical untreated disease progression. The second study is a Phase 2/3 randomized, placebo-controlled study in patients aged 2 to 25 years with later-onset SMA that showed motor function improvement or stabilization with risdiplam compared to motor function decline with placebo after one year. Data are promising but given the very limited data and lack of long-term safety data, exceedingly judicious prescribing and monitoring of therapy are warranted.

In May 2022, after interim results were published from the RAINBOWFISH trial that enrolled pre-symptomatic infants aged from birth to 6 weeks of age, the FDA updated its indication for risdiplam to include all pediatric patients with SMA.

Per Kaiser Permanente's Emerging Therapeutics Strategy Program guideline, for patients age < 6 months, based on the strength of current available data of onasemnogene abeparvovec-xioi (Zolgensma), KP consensus recommendation is to use onasemnogene abeparvovec-xioi as the preferred product for these patients.

Alternating treatments: There are no data supporting the efficacy and safety of alternating between risdiplam and nusinersen therapy; thus, alternating drug therapy is not recommended.

Hepatic impairment - relative precaution:
- Hepatic functional impairment via abnormal total bilirubin and/or abnormal PT (prothrombin time) and PTT (partial thromboplastin time) indicates need for further assessment prior to initiating risdiplam
- Avoid use in patients with hepatic impairment due to possible increased exposure to risdiplam which is primarily metabolized in the liver. The safety and efficacy of risdiplam have not been studied in patients with hepatic impairment.

FDA APPROVED INDICATIONS
Treatment of spinal muscular atrophy (SMA) in pediatric and adult patients

REFERENCES
1. Baranello G, Servais L, Day JW, et al. FIREFISH Part 1: 16-month safety and exploratory outcomes of risdiplam (RG7916) treatment in infants with Type 1 spinal muscular atrophy (SMA). 24th International Annual Congress of the World Muscle Society. Oct 2019.
2. Chiriboga CA, Mercuri E, Fischer D, et al. JEWELFISH: Safety and pharmacodynamic data in patients with spinal muscular atrophy (SMA) receiving treatment with risdiplam (RG7916) that have

previously been treated with nusinersen. 24th International Annual Congress of the World Muscle Society. Oct 2019.
3. NCT02913482. Investigate Safety, Tolerability, PK, PD and Efficacy of Risdiplam (RO7034067) in Infants WithType1 Spinal Muscular Atrophy (FIREFISH). https://clinicaltrials.gov/ct2/show/NCT02913482?term=risdiplam&draw=2&rank=4
4. NCT02908685. A Study to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Efficacy of Risdiplam (RO7034067) in Type 2 and 3 Spinal Muscular Atrophy (SMA) Participants (SUNFISH). https://clinicaltrials.gov/ct2/show/NCT02908685?term=risdiplam&draw=2&rank=8
5. NCT03032172. A Study of Risdiplam (RO7034067) in Adult and Pediatric Participants With Spinal Muscular Atrophy (Jewelfish). https://clinicaltrials.gov/ct2/show/NCT03032172?term=risdiplam&draw=2&rank=6
6. NCT03779334. A Study of Risdiplam in Infants With Genetically Diagnosed and Presymptomatic Spinal Muscular Atrophy (Rainbowfish). https://clinicaltrials.gov/ct2/show/NCT03779334?term=risdiplam&draw=2&rank=38.
7. MercuriE, et al. SUNFISH Part 2: Efficacy and Safety of Risdiplam (RG7916) in Patients with Type 2 or Non-Ambulant Type 3 Spinal Muscular Atrophy (SMA). Presented at: 2nd International Scientific and Clinical Congress on Spinal Muscular Atrophy; February 5-7 2020; Evry, France.
8. Servais L, et al. FIREFISH Part 2: Efficacy and safety of risdiplam (RG7916) in infants with Type 1 spinal muscular atrophy (SMA). Presented at the 2020 Cure SMA Research and Clinical Care Virtual Meeting. June 12, 2020
9. Finkel RS, Farrar MA, Vlodavets D, et al. RAINBOWFISH: Preliminary Efficacy and Safety Data in Risdiplam-Treated Infants with Presymptomatic SMA (P17-5.003). Neurology. 2022;98(18 Supplement):1636.

Creation Date: 3/2021
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

RISEDRONATE 35MG TABLET - STEP THERAPY

Generic	Brand	HICL	GCN	Exception/Other
RISEDRONATE SODIUM 35MG TABLET	ACTONEL		17378	

Step Therapy Criteria: Must meet ONE of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. The request is for generic risedronate 35 mg tablets and the patient has tried and failed or had an intolerance/allergy to alendronate.
2. The request is for brand Actonel, the patient has tried and failed or had an intolerance/allergy to alendronate, and Brand When Generic is Available nonformulary guidance is met as noted in a-d below:
    a. An authorized generic is not available.
    b. Patient has a documented allergic reaction to an inactive ingredient in the generic product (example: dye) not present in the brand name product and other generic equivalents to the brand are not available without the inactive ingredient which caused the allergic reaction.
    c. Patient has treatment failure, intolerance, or contraindication to at least three other formulary, therapeutic alternatives (Note: In cases where no other alternatives are available, only the generic equivalent needs to have been tried).
    d. Patient meets requirements for coverage for generic equivalent, when/if applicable.

If met, approve indefinitely based on product requested and step met:
- generic risedronate sodium 35mg tablets at GPID-G.
- brand Actonel 35 mg tablets at GPID.

If not met, do not approve.

Note: This step therapy does not include Atelvia or its generic DR tablet.

RATIONALE

Alendronate is the preferred, formulary oral bisphosphonate. Risedronate (Actonel) is a second line, non-formulary oral bisphosphonate for patients unable to take alendronate. For example, people with a history of gastrointestinal (GI) side effects to alendronate (but without esophageal disorders), risedronate can be substituted as some patients *may* have fewer GI side effects. Patients must try and fail alendronate prior to receiving nonformulary risedronate for benefit.

Regarding BWGA guidance noted: The Step regulation, CO 10-16-145, does not prohibit an organization from requiring a person to try a generic equivalent, a biosimilar drug, or an interchangeable biologic product UNLESS THE PATIENT OR PRESCRIBER REQUESTED A STEP THERAPY EXCEPTION AND THEY MEET ONE OF THE REQUIREMENTS.

Creation Date: 11/2023
Effective Date: 12/2023
Reviewed Date:
Revised Date:

RUXOLITINIB TOPICAL

Generic	Brand	HICL	GPID	Exception/Other
RUXOLITINIB PHOSPHATE	OPZELURA	38202	51172	ROUTE ≠ ORAL

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and currently stable on ruxolitinib cream for atopic dermatitis or vitiligo.
2. Prescribed by a CPMG or affiliated dermatology or allergy provider
3. The patient is 12 years of age or older

For atopic dermatitis: If met, approve for 6 total dispenses within 12 months max 60 grams per 28 days [max qty: 60, min ds: 28].
For vitiligo: If met, approve indefinitely, max 60 grams per 28 days [max qty: 60, min ds: 28].
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below or the provider has submitted justification and supporting clinical documentation that states one of the following: i) provider attests that the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

A. MILD TO MODERATE ATOPIC DERMATITIS
B. VITILIGO

A. DIAGNOSIS OF ATOPIC DERMATITIS: Must meet all the following:
   1. Prescribed by a CPMG or affiliated dermatology or allergy provider
   2. Patient has a diagnosis of mild to moderate atopic dermatitis
   3. The patient is 12 years of age or older
   4. Patient with inadequate response (after 6 weeks), intolerance, or contraindication to at least three of the following:
      a. 1 moderate potency or higher topical corticosteroid
      b. 1 topical calcineurin inhibitor
      c. Crisaborole (Eucrisa) 2% ointment (non-formulary)
      d. Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy

If met, approve for 6 total dispenses within 12 months max 60 grams per 28 days [max qty: 60, min ds: 28].
If not met, do not approve.

B. DIAGNOSIS OF VITILIGO: Must meet all the following:
   1. Prescribed by a CPMG or affiliated dermatology provider
   2. Patient has a diagnosis of vitiligo
   3. Treatment area is ≤ 10% BSA
   4. The patient is 12 years of age or older

5. Patient with inadequate response after 6 months, intolerance, or contraindication to topical corticosteroid, topical calcineurin inhibitor, or a mix of either.
6. Patient with inadequate response after 6 months, intolerance, or contraindication to phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy

If met, approve indefinitely, max 60 grams per 28 days [max qty: 60, min ds: 28].
If not met, do not approve.

RENEWAL CRITERIA FOR ATOPIC DERMATITIS: Must meet all the following:
1. Patient's atopic dermatitis been assessed by a dermatology or allergy provider in the past year
2. The patient has experienced or maintained improvement in pruritus and/or relapsing-remitting dermatitis

If met, approve for 6 total dispenses within 12 months max 60 grams per 28 days [max qty: 60, min ds: 28].
If not met, do not approve.

ESCALATION CRITERIA: Must meet indication specific criteria as follows:
1. ATOPIC DERMATITIS: Patient's atopic dermatitis is assessed to be > 10% but < 20% body surface area by a dermatology or allergy provider in the past year.

If met, approve for 6 total dispenses within 12 months max 120 grams per 28 days [max qty: 120, min ds: 28].
If not met, do not approve.

2. VITILIGO: Patient's vitiligo treatment area is > 3% but ≤ 10% body surface area by a dermatology provider in the past year.

If met, approve indefinitely, max 180 grams per 28 days [max qty: 180, min ds: 28].
If not met, do not approve.

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Opzelura.

Ruxolitinib (Opzelura) cream is indicated for:
1. Short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older. Opzelura clinical trials looked at up to 8 weeks of continuous use. Application area should not exceed 20% BSA. Consider alternative therapies for quantity beyond escalation criteria.
2. Treatment of nonsegmental vitiligo in non-immunocompromised patients 12 years of age and older. Application area should not exceed 10% BSA

REFERENCES

- Opzelura [Prescribing Information]. Wilmington, DE: Incyte, Corp., September 2022.
- Rosmarin D, Passeron T, Pandya AG, Grimes P, Harris JE, Desai SR, Lebwohl M, Ruer-Mulard M, Seneschal J, Wolkerstorfer A, Kornacki D, Sun K, Butler K, Ezzedine K; TRuE-V Study Group. Two Phase 3, Randomized, Controlled Trials of Ruxolitinib Cream for Vitiligo. N Engl J Med. 2022 Oct 20;387(16):1445-1455. doi: 10.1056/NEJMoa2118828. PMID: 36260792.

Creation date: 07/2022
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

FINGOLIMOD ODT (TASCENSO ODT)

Generic	Brand	HICL	GCN	Exception/Other
FINGOLIMOD ODT (0.25MG)	TASCENSO ODT	48165	52637	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days and is stable on the requested medication for the treatment of multiple sclerosis.

If met, approve x 3 months, then use Initial Criteria for full review and future coverage determination.
If not met, use Initial Criteria for full review and coverage determination.

INITIAL CRITERIA

A. Must meet all the following:
   1. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active Secondary-Progressive MS or Primary-Progressive MS)
   2. The patient is 10 years of age or older
   3. The patient is unable to swallow oral fingolimod 0.25mg capsules [NF], or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve at HICL x1 year.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA

A. ALL the following criteria must be met:
   1. The requesting provider is a CPMG or affiliated neurologist.
   2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include *non-active* Secondary-Progressive MS or Primary-Progressive MS)

If above renewal criteria are met, approve x1 year.
If above renewal criteria are not met, do not approve.

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FINGOLIMOD ODT (TASCENSO ODT)

Quantity and PA Approval Limits

Medication	Dosage Strength	Quantity limit for 30 days	Duration of Approval
Gilenya	0.25 mg capsules	#30 capsules	Approve for 1 year
	0.5 mg capsules	#30 capsules	
Tascenso ODT	0.25mg tablets	#30 tablets	Approve for 1 year
	0.5mg tablets	#30 tablets	Approve for 1 year
Mayzent	0.25 mg tablets	#12 tablets (for 5-day titration to reach 2mg/day)	Approve for 1 year
	2 mg tablets	#30 tablets for 2mg/day	
	0.25mg tablets	#7 tablets (for 4-day titration to reach 2mg/day)	
	2mg tablets	#15 tablets for 1mg/day	
Zeposia	0.23 mg capsules	#4 capsules (for titration day 1-4 titration)	Approve indefinitely
	0.46 mg capsules	#3 capsules (for titration day 5-7)	
	0.92 mg capsules	#1 capsule (for titration: day 8 and thereafter) #30 at full dose	
Ponesimod	2, 3, 4, 5, 6, 7, 8, 9, 10, and 20 mg tablets	For titration: #2 tablets (2mg: day 1-2) #2 tablets (3mg: day 3-4) #2 tablets (4mg: day 5-6) #1 tablet (5mg: day 7) #1 tablet (6mg: day 8) #1 tablet (7mg: day 9) #1 tablet (8mg: day 10) #1 tablet (9mg: day 11) #3 tablets (10mg: days 12-14) #30 tablets (20mg: starting day 15 and thereafter)	Approve for 1 year

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FINGOLIMOD ODT (TASCENSO ODT)

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	NP
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone;	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	NP
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	P
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand – NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Siponimod	Mayzent	Oral	NP
	Ponesimod	Ponvory	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	P
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-arrx	Biosimilar: Riabni	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

Off-label as a disease modifying treatment for MS

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FINGOLIMOD ODT (TASCENSO ODT)

RATIONALE
Per Plan.

This guideline replaces the 2019 Gilenya PA guideline (retire Gilenya PA guideline once the S1P rec modulator guideline becomes effective)

FDA APPROVED INDICATIONS
Treatment of patients with relapsing forms of multiple sclerosis

REFERENCES
KPCO Neurology Clinical Pharmacy Services

Creation date: 05/2020
Effective date: 01/2024
Reviewed date: 11/2023
Revised date: 11/2023

OZANIMOD (ZEPOSIA)

Generic	Brand	HICL	GCN	Exception/Other
OZANIMOD	ZEPOSIA	46431	47863, 47864, 47865, 54286	Nonformulary specialty tier

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

A. Patient is new to KPCO within the past 90 days and is stable on the requested medication for the treatment of multiple sclerosis.

If met, approve x 3 months, then use Initial Criteria for full review and future coverage determination.
If not met, use Initial Criteria for full review and coverage determination.

B. Patient is new to KPCO within the past 90 days, is being managed by a gastroenterologist, is 18 years of age or older, and is stable on ozanimod (Zeposia) for the treatment of ulcerative colitis.

If met, approve indefinitely.
If not met, use Initial Criteria for full review and coverage determination.

INITIAL CRITERIA: Must meet all the following based on diagnosis:

A. All Multiple Sclerosis requests

1. The requesting provider is a CPMG or affiliated neurologist
2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active Secondary-Progressive MS or Primary-Progressive MS)
3. The patient has an intolerance or contraindication to fingolimod, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve at HICL x1 year.
If initial criteria are not met, do not approve.

B. All Ulcerative Colitis requests

1. For ozanimod (Zeposia) UC requests, must meet all the following:
   a. The requesting provider is a CPMG or affiliated gastroenterologist.
   b. The patient has a diagnosis of moderate to severe ulcerative colitis.
   c. The patient is 18 years of age or older.
   d. The patient has failed or has an intolerance or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same

pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

i. at least 1 anti-TNF [infliximab (Inflectra or Remicade) [F], adalimumab (Amjevita) [F, PA], or golimumab (Simponi) [NF, PA]]
ii. at least one JAK-inhibitor indicated for ulcerative colitis [tofacitinib (Xeljanz) [F] or upadacitinib (Rinvoq) [NF, PA]]
iii. vedolizumab (Entyvio) [F]
iv. Ustekinumab (Stelara) [IL-12/23 Inhibitor, NF] OR risankizumab-rzaa (Skyrizi) [IL-23 Inhibitor, NF]

If initial criteria are met, then approve indefinitely at HICL, max 1 capsule per day.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA

A. For MS indications, ALL the following criteria must be met:
   1. The requesting provider is a CPMG or affiliated neurologist.
   2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include *non-active* Secondary-Progressive MS or Primary-Progressive MS)

If above renewal criteria are met, approve x1 year.
If above renewal criteria are not met, do not approve.

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OZANIMOD (ZEPOSIA)

Quantity and PA Approval Limits

Medication	Dosage Strength	Quantity limit for 30 days	Duration of Approval
Gilenya	0.25 mg capsules	#30 capsules	Approve for 1 year
	0.5 mg capsules	#30 capsules	
Tascenso ODT	0.25mg tablets	#30 tablets	Approve for 1 year
	0.5mg tablets	#30 tablets	Approve for 1 year
Mayzent	0.25 mg tablets	#12 tablets (for 5-day titration to reach 2mg/day)	Approve for 1 year
	2 mg tablets	#30 tablets for 2mg/day	
	0.25mg tablets	#7 tablets (for 4-day titration to reach 2mg/day)	
	2mg tablets	#15 tablets for 1mg/day	
Zeposia	0.23 mg capsules	#4 capsules (for titration day 1-4 titration)	Approve indefinitely
	0.46 mg capsules	#3 capsules (for titration day 5-7)	
	0.92 mg capsules	#1 capsule (for titration: day 8 and thereafter) #30 at full dose	
Ponesimod	2, 3, 4, 5, 6, 7, 8, 9, 10, and 20 mg tablets	For titration: #2 tablets (2mg: day 1-2) #2 tablets (3mg: day 3-4) #2 tablets (4mg: day 5-6) #1 tablet (5mg: day 7) #1 tablet (6mg: day 8) #1 tablet (7mg: day 9) #1 tablet (8mg: day 10) #1 tablet (9mg: day 11) #3 tablets (10mg: days 12-14) #30 tablets (20mg: starting day 15 and thereafter)	Approve for 1 year

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OZANIMOD (ZEPOSIA)

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	NP
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone;	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	NP
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	P
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand – NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Siponimod	Mayzent	Oral	NP
	Ponesimod	Ponvory	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	P
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-arrx	Biosimilar: Riabni	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

Off-label as a disease modifying treatment for MS

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OZANIMOD (ZEPOSIA)

RATIONALE
Per Plan.

This guideline replaces the 2019 Gilenya PA guideline (retire Gilenya PA guideline once the S1P rec modulator guideline becomes effective)

FDA APPROVED INDICATIONS
Treatment of patients with relapsing forms of multiple sclerosis
For ozanimod only: Treatment of moderately to severely active ulcerative colitis in adults

REFERENCES
KPCO Neurology Clinical Pharmacy Services
KPCO Gastroenterology Clinical Pharmacy Services

Creation date: 05/2020
Effective date: 01/2024
Reviewed date: 11/2023
Revised date: 11/2023

PLECANATIDE (TRULANCE)

Generic	Brand	HICL	GCN	Exception/Other
PLECANATIDE	TRULANCE	44054	42925	Formulary

GUIDELINES FOR COVERAGE

Must meet all the following:

1. The patient is 18 years of age or older with a diagnosis of IBS-C or CIC
2. The patient has tried and failed all of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. at least one bulk-forming laxative (a bulk forming laxative contains psyllium, methylcellulose, or polycarbophil and examples may include Metamucil, Citrucel, FiberCon)
    b. at least one osmotic laxative (an osmotic laxative contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)
    c. lubiprostone

If criteria are met, approve indefinitely at HICL, max 1 capsule per day.
If criteria are not met, do not approve.

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ePA Questions

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (bulk-forming laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Plan.

REFERENCES

Per Plan.

Creation date: 3/15/2017
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

PONESIMOD (PONVORY)

Generic	Brand	HICL	GCN	Exception/Other
PONESIMOD	PONVORY	47221	49395, 49396	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA
A. Patient is new to KPCO within the past 90 days and is stable on the requested medication for the treatment of multiple sclerosis.

If met, approve x 3 months, then use Initial Criteria for full review and future coverage determination.
If not met, use Initial Criteria for full review and coverage determination.

INITIAL CRITERIA
A. Must meet all the following:
   1. The requesting provider is a CPMG or affiliated neurologist
   2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active Secondary-Progressive MS or Primary-Progressive MS)
   3. The patient has an intolerance or contraindication to fingolimod, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve at HICL x1 year.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA
A. For MS indications, ALL the following criteria must be met:
   1. The requesting provider is a CPMG or affiliated neurologist.
   2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include *non-active* Secondary-Progressive MS or Primary-Progressive MS)

If above renewal criteria are met, approve x1 year.
If above renewal criteria are not met, do not approve.

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PONESIMOD (PONVORY)

Quantity and PA Approval Limits

Medication	Dosage Strength	Quantity limit for 30 days	Duration of Approval
Gilenya	0.25 mg capsules	#30 capsules	Approve for 1 year
	0.5 mg capsules	#30 capsules	
Tascenso ODT	0.25mg tablets	#30 tablets	Approve for 1 year
	0.5mg tablets	#30 tablets	Approve for 1 year
Mayzent	0.25 mg tablets	#12 tablets (for 5-day titration to reach 2mg/day)	Approve for 1 year
	2 mg tablets	#30 tablets for 2mg/day	
	0.25mg tablets	#7 tablets (for 4-day titration to reach 2mg/day)	
	2mg tablets	#15 tablets for 1mg/day	
Zeposia	0.23 mg capsules	#4 capsules (for titration day 1-4 titration)	Approve indefinitely
	0.46 mg capsules	#3 capsules (for titration day 5-7)	
	0.92 mg capsules	#1 capsule (for titration: day 8 and thereafter) #30 at full dose	
Ponesimod	2, 3, 4, 5, 6, 7, 8, 9, 10, and 20 mg tablets	For titration: #2 tablets (2mg: day 1-2) #2 tablets (3mg: day 3-4) #2 tablets (4mg: day 5-6) #1 tablet (5mg: day 7) #1 tablet (6mg: day 8) #1 tablet (7mg: day 9) #1 tablet (8mg: day 10) #1 tablet (9mg: day 11) #3 tablets (10mg: days 12-14) #30 tablets (20mg: starting day 15 and thereafter)	Approve for 1 year

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PONESIMOD (PONVORY)

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	NP
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone;	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	NP
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	P
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand – NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Siponimod	Mayzent	Oral	NP
	Ponesimod	Ponvory	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	P
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-arrx	Biosimilar: Riabni	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

Off-label as a disease modifying treatment for MS

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PONESIMOD (PONVORY)

RATIONALE
Per Plan.

This guideline replaces the 2019 Gilenya PA guideline (retire Gilenya PA guideline once the S1P rec modulator guideline becomes effective)

FDA APPROVED INDICATIONS
Treatment of patients with relapsing forms of multiple sclerosis

REFERENCES
KPCO Neurology Clinical Pharmacy Services

Creation date: 05/2020
Effective date: 01/2024
Reviewed date: 11/2023
Revised date: 11/2023

PRUCALOPRIDE (MOTEGRITY)

Generic	Brand	HICL	GCN	Exception/Other
PRUCALOPRIDE	MOTEGRITY	36920	28445, 28446	Nonformulary

GUIDELINES FOR COVERAGE

Must meet all the following:

1. The patient is 18 years of age or older with a diagnosis of Chronic Idiopathic Constipation (CIC)
2. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. at least one bulk-forming laxative (a bulk forming laxative contains psyllium, methylcellulose, or polycarbophil and examples may include Metamucil, Citrucel, FiberCon)
    b. at least one osmotic laxative (an osmotic laxative contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)
    c. lubiprostone
    d. Linzess and/or Trulance

If criteria are met, approve indefinitely at HICL, max 1 tablet per day.
If criteria are not met, do not approve.

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ePA Questions

1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (bulk-forming laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Plan.

REFERENCES

Per Plan.

Creation date: 3/15/2017
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

RAMELTEON (ROZEREM)

Generic	Brand	HICL	GCN	Exception/Other
RAMELTEON	ROZEREM	33126	25202	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Patient has insomnia characterized by difficulty with sleep onset.
2. Patient has tried and failed oral melatonin or has a contraindication to melatonin, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If the above criteria are met, approve generic ramelteon at HICL x 3 months.
   If the above criteria are not met, do not approve.

RENEWAL CRITERIA:
1. Documentation of a positive clinical response

   If met, approve indefinitely, maximum #1 tablet per day.
   If not met, do not approve.

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ePA Questions
Initial Review Questions
1. Does the patient have insomnia characterized by difficulty with sleep onset?
2. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
3. Is there reasoning why alternatives (melatonin) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Renewal Review Questions
1. Has the patient had a positive clinical response to therapy?

Creation date: 05/2018
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 09/2023

ADEMPAS (RIOCIGUAT)

Generic	Brand	HICL	GCN	Exception/Other
RIOCIGUAT	ADEMPAS	40644		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Adempas

If met, approve indefinitely at HICL.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the indications below and meet all the criteria associated with that indication:

A) Pulmonary Arterial Hypertension (PAH) (WHO Group 1): Must meet <u>all</u> the following:
1. Prescriber must be a cardiologist or a pulmonologist
2. Patient has a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) verified by right heart catheterization
3. Patient currently has WHO Functional Class II, III or IV symptoms
4. Patient has tried and failed or has an intolerance to or a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. One phosphodiesterase type 5 (PDE5) inhibitor: sildenafil (Revatio®) or tadalafil (Adcirca®)
   b. One endothelin receptor antagonist (ERA): Bosentan (Tracleer®), Ambrisentan (Letairis®), or macitentan (Opsumit®)

B) Chronic Thromboembolic Pulmonary Hypertension (CTEPH) (WHO Group 4): Must meet all the following:
1. Prescriber must be a pulmonologist or a cardiologist
2. Patient has a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4) verified by right heart catheterization
3. Patient is either not a candidate for pulmonary endarterectomy or the patient has persistent recurrent CTEPH after pulmonary endarterectomy

If criteria are met, approve indefinitely at HICL.
If criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS
- Treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to reduce risks of disease progression and hospitalization

- Treatment of chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class in adults

REFERENCES

1. Adempas (riociguat) [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; January 2018.
2. Adempas (riociguat) [product monograph]. Mississauga, Ontario, Canada: Bayer Inc: March 2020.

Creation Date: 8/18/2020
Effective Date: 01/01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

RISANKIZUMAB-RZZA (SKYRIZI)

Generic	Brand	HICL	GCN	Exception/Other
RISANKIZUMAB-RZAA	SKYRIZI	45699		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on therapy, medication is not being used in combination with another biologic for the same indication, and has one of the following indications prescribed by the appropriate specialist as noted:
   1. Patient has a diagnosis of Psoriatic Arthritis (PsA) prescribed by a CPMG or affiliated rheumatologist.
   2. Patient has a diagnosis of Psoriasis prescribed by a CPMG or affiliated dermatologist.
   3. Patient has a diagnosis of Crohn's Disease prescribed by a CPMG or affiliated gastroenterology specialist.

   If met, approve indefinitely, based on indication and medication:
   PsA:
   - Skyrizi: 1 pen/syringe per 84 days [max qty: 1, min ds: 84]

   Psoriasis:
   - Skyrizi: 1 pen/syringe per 84 days [max qty: 1, min ds: 84]

   Crohn's Disease:
   - Skyrizi [On-Body]: 1 single-dose prefilled cartridge per 56 days [max qty: 2.4 mL, min ds: 56]

   If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Psoriatic Arthritis (PsA)
B. Psoriasis
C. Crohn's Disease

A. Psoriatic Arthritis: All the following must be met:
   1. Patient has a diagnosis of psoriatic arthritis and medication is prescribed by a rheumatology provider
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response, intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. At least 2 DMARDs (including methotrexate) or has documented high disease activity in which traditional DMARDs would not be suitable treatment
      b. At least 1 TNF inhibitor (e.g., adalimumab-atto (Amjevita)-preferred [F, PA], etanercept (Enbrel) [F, PA], infliximab-dyyb (Inflectra)-preferred [F])
      c. Cosentyx [F]

If criteria are met, approve at HICL x 1 month, max 1 syringe per 28 days (loading dose) [max qty: 1, min ds: 28], then 1 syringe per 84 days (maintenance dose) indefinitely [max qty: 1, min ds: 84].
If criteria are not met, do not approve.

B. Psoriasis: All the following must be met:
   1. Patient has a diagnosis of moderate to severe psoriasis and medication is prescribed by a dermatology provider.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response (after at least 2 months), intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. A topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus), or the patient is reported as having very high disease activity (ex: > 50% BSA, erythrodermic, pustular psoriasis), disease affecting critical areas (ex: genitals, face), or prior biologic therapy within the past 4 months, skip and proceed to step 3c
      b. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Acitretin, Cyclosporine, Methotrexate, Apremilast (Otezla), Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
      c. At least one TNF inhibitor (adalimumab (Amjevita) - preferred [F, PA], infliximab (Inflectra) - preferred [F], etanercept (Enbrel) [F, PA]) - unless the patient has failed an IL-17 inhibitor
      d. At least one IL-17 inhibitor (secukinumab (Cosentyx) - preferred [F])

   If criteria are met, approve at HICL, with the following quantity limits: x 1 month, max 1 syringe per 28 days (loading dose) [max qty: 1, min ds: 28], then 1 syringe per 84 days (maintenance dose) indefinitely [max qty: 1, min ds: 84].
   If criteria are not met, do not approve.

C. Crohn's Disease: All the following must be met:
   1. Patient has a diagnosis of Crohn’s Disease, and the medication is prescribed by a gastroenterologist.
   2. Medication is not being used in combination with another biologic for the same indication
   3. Patient has experienced an inadequate response, intolerance, or has a contraindication to at least 1 TNF inhibitor (ex: infliximab [F], adalimumab [F, PA], or certolizumab [NF, PA]), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria are met, approve indefinitely at HICL, max 1 single-dose prefilled cartridge [Skyrizi On-Body] per 56 days [max qty: 2.4 mL, min ds: 56].
If criteria are not met, do not approve.

RENEWAL CRITERIA

1. The diagnosis for which the patient was originally authorized medication coverage, has been assessed by the applicable specialist in the past two years.
2. Medication is not being used in combination with another biologic for the same indication.

If met, approve indefinitely based on indication and medication:
PsA:
- Skyrizi: 1 pen/syringe per 84 days [max qty: 1, min ds: 84]

Psoriasis:
- Skyrizi: 1 pen/syringe per 84 days [max qty: 1, min ds: 84]

Crohn's Disease:
- Skyrizi [On-Body]: 1 single-dose prefilled cartridge per 56 days [max qty: 2.4 mL, min ds: 56]

If not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member, Initial, or Renewal PA Criteria prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval.

A. Patient with diagnosis of Crohn's disease
   1. For requests to start on escalated frequencies (1 syringe per less than 56 days):
      Provider states patient requires escalation based on medical necessity. Patient must have objective signs of disease activity as demonstrated on colonoscopy or with elevated inflammatory markers (fecal calprotectin or C-reactive protein).

      If met, approve at HICL x1 year, max 1 syringe per 28 days [max qty: 1, min ds: 28].
      If not met, then deny and offer maximum 1 syringe per 56 days indefinitely [max qty: 1, min ds: 56].

   2. For requests to continue escalated frequencies (1 syringe per less than 56 days):
      Patient must have been assessed by a gastroenterologist in the last 1 year, and the gastroenterologist evaluated if the frequency can be de-escalated and determined that the escalated frequency continues to be medically necessary.

      If met, approve at HICL x2 years, max 1 syringe per 28 days [max qty: 1, min ds: 28].
      If not met, deny and offer max 1 syringe per 56 days indefinitely [max qty: 1, min ds: 56].

RATIONALE

Ensure appropriate use consistent with FDA indication.

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

FDA APPROVED INDICATIONS

Plaque Psoriasis
Psoriatic Arthritis

Crohn's Disease

REFERENCES

Currently stable on medication means patient is tolerating well, appears to be effective and provider wishes to continue

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (ex: systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for psoriasis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*

Creation Date: 11/2019
Effective Date: 01/2024
Reviewed Date: 11/2023
Revised Date: 11/2023

SARILUMAB (KEVZARA)

Generic	Brand	HICL	GCN	Exception/Other
SARILUMAB	KEVZARA	44183	43223, 43224, 44269, 44277	Non-formulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and is stable on Kevzara.
2. Medication is not being used in combination with another biologic for the same indication.
3. Medication is being prescribed by a CPMG or affiliated rheumatologist.
4. Patient has ONE of the following diagnoses and is receiving the indicated drug as noted:
    a. Rheumatoid Arthritis (RA)
    b. Polymyalgia Rheumatica (PMR)

If met, approve indefinitely.
If not met, Use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications and must meet all indication-specific criteria.

A. Rheumatoid Arthritis (RA)
B. Polymyalgia Rheumatica (PMR)

A. **Rheumatoid Arthritis (RA):** All the following must be met:
1. Patient is 18 years or older, has a diagnosis of RA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. At least 2 of the following: Methotrexate, Leflunomide, Hydroxychloroquine, Sulfasalazine
    b. At least 1 TNF inhibitor (e.g. infliximab-dyyb (Inflectra) – preferred [F], adalimumab-atto (Amjevita) – preferred [F, PA])
    c. Patient has failure of or contraindication to Actemra.

If above criteria are met, approve at HICL indefinitely, max 2 pens/syringes per 28 days [MDD 0.09].
If above criteria are not met, do not approve.

B. **Polymyalgia Rheumatica (PMR):** All the following must be met:
1. Patient is 18 years or older, has a diagnosis of PMR, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.

3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Corticosteroids or cannot tolerate a corticosteroid taper
    b. Methotrexate
    c. Patient has failure of or contraindication to Actemra.

If above criteria are met, approve at HICL indefinitely, max 2 pens/syringes per 28 days [MDD 0.09].
If above criteria are not met, do not approve.

FDA APPROVED INDICATIONS
Actemra: RA, GCA, PJIA, SJIA, SSLD
Kevzara: RA, PMR

REFERENCES
1. Actemra:
    - Actemra ACTPen: 162 mg/0.9 mL (0.9 mL) Solution Auto-injector, Subcutaneous [preservative free]
    - Actemra 162 mg/0.9 mL (0.9 mL) Solution Prefilled Syringe, Subcutaneous [preservative free]
2. Kevzara:
    - Kevzara 150 mg/1.14 mL; 200 mg/1.14 mL Solution Auto-injector, Subcutaneous [preservative free]
    - Kevzara 150 mg/1.14 mL; 200 mg/1.14 mL Solution Prefilled Syringe, Subcutaneous [preservative free]
3. "*Currently stable*" means patient is tolerating well, medication appears to be effective, and provider wishes to continue therapy.
4. Bonelli M, Radner H, Kerschbaumer A, Mrak D, Durechova M, Stieger J, Husic R, Mandl P, Smolen JS, Dejaco C, Aletaha D. Tocilizumab in patients with new onset polymyalgia rheumatica (PMR-SPARE): a phase 2/3 randomised controlled trial. Ann Rheum Dis. 2022 Jun;81(6):838-844. doi: 10.1136/annrheumdis-2021-221126.
5. Assaraf M, Chevet B, Wendling D, Philippe P, Cailliau E, Roux C, Avouac J, Delacour M, Houvenagel E, Sellam J, Cortet B, Henry J, Flipo RM, Devauchelle-Pensec V. Efficacy and management of tocilizumab in polymyalgia rheumatica: results of a multicenter retrospective observational study. Rheumatology (Oxford). 2023 Aug 21:kead426. doi: 10.1093/rheumatology/kead426.

Creation Date: 11/2023
Effective Date: 02/2024
Reviewed Date:
Revised Date: 01/2024

SIPONIMOD (MAYZENT)

Generic	Brand	HICL	GCN	Exception/Other
SIPONIMOD	MAYZENT	45670	46133, 46134, 46135, 52075, 52076	Nonformulary specialty tier, least preferred

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

A. Patient is new to KPCO within the past 90 days and is stable on the requested medication for the treatment of multiple sclerosis.

If met, approve x 3 months, then use Initial Criteria for full review and future coverage determination.
If not met, use Initial Criteria for full review and coverage determination.

INITIAL CRITERIA

A. Must meet all the following:

1. The requesting provider is a CPMG or affiliated neurologist
2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include non-active Secondary-Progressive MS or Primary-Progressive MS)
3. The CYP2C9 genotype has been confirmed prior to starting treatment
    i. Patient does NOT have CYP2C9*3/*3 genotype (siponimod is contraindicated in this genotype)
    ii. For genotypes CYP2C9 *1/*3 and *2/*3 only: prescriber will not exceed FDA labeled dose of 1 mg/day
    iii. For all other genotypes: prescriber will not exceed FDA labeled maximum dose of 2 mg/day
4. The patient has an intolerance or contraindication to fingolimod, ozanimod, and/or ponesimod that is not expected to occur with siponimod, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve at HICL x1 year.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA

A. For MS indications, ALL the following criteria must be met:
    1. The requesting provider is a CPMG or affiliated neurologist.
    2. The patient has a diagnosis of relapsing or active form of multiple sclerosis. (This does not include *non-active* Secondary-Progressive MS or Primary-Progressive MS)

If above renewal criteria are met, approve x1 year.
If above renewal criteria are not met, do not approve.

SIPONIMOD (MAYZENT)

Quantity and PA Approval Limits

Medication	Dosage Strength	Quantity limit for 30 days	Duration of Approval
Gilenya	0.25 mg capsules	#30 capsules	Approve for 1 year
	0.5 mg capsules	#30 capsules	
Tascenso ODT	0.25mg tablets	#30 tablets	Approve for 1 year
	0.5mg tablets	#30 tablets	Approve for 1 year
Mayzent	0.25 mg tablets	#12 tablets (for 5-day titration to reach 2mg/day)	Approve for 1 year
	2 mg tablets	#30 tablets for 2mg/day	
	0.25mg tablets	#7 tablets (for 4-day titration to reach 2mg/day)	
	2mg tablets	#15 tablets for 1mg/day	
Zeposia	0.23 mg capsules	#4 capsules (for titration day 1-4 titration)	Approve indefinitely
	0.46 mg capsules	#3 capsules (for titration day 5-7)	
	0.92 mg capsules	#1 capsule (for titration: day 8 and thereafter) #30 at full dose	
Ponesimod	2, 3, 4, 5, 6, 7, 8, 9, 10, and 20 mg tablets	For titration: #2 tablets (2mg: day 1-2) #2 tablets (3mg: day 3-4) #2 tablets (4mg: day 5-6) #1 tablet (5mg: day 7) #1 tablet (6mg: day 8) #1 tablet (7mg: day 9) #1 tablet (8mg: day 10) #1 tablet (9mg: day 11) #3 tablets (10mg: days 12-14) #30 tablets (20mg: starting day 15 and thereafter)	Approve for 1 year

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SIPONIMOD (MAYZENT)

Disease Modifying Therapies

Class	Generic name	Brand or alternative name	Formulation	Preferred or Non-preferred per IR KP guidelines *(Does NOT refer to formulary status)*
Synthetic Cytokines	Interferon-beta 1a	Avonex	IM injection	NP
	Interferon-beta 1a	Plegridy	SQ injection	NP
	Interferon-beta 1a	Rebif	SQ injection	NP
	Interferon-beta 1b	Extavia	SQ injection	P
		Betaseron	SQ Injection	NP
Synthetic Myelin Basic Protein	Glatiramer acetate	Brand: Copaxone;	SQ injection	NP
		Generic: Glatopa (Sandoz)	SQ injection	NP
		Generic: Glatiramer acetate (Mylan)	SQ injection	NP
Reduced proliferation of activated T and B lymphocytes	Teriflunomide	Aubagio	Oral	NP
	Leflunomide** (pro-drug of teriflunomide)	Generic only (Brand: Arava)	Oral	P
Stimulator of Nrf2 pathway (aka Fumaric Acid Derivatives)	Dimethyl fumarate (pro-drug of MMF)	Tecfidera	Oral	Generic – P Brand – NP
	Diroximel fumarate (pro-drug of MMF)	Vumerity (bioequivalent to Tecfidera)	Oral	NP
	Monomethyl fumarate (active metabolite)	Bafiertam	Oral	NP
S1P Receptor Modulator	Fingolimod	Gilenya	Oral	P
	Ozanimod	Zeposia	Oral	NP
	Siponimod	Mayzent	Oral	NP
	Ponesimod	Ponvory	Oral	NP
T and B cell Depleting Small Molecule	Cladribine	Mavenclad	Oral	NP
T and B cell Depleting Antibody	Alemtuzumab	Lemtrada	Infusion	NP
Lymphocyte Anti-migration Antibody	Natalizumab	Tysabri	Infusion	P
B-cell Depleting Antibodies	Rituximab-abbs**	Biosimilar: Truxima,	Infusion	P
	Rituximab-arrx	Biosimilar: Riabni	Infusion	P
	Rituximab-pvvr**	Biosimilar: Ruxience	Infusion	NP
	Rituximab**	Brand: Rituxan	Infusion	NP
	Ocrelizumab	Ocrevus	Infusion	NP
	Ofatumumab	Kesimpta	SQ injection	NP
	Ublituximab	Briumvi	Infusion	NP

Off-label as a disease modifying treatment for MS

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SIPONIMOD (MAYZENT)

RATIONALE
Per Plan.

This guideline replaces the 2019 Gilenya PA guideline (retire Gilenya PA guideline once the S1P rec modulator guideline becomes effective)

FDA APPROVED INDICATIONS
Treatment of patients with relapsing forms of multiple sclerosis

REFERENCES
KPCO Neurology Clinical Pharmacy Services

Creation date: 05/2020
Effective date: 01/2024
Reviewed date: 11/2023
Revised date: 11/2023

SABA - NON-PREFERRED ALBUTEROL HFA NON-FORMULARY GUIDELINE

Generic	Brand	HICL	GCN	Exception/Other
ALBUTEROL SULFATE	VENTOLIN HFA		22913	Non-Formulary - Preferred
ALBUTEROL SULFATE	PROAIR RESPICLICK		38212	Non-Formulary - 2nd Preferred
ALBUTEROL SULFATE	PROVENTIL HFA		22913	Non-Formulary - 3rd Preferred
ALBUTEROL SULFATE	PROAIR DIGIHALER		47012	Non-Formulary - Least Preferred

Non-Formulary Criteria
Review based on drug requested:

1. Ventolin HFA: Do not approve. Patient must use the AG [NDC: 66993-0019-68].

2. Proventil HFA: Do not approve. Patient must use an AG [NDC: 00254-1007-52 or 00781-7296-85].

3. ProAir HFA: Obsolete as of 10/1/22. Patient must use the AG [NDC: 00093-3174-31].

4. ProAir Respiclick: Must meet all the following:
    a. Patient does not have an allergy or intolerance to albuterol sulfate
    b. Patient has documented allergy to an inactive ingredient, intolerance (patient states doesn't work as well, tastes bad, etc.), or clinical failure (patient states has to use more puffs or ineffective) to at least one of the following (listed in preferred order), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        i. Proventil HFA authorized generic - 00254-1007-52 or 00781-7296-85
        ii. ProAir HFA authorized generic - 00093-3174-31
        iii. Ventolin HFA authorized generic - 66993-0019-68

If criteria are met, approve formulary override at NDC-9 level indefinitely.
If criteria are not met, do not approve. [If patient has an allergy or intolerance to albuterol sulfate itself, recommend levalbuterol HFA.]

5. ProAir Digihaler: Must meet all the following:
    a. Patient does not have an allergy or intolerance to albuterol sulfate.
    b. Patient has documented allergy to an inactive ingredient, intolerance (patient states doesn't work as well, tastes bad, etc.), or clinical failure (patient states has to use more puffs or ineffective) to at least one of the following (listed in preferred order), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack

of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

i. Proventil HFA authorized generic - 00254-1007-52 or 00781-7296-85
ii. ProAir HFA authorized generic - 00093-3174-31
iii. Ventolin HFA authorized generic - 66993-0019-68
iv. ProAir Respiclick

If criteria are met, approve formulary override at NDC-9 level indefinitely.
If criteria are not met, do not approve. [If patient has an allergy or intolerance to albuterol sulfate itself, recommend levalbuterol HFA.]

RATIONALE
Per Health Plan.
Brand name Ventolin HFA and Proventil HFA will not be covered when an authorized generic (AG) is available, as these are identical products with differences only in the labeling.

> The term “authorized generic” drug is most commonly used to describe an approved brand name drug that is marketed without the brand name on its label. Other than the fact that it does not have the brand name on its label, it is the exact same drug product as the branded product.1

ProAir Respiclick and ProAir Digihaler may be considered after failure of formulary preferred albuterol HFA products.

Patients noted to have an allergy to albuterol sulfate should be prescribed levalbuterol.

FDA APPROVED INDICATIONS
See individual medications.

REFERENCES
1. https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/fda-list-authorized-generic-drugs#:~:text=The%20term%20%E2%80%9Cauthorized%20generic%E2%80%9D%20drug,product%20as%20the%20branded%20product.
2. 00254-1007-52 and 00781-7296-85 is authorized generic for Proventil HFA
3. 00093-3174-31 is authorized generic for ProAir HFA
4. 66993-0019-68 is authorized generic for Ventolin HFA

Creation date: 03/2021
Effective date: 01/2024
Reviewed date: 09/2023
Revised date: 09/2023

SATRALIZUMAB (ENSPRYNG)

Generic Name	Brand Name	HICL	GPID	Comments
SATRALIZUMAB-MWGE	ENSPRYNG	46781	48477	Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
For patients new to KPCO within the past 90 days stable on satralizumab (Enspryng).

Approve x3 months for transitional supply.

INITIAL CRITERIA: For new starts and for new members after the one-time transitional approval: Must meet all the following:
1. Patient must be age 18 or older
2. Medication must be prescribed by a Neurologist
3. At the time of request, the patient does not have either of the following: active hepatitis B infection (positive results for hepatitis B surface antigen and anti-hepatitis B virus tests), or active or untreated latent tuberculosis
4. Patient has a diagnosis of Neuromyelitis Optica Spectrum Disorder (NMOSD) with positive serologic test for anti-AQP4 antibodies.
5. Patient must have experienced one of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. A severe* breakthrough relapse while on rituximab or biosimilar for at least 6-months at recommended NMOSD dosing** not attributed rapid steroid withdrawal or discontinuation
    b. Recurrent breakthrough relapse after 6-month trial of rituximab or its biosimilar at recommended NMOSD dosing** in combination with maximum tolerated doses of either mycophenolate mofetil or azathioprine
    c. Patient has a severe intolerance or contraindication to rituximab or its biosimilar.

    If initial criteria are met, approve at HICL (override PA Res and Formulary) x 6 months.
    If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Patient is responding positively to therapy including, but not limited to, improvement or stabilization in any one of the following parameters: frequency of relapse, pain, fatigue, motor function, progression of symptoms, or visual acuity.

    If renewal criteria are met, approve at HICL (override PA Res and Formulary) x1 year.
    If renewal criteria are not met, do not approve.

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ePA Questions
Initial Review Questions

1. Does the patient have either of the following: active hepatitis B infection, or active or untreated latent tuberculosis?
2. Does the patient have a diagnosis of Neuromyelitis Optica Spectrum Disorder (NMOSD) with positive serologic test for anti-AQP4 antibodies?
3. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
4. Is there reasoning why alternatives (rituximab or biosimilar) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Renewal Review Questions

1. Has the patient experienced improvement or stabilization in any of the following since starting satralizumab? (Please check any/all boxes that apply.)
    a. frequency of relapse
    b. pain
    c. fatigue
    d. motor function
    e. progression of symptoms
    f. visual acuity

RATIONALE

Current treatment for relapse prevention in NMOSD are off-label immunosuppressive therapies including corticosteroids and immunosuppressive drugs such as rituximab (or biosimilar), tocilizumab, mycophenolate mofetil, and azathioprine in both AQP4 antibody positive and negative patients. Treatment with these agents was associated with significant reductions in annualized relapse rates in the range of 72%-88%. Satralizumab (Enspryng) is a humanized monoclonal antibody targeting the interleukin 6 (IL-6) receptor and is given via subcutaneous injection every 4 weeks. There is no data that satralizumab is more effective or safer than current standards of treatment. Satralizumab was designed to be a longer lasting, subcutaneous version of tocilizumab. Satralizumab is the third FDA-approved agent for patient with AQP4 antibody-positive NMOSD and the first self-administered product available. It follows the approval of eculizumab (Soliris) and inebilizumab (Uplizna).

FDA APPROVED INDICATIONS

Satralizumab is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

APPENDIX

*Examples of severe breakthrough relapse include but are not limited to:

- Hospitalization for neurological deficits from NMOSD relapse (e.g., muscle weakness that affects both legs (paraparesis); muscle weakness that affects one side of body such as left arm and left leg (hemiparesis); muscle weakness that affects all four limbs (quadriparesis)
- Optic neuritis severity (hand motion only or worse) confirmed by an ophthalmologist

**NMO dosing for rituximab or biosimilar requires a minimum of 1000mg at a fixed interval of every 6 months dosing.

REFERENCES

1. Enspryng [package insert]. South San Francisco, CA: Genentech, Inc.; March 2022.
2. Glisson CC. Neuromyelitis optica spectrum disorders. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed December 2022.

3. Damato V, Evoli A, Iorio R. Efficacy and Safety of Rituximab Therapy in Neuromyelitis Optica Spectrum Disorders A Systematic Review and Meta-analysis. JAMA Neurol 2016;73:1342-48.
4. Brownlee W, Bourdette D, Broadley S et al. Treatment multiple sclerosis and neuromyelitis optica spectrum disorder during the COVID-19 pandemic. Neurology. 2020; 94:949-52.
5. Burton J, Costello F. Developing evidence-based guidelines for the diagnosis and treatment of NMOSD in Alberta, Canada. Neurology. 2018; 90(15 Supplement) S13.001
6. Collongues N, Ayme-Dietrich E, Monassier L, et al. Pharmacotherapy for Neuromyelitis Optica Spectrum Disorders: Current Management and Future Options. Drugs 2019;79:125–142. https://doi.org/10.1007/s40265-018-1039-7
7. Tahara M, Oeda T, Okada K, et al. Safety and efficacy of rituximab in neuromyelitis optica spectrum disorders (RIN-1 study): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet Neurol 2020;19:298–306
8. Poupart J, Gioivannelli J, Deschamps R, et al. Evaluation of efficacy and tolerability of first-line therapies in NMOSD. Neurology. 2020;94:1-12. doi:10.1212/WNL.0000000000009245.
9. Zhang C, Zhang M, Qiu W, et al. Safety and efficacy of tocilizumab versus azathioprine in highly relapsing neuromyelitis optica spectrum disorder (TANGO): an open-label, multicentre, randomised, phase 2 trial. Lancet Neurol 2020;19:391-401.
10. Kim, SH, Hyun, JW, Joung, A, Park, EY, Joo, J, Kim, HJ, 2017. Predictors of response to first-line immune-suppressive therapy in neuromyelitis optica spectrum disorders. Mult. Scler. 23, 1902–1908. https://doi.org/10.1177/1352458516687403.

Creation Date: 3/2021
Effective Date: 04/2024
Reviewed Date: 3/2024
Revised Date: 9/2023

SELEXIPAG

Generic	Brand	HICL	GCN	Exception/Other
SELEXIPAG	UPTRAVI	42922	40378 GPID 40355 GPID 42922 HICL 2/day	

GUIDELINES FOR COVERAGE:
NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Uptravi

If met, approve at HICL indefinitely.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Prescriber must be either a pulmonologist or a cardiologist
2. Patient has a diagnosis of pulmonary arterial hypertension (PAH, WHO Group 1) verified by right heart catheterization
3. Patient currently has WHO Functional Class II, III or IV symptoms
4. Patient has tried and failed, has an intolerance to or a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. one phosphodiesterase type 5 (PDE5) inhibitor (e.g., Adcirca, Revatio)
   b. one endothelin receptor antagonist (ERA) [e.g., Tracleer, Letairis or Opsumit]

If all criteria above are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Per Health Plan.

FDA APPROVED INDICATIONS
Indicated for the treatment of pulmary arterial hypertension (PAH, WHO group I) to delay disease progression and reduce the risk of hospitalization for PAH.

REFERENCES
1. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmacueticals US, Inc.; Revised 12/2017
2. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol. 2013; 62:034-841.

Creation date: 3/15/2017
Effective date: 01/01/2024
Reviewed date: 05/2023
Revised date: 05/2023

SELINEXOR (XPOVIO)

Generic	Brand	HICL	GCN/GPID	Exception/Other
SELINEXOR	XPOVIO	45854		Non-formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following criteria:

A. Patient must be age 18 or older
B. Must be prescribed by a Hematologist/Oncologist
C. Must have a diagnosis of multiple myeloma or diffuse large B cell lymphoma
D. Must meet the diagnosis/drug specific criteria below:
   1. Multiple Myeloma - using in combination with bortezomib (Velcade) AND dexamethasone: Patient must have received at least 1 prior therapy for treatment of multiple myeloma.

      If all above criteria are met, approve x 12 months.
      If all above criteria are not met, do not approve.

   2. Multiple Myeloma - using in combination with dexamethasone only: Patient must have been treated with at least 4 prior therapies and whose disease is refractory to at least two proteasome inhibitors (bortezomib, carfilzomib, ixazomib), at least two immunomodulatory agents (thalidomide, lenalidomide, pomalidomide) and one anti-CD38 monoclonal antibody (daratumumab, daratumumab and hyaluronidase-fihi, or isatuximab-irfc).

      If all the above criteria are met, approve x 3 months.
      If all above criteria are not met, do not approve.

   3. Diffuse Large B-cell Lymphoma: Patient must have been treated with at least 2 prior lines of systemic therapy.

      If all the above criteria are met, approve x 3 months.
      If all above criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the diagnosis specific criteria below:

A. Multiple Myeloma: Patient's disease has not progressed since initiation of medication OR treating provider believes patient is deriving significant clinical benefit to justify treatment continuation.
B. Diffuse Large B-cell Lymphoma: Patient's disease has not progressed since initiation of medication OR treating provider believes patient is deriving significant clinical benefit to justify treatment continuation.

   If met, approve x 3 months.
   If not met, do not approve.

RATIONALE

Selinexor is a newly approved agent with specific criteria included in the FDA indication intended to direct therapy to the patients who may be most likely to respond in terms of the risk/benefit. Clinical trials have illustrated that this agent is quite toxic and thus may not be worth the risk of treatment in patients who have not progressed on lesser lines of therapy. The duration of approval and renewal is based upon the typical duration seen for patients to respond to treatment.

FDA APPROVED INDICATIONS

XPOVIO is a nuclear export inhibitor indicated:

- **In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy**
- In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody
- For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy

REFERENCES

1. Xpovio prescribing information. Viewed at: https://www.karyopharm.com/wp-content/uploads/2019/07/NDA-212306-SN-0071-Prescribing-Information-01July2019.pdf. Accessed September 2, 2020
2. Kalakonda N, et al. Lancet Haematol. 2020;7:e511-22
3. Chari A, et al. N Engl J Med. 2019;381:727-38
4. Grosicki S, et al. Lancet. 2020; 396(10262): 1563-1573

Creation Date: 09/2020
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2023

SHORT-ACTING AND RAPID-ACTING INSULIN VIALS
ASPART

Generic	Brand	HICL	GCN	Exception/Other
INSULIN ASPART	NOVOLOG VIAL		92326	

GUIDELINES FOR COVERAGE

Must meet criteria based on requested product, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Request for insulin aspart (Novolog) vial:
   a. Has failed insulin lispro (Humalog) due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent
   b. If DM2, has failed regular insulin (Humulin R) due to difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent

   If above criteria are met, then approve generic only at GPID indefinitely.
   If above criteria are not met, do not approve.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Regular insulin (Humulin R) and insulin lispro (Humalog) are KPCO preferred bolus insulin options based on their competitive cost advantage for patients and KPCO.

FDA APPROVED INDICATIONS

Diabetes type 1 and type 2 treatment

REFERENCES

Per Plan

Creation date: 07/2022
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

SHORT-ACTING AND RAPID-ACTING INSULIN VIALS
ASPART NIACINAMIDE

Generic	Brand	HICL	GCN	Exception/Other
INSULIN ASPART (NIACINAMIDE)	FIASP VIAL		43054	Ultra rapid

GUIDELINES FOR COVERAGE

Must meet criteria based on requested product, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Request for insulin aspart with niacinimide (Fiasp) vial: Must meet ALL below criteria:
   a. Has failed insulin lispro (Humalog) due to difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent
   b. Has failed insulin aspart (Novolog) due to difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent
   c. Has failed insulin lispro aabc (Lyumjev) due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent

   If above criteria are met, then approve at GPID indefinitely.
   If above criteria are not met, do not approve.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Regular insulin (Humulin R) and insulin lispro (Humalog) are KPCO preferred bolus insulin options based on their competitive cost advantage for patients and KPCO.

FDA APPROVED INDICATIONS

Diabetes type 1 and type 2 treatment

REFERENCES

Per Plan

Creation date: 07/2022
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

KAISER PERMANENTE

KAISER COLORADO HMO MR GUIDELINES

SHORT-ACTING AND RAPID-ACTING INSULIN VIALS
GLULISINE

Generic	Brand	HICL	GCN	Exception/Other
INSULIN GLULISINE	APIDRA VIAL		25936	

GUIDELINES FOR COVERAGE

Must meet criteria based on requested product, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Request for insulin glulisine (Apidra) vial:
   a. Has failed insulin lispro (Humalog) due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent
   b. If DM2, has failed regular insulin (Humulin R) due to difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent
   c. Has failed insulin aspart (Novolog) due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent
   d. Has failed insulin lispro aabc (Lyumjev) due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent

   If above criteria are met, then approve at GPID indefinitely.
   If above criteria are not met, do not approve.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Regular insulin (Humulin R) and insulin lispro (Humalog) are KPCO preferred bolus insulin options based on their competitive cost advantage for patients and KPCO.

FDA APPROVED INDICATIONS

Diabetes type 1 and type 2 treatment

REFERENCES

Per Plan

Creation date: 07/2022
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

SHORT-ACTING AND RAPID-ACTING INSULIN VIALS
LISPRO AABC

Generic	Brand	HICL	GCN	Exception/Other
INSULIN LISPRO-AABC	LYUMJEV VIAL		48226	1st insulin approved as a biologic Ultra rapid

GUIDELINES FOR COVERAGE

Must meet criteria based on requested product, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Request for insulin lispro aabc (Lyumjev) vial: Must meet ALL below criteria:
   a. Has failed insulin lispro (Humalog) due to difficulties with timing of mealtime doses, late hypoglycemia, or due to an adverse drug reaction/intolerance that is not expected to occur with the requested agent

   If above criteria are met, then approve at GPID indefinitely.
   If above criteria are not met, do not approve.

RATIONALE

There is evidence to say that all insulin products are equally efficacious and safe if used appropriately. Insulin choice depends on insulin pharmacokinetics and patients' ability to safely handle various dosage forms. Regular insulin (Humulin R) and insulin lispro (Humalog) are KPCO preferred bolus insulin options based on their competitive cost advantage for patients and KPCO.

FDA APPROVED INDICATIONS

Diabetes type 1 and type 2 treatment

REFERENCES

Per Plan

Creation date: 07/2022
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

SHORT-ACTING MUSCARINIC ANTAGONIST (SAMA) CLASS
IPRATROPIUM BROMIDE HFA

Generic name	Brand name	HICL	GPID	Comments
IPRATROPIUM BROMIDE	ATROVENT HFA		24621	

GUIDELINES FOR COVERAGE: Must meet criteria below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed another drug in the same pharmacological class or with the same mechanism of action as the required drug(s) and the drug was discontinued due to lack of efficacy, diminished effect, or adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Patient has a diagnosis of COPD.
2. Patient must be age 18 or older.
3. Patient has tried and failed, or has an intolerance or a contraindication to, Spiriva Respimat 2.5 mcg/inhalation (tiotropium) and Stiolto (tiotropium/olodaterol).
4. Medication will not be used in combination with any long-acting anticholinergic inhaler [Spiriva (tiotropium), Stiolto (tiotropium/olodaterol), etc.].
5. Patient must have tried and failed, or has an intolerance or a contraindication to, Combivent Respimat.

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Guidelines recommend use of a long-acting bronchodilator (i.e., Spiriva) in patients whose symptoms are not controlled with intermittent use of a short-acting bronchodilator (i.e., albuterol). In a systematic review that compared tiotropium (long-acting anticholinergic) with ipratropium (short-acting anticholinergic) in patients with COPD, tiotropium was associated with improved lung function, fewer hospitalizations, fewer exacerbations of COPD, and improved quality of life.

FDA APPROVED INDICATIONS
Atrovent HFA is an anticholinergic indicated for the maintenance treatment of bronchospasm associated with COPD. Combivent Respimat is indicated for the treatment of COPD in those patients who are currently on a regular bronchodilator who continue to have bronchospasms and require a second bronchodilator.

Neither Combivent Respimat nor Atrovent HFA are FDA-indicated for use in patients with asthma. Compared to short-acting beta agonists (SABA), ipratropium has a slower onset (15-20 minutes) and achieves less bronchodilation in patients with asthma. Ipratropium may be recommended for management of a severe asthma exacerbation in a primary care or acute care facility. A meta-analysis showed that except in the setting of acute, severe asthmatic attacks, combination therapy with ipratropium and SABA is not superior to SABA alone in adults with asthma.

REFERENCES
Per Health Plan.

Creation Date: 05/2022

Effective Date: 01/2024
Reviewed Date: 05/2023
Revised Date: 05/2023

SHORT-ACTING MUSCARINIC ANTAGONIST (SAMA) CLASS
IPRATROPIUM BROMIDE/ALBUTEROL

Generic name	Brand name	HICL	GPID	Comments
IPRATROPIUM BROMIDE/ALBUTEROL	COMBIVENT RESPIMAT		32395	

GUIDELINES FOR COVERAGE: Must meet criteria below, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed another drug in the same pharmacological class or with the same mechanism of action as the required drug(s) and the drug was discontinued due to lack of efficacy, diminished effect, or adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Patient has a diagnosis of COPD.
2. Patient must be age 18 or older.
3. Patient has tried and failed, or has an intolerance or a contraindication to, Spiriva Respimat 2.5 mcg/inhalation (tiotropium) and Stiolto (tiotropium/olodaterol).
4. Medication will not be used in combination with any long-acting anticholinergic inhaler [Spiriva (tiotropium), Stiolto (tiotropium/olodaterol), etc.].

If criteria are met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE
Guidelines recommend use of a long-acting bronchodilator (i.e., Spiriva) in patients whose symptoms are not controlled with intermittent use of a short-acting bronchodilator (i.e., albuterol). In a systematic review that compared tiotropium (long-acting anticholinergic) with ipratropium (short-acting anticholinergic) in patients with COPD, tiotropium was associated with improved lung function, fewer hospitalizations, fewer exacerbations of COPD, and improved quality of life.

FDA APPROVED INDICATIONS
Atrovent HFA is an anticholinergic indicated for the maintenance treatment of bronchospasm associated with COPD. Combivent Respimat is indicated for the treatment of COPD in those patients who are currently on a regular bronchodilator who continue to have bronchospasms and require a second bronchodilator.

Neither Combivent Respimat nor Atrovent HFA are FDA-indicated for use in patients with asthma. Compared to short-acting beta agonists (SABA), ipratropium has a slower onset (15-20 minutes) and achieves less bronchodilation in patients with asthma. Ipratropium may be recommended for management of a severe asthma exacerbation in a primary care or acute care facility. A meta-analysis showed that except in the setting of acute, severe asthmatic attacks, combination therapy with ipratropium and SABA is not superior to SABA alone in adults with asthma.

REFERENCES
Per Health Plan.

Creation Date: 05/2022
Effective Date: 01/2024

Reviewed Date: 05/2023
Revised Date: 05/2023

SIMPONI (GOLIMUMAB)

Generic	Brand	HICL	GCN	Exception/Other
GOLIMUMAB	SIMPONI	36278	22533, 22536, 35001, 34697	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO within the past 90 days, is currently stable on Simponi, medication is not being used in combination with another biologic for the same indication, and has one of the following indications managed by the appropriate specialist as noted below:
   1. Patient has a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), or Ankylosing Spondylitis or subtype and is being managed by a CPMG or affiliated rheumatologist.
   2. Patient has a diagnosis of Ulcerative Colitis and is being managed by a CPMG or affiliated gastroenterology specialist..

   If met, approve indefinitely, max 1 pen/syringe per 28 days.
   If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Rheumatoid Arthritis (RA)
B. Psoriatic Arthritis (PsA)
C. Ankylosing Spondylitis or subtype
D. Ulcerative Colitis

A. RHEUMATOID ARTHRITIS: All the following must be met:
   1. Patient has a diagnosis of RA, and medication is prescribed by a rheumatologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. at least 2 DMARDs (including methotrexate)
   b. at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred [F], adalimumab-atto (Amjevita)-preferred [F, PA])
   c. at least 2 non-TNF inhibitor biologics

   If above criteria are met, then approve 1 pen/syringe per 28 days indefinitely.
   If above criteria are not met, then do not approve.

B. PSORIATIC ARTHRITIS (PsA): All the following must be met:
   1. Patient has a diagnosis of PsA, and medication is prescribed by a rheumatologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least 2 DMARDs (including methotrexate) or the patient has documented high disease activity in which these medications would not be suitable treatment
      b. at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred [F], adalimumab-atto (Amjevita)-preferred [F, PA])
      c. secukinumab (Cosentyx) [F]
      d. guselkumab (Tremfya) [NF, PA]
      e. At least 1 of the following:
         i. ustekinumab (Stelara) [NF, PA]
         ii. abatacept (Orencia) [F, PA]
         iii. risankizumab (Skyrizi) [NF, PA]
         iv. JAK inhibitor [e.g., tofacitinib (Xeljanz)]

   If above criteria are met, then approve 1 pen/syringe per 28 days indefinitely.
   If above criteria are not met, then do not approve.

C. ANKYLOSING SPONDYLITIS: All the following must be met:
   1. Medication must be prescribed by a rheumatologist, and the patient has a diagnosis of ankylosing spondylitis or one of the following subtype diagnoses: spondyloarthritis (SpA), axial SpA, nonradiographic axial SpA, radiographic axial SpA, sacroiliitis, undifferentiated spondyloarthropathy, spondyloarthropathy, or enteropathic arthropathy.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred, adalimumab-atto (Amjevita)-preferred)
      b. secukinumab (Cosentyx) [F]

   If above criteria are met, then approve 1 pen/syringe per 28 days indefinitely.
   If above criteria are not met, then do not approve.

D. ULCERATIVE COLITIS: All the following must be met:
   1. Patient has a diagnosis of ulcerative colitis or indeterminant colitis with ulcerative colitis features, and the medication is prescribed by a gastroenterologist.
   2. Patient is 6 years of age or older.
   3. Medication is not being used in combination with another biologic for the same indication.
   4. Patient with failure, intolerance, or contraindication to at least one TNF inhibitor (e.g. infliximab [F], adalimumab (Amjevita) [F, PA]), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If above criteria are met, then approve 3 pens/syringes (loading dose) per 28 days, followed by 1 pen/syringe per 28 days (maintenance dose) indefinitely.
   If above criteria are not met, then do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. The diagnosis for which the patient was originally authorized medication coverage has been assessed by the applicable specialist in the past two years.
2. Medication is not being used in combination with another biologic for the same indication.

   If met, approve indefinitely, max 1 pen/syringe per 28 days.
   If not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member, Initial, or Renewal PA Criteria prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval.

Applicable only to patients with a diagnosis of Ulcerative Colitis
1. Documentation by gastroenterology provider of the patient resuming therapy after a gap 3 months or longer in treatment (to reload)

   If met, then approve 3 pens/syringes (loading dose) per 28 days, then 1 pen/syringe per 28 days indefinitely.
   If not met, then deny and offer maximum 1 pen/syringe per 28 days indefinitely.

2. For requests to start on escalated doses (>1 pen/syringe per 28 days): Patient must have been on standard maintenance dose of 1 pen/syringe per 28 days at least 3 months with inadequate drug level (< 2.4 mcg/mL)

   If met, then approve 2 pens/syringes per 28 days x1 year.
   If not met, then deny and offer maximum 1 pen/syringe per 28 days indefinitely.

3. For requests to continue escalated doses (2 pens/syringes per 28 days): Patient has been assessed by a gastroenterologist in the last 1 year, and the gastroenterologist has evaluated if the dose can be de-escalated and determined that the escalated dose continues to be medically necessary

If met, then approve 2 pens/syringes per 28 days x 2 years.
If not met, then deny and offer maximum 1 pen/syringe per 28 days indefinitely.

REFERENCES:
Currently stable on medication means patient is tolerating well, appears to be effective and provider wishes to continue.

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

ICD-10 Diagnosis Codes

Diagnosis	ICD-10 code
ankylosing spondylitis (also termed radiographic axial spondyloarthritis)	subcategory M45*
spondyloarthritis (SpA)	M47.9, M47.812, M47.12, M47.813, M47.816, M47.16, M47.817, M47.811, M47.818, M47.10, M47.819, M46.814, M46.815
axial SpA	subcategory M46.8
nonradiographic axial SpA	subcategory M46.8
sacroiliitis	M12.9, M46.1
undifferentiated spondyloarthropathy	M47.9
spondyloarthropathy	M47.9
enteropathic arthropathy	M07.60

Created: 11/2020
Effective: 06/20/2023
Reviewed: 11/2023
Revised: 11/2023

SODIUM OXYBATE (XYREM)

Generic	Brand	HICL	GCN	Exception/Other
SODIUM OXYBATE	XYREM* (Brand name excluded while AG is available)	12346	18104	3rd preferred in narcolepsy class (generic only*)

GUIDELINES FOR COVERAGE

CRITERIA FOR ALL PATIENTS CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

1. Medication is prescribed by a Neurology or a Board-Certified Sleep Medicine provider.
2. Medication is being prescribed for Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; or Cataplexy (not excessive daytime sleepiness) due to narcolepsy.
3. Medication requested is not be used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xywav, Lumryz).

If criteria are met, approve indefinitely, max 18 mL/day.
If criteria are not met, do not approve.

CRITERIA FOR ANY PATIENT NOT CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

A. Medication is prescribed by Neurology or a Board-Certified Sleep Medicine provider.
B. Medication requested is not be used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xywav, Lumryz).
C. Patient must have one of the following indications and meet all criteria pertaining to that indication:
    1. Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia: Must meet all the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        a. Patient must have tried and failed or have a contraindication to each of the following: amphetamines, methylphenidate, and either modafinil or armodafinil.
        b. Patient must have tried and failed or have a contraindication to Sunosi and Wakix [Prior Authorization required for all].

    If criteria are met, approve indefinitely, max 18 mL/day.
    If criteria are not met, do not approve.

    2. Cataplexy (not excessive daytime sleepiness) due to narcolepsy: Must meet all the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv)

the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

a. Patient must have tried and failed or have a contraindication to each of the following: a tricyclic antidepressant (TCA), a selective serotonin reuptake inhibitor (SSRI), and a selective serotonin-norepinephrine (SNRI).
b. Patient must have tried and failed or have a contraindication to Wakix [Prior Authorization required].

If critieria are met, approve indefinitely, max 18 mL/day.
If criteria are not met, do not approve.

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ePA Questions

1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; Cataplexy (not excessive daytime sleepiness) due to narcolepsy]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia

   1. Is the patient stable on therapy with this medication?
   2. For patients noted stable on therapy, start date of therapy (MMDDYY):
   3. Is the medication being used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xywav, Lumryz)?
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (amphetamines, methylphenidate, modafinil, armodafinil) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Cataplexy (not excessive daytime sleepiness) due to narcolepsy

   1. Is the patient stable on therapy with this medication?
   2. For patients noted stable on therapy, start date of therapy (MMDDYY):
   3. Is the medication being used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xywav, Lumryz)?
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (amitriptyline tablets, desipramine tablets, nortriptyline capsules; citalopram tablets/solution, escitalopram tablets, fluoxetine capsules/solution, paroxetine IR tablets, sertraline tablets/susp; venlafaxine ER capsules (37.5 mg, 75 mg, 150 mg), duloxetine capsules (20 mg, 30 mg, 60 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE

Per Dr. Richey and Health Plan
Brand Xyrem is excluded from coverage as an authorized generic [AG] is available.

Is an Authorized Generic Drug the Same Thing as a Generic Drug? No.

AUTHORIZED GENERIC [AG]: The term “authorized generic” drug is most commonly used to describe an approved brand name drug that is marketed without the brand name on its label. Other than the fact that it does not have the brand name on its label, **it is the exact same drug**

product as the branded product. An authorized generic may be marketed by the brand name drug company, or another company with the brand company's permission. In some cases, even though it is the same as the brand name product, a company may choose to sell the authorized generic at a lower cost than the brand name drug.

GENERIC: A generic drug, as that term is commonly understood and referred to by health care providers and insurers, is a copy of a brand-name drug that is developed and made by a company other than the company that makes the brand-name drug. A generic drug is the same as the brand-name drug in active ingredient, conditions of use, dosage form, strength, route of administration, and (with certain permissible differences) labeling. However, a generic drug may have certain minor differences from the brand-name product, such as different inactive ingredients.

https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/fda-list-authorized-generic-drugs

FDA APPROVED INDICATIONS AND SUPPORTED OFF-LABEL INDICATIONS

Xyrem/Xywav/Lumryz = Cataplexy; Narcolepsy; Idiopathic hypersomnia
Sunosi = Narcolepsy; Idiopathic hypersomnia; Hypersomnia associated with Obstructive sleep apnea
Wakix = Cataplexy; Narcolepsy; Idiopathic hypersomnia

Creation date: 03/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

SODIUM OXYBATE EXTENDED RELEASE (LUMRYZ)

Generic	Brand	HICL	GCN	Exception/Other
SODIUM OXYBATE EXTENDED RELEASE	LUMRYZ	12346	54076, 54077, 54079, 54092	5th preferred in narcolepsy class

GUIDELINES FOR COVERAGE

CRITERIA FOR ALL PATIENTS CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

1. Medication is prescribed by a Neurology or a Board-Certified Sleep Medicine provider.
2. Medication is being prescribed for Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; or Cataplexy (not excessive daytime sleepiness) due to narcolepsy.
3. Medication requested is not be used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xyrem, Xywav).
4. Patient must have tried and failed or have intolerance or contraindication to sodium oxybate (generic Xyrem) and/or Xywav [Prior Authorization required for all], or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria are met, approve indefinitely, max 1 packet/day.
If criteria are not met, do not approve.

CRITERIA FOR ANY PATIENT NOT CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

A. Medication is prescribed by Neurology or a Board-Certified Sleep Medicine provider.
B. Medication requested is not be used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xyrem, Xywav).
C. Patient must have one of the following indications and meet all criteria pertaining to that indication:
    1. Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia: Must meet all the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
        a. Patient must have tried and failed or have a contraindication to each of the following: amphetamines, methylphenidate, and either modafinil or armodafinil.
        b. Patient must have tried and failed or have a contraindication to Sunosi, Wakix, and sodium oxybate (generic Xyrem) or Xywav [Prior Authorization required for all].

        If criteria are met, approve indefinitely, max 1 packet/day.
        If criteria are not met, do not approve.

2. Cataplexy (not excessive daytime sleepiness) due to narcolepsy: Must meet all the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Patient must have tried and failed or have a contraindication to each of the following: a tricyclic antidepressant (TCA), a selective serotonin reuptake inhibitor (SSRI), and a selective serotonin-norepinephrine (SNRI).
   b. Patient must have tried and failed or have a contraindication to Wakix, and sodium oxybate (generic Xyrem) or Xywav [Prior Authorization required for all].

   If critieria are met, approve indefinitely, max 1 packet/day.
   If criteria are not met, do not approve.

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ePA Questions

1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; Cataplexy (not excessive daytime sleepiness) due to narcolepsy]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia

   1. Is the patient stable on therapy with this medication?
   2. For patients noted stable on therapy, start date of therapy (MMDDYY):
   3. Is the medication being used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xywav, Xyrem)?
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (amphetamines, methylphenidate, modafinil, armodafinil) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Cataplexy (not excessive daytime sleepiness) due to narcolepsy

   1. Is the patient stable on therapy with this medication?
   2. For patients noted stable on therapy, start date of therapy (MMDDYY):
   3. Is the medication being used in combination with solriamfetol (Sunosi), pitolisant (Wakix) or any other oxybate product (i.e. Xywav, Xyrem)?
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (amitriptyline tablets, desipramine tablets, nortriptyline capsules; citalopram tablets/solution, escitalopram tablets, fluoxetine capsules/solution, paroxetine IR tablets, sertraline tablets/susp; venlafaxine ER capsules (37.5 mg, 75 mg, 150 mg), duloxetine capsules (20 mg, 30 mg, 60 mg)) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Dr. Richey and Health Plan

FDA APPROVED INDICATIONS AND SUPPORTED OFF-LABEL INDICATIONS
Xyrem/Xywav/Lumryz = Cataplexy; Narcolepsy; Idiopathic hypersomnia
Sunosi = Narcolepsy; Idiopathic hypersomnia; Hypersomnia associated with Obstructive sleep apnea
Wakix = Cataplexy; Narcolepsy; Idiopathic hypersomnia

Creation date: 03/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

SODIUM PHENYLBUTYRATE AND TAURURSODIOL (RELYVRIO)

Generic	Brand	HICL	GCN	Exception/Other
SODIUM PHENYLBUTYRATE AND TAURURSODIOL (ORAL)	RELYVRIO FOR ORAL SUSPENSION	48081	52696	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and stable on therapy.

If met, approve x3 months.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Medication is prescribed by a CPMG or affiliated neurologist
2. The patient has a diagnosis of clinical ALS and is less than 18-months from onset of first symptom
3. Normal Respiratory Function defined as a Forced Vital Capacity (FVC) greater than 60% obtained within past two months
4. The patient is currently taking riluzole or has previously tried riluzole, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If initial criteria are met, approve x 1 year at GPID.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
1. The patient is not dependent on invasive ventilation or tracheostomy.

If met, approve x 1 year at GPID.
If not met, do not approve.

RATIONALE
Promote appropriate utilization of Relyvrio based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS
Relyvrio is an orally administered fixed dose combination of sodium phenylbutyrate and taurursodiol indicated for the treatment of amyotrophic lateral sclerosis (ALS).

DOSAGE AND ADMINISTRATION
The recommended dosage of Relyvrio one single dose packet orally once daily for 21 days, then increase to 1 single-dose packet twice daily.

REFERENCES
Relyvrio [prescribing information]. Cambridge, MA: Amylyx Pharmaceuticals, Inc.; September 2022.

Creation Date: 01/2023
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

SOLRIAMFETOL (SUNOSI)

Generic	Brand	HICL	GCN	Exception/Other
SOLRIAMFETOL HCL	SUNOSI	45666	46126, 46127	Most Preferred in Narcolepsy class

GUIDELINES FOR COVERAGE

CRITERIA FOR ALL PATIENTS CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

1. Medication is prescribed by a Neurology or a Board-Certified Sleep Medicine provider.
2. Medication is being prescribed for Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; or Hypersomnia associated with obstructive sleep apnea (OSA).
3. Medication requested is not be used in combination with pitolisant (Wakix) or any oxybate product (i.e. Xyrem, Xywav, Lumryz).

If criteria are met, approve indefinitely, max 1 tablet/day.
If criteria are not met, do not approve.

CRITERIA FOR ANY PATIENT NOT CURRENTLY TAKING THE REQUESTED MEDICATION: MUST MEET ALL THE FOLLOWING:

1. Medication is prescribed by Neurology or a Board-Certified Sleep Medicine provider.
2. Medication requested is not be used in combination with pitolisant (Wakix) or any oxybate product (i.e. Xyrem, Xywav, Lumryz).
3. Medication is being prescribed for Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; or Hypersomnia associated with obstructive sleep apnea (OSA).
4. Patient must have tried and failed or have a contraindication to each of the following, or the provider submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or will likely cause an adverse reaction or harm; ii) the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception: amphetamines, methylphenidate, and either modafinil or armodafinil.

If criteria are met, approve indefinitely, max 1 tablet/day.
If criteria are not met, do not approve.

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ePA Questions

1. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Excessive daytime sleepiness due to narcolepsy or idiopathic hypersomnia; Hypersomnia associated with obstructive sleep apnea (OSA)]
2. Is the medication being used in combination with pitolisant (Wakix) or any other oxybate product (i.e. Xywav, Xyrem, Lumryz)?
3. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
4. Is there reasoning why alternatives (amphetamines, methylphenidate, modafinil, armodafinil) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Dr. Richey and Health Plan

FDA APPROVED INDICATIONS AND SUPPORTED OFF-LABEL INDICATIONS
Xyrem/Xywav/Lumryz = Cataplexy; Narcolepsy; Idiopathic hypersomnia
Sunosi = Narcolepsy; Idiopathic hypersomnia; Hypersomnia associated with Obstructive sleep apnea
Wakix = Cataplexy; Narcolepsy; Idiopathic hypersomnia

Creation date: 03/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

SOMATROPIN - GROWTH HORMONE

Generic	Brand	HICL	GCN	Exception/Other
LONAPEGSOMATROPIN-TCGD	SKYTROFA	47565		Once weekly non-preferred
SOMAPACITAN-BECO	SOGROYA	46831		Once weekly non-preferred

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-G below:

A) Pediatric (<18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi Syndrome
B) Pediatric (<18yrs) Small for Gestational Age (SGA)
C) Adults (>18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism)
D) Short Bowel Syndrome
E) Growth failure due to renal disease
F) HIV/AIDS-wasting syndrome/Cachexia
G) All other indications

A. For Pediatric patients, age less than 18 years, diagnosed with growth hormone deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi syndrome: Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order] :
      a. Omnitrope cartridges: no additional criteria.
         If initial criteria above are met, approve at GPID indefinitely.
         If criteria above are not met, do not approve.
      b. Genotropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges
         If meets above initial criteria, approve at GPID indefinitely
         If criteria above are not met, do not approve.
      c. Omnitrope vials: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges and/or Genotropin
         If meets above initial criteria, approve at GPID indefinitely
         If criteria above are not met, do not approve.
      d. Saizen: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, and/or Omnitrope vials
         If meets above initial criteria, approve at GPID indefinitely
         If criteria above are not met, do not approve.
      e. Nutropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, and/or Saizen

If meets above initial criteria, approve at GPID indefinitely
If criteria above are not met, do not approve.

f. Humatrope: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, and/or Nutropin
If meets above initial criteria, approve at GPID indefinitely.
If criteria above are not met, do not approve.

g. Norditropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, and/or Humatrope
If meets above initial criteria, approve at GPID indefinitely
If criteria above are not met, do not approve.

h. Zomacton: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, and/or Norditropin
If meets above initial criteria, approve at GPID indefinitely
If criteria above are not met, do not approve.

i. Sogroya: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, Norditropin, and/or Zomacton
If meets above initial criteria, approve at GPID indefinitely
If criteria above are not met, do not approve.

j. Skytrofa: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, Norditropin, Zomacton, and/or Sogroya
If meets above initial criteria, approve at GPID indefinitely
If criteria above are not met, do not approve.

B. Pediatric patients, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
1. Medication is prescribed by, or in consultation with an Endocrinologist
2. Patient with no 'catch-up growth' by 2 years of age
3. Patient’s height is either 2 or more standard deviations (SD) below the mean height for children of the same age and sex, or less than the second percentile for their age and sex
4. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Omnitrope cartridges: no additional criteria.
If meets above initial criteria, approve at GPID x1 year
If criteria above are not met, do not approve.
b. Genotropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges
If meets above initial criteria, approve at GPID x1 year
If criteria above are not met, do not approve.
c. Omnitrope vials: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges and/or Genotropin

If meets above initial criteria, approve at GPID x1 year
If criteria above are not met, do not approve.

d. Saizen: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, and/or Omnitrope vials
If meets above initial criteria, approve at GPID x1 year
If criteria above are not met, do not approve.
e. Nutropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, and/or Saizen
If meets above initial criteria, approve at GPID x1 year
If criteria above are not met, do not approve.
f. Humatrope: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, and/or Nutropin
If meets above initial criteria, approve at GPID x1 year
If criteria above are not met, do not approve.
g. Norditropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, and/or Humatrope
If meets above initial criteria, approve at GPID x1 year
If criteria above are not met, do not approve.
h. Zomacton: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, and/or Norditropin
If meets above initial criteria, approve at GPID x1 year
If criteria above are not met, do not approve.
i. Sogroya: do not approve. Not indicated for treatment of SGA
j. Skytrofa: do not approve. Not indicated for treatment of SGA

C. For adults, age 18 years or older, with continued Growth Hormone Deficiency or Growth Hormone Deficiency associated with multiple hormone deficiencies (ex: hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma: Must meet all the following:
1. Patient has a diagnosis of Growth Hormone Deficiency alone or associated with hormone deficiencies resulting from pituitary disease, hypothalamic disease, surgery, radiation therapy or trauma
2. Medication is prescribed by, or in consultation with, an Endocrinologist
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Omnitrope cartridges: no additional criteria.
If meets above criteria, approve at GPID indefinitely
If criteria above are not met, do not approve.
b. Genotropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges
If meets above criteria, approve at GPID indefinitely
If criteria above are not met, do not approve.

c. Omnitrope vials: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges and/or Genotropin
   If meets above criteria, approve at GPID indefinitely
   If criteria above are not met, do not approve.
d. Saizen: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, and/or Omnitrope vials
   If meets above criteria, approve at GPID indefinitely
   If criteria above are not met, do not approve.
e. Nutropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, and/or Saizen
   If meets above criteria, approve at GPID indefinitely
   If criteria above are not met, do not approve.
f. Humatrope: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, and/or Nutropin
   If meets above criteria, approve at GPID indefinitely
   If criteria above are not met, do not approve.
g. Norditropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, and/or Humatrope
   If meets above criteria, approve at GPID indefinitely
   If criteria above are not met, do not approve.
h. Zomacton: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, and/or Norditropin
   If meets above criteria, approve at GPID indefinitely
   If criteria above are not met, do not approve.
i. Sogroya: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, Norditropin, and/or Zomacton
   If meets above initial criteria, approve at GPID indefinitely.
   If criteria above are not met, do not approve.
j. Skytrofa: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, Norditropin, Zomacton, and/or Sogroya
   If meets above initial criteria, approve at GPID indefinitely.
   If criteria above are not met, do not approve.

D. To treat Short Bowel Syndrome: (Therapy is only 4 weeks per lifetime): Must meet all the following:
   1. Patient has a diagnosis of Short Bowel Syndrome
   2. Requested medication is Zorbtive (only medication with literature support)
   3. Medication is prescribed by or in consultation with nutritional support specialists or gastroenterology specialists
   4. Patient is currently on specialized nutritional support, such as a high carbohydrate, low-fat diet
   5. Patient has not received a course of Zorbtive to treat Short Bowel Syndrome in the past
   If initial criteria above are met, approve Zorbtive at GPID x4 weeks, MDD 1 vial
   If criteria above are not met, do not approve.

E. For pediatric patients, less than 18 years of age, with growth failure with pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or in consultation with, an Endocrinologist or a Nephrologist

2. Patient has a diagnosis of CRI/CKD with GHD and awaiting transplant
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
    a. Omnitrope cartridges
        If meets above initial criteria, approve at GPID x1 year
        If criteria above are not met, do not approve.
    b. Genotropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges
        If meets above initial criteria, approve at GPID x1 year
        If criteria above are not met, do not approve.
    c. Omnitrope vials: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges and/or Genotropin
        If meets above initial criteria, approve at GPID x1 year
        If criteria above are not met, do not approve.
    d. Saizen: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, and/or Omnitrope vials
        If meets above initial criteria, approve at GPID x1 year
        If criteria above are not met, do not approve.
    e. Nutropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, and/or Saizen
        If meets above initial criteria, approve at GPID x1 year
        If criteria above are not met, do not approve.
    f. Humatrope: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, and/or Nutropin
        If meets above initial criteria, approve at GPID x1 year
        If criteria above are not met, do not approve.
    g. Norditropin: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, and/or Humatrope
        If meets above initial criteria, approve at GPID x1 year
        If criteria above are not met, do not approve.
    h. Zomacton: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, and/or Norditropin
        If meets above criteria, approve at GPID x1 year
        If criteria above are not met, do not approve.
    k. Sogroya: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, Norditropin, and/or Zomacton
        If meets above initial criteria, approve at GPID indefinitely
        If criteria above are not met, do not approve.
    l. Skytrofa: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, Norditropin, Zomacton, and/or Sogroya

If meets above initial criteria, approve at GPID indefinitely
If criteria above are not met, do not approve.

F. To treat HIV/AIDS-wasting syndrome/cachexia: Must meet all the following criteria: [New members currently using Growth Hormone use Renewal Criteria below]
   1. Patient has a diagnosis of HIV/AIDS
   2. Requested medication is Serostim (only medication with literature support)
   3. Medication is prescribed by infectious disease specialists or gastroenterology specialists
   4. Patient is on anti-retroviral therapy for HIV/AIDs
   5. Patient meets one of the following criteria:
      a. 10% unintentional weight loss over 12 months
      b. 7.5% unintentional weight loss over 6 months
      c. 5% body cell mass (BCM) loss within 6 months
      d. In men: BCM < 35% of total body weight and body mass index (BMI) < 27kg/m2
      e. In women: BCM < 23% of total body weight and BMI < 27kg/m2
      f. BMI < 20kg/m2
   6. Patient has had an inadequate response or contraindication to the following cyproheptadine, dronabinol, testosterone, and megestrol acetate

If criteria above are met, approve Serostim at GPID x3 months, max daily dose 1 vial.
If criteria above are not met, do not approve.

G. All other indications: The following indications are not covered:
   1. Idiopathic Short Stature (non-GH deficiency)
   2. Athletic Enhancement
   3. Anti-aging
   4. Infertility (female)
   5. Other indications not listed in A-F above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) Pediatric (<18yrs) Small for Gestational Age (SGA)
B) Growth failure due to renal disease
C) HIV/AIDS-wasting syndrome/Cachexia

A) Pediatric patient, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient's height has increased by 2 cm or more from previous year, or the patient has not yet reached the 50th percentile of predicted height

   If meets above renewal criteria, approve x 12 months.
   If criteria above are not met, do not approve.

B) For Pediatric patients, age less than 18 years, growth failure due to pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or consultation with an Endocrinologist or Nephrologist
   2. Patient has not received kidney transplant

   If meets above renewal criteria, approve x12 months.
   If criteria above are not met, do not approve.

C) For HIV/AIDS-wasting syndrome/cachexia: New members on Growth Hormone and Renewals must meet all the following:
   1. Medication is prescribed by infectious disease specialists or gastroenterology specialists
   2. Requested medication is Serostim (only medication with literature support)
   3. Patient is on anti-retroviral therapy for HIV/AIDs
   4. Patient has shown a clinical benefit as demonstrated by an increase in muscle mass and weight from baseline (weight gain more than 2kg), while on growth hormone replacement
   5. Patient has not received more than 48 weeks of therapy. [There is no data supporting more than 48 weeks of therapy.]

   If meets above renewal criteria, approve Serostim at GPID x8 months, max daily dose 1 vial.
   If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).
HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.

OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.
SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).
SOGROYA is a human growth hormone analog indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency and treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

REFERENCES

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCE & M 2000; 85(11):3990-3.
3. Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.
4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.
10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
12. Vetter Pharma-Fertigung GmBH & Co. KG. Genotropin package insert. Ravensburg, Germany. August 2009.
13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
18. EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.

20. EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
21. Sandoz GmbH. Omnitrope package insert. Austria. June 2010.
22. Lonapegsomatropin-tcgd (Skytrofa). New drug review. IPD Analytics RxInsights. September 2021
23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

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SOMATROPIN - GROWTH HORMONE
GENOTROPIN

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	GENOTROPIN		50177, 50187, 50197, 50207, 21450, 21451, 21452, 21453, 10554, 50217, 21454, 63408	Omnitrope is Formulary All others are Non-Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-E below:

A) Pediatric (<18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi Syndrome
B) Pediatric (<18yrs) Small for Gestational Age (SGA)
C) Adults (>18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism)
D) Growth failure due to renal disease
E) All other indications

A. For Pediatric patients, age less than 18 years, diagnosed with growth hormone deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi syndrome: Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order] :
      a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges

         If meets above initial criteria, approve at GPID indefinitely.
         If criteria above are not met, do not approve.

B. Pediatric patients, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient with no 'catch-up growth' by 2 years of age

3. Patient's height is either 2 or more standard deviations (SD) below the mean height for children of the same age and sex, or less than the second percentile for their age and sex
4. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
    a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges
        If meets above initial criteria, approve at GPID x1 year.
        If criteria above are not met, do not approve.

C. For adults, age 18 years or older, with continued Growth Hormone Deficiency or Growth Hormone Deficiency associated with multiple hormone deficiencies (ex: hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma: Must meet all the following:
    1. Patient has a diagnosis of Growth Hormone Deficiency alone or associated with hormone deficiencies resulting from pituitary disease, hypothalamic disease, surgery, radiation therapy or trauma
    2. Medication is prescribed by, or in consultation with, an Endocrinologist
    3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
        a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges
            If meets above criteria, approve at GPID indefinitely.
            If criteria above are not met, do not approve.

D. For pediatric patients, less than 18 years of age, with growth failure with pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
    1. Medication is prescribed by, or in consultation with, an Endocrinologist or a Nephrologist
    2. Patient has a diagnosis of CRI/CKD with GHD and awaiting transplant
    3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested

drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges

If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

E. All other indications: The following indications are not covered:
1. Idiopathic Short Stature (non-GH deficiency)
2. Athletic Enhancement
3. Anti-aging
4. Infertility (female)
5. Other indications not listed in A-D above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) Pediatric (<18yrs) Small for Gestational Age (SGA)
B) Growth failure due to renal disease

A) Pediatric patient, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
1. Medication is prescribed by, or in consultation with an Endocrinologist
2. Patient's height has increased by 2 cm or more from previous year, or the patient has not yet reached the 50th percentile of predicted height

If meets above renewal criteria, approve x 12 months
If criteria above are not met, do not approve.

B) For Pediatric patients, age less than 18 years, growth failure due to pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
1. Medication is prescribed by, or consultation with an Endocrinologist or Nephrologist
2. Patient has not received kidney transplant

If meets above renewal criteria, approve x12 months
If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).

HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.
SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).
SOGROYA is a human growth hormone analog indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency and treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

REFERENCES

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCE & M 2000; 85(11):3990-3.
3. Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.
4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.

5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.
10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
12. Vetter Pharma-Fertigung GmBH & Co. KG. Genotropin package insert. Ravensburg, Germany. August 2009.
13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
18. EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.
20. EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
21. Sandoz GmbH. Omnitrope package insert. Austria. June 2010.
22. Lonapegsomatropin-tcgd (Skytrofa). New drug review. IPD Analytics RxInsights. September 2021
23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

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SOMATROPIN - GROWTH HORMONE
HUMATROPE

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	HUMATROPE		575, 25957, 25963, 25969	Omnitrope is Formulary All others are Non-Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-E below:
A) Pediatric (<18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi Syndrome
B) Pediatric (<18yrs) Small for Gestational Age (SGA)
C) Adults (>18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism)
D) Growth failure due to renal disease
E) All other indications

A. For Pediatric patients, age less than 18 years, diagnosed with growth hormone deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi syndrome: Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order] :
      a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, and/or Nutropin
         If meets above initial criteria, approve at GPID indefinitely.
         If criteria above are not met, do not approve.

B. Pediatric patients, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient with no 'catch-up growth' by 2 years of age
   3. Patient’s height is either 2 or more standard deviations (SD) below the mean height for children of the same age and sex, or less than the second percentile for their age and sex
   4. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested

drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, and/or Nutropin
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

C. For adults, age 18 years or older, with continued Growth Hormone Deficiency or Growth Hormone Deficiency associated with multiple hormone deficiencies (ex: hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma: Must meet all the following:
1. Patient has a diagnosis of Growth Hormone Deficiency alone or associated with hormone deficiencies resulting from pituitary disease, hypothalamic disease, surgery, radiation therapy or trauma
2. Medication is prescribed by, or in consultation with, an Endocrinologist
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, and/or Nutropin
If meets above criteria, approve at GPID indefinitely.
If criteria above are not met, do not approve.

D. For pediatric patients, less than 18 years of age, with growth failure with pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
1. Medication is prescribed by, or in consultation with, an Endocrinologist or a Nephrologist
2. Patient has a diagnosis of CRI/CKD with GHD and awaiting transplant
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, and/or Nutropin
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

E. All other indications: The following indications are not covered:
1. Idiopathic Short Stature (non-GH deficiency)

2. Athletic Enhancement
3. Anti-aging
4. Infertility (female)
5. Other indications not listed in A-D above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) Pediatric (<18yrs) Small for Gestational Age (SGA)
B) Growth failure due to renal disease

A) Pediatric patient, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient's height has increased by 2 cm or more from previous year, or the patient has not yet reached the 50th percentile of predicted height

   If meets above renewal criteria, approve x 12 months.
   If criteria above are not met, do not approve.

B) For Pediatric patients, age less than 18 years, growth failure due to pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or consultation with an Endocrinologist or Nephrologist
   2. Patient has not received kidney transplant

   If meets above renewal criteria, approve x12 months.
   If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).
HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease,

hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.
SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).
SOGROYA is a human growth hormone analog indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency and treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

REFERENCES

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCE & M 2000; 85(11):3990-3.
3. Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.
4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.

10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
12. Vetter Pharma-Fertigung GmBH & Co. KG. Genotropin package insert. Ravensburg, Germany. August 2009.
13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
18. EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.
20. EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
21. Sandoz GmbH. Omnitrope package insert. Austria. June 2010.
22. Lonapegsomatropin-tcgd (Skytrofa). New drug review. IPD Analytics RxInsights. September 2021
23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

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SOMATROPIN - GROWTH HORMONE
NORDITROPIN

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	NORDITROPIN		24145, 24146, 24147, 25816	Omnitrope is Formulary All others are Non-Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-E below:

A) Pediatric (<18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi Syndrome
B) Pediatric (<18yrs) Small for Gestational Age (SGA)
C) Adults (>18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism)
D) Growth failure due to renal disease
E) All other indications

A. For Pediatric patients, age less than 18 years, diagnosed with growth hormone deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi syndrome: Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order] :
      a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, and/or Humatrope
         If meets above initial criteria, approve at GPID indefinitely.
         If criteria above are not met, do not approve.

B. Pediatric patients, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient with no 'catch-up growth' by 2 years of age
   3. Patient’s height is either 2 or more standard deviations (SD) below the mean height for children of the same age and sex, or less than the second percentile for their age and sex
   4. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested

drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, and/or Humatrope
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

C. For adults, age 18 years or older, with continued Growth Hormone Deficiency or Growth Hormone Deficiency associated with multiple hormone deficiencies (ex: hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma: Must meet all the following:
1. Patient has a diagnosis of Growth Hormone Deficiency alone or associated with hormone deficiencies resulting from pituitary disease, hypothalamic disease, surgery, radiation therapy or trauma
2. Medication is prescribed by, or in consultation with, an Endocrinologist
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, and/or Humatrope
If meets above criteria, approve at GPID indefinitely.
If criteria above are not met, do not approve.

D. For pediatric patients, less than 18 years of age, with growth failure with pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
1. Medication is prescribed by, or in consultation with, an Endocrinologist or a Nephrologist
2. Patient has a diagnosis of CRI/CKD with GHD and awaiting transplant
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, and/or Humatrope
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

E. All other indications: The following indications are not covered:
1. Idiopathic Short Stature (non-GH deficiency)

2. Athletic Enhancement
3. Anti-aging
4. Infertility (female)
5. Other indications not listed in A-D above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) Pediatric (<18yrs) Small for Gestational Age (SGA)
B) Growth failure due to renal disease

A) Pediatric patient, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient's height has increased by 2 cm or more from previous year, or the patient has not yet reached the 50th percentile of predicted height

   If meets above renewal criteria, approve x 12 months.
   If criteria above are not met, do not approve.

B) For Pediatric patients, age less than 18 years, growth failure due to pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or consultation with an Endocrinologist or Nephrologist
   2. Patient has not received kidney transplant

   If meets above renewal criteria, approve x12 months.
   If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).
HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease,

hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
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SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).
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REFERENCES

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
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3. Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.
4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.

10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
12. Vetter Pharma-Fertigung GmBH & Co. KG. Genotropin package insert. Ravensburg, Germany. August 2009.
13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
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19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.
20. EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
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23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

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SOMATROPIN - GROWTH HORMONE
NUTROPIN AQ

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	NUTROPIN AQ		17475, 99320, 27846	Omnitrope is Formulary All others are Non-Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-E below:

A) Pediatric (<18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi Syndrome
B) Pediatric (<18yrs) Small for Gestational Age (SGA)
C) Adults (>18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism)
D) Growth failure due to renal disease
E) All other indications

A. For Pediatric patients, age less than 18 years, diagnosed with growth hormone deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi syndrome: Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order] :
      a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, and/or Saizen
      If meets above initial criteria, approve at GPID indefinitely.
      If criteria above are not met, do not approve.

B. Pediatric patients, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient with no 'catch-up growth' by 2 years of age
   3. Patient’s height is either 2 or more standard deviations (SD) below the mean height for children of the same age and sex, or less than the second percentile for their age and sex
   4. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested

drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, and/or Saizen
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

C. For adults, age 18 years or older, with continued Growth Hormone Deficiency or Growth Hormone Deficiency associated with multiple hormone deficiencies (ex: hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma: Must meet all the following:
1. Patient has a diagnosis of Growth Hormone Deficiency alone or associated with hormone deficiencies resulting from pituitary disease, hypothalamic disease, surgery, radiation therapy or trauma
2. Medication is prescribed by, or in consultation with, an Endocrinologist
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, and/or Saizen
If meets above criteria, approve at GPID indefinitely.
If criteria above are not met, do not approve.

D. For pediatric patients, less than 18 years of age, with growth failure with pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
1. Medication is prescribed by, or in consultation with, an Endocrinologist or a Nephrologist
2. Patient has a diagnosis of CRI/CKD with GHD and awaiting transplant
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, and/or Saizen
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

E. All other indications: The following indications are not covered:
1. Idiopathic Short Stature (non-GH deficiency)

2. Athletic Enhancement
3. Anti-aging
4. Infertility (female)
5. Other indications not listed in A-D above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) Pediatric (<18yrs) Small for Gestational Age (SGA)
B) Growth failure due to renal disease

A) Pediatric patient, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient's height has increased by 2 cm or more from previous year, or the patient has not yet reached the 50th percentile of predicted height

   If meets above renewal criteria, approve x 12 months.
   If criteria above are not met, do not approve.

B) For Pediatric patients, age less than 18 years, growth failure due to pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or consultation with an Endocrinologist or Nephrologist
   2. Patient has not received kidney transplant

   If meets above renewal criteria, approve x12 months.
   If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).
HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease,

hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.
SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).
SOGROYA is a human growth hormone analog indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency and treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

REFERENCES

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCE & M 2000; 85(11):3990-3.
3. Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.
4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.

10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
12. Vetter Pharma-Fertigung GmBH & Co. KG. Genotropin package insert. Ravensburg, Germany. August 2009.
13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
18. EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.
20. EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
21. Sandoz GmbH. Omnitrope package insert. Austria. June 2010.
22. Lonapegsomatropin-tcgd (Skytrofa). New drug review. IPD Analytics RxInsights. September 2021
23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

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SOMATROPIN - GROWTH HORMONE
OMNITROPE

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	OMNITROPE		92366, 92386, 93215	Omnitrope is Formulary All others are Non-Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-E below:

A) Pediatric (<18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi Syndrome
B) Pediatric (<18yrs) Small for Gestational Age (SGA)
C) Adults (>18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism)
D) Growth failure due to renal disease
E) All other indications

A. For Pediatric patients, age less than 18 years, diagnosed with growth hormone deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi syndrome: Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order] :
      a. Omnitrope cartridges: no additional criteria.
         If initial criteria above are met, approve at GPID indefinitely.
         If criteria above are not met, do not approve.
      b. Omnitrope vials: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges and/or Genotropin
         If meets above initial criteria, approve at GPID indefinitely.
         If criteria above are not met, do not approve.

B. Pediatric patients, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient with no 'catch-up growth' by 2 years of age
   3. Patient’s height is either 2 or more standard deviations (SD) below the mean height for children of the same age and sex, or less than the second percentile for their age and sex
   4. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the

required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

a. Omnitrope cartridges: no additional criteria.
   If meets above initial criteria, approve at GPID x1 year.
   If criteria above are not met, do not approve.
b. Omnitrope vials: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges and/or Genotropin
   If meets above initial criteria, approve at GPID x1 year.
   If criteria above are not met, do not approve.

C. For adults, age 18 years or older, with continued Growth Hormone Deficiency or Growth Hormone Deficiency associated with multiple hormone deficiencies (ex: hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma: Must meet all the following:
   1. Patient has a diagnosis of Growth Hormone Deficiency alone or associated with hormone deficiencies resulting from pituitary disease, hypothalamic disease, surgery, radiation therapy or trauma
   2. Medication is prescribed by, or in consultation with, an Endocrinologist
   3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
      a. Omnitrope cartridges: no additional criteria.
         If meets above criteria, approve at GPID indefinitely.
         If criteria above are not met, do not approve.
      b. Omnitrope vials: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges and/or Genotropin
         If meets above criteria, approve at GPID indefinitely.
         If criteria above are not met, do not approve.

D. For pediatric patients, less than 18 years of age, with growth failure with pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or in consultation with, an Endocrinologist or a Nephrologist
   2. Patient has a diagnosis of CRI/CKD with GHD and awaiting transplant
   3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested

drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:

a. Omnitrope cartridges
   If meets above initial criteria, approve at GPID x1 year.
   If criteria above are not met, do not approve.
b. Omnitrope vials: Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges and/or Genotropin
   If meets above initial criteria, approve at GPID x1 year.
   If criteria above are not met, do not approve.

E. All other indications: The following indications are not covered:
   1. Idiopathic Short Stature (non-GH deficiency)
   2. Athletic Enhancement
   3. Anti-aging
   4. Infertility (female)
   5. Other indications not listed in A-D above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) Pediatric (<18yrs) Small for Gestational Age (SGA)
B) Growth failure due to renal disease

A) Pediatric patient, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient's height has increased by 2 cm or more from previous year, or the patient has not yet reached the 50th percentile of predicted height

   If meets above renewal criteria, approve x 12 months.
   If criteria above are not met, do not approve.

B) For Pediatric patients, age less than 18 years, growth failure due to pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or consultation with an Endocrinologist or Nephrologist
   2. Patient has not received kidney transplant

   If meets above renewal criteria, approve x12 months.
   If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age

of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).
HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.
SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).
SOGROYA is a human growth hormone analog indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency and treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

REFERENCES

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCE & M 2000; 85(11):3990-3.
3. Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.

4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.
10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
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13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
18. EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.
20. EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
21. Sandoz GmbH. Omnitrope package insert. Austria. June 2010.
22. Lonapegsomatropin-tcgd (Skytrofa). New drug review. IPD Analytics RxInsights. September 2021
23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

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SOMATROPIN - GROWTH HORMONE
SAIZEN

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	SAIZEN		23695	Omnitrope is Formulary All others are Non-Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-E below:

A) Pediatric (<18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi Syndrome
B) Pediatric (<18yrs) Small for Gestational Age (SGA)
C) Adults (>18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism)
D) Growth failure due to renal disease
E) All other indications

A. For Pediatric patients, age less than 18 years, diagnosed with growth hormone deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi syndrome: Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order] :
      a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, and/or Omnitrope vials
      If meets above initial criteria, approve at GPID indefinitely.
      If criteria above are not met, do not approve.

B. Pediatric patients, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient with no 'catch-up growth' by 2 years of age
   3. Patient’s height is either 2 or more standard deviations (SD) below the mean height for children of the same age and sex, or less than the second percentile for their age and sex
   4. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested

drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, and/or Omnitrope vials
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

C. For adults, age 18 years or older, with continued Growth Hormone Deficiency or Growth Hormone Deficiency associated with multiple hormone deficiencies (ex: hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma: Must meet all the following:
1. Patient has a diagnosis of Growth Hormone Deficiency alone or associated with hormone deficiencies resulting from pituitary disease, hypothalamic disease, surgery, radiation therapy or trauma
2. Medication is prescribed by, or in consultation with, an Endocrinologist
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, and/or Omnitrope vials
If meets above criteria, approve at GPID indefinitely.
If criteria above are not met, do not approve.

D. For pediatric patients, less than 18 years of age, with growth failure with pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
1. Medication is prescribed by, or in consultation with, an Endocrinologist or a Nephrologist
2. Patient has a diagnosis of CRI/CKD with GHD and awaiting transplant
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, and/or Omnitrope vials
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

E. All other indications: The following indications are not covered:
1. Idiopathic Short Stature (non-GH deficiency)

2. Athletic Enhancement
3. Anti-aging
4. Infertility (female)
5. Other indications not listed in A-D above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) Pediatric (<18yrs) Small for Gestational Age (SGA)
B) Growth failure due to renal disease

A) Pediatric patient, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient's height has increased by 2 cm or more from previous year, or the patient has not yet reached the 50th percentile of predicted height

   If meets above renewal criteria, approve x 12 months.
   If criteria above are not met, do not approve.

B) For Pediatric patients, age less than 18 years, growth failure due to pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or consultation with an Endocrinologist or Nephrologist
   2. Patient has not received kidney transplant

   If meets above renewal criteria, approve x12 months.
   If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).
HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease,

hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.
SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).
SOGROYA is a human growth hormone analog indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency and treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

REFERENCES

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCE & M 2000; 85(11):3990-3.
3. Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.
4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.

10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
12. Vetter Pharma-Fertigung GmBH & Co. KG. Genotropin package insert. Ravensburg, Germany. August 2009.
13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
18. EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.
20. EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
21. Sandoz GmbH. Omnitrope package insert. Austria. June 2010.
22. Lonapegsomatropin-tcgd (Skytrofa). New drug review. IPD Analytics RxInsights. September 2021
23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

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SOMATROPIN (SEROSTIM)

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	SEROSTIM		63405, 25955, 25960	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) HIV/AIDS-wasting syndrome/Cachexia
B) All other indications

A. To treat HIV/AIDS-wasting syndrome/cachexia: Must meet all the following criteria: [New members currently using Growth Hormone use Renewal Criteria below]
   1. Patient has a diagnosis of HIV/AIDS
   2. Medication is prescribed by infectious disease specialists or gastroenterology specialists
   3. Patient is on anti-retroviral therapy for HIV/AIDs
   4. Patient meets one of the following criteria:
      a. 10% unintentional weight loss over 12 months
      b. 7.5% unintentional weight loss over 6 months
      c. 5% body cell mass (BCM) loss within 6 months
      d. In men: BCM < 35% of total body weight and body mass index (BMI) < 27kg/m2
      e. In women: BCM < 23% of total body weight and BMI < 27kg/m2
      f. BMI < 20kg/m2
   5. Patient has had an inadequate response or contraindication to the following cyproheptadine, dronabinol, testosterone, and megestrol acetate

If criteria above are met, approve Serostim at GPID x3 months, max daily dose 1 vial.
If criteria above are not met, do not approve.

B. All other indications: The following indications are not covered:
   1. Idiopathic Short Stature (non-GH deficiency)
   2. Athletic Enhancement
   3. Anti-aging
   4. Infertility (female)
   5. Other indications not listed in A above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined below:

A) For HIV/AIDS-wasting syndrome/cachexia: New members on Growth Hormone and Renewals must meet all the following:
   1. Medication is prescribed by infectious disease specialists or gastroenterology specialists
   2. Requested medication is Serostim (only medication with literature support)
   3. Patient is on anti-retroviral therapy for HIV/AIDs
   4. Patient has shown a clinical benefit as demonstrated by an increase in muscle mass and weight from baseline (weight gain more than 2kg), while on growth hormone replacement
   5. Patient has not received more than 48 weeks of therapy. [There is no data supporting more than 48 weeks of therapy.]

   If meets above renewal criteria, approve Serostim at GPID x8 months, max daily dose 1 vial.
   If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).
HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.
SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).

SOGROYA is a human growth hormone analog indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency and treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

REFERENCES

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4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.
10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
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13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
18. EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.
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21. Sandoz GmbH. Omnitrope package insert. Austria. June 2010.
22. Lonapegsomatropin-tcgd (Skytrofa). New drug review. IPD Analytics RxInsights. September 2021
23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

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SOMATROPIN - GROWTH HORMONE
ZOMACTON

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	ZOMACTON		25967, 25955	Omnitrope is Formulary All others are Non-Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Review based on diagnosis/indication as outlined, A-E below:

A) Pediatric (<18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi Syndrome
B) Pediatric (<18yrs) Small for Gestational Age (SGA)
C) Adults (>18yrs) Growth Hormone Deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism)
D) Growth failure due to renal disease
E) All other indications

A. For Pediatric patients, age less than 18 years, diagnosed with growth hormone deficiency (GHD) alone or with multiple hormone deficiencies (ex: hypopituitarism), Turner Syndrome, or Prader Willi syndrome: Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order] :
      a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, and/or Norditropin
         If meets above initial criteria, approve at GPID indefinitely.
         If criteria above are not met, do not approve.

B. Pediatric patients, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient with no 'catch-up growth' by 2 years of age
   3. Patient’s height is either 2 or more standard deviations (SD) below the mean height for children of the same age and sex, or less than the second percentile for their age and sex
   4. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested

drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, and/or Norditropin
If meets above initial criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

C. For adults, age 18 years or older, with continued Growth Hormone Deficiency or Growth Hormone Deficiency associated with multiple hormone deficiencies (ex: hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma: Must meet all the following:
1. Patient has a diagnosis of Growth Hormone Deficiency alone or associated with hormone deficiencies resulting from pituitary disease, hypothalamic disease, surgery, radiation therapy or trauma
2. Medication is prescribed by, or in consultation with, an Endocrinologist
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, and/or Norditropin
If meets above criteria, approve at GPID indefinitely.
If criteria above are not met, do not approve.

D. For pediatric patients, less than 18 years of age, with growth failure with pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
1. Medication is prescribed by, or in consultation with, an Endocrinologist or a Nephrologist
2. Patient has a diagnosis of CRI/CKD with GHD and awaiting transplant
3. And based on requested drug or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed below in preferential order]:
a. Patient has tried and failed, or has an intolerance or contraindication to Omnitrope cartridges, Genotropin, Omnitrope vials, Saizen, Nutropin, Humatrope, and/or Norditropin
If meets above criteria, approve at GPID x1 year.
If criteria above are not met, do not approve.

E. All other indications: The following indications are not covered:
1. Idiopathic Short Stature (non-GH deficiency)

2. Athletic Enhancement
3. Anti-aging
4. Infertility (female)
5. Other indications not listed in A-D above

RENEWAL CRITERIA: Review based on diagnosis/indication as outlined, A-B below:

A) Pediatric (<18yrs) Small for Gestational Age (SGA)
B) Growth failure due to renal disease

A) Pediatric patient, age less than 18 years, Small for Gestational Age (SGA): Must meet all the following:
   1. Medication is prescribed by, or in consultation with an Endocrinologist
   2. Patient's height has increased by 2 cm or more from previous year, or the patient has not yet reached the 50th percentile of predicted height

   If meets above renewal criteria, approve x 12 months.
   If criteria above are not met, do not approve.

B) For Pediatric patients, age less than 18 years, growth failure due to pediatric chronic renal insufficiency (CRI)/chronic kidney disease (CKD) prior to renal transplant: Must meet all the following:
   1. Medication is prescribed by, or consultation with an Endocrinologist or Nephrologist
   2. Patient has not received kidney transplant

   If meets above renewal criteria, approve x12 months.
   If criteria above are not met, do not approve.

RATIONALE

Ensure appropriate use of growth hormones with respect to evidence-based guidelines and direct usage to formulary agents. KPCO generally does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.

GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).
HUMATROPE is indicated for Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age at birth. Adult Patients: Treatment of adults with either childhood-onset or adult-onset GH deficiency.
NORDITROPIN, FLEXPRO AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency, either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease,

hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.
NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
OMNITROPE is indicated for Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi Syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature. Adult Patients: Treatment of adults with either adult onset or childhood onset GHD.
SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.
SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.
ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.
SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).
SOGROYA is a human growth hormone analog indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency and treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

REFERENCES

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCE & M 2000; 85(11):3990-3.
3. Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.
4. Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
5. National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
6. Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
7. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
8. Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
9. Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.

10. Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
11. Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.
12. Vetter Pharma-Fertigung GmBH & Co. KG. Genotropin package insert. Ravensburg, Germany. August 2009.
13. Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
14. Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
15. Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
16. Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
17. EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
18. EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
19. Ferring Pharmaceuticals, Inc. Zomacton package insert. Parisppany, NJ. March, 2015.
20. EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
21. Sandoz GmbH. Omnitrope package insert. Austria. June 2010.
22. Lonapegsomatropin-tcgd (Skytrofa). New drug review. IPD Analytics RxInsights. September 2021
23. Allen DB, Backeljauw P, Bidlingmaier M, Biller BMK, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. European Journal of Endocrinology (2016) 174 (2). doi:10.1530/EJE-15-0873 (ghresearchsociety.org)
24. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. Horm Res Paediatr. 2016;86(6):361-397. doi: 10.1159/000452150.

Creation Date: 11/16/2016
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

SONIDEGIB (ODOMZO)

Generic Name	Brand Name	HICL	GPID	Comments
SONIDEGIB PHOSPHATE	ODOMZO 200MG CAPSULE	42369	39217	Preferred for BCC

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO in the past 90 days and stable on therapy.

If new member criteria are met, approve x1 year.
If new member criteria are not met, proceed to Initial Criteria.

INITIAL CRITERIA: Must have all of the criteria below:

A. Medication is prescribed by a CPMG or affiliated Dermatologist or Oncologist
B. Patient has a diagnosis of Basal Cell Carcinoma (BCC) and one of the following: metastatic disease, recurrence of BCC following surgery or radiation therapy, locally advanced disease and medication is being used to shrink tumor to allow the patient to become a surgical candidate, or the patient is not a candidate for surgery or radiation therapy

If initial criteria above are met, approve x2 years.
If initial criteria above are not met, do not approve.

RENEWAL CRITERIA:
Patient's disease has not progressed since treatment initiation as assessed by treating physician OR treating physician believes patient is deriving significant clinical benefit to justify treatment continuation.

If renewal criteria above are met, then approve x1 year.
If renewal criteria are not met, do not approve.

RATIONALE

Per KPCO treatment guidelines

- Sonidegib is the preferred hedgehog inhibitor per KP National guidelines.
- Sonidegib and vismodegib are accepted as equal in terms of efficacy.
- If patient has contraindication to either sonidegib or vismodegib, they would be considered to have a contraindication to the other.
- A patient may have intolerable toxicities with sonidegib that might not occur with vismodegib.
- If a patient has progression of disease with sonidegib, there is no value in trying vismodegib based on currently available data.

FDA APPROVED INDICATIONS

ODOMZO™ (sonidegib) is a hedgehog pathway inhibitor indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.

REFERENCES

Ekim Ekinci, Stephanie Cho

Creation Date: 3/8/2019
Revised: 3/29/2024

Effective Date: 1/2024
Reviewed Date: 1/2024
Revised Date: 1/2024

SOTAGLIFLOZIN (INPEFA)

Generic	Brand	HICL	GCN	Exception/Other
SOTAGLIFLOZIN	INPEFA	48976		

GUIDELINES FOR COVERAGE
Must be used for one of the following indications and meet all related criteria as follows:

A. Heart failure
B. DM2 plus CKD plus CV risk factor(s)

A. Heart Failure: Must meet all the following:
   1. 18 years of age or older
   2. Has heart failure (includes HFrEF, HFpEF, HFmrEF, HFimpEF)
   3. eGFR greater than or equal to 25 ml/min
   4. Has contraindications to, is currently using, or has failed all of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. ACE-I or ARB or ARNI (Entresto)
      b. Beta blocker
      c. Aldosterone antagonist (e.g., spironolactone, eplerenone)
      d. Empagliflozin (Jardiance)

If all criteria met, approve at HICL indefinitely, max 1 tablet per day.
If criteria are not met, do not approve.

B. DM2 plus CKD plus CV risk factor(s): Must meet all the following:
   1. 18 years of age or older
   2. Has type 2 diabetes (DM2)
   3. Has chronic kidney disease (CKD) defined as eGFR of at least 25 ml/min but less than 60 mL/min)
   4. Has 1 or more of the following CV risk factors: HF hospitalization in past 2 years, LVEF less than or equal to 40%, left ventricular hypertrophy, coronary artery calcium (CAC) score greater than or equal to 300, NT-proBNP greater than or equal to 400 pg/mL, high sensitivity troponin greater than 15 pg/mL for men or 10 pg/mL for women, hs-CRP greater than 3 mg/L, urinary albumin-to-creatinine ratio greater than or equal to 300 mg/g
   5. Has contraindications to, is currently using or has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. ACE-I or ARB
      b. Empagliflozin (Jardiance)

If all criteria met, approve at HICL indefinitely, max 1 tablet per day
If criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

KPCO Preferred order of agents:
1. Empagliflozin (Jardiance), formulary without PA, is the preferred agent for ASCVD, CKD, and HF due to strength of clinical trial data, range of approved indications, and cost (1/2 tab regimen)
2. Canagliflozin (Invokana), non-formulary with PA, is the 2nd preferred option for ASCVD, CKD and DM2 patients without compelling indications. due to broad range of indications and cost (1/2 tab regimen).
3. Dapagliflozin (Farxiga), non-formulary with PA, is the 2nd preferred option for HF, and the 3rd preferred option for ASCVD, CKD and DM2 patients without compelling indications due to broad range of indications but at high cost.
4. Ertugliflozin (Steglatro), non-formulary with PA, is least preferred due to high cost, paucity of positive clinical trial data, and lack of additional FDA-approved indications. Specifically, ertugliflozin has been studied in patients with type 2 diabetes and ASCVD and did not improve cardiovascular outcomes while all three other SGLT-2i have demonstrated such benefits in this population.
5. Bexagliflozin (Brenzavvy): non-formulary with PA, is least preferred due to high cost lack of additional FDA-approved indications.
6. Sotagliflozin (Inpefa): non-formulary with PA, is 3rd preferred for HF given shorter history of postmarketing safety data compared to other SGLT2i's approved for HF as well as the need to titrate sotagliflozin dose for when others are fixed-dose regimens. Sotagliflozin (Inpefa) is least preferred for glycemic control due to lack of clinical trial data and FDA-approved indication as well as its high cost.

FDA APPROVED INDICATIONS for SGLT2 Inhibitors
Empagliflozin (Jardiance)
1. Improve glycemic control in patients with DM2
2. Reduce the risk of CV death in pts with DM2 + CVD
3. Reduce risk of CVD death and HF hospitalizations in pts with HF
4. Reduce risk of sustained eGFR decline, ESRD, CV death and hospitalizations in adults with CKD at risk of progression

Canagliflozin (Invokana)
1. Improve glycemic control in patients with DM2
2. Reduce risk of MACE in pts with DM2 + CVD
3. Reduce the risk of ESRD, doubling of creatinine, CV death, or HF hospitalization in pts with DM2 + diabetic nephropathy

Dapagliflozin (Farxiga)
1. Improve glycemic control in patients with DM2
2. Reduce risk of HF hosp in pts with DM2 + CVD/multiple CV RFs
3. Reduce the risk of CV death and HF hosp in patients with HFrEF NYHA II-IV
4. Reduce risk of sustained eGFR decline, ESRD, CV death, and hospitalization for HF in adults with CKD at risk of progression

Ertugliflozin (Steglatro)

1. Improve glycemic control in patients with DM2

Bexagliflozin (Brenzavvy)
1. Improve glycemic control in patients with DM2

Sotagliflozin (Inpefa)
1. Reduce the risk of CV death and HF hosp in pts with heart failure
2. Reduce the risk of CV death and HF hosp in pts with DM2 + CKD + CV RF(s)

REFERENCES
1. Inpefa [Package Insert], Lexicon Pharmaceuticals, Inc.: The Woodlands, TX; 2023
2. Bhatt DL, Szarek M, Steg PG, et al. Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure. NEJM. 2021;384:117-28.
3. Bhatt DL, Szarek M, Pitt B, et al. Sotagliflozin in Patients with Diabetes and Chronic Kidney Disease. NEJM. 2021;384:129-139.
4. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. JACC. 2022;145(18):e895–e1032

Creation date: 01/2024
Effective date: 02/2024
Reviewed date:
Revised date:

FILSPARI (SPARSENTAN)

Generic	Brand	HICL	GCN	Exception/Other
SPARSENTAN	FILSPARI	48721	53742, 53743	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
1. Patient is new to KPCO within the past 90 days and is currently stable on Filspari.

If met, approve indefinitely at HICL.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. The patient is 18 years of age or older.
2. Therapy is prescribed by a nephrologist.
3. The patient has a diagnosis of primary immunoglobulin A nephropathy (IgAN).
4. The patient's diagnosis is confirmed by a biopsy.
5. The patient is at risk of rapid disease progression (e.g., urine protein-to-creatinine ration (UPCR) 1.5 g/g or greater).
6. The patient has proteinuria of at least 1g/day.
7. The patient has an intolerance or contraindication to, or has failed an ACE inhibitor (e.g. lisinopril) or an ARB (e.g. losartan) after at least 12 weeks of therapy, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.
8. Filspari will NOT be used concurrently with an ACE inhibitor (e.g. lisinopril) or an ARB (e.g. losartan), an endothelin receptor antagonist (e.g. ambrisentan), or aliskiren.

If met, approve for 12 months at HICL, max #1 per day.
If not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. The patient has had a reduction in proteinuria, or the patient has improved or stable kidney function compared to baseline.
2. Filspari will not be used concurrently with an ACE inhibitor (e.g. lisinopril), an ARB (e.g. losartan), an endothelin receptor antagonist (e.g. ambrisentan), or aliskiren.

If met, approve for 12 months at HICL, max #1 per day.
If not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS
FILSPARI (sparsentan): primary immunoglobulin A nephropathy (IgAN)

REFERENCES

Filspari Prescribing Information. San Diego, CA: Travere Therapeutics, Inc.; February 2023.

Creation Date: 11/2023
Effective Date: 12/2023
Reviewed Date:
Revised Date:

SPIRONOLACTONE (CAROSPIR) ORAL SOLUTION - AGE RESTRICTION CRITERIA

Generic	Brand	HICL	GCN	Exception/Other
SPIRONOLACTONE ORAL SOLUTION	CAROSPIR	02901	15596	

GUIDELINES FOR COVERAGE

INITIAL AND RENEWAL CRITERIA: ONE of the following criteria must be met:

1. Patient must be less than or equal to 10 years of age
2. Patient is using an alternative route of administration, such as a gastrostomy tube
3. Dose cannot be administered by using halved, whole or combinations of the 25-, 50-, or 100-mg tablets
4. Patient cannot swallow whole, halved, or crushed tablets (with or without mixing in apple sauce)

If any of the above criteria are met, approve x 1 year.
If none of the above criteria are met, do not approve.

RATIONALE

Per Health Plan

FDA APPROVED INDICATIONS

Edema: Management of edema for cirrhosis of liver when unresponsive to fluid and sodium restriction

Heart failure: To increase survival, manage edema and reduce hospitalization for heart failure in patients with New York Heart Association (NYHA) class III to IV and reduced ejection fraction; usually administered in conjunction with other heart failure therapies

Hypertension: Management of hypertension unresponsive to other therapies. Note: Not recommended for the initial treatment of hypertension (ACC/AHA [Whelton 2017]).

REFERENCES

Per Health Plan

Creation date: 09/26/2018
Effective date: 03/2024
Reviewed date: 12/2023
Revised date: 12/2023

SUVOREXANT (BELSOMRA)

Generic Name	Brand Name	HICL	GPID	Comments
SUVOREXANT	BELSOMRA	41333		Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all General Criteria and all Age Criteria in applicable age section

A. **General Criteria for All Requests:** Must meet all the following:
   1. Medication is prescribed by Behavioral Health or Sleep Medicine provider
   2. Patient must be age 18 or older
   3. Diagnosis of insomnia characterized by difficulties with sleep onset and/or sleep maintenance
   4. Potential factors contributing to sleep disturbances have been addressed (e.g., inappropriate sleep hygiene, sleep environment issues and co-morbid conditions contributing to insomnia)
   5. Patient has no history of substance abuse
   6. Patient has no history of narcolepsy

B. **Age 65 Years or Older:** Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to trazodone
   2. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to ramelteon or OTC melatonin
   3. Trial and failure of, contraindication, or intolerance to lemborexant (Dayvigo)

   If initial criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.
   If initial criteria are not met, do not approve.

C. **Age Less Than 65 Years:** Must meet all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   1. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to trazodone
   2. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to ramelteon or OTC melatonin
   3. Trial and failure of (after at least 2 weeks on therapy), contraindication, or intolerance to at least ONE of the following sedative-hypnotic alternatives: zolpidem (F), zaleplon (NF), eszopiclone (NF)
   4. Trial and failure of, contraindication, or intolerance to lemborexant (Dayvigo)

If initial criteria are met, approve at indefinitely, max daily dose of 1 tablet.
If initial criteria are not met, do not approve.

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ePA Questions

1. Have factors that could contribute to sleep disturbances been addressed (e.g., inappropriate sleep hygiene, sleep environment issues and co-morbid conditions contributing to insomnia)?
2. Does the patient have history of substance abuse?
3. Does the patient have history of narcolepsy?
4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
5. Is there reasoning why alternatives (OTC melatonin, trazodone, zolpidem IR tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

FDA APPROVED INDICATIONS

Dayvigo (lemborexant) and Belsomra (suvorexant), and Quviviq (daridorexant) are indicated for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.

REFERENCES

Per Health Plan

Creation Date: 03/2021
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 03/2024

SYNAREL (NAFARELIN)

Generic	Brand	HICL	GCN	Exception/Other
NAFARELIN	SYNAREL	21103	84354	Formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by an Obstetrician/Gynecologist or an Endocrinologist
2. Must have a diagnosis of either endometriosis or central precocious puberty
3. Must have trial and failure of, or intolerance or contraindication to, leuprolide acetate, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If initial criteria are met, approve x 6 months.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Adherence to nafarelin therapy
2. Significant improvement of treated condition:
   a. Endometriosis: Pain, abnormal menstrual bleeding, or other symptoms of endometriosis
   b. Central precocious puberty: Suppression of pubertal growth as measured by height, bone measurements, etc.

If renewal criteria are met, approve x 12 months.
If renewal criteria are not met, do not approve.

RATIONALE
Per Health Plan and current treatment guidelines

FDA APPROVED INDICATIONS
Endometriosis
Central precocious puberty

REFERENCES

Creation Date: 10/2021
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 09/2023

TAFAMIDIS (VYNDAMAX, VYNDAQEL)

Generic	Brand	HICL	GCN	Exception/Other
TAFAMIDIS	VYNDAMAX	45729	46258	
TAFAMIDIS MEGLUMINE	VYNDAQEL	41631	37584	

GUIDELINES FOR COVERAGE

Tafamidis will be approved if ALL the following are met:
1. Patient is at least 18 years of age
2. Patient has a diagnosis of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) documented by patient with positive biopsy demonstrating transthyretin (TTR)-amyloid deposition OR meeting all three of the following:
   a. Diagnosis of heart failure (defined as stage C hear failure (HF) plus New York Heart Association (NYHA class I, II or III), AND either:
      i. Echocardiogram with end-diastolic interventricular septal wall thickness of at least 12mm
      OR
      ii. Cardiac MRI consistent with, or suggestive of, amyloidosis
   b. Pyrophosphate (PYP) scintigraphy cardiac uptake visual score of either:
      i. Grade 2 or 3 using the Perugini Grade 1-3 scoring system
      OR
      ii. Calculated heart-to-contralateral lung (H/CL) ratio of at least 1.5
   c. Absence of a monoclonal gammopathy to rule out light-chain (AL) amyloidosis as determined by meeting the following:
      i. Serum protein electrophoresis (SPEP): no M spike detected, AND
      ii. Kappa/lambda serum free light chains: kappa/lambda free ration within normal limits
      iii. If SPEP and/or kappa lambda serum free light chains are abnormal, serum immunofixation (IFE) is required to be negative (“No monoclonal proteins detected”)
      iv. If results of any of these are unclear such that criteria are not met, a consultation by the Oncology Dept determining that patient does not have AL amyloidosis is adequate to meet this criterion.
3. Patient has medical history of heart failure (HF) with at least 1 of the following:
   a. Prior hospitalization for HF
   b. Clinical evidence of HF (without hospitalization) manifested by signs or symptoms of volume overload or elevated intracardiac pressures that required diuretic
4. Patient has glomerular filtration rate (GFR) of at least 25mL/min and is not requiring dialysis
5. Patient is not currently taking inotersen (Tegsedi) or patisiran (Onpattro)
6. Patient has no history of heart or liver transplantation
7. Patient has no implanted cardiac mechanical assist devices
8. Patient's life expectancy is greater than 1 year

If all the above are met, approve indefinitely.
If any of the above are not met, do not approve.

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ePA Questions

1. Does the patient have a diagnosis of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) documented by positive biopsy demonstrating transthyretin (TTR)-amyloid deposition OR meeting all three of the following:
   1. Diagnosis of heart failure (defined as stage C hear failure (HF) plus New York Heart Association (NYHA class I, II or III), AND either:

   a. Echocardiogram with end-diastolic interventricular septal wall thickness of at least 12mm
   OR
   b. Cardiac MRI consistent with, or suggestive of, amyloidosis
2. Pyrophosphate (PYP) scintigraphy cardiac uptake visual score of either:
   a. Grade 2 or 3 using the Perugini Grade 1-3 scoring system
   OR
   b. Calculated heart-to-contralateral lung (H/CL) ratio of at least 1.5
3. Absence of a monoclonal gammopathy to rule out light-chain (AL) amyloidosis as determined by meeting the following:
   a. Serum protein electrophoresis (SPEP): no M spike detected, AND
   b. Kappa/lambda serum free light chains: kappa/lambda free ration within normal limits
   c. If SPEP and/or kappa lambda serum free light chains are abnormal, serum immunofixation (IFE) is required to be negative ("No monoclonal proteins detected")
   d. If results of any of these are unclear such that criteria are not met, a consultation by the Oncology Dept determining that patient does not have AL amyloidosis is adequate to meet this criterion.

2. Has the patient had prior hospitalization for HF?
3. Does the patient have clinical evidence of HF (without hospitalization) manifested by signs or symptoms of volume overload or elevated intracardiac pressures that required diuretic?
4. Is the patient requiring dialysis?
5. Lab: glomerular filtration rate (GFR):
6. Date of GFR Lab (MMDDYY):
7. Is the patient taking inotersen (Tegsedi) or patisiran (Onpattro)?
8. Has the patient had heart or liver transplant?
9. Does the patient have an implanted cardiac mechanical assist device?
10. Is the patient's life expectancy greater than 1 year?

RATIONALE
KP Interregional Practice Recommendations for Tafamidis 2019

FDA APPROVED INDICATIONS
Treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization

REFERENCES
1. Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. N Engl J Med 2018; 379:1007-1016
2. Vyndaqel and Vyndamax [package insert]. New York, NY: Pfizer Laboratories; revised 4/2020.
3. Damy T, Garcia-Pavia P, Hanna M, et al. Efficacy and safety of tafamidis doses in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT) and long-term extension study. Eur J Heart Fail 2020; doi:10.1002/ejhf.2027

Creation Date: 3/2020
Effective Date: 4/2024
Reviewed Date: 3/2024
Revised Date: 3/2024

TASIMELTEON (HETLIOZ)

Generic	Brand	HICL	GCN	Exception/Other
TASIMELTEON	HETLIOZ	40927	36068	
TASIMELTEON SUSPENSION	HETLIOZ LQ	40927	48937	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: ONE of the following must be met:

1. Patient has a diagnosis of Non-24-Hour Sleep Wake Disorder (N24HSWD) and must meet all of the following:
   a. Prescribed by a Sleep Specialist (CPMG or affiliated network provider with active referral as necessary)
   b. Patient has tried oral melatonin and ramelteon, if no contraindication to use exists, for at least 1 month without efficacy, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
   c. Patient has used non-pharmacologic sleep entrainment (alignment of the internal biological clock rhythm to external time cues, such as the natural dark-light cycles) including bright light therapy (in patients with light perception) and/or optimizing sleep therapy

OR

2. Patient is already stable on the drug

OR

3. Patient has a diagnosis of nighttime sleep disturbances in Smith-Magenis syndrome (SMS) and must meet all of the following:
   a. Prescribed by a Sleep Specialist (CPMG or affiliated network provider with active referral as necessary)
   b. Patient has tried and failed maximally tolerated melatonin therapy, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

   If met, approve x 3 months with a maximum daily dose 1 tablet. Prescriber to re-evaluate treatment after 2 months.
   If not met, do not approve.

RENEWAL CRITERIA:

1. Documentation of a positive clinical response

If met, approve x 2 years, maximum #1 tablet per day.

If not met, do not approve.

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ePA Questions
Initial Review Questions
1. Is the patient stable on therapy with tasimelteon?
2. For patients noted stable on therapy, start date of therapy (MMDDYY):
3. Diagnosis associated with this request: [check boxes for all diagnoses listed in criteria: Non-24-Hour Sleep Wake Disorder (N24HSWD); Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS)]

   QUESTIONS BASED ON DIAGNOSIS SELECTED

   Non-24-Hour Sleep Wake Disorder (N24HSWD)
   1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   2. Is there reasoning why alternatives (melatonin and ramelteon) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

   Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS)
   4. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
   5. Is there reasoning why alternatives (melatonin) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Renewal Review Questions
1. Has the patient had a positive clinical response to therapy?

RATIONALE
Promote appropriate utilization of Hetlioz based on FDA approved indication and dosage.

Hetlioz is the first FDA approved treatment for non-24 hour sleep-wake disorder (N24HSWD), a chronic circadian rhythm disorder in which a person's day length is not synchronized with the 24-hour day-night cycle. Hetlioz is a melatonin receptor agonist that has high affinity for MT1 and MT2 receptors in the suprachiasmatic nucleus of the brain, which are thought to synchronize the body's melatonin and cortisol circadian rhythms with the day-night cycle.

The majority of people with N24HSWD are completely blind due to the lack of light information received from the eyes, which normally regulates the 24-hour day-night cycle. Currently there are 1.3 million legally blind people in the United States (US); 130,000 are completely blind and approximately 70% of those people suffer from N24HSWD.

Treatments for N24HSWD are aimed at resynchronizing the patient's internal body clock to the 24-hour day-night cycle. Phototherapy and dietary melatonin are commonly used to help manage symptoms, as there is no permanent cure for the disorder. In sighted patients, exposure to bright light may counteract the tendency for circadian rhythms to delay. It involves 30-120 minutes of exposure to 3,000 to 10,000 lux light intensity upon awakening daily. Use of melatonin may also be successful in advancing a patient’s circadian rhythm; however the dosage and time of administration need to be adjusted on an individual basis.

Aside from Hetlioz, Rozerem (ramelteon) is the only other melatonin receptor agonist approved in the US. However, Rozerem is not indicated for N24HSWD, but rather for the treatment of insomnia

characterized by difficulty with sleep onset. Hetlioz offers another option for the treatment of N24HSWD in which there is FDA oversight and regulation, unlike over-the-counter dietary melatonin.

The most frequently reported adverse reactions in patients receiving Hetlioz include headache (17%), alanine aminotransferase increase (10%), nightmare/abnormal dreams (10%), upper respiratory tract infection (7%), and urinary tract infection (7%). In placebo-controlled studies, 6% of patients exposed to Hetlioz discontinued treatment due to an adverse event, compared with 4% of patients who received placebo.

There were no signs or symptoms indicative of abuse potential or physical dependence in clinical studies with Hetlioz. Discontinuation of Hetlioz following chronic administration did not produce withdrawal signs.

DOSE
The recommended dosage of Hetlioz is 20 mg per day taken before bedtime, at the same time every night. Because of individual differences in circadian rhythms, drug effect may not occur for weeks or months. Hetlioz should be taken without food.

FDA APPROVED INDICATIONS
Hetlioz is a melatonin receptor agonist indicated for the treatment of non-24-hour sleep-wake disorder and nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in patients who are 16 years of age and older.

REFERENCES
1. KPWA Hetlioz prior authorization criteria from 9/2018
2. Hetlioz [Prescribing Information]. Washington, D.C., Vanda Pharmaceuticals, Inc., Jan 2014.
3. FDA News Release on Jan 31, 2014: FDA approves Hetlioz: first treatment for non-24 hour sleepwake disorder in blind individuals. Available online at: http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm384092.html
4. Circadian Sleep Disorders Network. http://www.circadiansleepdisorders.org/index.php

Creation date: 05/2018
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 09/2023

TEDUGLUTIDE (GATTEX)

Generic	Brand	HICL	GCN	Exception/Other
TEDUGLUTIDE	GATTEX	39890	33927	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Requesting provider is a CPMG or affiliated gastroenterologist
2. Patient is at least 1 year old with documented short bowel syndrome (SBS)
3. Patient has been dependent on parenteral nutrition (PN) for greater than or equal to 12 months
4. If the patient is an adult and has a colon, they must have had a colonoscopy in the past 6 months
5. If the patient is under 18 years of age and has a colon, they must have had a fecal occult blood test in the past 6 months, with a follow up colonoscopy/sigmoidoscopy if unexplained blood was found
6. Patient has an intolerance or contraindication to, or has failed (after adequate trial of at least 4 weeks) BOTH of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   a. Antisecretory agent (e.g., histamine-2 receptor antagonist, proton pump inhibitor, octreotide, clonidine)
   b. Antimotility agent (e.g., loperamide, diphenoxylate with atropine, opioid such as codeine)

If initial criteria above are met, then approve x 6 months with a max daily dose of 1 vial per day.
If initial criteria above are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Patient is still under the care of a CPMG or an affiliated gastroenterologist
2. There is documentation demonstrating a decreased need for parenteral support compared to baseline
3. If the patient is an adult and has a colon, the patient is up to date with screening colonoscopies (due after 1 year of treatment with teduglutide, then every 5 years or more frequently if polyps found)
4. If the patient is pediatric and has a colon, the patient is up to date with screening colonoscopies (due after 1 year of treatment with teduglutide, then every 5 years, or if new/unexplained gastrointestinal bleeding). Annual fecal occult blood tests have been performed in years colonoscopy has not been performed.

If renewal criteria above are met, then approve x 1 year, with max daily dose of 1 vial per day.
If renewal criteria above are not met, do not approve.

RATIONALE

Teduglutide is a recombinant analog of human glucagon-like peptide-2 (GLP-2) improving the small intestine's ability to absorb fluids, electrolytes and nutrients. Teduglutide 0.05 mg/kg/day and 0.1 mg/kg/day were compared to placebo in a clinical trial (n=84). The lower dose was statistically better than placebo regarding the percent of patients who achieved at least 20% reduction in PN/IVF volume (46% vs 6%, $p<0.01$). The higher dose was not statistically significant compared to placebo. The

reason for this variation with the two strengths is unclear but may be due to the strict weaning protocol to which the study subjects were restricted. In a second trial (n=86), teduglutide 0.05 mg/kg/day had a higher percent of patients who achieved at least 20% reduction in PN/IVF volume (63% vs 30%, p<0.001) than placebo. Across both of the 6-month trials, two patients treated with teduglutide became completely independent of PN/IVF.

In the cases where TPN cannot be weaned off completely, the clinical significance of TPN volume reduction is unclear.

There are many long-term safety concerns, as teduglutide's mechanism of action promotes cell growth. Long term data is necessary to determine the safety and efficacy of this medication.

FDA APPROVED INDICATIONS
Treatment of adult and pediatric patients 1 year of age and older with short bowel syndrome (SBS) who are dependent on parenteral support.

REFERENCES
1. Kaiser Permanente Drug Information Services, Drug Monograph: Teduglutide (Gattex). May 22, 2013.
2. Kaiser Foundation Health Plan of Washington Group Health Formulary Minutes from Statewide Pharmacy & Therapeutics Committee Meeting: June 12, 2013.
3. KPNW Gattex non-Medicare guideline, 2019.
4. Parrish CR, DiBaise JK. Managing the Adult Patient With Short Bowel Syndrome. Gastroenterol Hepatol (N Y). 2017 Oct;13(10):600-608.

Creation Date:7/25/2018
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

TENAPANOR (IBSRELA)

Generic	Brand	HICL	GCN	Exception/Other
TENAPANOR	IBSRELA	46009	46915	Nonformulary

GUIDELINES FOR COVERAGE
Must meet all the following:
1. The patient is 18 years of age or older with a diagnosis of IBS-C
2. The patient has tried and failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. at least one bulk-forming laxative (a bulk forming laxative contains psyllium, methylcellulose, or polycarbophil and examples may include Metamucil, Citrucel, FiberCon)
    b. at least one osmotic laxative (an osmotic laxative contains magnesium hydroxide, polyethylene glycol, lactulose, magnesium citrate, or glycerin and examples may include milk of magnesia or Miralax)
    c. lubiprostone
    d. Linzess and/or Trulance

If criteria are met, approve indefinitely at HICL, max 2 tablets per day.
If criteria are not met, do not approve.

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ePA Questions
1. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
2. Is there reasoning why alternatives (bulk-forming laxative, osmotic laxative) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Per Plan.

REFERENCES
Per Plan.

Creation date: 3/15/2017
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

TERIPARATIDE (FORTEO)

Generic name	Brand name	HICL	GCN/GPID	Other
TERIPARATIDE	FORTEO		14404	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all General Criteria and Drug Specific Criteria below:

A. General Criteria for all requests:
   1. Must be prescribed by an endocrinology or rheumatology provider
   2. No history of osteosarcoma
   3. Diagnosis of osteoporosis and meets one of the following criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Must be considered very high risk for fracture with one of the following:
         i. T-score of -2.5 or less, and 1 or more fragility fractures
         ii. BMD with t-score of -3.5 or less
         iii. History of multiple vertebral compression fractures
         iv. History of multiple fragility fractures
      b. Decline in BMD by more than 2% at hip or more than 2.5% at spine per year, after at least one year of oral alendronate or risedronate, IV zoledronic acid, or denosumab (Prolia), with at least 75% adherence to therapy
      c. T-score remains or has dropped to <-3.5 after at least one year of oral alendronate or risedronate, IV zoledronic acid, or denosumab (Prolia)
      d. Experienced 2 or more fragility fractures while adherent (at least 75% proportion days covered) to oral alendronate or risedronate, IV zoledronic acid, or denosumab (Prolia) for at least one year
      e. Unable to use alendronate or risedronate and IV zoledronic acid due to contraindications or adverse effects, or unable to use denosumab (Prolia) due to contraindications or adverse effects

B. Drug Specific Criteria: Must meet all criteria specific to medication requested below:
   1. Forteo: No additional criteria.
   2. Non-AB rated generic teriparatide 20mcg: Do not approve, must use brand Forteo

If initial criteria are met, approve x2 years.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:

1. Must be prescribed by an endocrinology or rheumatology provider
2. Remains high risk for fracture based on current T-score of -2.5 or less or hip or vertebral fracture prior to therapy with Forteo, AND meets one of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy,

diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

a. Chronic glucocorticoid-treated patient (2.5mg or more per day of prednisone or equivalent) and provider indicates is unable to transition to oral alendronate or risedronate, IV zoledronic acid, or denosumab (Prolia)
b. Multiple compression fractures but none while on teriparatide
c. Other high risk fracture condition (i.e., adynamic renal bone disease, elevated P1NP level, severe COPD and compression factures) and provider indicates is unable to transition to oral alendronate or risedronate, IV zoledronic acid, or denosumab (Prolia)

If renewal criteria are met, approve x2 years.
If renewal criteria are not met, do not approve.

RATIONALE

Initial criteria -

- For initial therapy in patients at high risk, there is some evidence that teriparatide could be started first and then followed by an antiresorptive agent (e.g., bisphosphonate) because the bone formation effects of teriparatide may be reduced if started after treatment with an antiresorptive agent. Criteria would allow for use in patients who are at highest risk for fracture prior to starting alternative therapy.
- Patients with history of fragility fracture and BMD with initial t-score in osteoporosis range (<-2.5) but without severe osteoporosis (<-3.5) are generally managed in primary care with use of IV or oral bisphosphonates, with evidence to support use in fracture risk reduction with treatment duration of up to 6-10 years as long as no significant declines in BMD or multiple fragility fractures while on bisphosphonate therapy. Evidence that transition to anabolic agent after use of bisphosphonates may not have as much of a robust response in BMD improvements compared to initial treatment. Therefore, for patients without severe disease or evidence of bisphosphonate failure, continuation of initial therapy is reasonable.
- Based on the landmark pivotal trials for teriparatide and abaloparatide, there is no clinically significant difference in efficacy or recommended treatment durations between teriparatide and abaloparatide for postmenopausal women with osteoporosis.
- There is no head-to-head comparative trial between teriparatide and abaloparatide. Each agent has only been compared to placebo. When compared to placebo, both have demonstrated comparable BMD improvements and fracture reduction with similar treatment durations for efficacy.
- Given similar efficacy and teriparatide being more cost effective, reasonable to preferentially use teriparatide over abaloparatide.
- Both teriparatide and abaloparatide are viable options for treatment of osteoporosis in those with contraindications or intolerances to bisphosphonates when other alternatives (ex. denosumab or romosozumab would also be contraindicated such as in the case of osteonecrosis of the jaw and atypical femur fractures).

Renewal criteria -

- In November 2020, the FDA removed the 2-year lifetime limitation to treatment with teriparatide due to the risk of osteosarcoma:
  - The osteosarcoma warning was based upon studies in rats that high doses (3x greater than human dosing) administered over most of the rats' lifespan (about 24 months) increased the risk of osteosarcoma.
  - Since the teriparatide clinical trials were happening at that time, the trials were terminated early (~19 months).

  - In the 18 years since teriparatide was approved, no increase in osteosarcoma risk has been reported in studies in animals with bone remodeling similar to that in humans (e.g., monkeys). However osteosarcoma is rare (about 1 in 250,000 adults per year) so would need very large sample sizes.
  - The observed incidence of osteosarcoma during a 15-year post marketing surveillance study was no different than the background incidence rate.
  - Teriparatide has been studied for up to 3 years for the treatment of glucocorticoid-induced osteoporosis.
- Abaloparatide still has 2-year treatment duration in FDA labeling

FDA APPROVED INDICATIONS

FORTEO (teriparatide)

- **Osteoporosis:** Treatment of osteoporosis in postmenopausal females who are at high risk for fracture (defined as history of osteoporotic fracture or multiple risk factors for fracture); treatment to increase bone mass in males with primary or hypogonadal osteoporosis who are high risk for fracture; treatment of males and females with glucocorticoid-induced osteoporosis associated with chronic systemic glucocorticoids with a prednisone dosage of ≥5 mg/day (or equivalent) at a high risk for fracture. May also be used in patients who have failed or are intolerant to other available osteoporosis therapy.

TYMLOS (abaloparatide)

- **Osteoporosis, postmenopausal, fracture risk reduction:** Indicated to reduce risk of vertebral and nonvertebral fractures in postmenopausal women with osteoporosis at high risk for fracture or who failed or intolerant to other available osteoporosis therapy.
- **Osteoporosis, Men at high risk of fracture or who have failed or are intolerant to other osteoporosis therapy:** Indicated to increase bone density in men with osteoporosis at high risk for fracture (defined as a history of osteoporotic fracture or multiple risk factors for fracture), or patients who have failed or are intolerant to other available osteoporosis therapy.

REFERENCES

1. Eastell R, Rosen CJ, Black DM, Cheung AM, Murad MH, Shoback D. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2019;104(5):1595–1622.
2. Tsai JN, Uihlein AV, Lee H, et al. Teriparatide and denosumab, alone or combined, in women with postmenopausal osteoporosis: the DATA study randomized trial. *Lancet* 2013; 382(9886):50–56.
3. Cosman F, Nieves JW, Dempster DW. Treatment sequence matters: anabolic and
4. antiresorptive therapy for osteoporosis. J Bone Miner Res. 2017;32(2):198–202.
5. Miller PD, Lewiecki EM, Krohn K, Schwartz E. Teriparatide: Label changes and identifying patients for long-term use. *Cleveland Clinic Journal of Medicine*. 2021;88(9):489-493. https://www.ccjm.org/content/88/9/489

Creation Date: 05/2022
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

TESTOSTERONE UNDECANOATE ORAL CAPSULES
JATENZO

Generic	Brand	HICL	GCN/GPID	Exception/Other
TESTOSTERONE UNDECANOATE	JATENZO		46152, 46153, 46144	Non-formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by an Endocrinology specialist
2. Patient must be age 18 years or older
3. Patient has a diagnosis of primary hypogonadism or hypogonadotropic hypogonadism with supporting documentation demonstrating serum testosterone concentrations below normal range
4. Patient has persistent signs and symptoms (e.g., depressed mood, decreased energy, progressive decrease in muscle mass, osteoporosis, loss of libido) of androgen deficiency prior to treatment
5. Documentation of inadequate response (<400ng/dL total testosterone while adherent to appropriately dosed therapy), intolerance, or contraindication to all the following alternative generic testosterone formulations, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Testosterone cypionate (or enanthate) intramuscular injection*
    b. Testosterone topical gels - 1% and 1.62%
    c. Testosterone transdermal solution (e.g., testosterone 30mg/actuation solution)

If all initial criteria are met, approve x2 years at HICL with max daily dose per below:
- Jatenzo 158 mg capsules = 4 caps/day
- Jatenzo 198 mg capsules = 4 caps/day
- Jatenzo 237 mg capsules = 2 caps/day

If all initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:
1. Patients' blood pressure is adequately controlled (≤140/90)
2. Patient does NOT have carcinomas of the breast or prostate
3. Patient has shown an adequate response to therapy as demonstrated by testosterone levels of ≥400-600 ng/dL total testosterone, within the most recent year

If all renewal criteria are met, approve x2 years at HICL, with max daily dose per below:
- Jatenzo 158 mg capsules = 4 caps/day
- Jatenzo 198 mg capsules = 4 caps/day
- Jatenzo 237 mg capsules = 2 caps/day

If all renewal criteria are not met, do not approve.

* *Documentation of a member having a needle phobia does not qualify as a medically acceptable contraindication or clinical inappropriateness to injectable products.*

RATIONALE
Quantity limits:

Jatenzo 158mg capsules	4 capsules/day
Jatenzo 198mg capsules	4 capsules/day
Jatenzo 237mg capsule	2 capsules/day
Tlando 112.5 mg capsules	4 capsules/day
Kyzatrex 100 mg capsules	2 capsules/day
Kyzatrex 150 mg capsules	4 capsules/day
Kyzatrex 200 mg capsules	4 capsules/day

FDA APPROVED INDICATIONS:
Testosterone replacement therapy for adult (18 years +) males with primary hypogonadism (congenital or acquire) or hypogonadotropic hypogonadism (congenital or acquired).

REFERENCES
Note: HICL includes injectable vial - Aveed 750mg/3ml as well as all Jatenzo, Tlando and Kyzatrex strengths

Creation Date: 11/2020
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

TESTOSTERONE UNDECANOATE ORAL CAPSULES
KYZATREX

Generic	Brand	HICL	GCN/GPID	Exception/Other
TESTOSTERONE UNDECANOATE	KYZATREX		52646, 52647, 52648	Non-formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by an Endocrinology specialist
2. Patient must be age 18 years or older
3. Patient has a diagnosis of primary hypogonadism or hypogonadotropic hypogonadism with supporting documentation demonstrating serum testosterone concentrations below normal range
4. Patient has persistent signs and symptoms (e.g., depressed mood, decreased energy, progressive decrease in muscle mass, osteoporosis, loss of libido) of androgen deficiency prior to treatment
5. Documentation of inadequate response (<400ng/dL total testosterone while adherent to appropriately dosed therapy), intolerance, or contraindication to all the following alternative generic testosterone formulations, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Testosterone cypionate (or enanthate) intramuscular injection*
    b. Testosterone topical gels - 1% and 1.62%
    c. Testosterone transdermal solution (e.g., testosterone 30mg/actuation solution)

If all initial criteria are met, approve x2 years at HICL with max daily dose per below:
- Kyzatrex 100mg capsules = 2 caps/day
- Kyzatrex 150mg capsules = 4 caps/day
- Kyzatrex 200mg capsules = 4 caps/day

If all initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:
1. Patients' blood pressure is adequately controlled (≤140/90)
2. Patient does NOT have carcinomas of the breast or prostate
3. Patient has shown an adequate response to therapy as demonstrated by testosterone levels of ≥400-600 ng/dL total testosterone, within the most recent year

If all renewal criteria are met, approve x2 years at HICL, with max daily dose per below:
- Kyzatrex 100mg capsules = 2 caps/day
- Kyzatrex 150mg capsules = 4 caps/day
- Kyzatrex 200mg capsules = 4 caps/day

If all renewal criteria are not met, do not approve.

* *Documentation of a member having a needle phobia does not qualify as a medically acceptable contraindication or clinical inappropriateness to injectable products.*

RATIONALE
Quantity limits:

Jatenzo 158mg capsules	4 capsules/day
Jatenzo 198mg capsules	4 capsules/day
Jatenzo 237mg capsule	2 capsules/day
Tlando 112.5 mg capsules	4 capsules/day
Kyzatrex 100 mg capsules	2 capsules/day
Kyzatrex 150 mg capsules	4 capsules/day
Kyzatrex 200 mg capsules	4 capsules/day

FDA APPROVED INDICATIONS:
Testosterone replacement therapy for adult (18 years +) males with primary hypogonadism (congenital or acquire) or hypogonadotropic hypogonadism (congenital or acquired).

REFERENCES
Note: HICL includes injectable vial - Aveed 750mg/3ml as well as all Jatenzo, Tlando and Kyzatrex strengths

Creation Date: 11/2020
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

KAISER PERMANENTE

KAISER COLORADO HMO MR GUIDELINES

TESTOSTERONE UNDECANOATE ORAL CAPSULES
TLANDO

Generic	Brand	HICL	GCN/GPID	Exception/Other
TESTOSTERONE UNDECANOATE	TLANDO	07304	52120	Non-formulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Must be prescribed by an Endocrinology specialist
2. Patient must be age 18 years or older
3. Patient has a diagnosis of primary hypogonadism or hypogonadotropic hypogonadism with supporting documentation demonstrating serum testosterone concentrations below normal range
4. Patient has persistent signs and symptoms (e.g., depressed mood, decreased energy, progressive decrease in muscle mass, osteoporosis, loss of libido) of androgen deficiency prior to treatment
5. Documentation of inadequate response (<400ng/dL total testosterone while adherent to appropriately dosed therapy), intolerance, or contraindication to all the following alternative generic testosterone formulations, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Testosterone cypionate (or enanthate) intramuscular injection*
    b. Testosterone topical gels - 1% and 1.62%
    c. Testosterone transdermal solution (e.g., testosterone 30mg/actuation solution)

If all initial criteria are met, approve x2 years at HICL, with max daily dose of 4 caps per day.
If all initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:
1. Patients' blood pressure is adequately controlled (≤140/90)
2. Patient does NOT have carcinomas of the breast or prostate
3. Patient has shown an adequate response to therapy as demonstrated by testosterone levels of ≥400-600 ng/dL total testosterone, within the most recent year

If all renewal criteria are met, approve x2 years at HICL, with max daily dose of 4 caps per day.
If all renewal criteria are not met, do not approve.

* *Documentation of a member having a needle phobia does not qualify as a medically acceptable contraindication or clinical inappropriateness to injectable products.*

RATIONALE
Quantity limits:

Jatenzo 158mg capsules	4 capsules/day
Jatenzo 198mg capsules	4 capsules/day
Jatenzo 237mg capsule	2 capsules/day
Tlando 112.5 mg capsules	4 capsules/day

Kyzatrex 100 mg capsules	2 capsules/day
Kyzatrex 150 mg capsules	4 capsules/day
Kyzatrex 200 mg capsules	4 capsules/day

FDA APPROVED INDICATIONS:
Testosterone replacement therapy for adult (18 years +) males with primary hypogonadism (congenital or acquire) or hypogonadotropic hypogonadism (congenital or acquired).

REFERENCES
Note: HICL includes injectable vial - Aveed 750mg/3ml as well as all Jatenzo, Tlando and Kyzatrex strengths

Creation Date: 11/2020
Effective Date: 01/2024
Reviewed Date: 09/2023
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TEZACAFTOR/IVACAFTOR (SYMDEKO)

Generic	Brand	HICL	GCN	Exception/Other
TEZACAFTOR/IVACAFTOR	SYMDEKO	44771		

GUIDELINES FOR USE

Requests for TEZACAFTOR/IVACAFTOR will be approved if ALL the following are met:
1. Prescribed by a pulmonologist
2. Patient has a diagnosis of cystic fibrosis (CF) and
    a. is homozygous for the F508del mutation
    OR
    b. has at least one of mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor (verified by testing) [Consult Symdeko website to check eligibility mutations: https://www.Symdeko.com]
3. Patient is at least 6 years old

If above criteria are met, approve indefinitely, max #2/day
If above criteria are not met, do not approve.

RATIONALE

Ensure appropriate utilization of tezacaftor/ivacaftor. TEZ/IVA (Symdeko) has potential safety advantages over LUM/IVA (Orkambi) including fewer drug-drug interactions and a lower incidence of respiratory adverse effects. TEZ/IVA has not been demonstrated to have improved efficacy compared to LUM/IVA, as there are no head-to-head studies. One study, EXPAND, reported modest improvements in lung function for TEZ/IVA compared to IVA (Kalydeco) for patients ⩾12 years with cystic fibrosis who were heterozygous for the F508del mutation and a CFTR mutation associated with residual CFTR function.

FDA APPROVED INDICATIONS

Cystic fibrosis: Treatment of patients with cystic fibrosis (CF) aged ⩾6 years who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.

REFERENCES

Kaiser Permanente Drug Information Services, Drug Monograph: tezacaftor/ivacaftor and ivacaftor (Symdeko). May 2018.

Symdeko [package insert]. Boston, MA: Vertex Pharmaceuticals Incorporated; 2022.

Creation date: 07/2018
Effective date: 01/2024
Reviewed date: 07/2023
Revised date: 07/2023

TOCILIZUMAB (ACTEMRA)

Generic	Brand	HICL	GCN	Exception/Other
TOCILIZUMAB	ACTEMRA SYRINGE, ACTEMRA ACTPEN	36466	35486, 45082	Formulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and is stable on Actemra.
2. Medication is not being used in combination with another biologic for the same indication.
3. Medication is being prescribed by a CPMG or affiliated rheumatologist.
4. Patient has ONE of the following diagnoses and is receiving the indicated drug as noted:
    a. Rheumatoid Arthritis (RA)
    b. Polymyalgia Rheumatica (PMR)
    c. Giant cell arteritis (GCA)
    d. Polyarticular juvenile idiopathic arthritis (PJIA)
    e. Systemic juvenile idiopathic arthritis (SJIA)
    f. Systemic sclerosis-associated lung disease (SSLD)

If met, approve indefinitely.
If not met, Use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications and must meet all indication-specific criteria.

A. Rheumatoid Arthritis (RA)
B. Polymyalgia Rheumatica (PMR)
C. Giant cell arteritis (GCA)
D. Polyarticular juvenile idiopathic arthritis (PJIA)
E. Systemic juvenile idiopathic arthritis (SJIA)
F. Systemic sclerosis-associated lung disease (SSLD)

A. **Rheumatoid Arthritis (RA):** All the following must be met:
1. Patient is 18 years or older, has a diagnosis of RA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. At least 2 of the following: Methotrexate, Leflunomide, Hydroxychloroquine, Sulfasalazine
    b. At least 1 TNF inhibitor (e.g. infliximab-dyyb (Inflectra) – preferred [F], adalimumab-atto (Amjevita) – preferred [F, PA])

If above criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.13].

If above criteria are not met, do not approve.

B. **Polymyalgia Rheumatica (PMR):** All the following must be met:
1. Patient is 18 years or older, has a diagnosis of PMR, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Corticosteroids or cannot tolerate a corticosteroid taper
    b. Methotrexate

If above criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.13].
If above criteria are not met, do not approve.

C. **Giant Cell Arteritis (GCA):** All the following must be met:
1. Patient is 18 years or older, has a diagnosis of GCA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to a corticosteroid

If above criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.13].
If above criteria are not met, do not approve.

D. **Polyarticular Juvenile Idiopathic Arthritis (PJIA):** All the following must be met:
1. Patient is 2 years old, has a diagnosis of PJIA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to at least 1 of the following medications, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Methotrexate
    b. Leflunomide
    c. Hydroxychloroquine
    d. Sulfasalazine

If above criteria are met, approve at HICL indefinitely, max 2 pens/syringes per 28 days [MDD 0.07].
If above criteria are not met, do not approve.

E. **Systemic juvenile idiopathic arthritis (SJIA):** All the following must be met:
1. Patient is 2 years old, has a diagnosis of SJIA, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.
3. Patient with failure, intolerance, or contraindication to at least 1 of the following medications, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
    a. Methotrexate
    b. Leflunomide
    c. Hydroxychloroquine
    d. Sulfasalazine

If above criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.13].
If above criteria are not met, do not approve.

F. **Systemic sclerosis-associated lung disease (SSLD):** All the following must be met:
1. Patient is 18 years or older, has a diagnosis of SSLD, and medication is prescribed by a CPMG or affiliated rheumatologist.
2. Medication is not being used in combination with another biologic for the same indication.

If above criteria are met, approve at HICL indefinitely, max 4 pens/syringes per 28 days [MDD 0.13].
If above criteria are not met, do not approve.

FDA APPROVED INDICATIONS
Actemra: RA, GCA, PJIA, SJIA, SSLD
Kevzara: RA, PMR

REFERENCES
1. Actemra:
    - Actemra ACTPen: 162 mg/0.9 mL (0.9 mL) Solution Auto-injector, Subcutaneous [preservative free]
    - Actemra 162 mg/0.9 mL (0.9 mL) Solution Prefilled Syringe, Subcutaneous [preservative free]
2. "*Currently stable*" means patient is tolerating well, medication appears to be effective, and provider wishes to continue therapy.
3. Bonelli M, Radner H, Kerschbaumer A, Mrak D, Durechova M, Stieger J, Husic R, Mandl P, Smolen JS, Dejaco C, Aletaha D. Tocilizumab in patients with new onset polymyalgia rheumatica (PMR-SPARE): a phase 2/3 randomised controlled trial. Ann Rheum Dis. 2022 Jun;81(6):838-844. doi: 10.1136/annrheumdis-2021-221126.
4. Assaraf M, Chevet B, Wendling D, Philippe P, Cailliau E, Roux C, Avouac J, Delacour M, Houvenagel E, Sellam J, Cortet B, Henry J, Flipo RM, Devauchelle-Pensec V. Efficacy and management of tocilizumab in polymyalgia rheumatica: results of a multicenter retrospective observational study. Rheumatology (Oxford). 2023 Aug 21:kead426. doi: 10.1093/rheumatology/kead426.

Creation Date: 11/2023
Effective Date: 02/2024
Reviewed Date:
Revised Date: 01/2024

TOLTERODINE ER (DETROL LA)

Generic	Brand	HICL	GCN	Exception/Other
TOLTERODINE ER	DETROL LA	18047	12263, 12264	Max daily dose 1 cap per day

GUIDELINES FOR COVERAGE

Review based on patient cognitive status noted in section A or B:

A. Patients with a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin and/or trospium IR, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely (max daily dose of 1 capsule/day).
      If criteria are not met, do not approve.

B. Patients WITHOUT a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin, and/or trospium IR, and/or oxybutynin tablet/syrup, the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely (max daily dose of 1 capsule/day).
      If criteria are not met, do not approve.

RATIONALE

Per Health Plan.

- An adequate response is defined as one less episode of frequency or incontinence per day after an adequate trial of 4-6 weeks.
- Preferred formulary agents, in order: oxybutynin ER, oxybutynin IR, solifenacin, trospium IR and oxybutynin syrup.

- Preferred nonformulary agents in order: tolterodine IR, tolterodine ER, darifenacin, fesoterodine, trospium ER, mirabegron and vibegron. Oxybutynin gel (Gelnique) and oxybutynin patch (Oxytrol) are excluded from coverage.
- Agents preferred in cognitive impairment include, in order: solifenacin, trospium IR, darifenacin ER, trospium ER.

Creation date: 01/15/2019
Effective date: 01/2024
Reviewed date: 09/2023
Revised date: 09/2023

TOLTERODINE IR (DETROL)

Generic	Brand	HICL	GCN	Exception/Other
TOLTERODINE IR	DETROL	18047	37061, 37062	

GUIDELINES FOR COVERAGE

Review based on patient cognitive status noted in section A or B:

A. Patients with a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin and/or trospium IR, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely.
      If criteria are not met, do not approve.

B. Patients WITHOUT a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin, and/or trospium IR, and/or oxybutynin tablet/syrup, the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely.
      If criteria are not met, do not approve.

RATIONALE

Per Health Plan.

- An adequate response is defined as one less episode of frequency or incontinence per day after an adequate trial of 4-6 weeks.
- Preferred formulary agents, in order: oxybutynin ER, oxybutynin IR, solifenacin, trospium IR and oxybutynin syrup.

- Preferred nonformulary agents in order: tolterodine IR, tolterodine ER, darifenacin, fesoterodine, trospium ER, mirabegron and vibegron. Oxybutynin gel (Gelnique) and oxybutynin patch (Oxytrol) are excluded from coverage.
- Agents preferred in cognitive impairment include, in order: solifenacin, trospium IR, darifenacin ER, trospium ER.

Creation date: 01/15/2019
Effective date: 01/2024
Reviewed date: 09/2023
Revised date: 09/2023

TOPICAL ONYCHOMYCOSIS AGENTS

Generic	Brand	HICL	GCN	Comments
CICLOPIROX/UREA/CAMPH/MEN/EUC 8% SOLN	CICLODAN		29988	Nonformulary

GUIDELINES FOR COVERAGE

Review based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Must have tried and failed, have a contraindication or intolerance to 6 weeks of oral terbinafine tablets for fingernails and 12 weeks of oral terbinafine tablets for toenails

   If criteria are met, approve at GPID for 48 weeks.
   If criteria are not met, do not approve.

RATIONALE

Per plan.

Creation Date: 07/2022
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

TOPICAL ONYCHOMYCOSIS AGENTS

Generic	Brand	HICL	GCN	Comments
CICLOPIROX 8% SOLN	CICLODAN		8040	Nonformulary

GUIDELINES FOR COVERAGE

Review based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Must have tried and failed, have a contraindication or intolerance to 6 weeks of oral terbinafine tablets for fingernails and 12 weeks of oral terbinafine tablets for toenails

   If criteria are met, approve at GPID for 48 weeks.
   If criteria are not met, do not approve.

RATIONALE

Per plan.

Creation Date: 07/2022
Effective Date: 01/2024
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TOPICAL ONYCHOMYCOSIS AGENTS

Generic	Brand	HICL	GCN	Comments
EFINACONAZOLE	JUBLIA		36653	Nonformulary

GUIDELINES FOR COVERAGE
Review based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

A. Must meet all the following:
   1. Must have tried and failed, have a contraindication or intolerance to 6 weeks of oral terbinafine tablets for fingernails and 12 weeks of oral terbinafine tablets for toenails
   2. Must have tried and failed 48 weeks of topical ciclopirox solution
   3. Must have tried and failed 48 weeks of topical tavaborole solution
   4. Must have mycology labs showing either a positive nail fungal culture or positive PAS staining of nail clipping in formalin

   If criteria are met, approve at GPID for 48 weeks.
   If criteria are not met, do not approve.

RATIONALE
Per plan.

Creation Date: 07/2022
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

TOPICAL ONYCHOMYCOSIS AGENTS

Generic	Brand	HICL	GCN	Comments
TAVABOROLE 5%	KERYDIN		36997	Nonformulary

GUIDELINES FOR COVERAGE
Review based on medication requested, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

A. Must meet all the following:
   1. Must have tried and failed, have a contraindication or intolerance to 6 weeks of oral terbinafine tablets for fingernails and 12 weeks of oral terbinafine tablets for toenails
   2. Must have tried and failed 48 weeks of topical ciclopirox solution

   If criteria are met, approve at GPID for 48 weeks.
   If criteria are not met, do not approve.

RATIONALE
Per plan.

Creation Date: 07/2022
Effective Date: 01/2024
Reviewed Date: 07/2023
Revised Date: 07/2023

TOPICAL TRETINOIN COVERAGE RULES

Generic name	Brand name	HICL	GPID	Exception/Other
TRETINOIN (TOPICAL)		02468, 32888	22874, 31777, 17443, 31776, 44075, 36604, 22881, 22880, 22871, 22882, 22872, 22870	

GUIDELINES FOR COVERAGE

Must meet one of the following criteria:

1. Patient must be age 35 or younger
2. Must have one of the following acne, actinic keratosis or verruca plana diagnoses:
   a) L70.0 - acne vulgaris
   b) L70.1 - acne conglobate
   c) L70.2 - acne varioliformis
   d) L70.3 - acne tropica
   e) L70.8 - Other acne
   f) L70.9 - acne, unspecified
   g) L57.0 - actinic keratosis
   h) B07.8 - verruca plana

If one of the above criteria are met, then approve at HICL-G indefinitely.
If criteria not met, do not approve.

FDA APPROVED INDICATIONS

Topical tretinoin products are FDA approved for acne, wrinkles, hyperpigmentation of skin and roughness of skin. Supported off-label indications include keratosis and ultraviolet-induced change in normal skin. Per CMS guidance all except acne and keratosis are cosmetic indications and are excluded from benefit.

REFERENCES

Topical vitamin A treatment of recalcitrant common warts - PMC (nih.gov)

Creation Date: 01/2023
Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

TOPIRAMATE 25 MG/ML SOLUTION - AGE RESTRICTION CRITERIA

Generic	Brand	HICL	GCN	Exception/Other
TOPIRAMATE SOLUTION 25 MG/ML	EPRONTIA		51457	

GUIDELINES FOR COVERAGE

INITIAL AND RENEWAL CRITERIA: ONE of the following criteria must be met:
1. Patient is less than or equal to 10 years old
2. Patient is using an alternative administration route, such as a gastrostomy tube
3. Dose cannot be administered by using half, whole or combo of the topiramate tablets or combo of the topiramate capsules
4. Patient cannot swallow opened capsules or other tablets whole, halved, or crushed (with or without mixing in apple sauce)

If any criterion is met, approve x1 year.
If no criteria are met, do not approve, and suggest either changing to capsules that can be opened and sprinkled on a teaspoonful of soft food or tablet strengths that can be halved or used in combination, or crushing topiramate tablets before administration and taking with or without applesauce.

RATIONALE
Per Health Plan.

General Clinical Criteria for solutions/suspension
1. Age is less than or equal to 10 years old
2. Presence of gastrostomy
3. Dose does not allow use of halved, whole or combo of tablet
4. Dose does not use whole capsule (cannot “cut” capsules in half)
5. Clinical condition where unable to swallow crushed/opened tablets/capsules (i.e., esophageal stricture)

FDA APPROVAL
1. Prophylaxis of migraine headache in patients ≥12 years of age
2. Monotherapy or adjunctive therapy in patients ≥2 years of age (immediate release and Qudexy XR) or ≥6 years of age (Trokendi XR) with focal (partial) onset or primary generalized tonic-clonic seizures
3. Adjunctive therapy in patients ≥2 years of age (immediate release and Qudexy XR) or ≥6 years of age (Trokendi XR only) with seizures associated with Lennox-Gastaut syndrome

REFERENCES
Per Health Plan

Creation date: 09/2023
Effective date: 03/2024
Reviewed date: 12/2023
Revised date: 12/2023

TRALOKINUMAB-LDRM (ADBRY)

Generic	Brand	HICL	GCN	Exception/Other
TRALOKINUMAB-LDRM	ADBRY	47741		Formulary Specialty tier

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: All the following must be met:
1. Patient is new to KPCO within the past 90 days and currently stable on tralokinumab (Adbry)
2. Must be prescribed by a CPMG or an affiliated dermatologist or allergist with an active referral if necessary.
3. Medication is not being used in combination with another biologic for the same indication.

If above criteria are met, approve indefinitely, max 4 syringes per 28 days.
If above criteria are not met, review by Initial Criteria.

INITIAL CRITERIA: All the following must be met:
1. Must be prescribed by a CPMG or an affiliated dermatologist or allergist with an active referral if necessary.
2. Diagnosis of moderate to severe atopic dermatitis
3. Medication is not being used in combination with another biologic for the same indication.
4. Patient has experienced all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception: [Skip if patient has been on an atopic dermatitis biologic or oral JAKi therapy within the past 4 months (excludes sample trials)]
    a. Inadequate response, intolerance, or contraindication to at least one topical corticosteroid OR topical calcineurin inhibitor (pimecrolimus, tacrolimus)
    b. Inadequate response (after at least 2 months) or intolerance to at least one, or contraindication to at least two of the below pre-biologic therapies:
        i. Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
        ii. Azathioprine
        iii. Cyclosporine
        iv. Methotrexate
        v. Mycophenolate

If above criteria are met, approve at HICL x1 fill, max 6 syringes per 28 days (loading dose), then 4 syringes per 28 days (maintenance dose) indefinitely.
If above criteria are not met, do not approve.

RATIONALE
Per Health Plan and current treatment guidelines

FDA APPROVED INDICATIONS
Atopic Dermatitis (Moderate to Severe)

REFERENCES

1. Eichenfield LF, Tom WL, Chamlin SL, Feldman SR, Hanifin JM, Simpson EL, Berger TG, Bergman JN, Cohen DE, Cooper KD, Cordoro KM, Davis DM, Krol A, Margolis DJ, Paller AS, Schwarzenberger K, Silverman RA, Williams HC, Elmets CA, Block J, Harrod CG, Smith Begolka W, Sidbury R. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014 Feb;70(2):338-51.
2. Fishbein AB, Silverberg JI, Wilson EJ, Ong PY. Update on Atopic Dermatitis: Diagnosis, Severity Assessment, and Treatment Selection. J Allergy Clin Immunol Pract. 2020 Jan;8(1):91-101

Table 3: Relative contraindications of various treatments

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses* (ex: *systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for atopic dermatitis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities,* active malignancy, *and hypersensitivity*
Acitretin	*Women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*
Mycophenolate	*Hypersensitivity to mycophenolate, active malignancy, pregnancy, breastfeeding, women of childbearing age not using highly effective contraceptive methods. Mycophenolate requires REMS program for females of childbearing age.*

Table 4: Home UV phototherapy criteria and contracted provider information (Daavlin)

KPCO home phototherapy contracted provider: Daavlin
KPCO contracts with Daavlin for home phototherapy units Submit orders to Daavlin (see form link below), and they will work with the patient directly and help coordinate insurance coverage, billing, shipping, and technical support if needed Daavlin Phone: 1-800-322-8546; Daavlin Fax: 1-419-636-1739 https://www.daavlin.com/physicians/ https://www.daavlin.com/wp-content/uploads/2017/08/Home-Phototherapy-Order-Packet-042017.pdf Units: DermaPal: hand-held scalp spot unit 1 Series: small panel unit (ideal for patients with limited disease [ex: only hand / foot involvement]) 4 Series: mid-sized panel unit (ideal for patients with regional disease [ex: those with lower leg, arm involvement) 7 Series: large 6' panel unit (most used unit, allows for full body treatment)

Creation Date: 07/2022
Effective Date: 01/2024
Revised Date: 07/2023
Reviewed Date: 07/2023

TRAMETINIB DIMETHYL SULFOXIDE (MEKINIST)

Generic Name	Brand Name	HICL	GPID	Comments
TRAMETINIB	MEKINIST	40361	34726, 34727	Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
1. Patient is new to KPCO within the past 90 days and is stable on therapy.

   If met, approve based on the following:
   - For adjuvant setting: Approve for duration needed to complete a total of 12 months of adjuvant treatment, max 3 per day.
   - For unresectable or metastatic setting: Approve indefinitely, max 3 per day.

   If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
A. Must be prescribed by an oncologist
B. Must meet the diagnosis/drug specific criteria below-
   1. CUTANEOUS MELANOMA (ADJUVANT SETTING)
      a. Must be requested in the adjuvant treatment setting
      b. Must have a BRAF V600 activating mutation positive tumor
      c. Must be requested in combination with dabrafenib (Tafinlar)

      If met, then approve x 12 months with max daily dose of 3 tablets/day.
      If not met, do not approve.

   2. CUTANEOUS MELANOMA (UNRESECTABLE OR METASTATIC SETTING)
      a. Must be requested in unresectable or metastatic (advanced) setting
      b. Must have a BRAF V600 activating mutation positive tumor
      c. Must be requested in combination with dabrafenib (Tafinlar)
      d. Must NOT have progressed through other MEK-targeted therapies (ex: cobimetinib (Cotellic), binimetinib (Mektovi)) in the unresectable or metastatic (advanced) setting
      e. Must have confirmed brain metastasis OR patient has tried and is unable to tolerate cobimetinib (Cotellic) due to unacceptable toxicities despite adequate dose reductions

      If met, approve indefinitely, max 3 tablets/day.
      If not met, do not approve. Use specific notations below for denial as applicable:
      - If criteria 2.b. is not met, deny noting that trametinib must be used in combination with dabrafenib.
      - If criteria 2.c. is not met, deny noting that there is not enough evidence to support use of trametinib after progression on other MEK-targeted therapies in the unresectable or metastatic (advanced) setting.
      - If criteria 2.d. is not met, deny noting the patient must use cobimetinib (in combination with vemurafenib).

   3. NON-SMALL CELL LUNG CANCER
      a. Must be requested in the unresectable or metastatic setting
      b. Must have BRAF V600E mutation positive tumor

If met, approve indefinitely, max 3 per day.
If not met, do not approve.

4. THYROID CANCER
   a. Must be requested in the locally advanced or metastatic setting
   b. Must have anaplastic thyroid cancer
   c. Must have BRAF V600E mutation positive tumor

   If met, approve indefinitely, max 3 per day.
   If not met, do not approve.

5. SOLID TUMORS
   a. Must be requested in the unresectable or metastatic setting
   b. Must have BRAF V600E mutation positive tumor
   c. Must have progressed through prior treatment and have no satisfactory alternative treatment options

   If met, approve indefinitely, max 3 per day.
   If not met, do not approve.

6. OVARIAN CANCER
   a. Must have low-grade serous carcinoma
   b. Must have recurrent disease

   If met, approve indefinitely, max 3 per day.
   If not met, do not approve.

RENEWAL CRITERIA

1. Request for continued coverage is in the unresectable or metastatic setting only. [No indication for treatment beyond 12 months in the adjuvant setting]
2. Patient's disease has not progressed since treatment initiation OR treating provider believes patient is deriving significant clinical benefit to justify treatment continuation
   Note that provider does NOT need to prove lack of progression via imaging, a clinical evaluation suffices

   If met, approve indefinitely, max 3 per day.
   If not met, do not approve.

RATIONALE

FDA labeling
Steering use toward preferred products

FDA APPROVED INDICATIONS

Melanoma (adjuvant, unresectable/metastatic), NSCLC (metastatic), anaplastic thyroid cancer (locally advanced, metastatic), solid tumors (unresectable, metastatic) with BRAF V600 activating mutations

REFERENCES

Package insert

Creation Date: 03/2020

Effective Date: 02/2024
Reviewed Date: 01/2024
Revised Date: 01/2024

TYVASO (TREPROSTINIL)

Generic	Brand	HICL	GCN	Exception/Other
TREPROSTINIL SOLUTION FOR INHALATION	TYVASO	36541	27492	
TREPROSTINIL DRY POWDER FOR INHALATION	TYVASO DPI	36541	52362, 52387, 52382, 52376, 52377, 52378	

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Tyvaso or Tyvaso DPI

If met, approve indefinitely at HICL.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must have one of the following indications and meet indication-specific criteria as noted:

A. Pulmonary Arterial Hypertension (PAH) (WHO Group 1): Must meet all the following:
   1. Prescriber must be a cardiologist or a pulmonologist.
   2. Patient has a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) verified by right heart catheterization.
   3. Patient currently has WHO Functional Class II, III or IV symptoms.
   4. Patient has tried and failed, or has an intolerance to, or a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. One phosphodiesterase type 5 (PDE5) inhibitor: sildenafil (Revatio®) or tadalafil (Adcirca®)
      b. One endothelin receptor antagonist (ERA): Bosentan (Tracleer®), Ambrisentan (Letairis®), or macitentan (Opsumit®)
      c. Orenitram (treprostinil oral tablet)

   If criteria are met, approve indefinitely at HICL.
   If criteria are not met, do not approve.

B. Pulmonary Hypertension associated with Interstitial Lung Disease (PH-ILD) (WHO Group 3): Must meet all the following:
   1. Prescriber must be a pulmonologist or a cardiologist.
   2. Patient has a diagnosis of pulmonary hypertension associated with interstitial lung disease (WHO Group 3) verified by right heart catheterization.

   If criteria are met, approve indefinitely at HICL.
   If criteria are not met, do not approve.

RATIONALE
Ensure appropriate use consistent with FDA indication(s).

FDA APPROVED INDICATIONS
- TYVASO (solution for inhalation)
  - Treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to reduce risks of disease progression and hospitalization.
- TYVASO DPI (dry powder for inhalation)
  - Treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to reduce risks of disease progression and hospitalization.
  - Treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD) (WHO Group 3).

REFERENCES
1. Tyvaso (treprostinil solution for inhalation) [prescribing information]. Research Triangle Park, NC: United Therapeutics Corp; May 2022.
2. Tyvaso DPI (treprostinil dry powder for inhalation) [prescribing information]. Research Triangle Park, NC: United Therapeutics Corp; June 2023.

Creation Date: 11/2023
Effective Date: 12/2023
Reviewed Date:
Revised Date:

TROFINETIDE (DAYBUE)

Generic	Brand	HICL	GCN	COMMENTS
TROFINETIDE 200 MG/ML SOLN	DAYBUE SOLN	48773	53839	Non-Formulary

GUIDELINES FOR COVERAGE

Must meet all the following:

1. Medication is prescribed by a neurologist or medical geneticist.
2. The patient is 2 years of age or older.
3. The patient has a diagnosis of Rett syndrome confirmed by genetic testing showing disease-causing mutation in the MECP2 gene.

If met, approve indefinitely, max daily dose: 120 mL.
If not met, do not approve.

RATIONALE

Ensure appropriate use consistent with FDA indication.

FDA APPROVED INDICATIONS

Rett syndrome: Treatment of Rett syndrome in adults and pediatric patients ≥2 years of age.

REFERENCES

Daybue (trofinetide) [prescribing information]. San Diego, CA: Acadia Pharmaceuticals Inc; March 2023.

Creation Date: 11/2023
Effective Date: 12/2023
Reviewed Date:
Revised Date:

TROSPIUM ER (SANCTURA XR)

Generic	Brand	HICL	GCN	Exception/Other
TROSPIUM ER	SANCTURA XR		99193	Max daily dose 1 cap per day

GUIDELINES FOR COVERAGE

Review based on patient cognitive status noted in section A or B:

A. Patients with a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin and/or trospium IR, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely (max daily dose 1 capsule/day).
      If criteria are not met, do not approve.

B. Patients WITHOUT a history of cognitive issues (dementia, memory impairment, delirium): Must meet all the following:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to solifenacin, and/or trospium IR, and/or oxybutynin tablet/syrup, the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

      If criteria are met, approve indefinitely (max daily dose 1 capsule/day).
      If criteria are not met, do not approve.

RATIONALE

Per Health Plan.

- An adequate response is defined as one less episode of frequency or incontinence per day after an adequate trial of 4-6 weeks.
- Preferred formulary agents, in order: oxybutynin ER, oxybutynin IR, solifenacin, trospium IR and oxybutynin syrup.

- Preferred nonformulary agents in order: tolterodine IR, tolterodine ER, darifenacin, fesoterodine, trospium ER, mirabegron and vibegron. Oxybutynin gel (Gelnique) and oxybutynin patch (Oxytrol) are excluded from coverage.
- Agents preferred in cognitive impairment include, in order: solifenacin, trospium IR, darifenacin ER, trospium ER.

Creation date: 01/15/2019
Effective date: 01/2024
Reviewed date: 09/2023
Revised date: 09/2023

KAISER PERMANENTE

KAISER COLORADO HMO MR GUIDELINES

TUCATINIB (TUKYSA) QUANTITY LIMIT

GUIDELINES FOR QUANTITY LIMIT:

- **Maximum 4 tablets per day per strength**
- **If patient requires a dose that exceeds 4 tablets per day, two separate prescriptions must be used (one for each strength) to result in desired dose**

Rationale:

- Tukysa comes in 50mg, bottle of #60, and 150mg tablets, bottles of #60 or #120
- Must be dispensed in original bottle due to a desiccant required for stability
- Tukysa 150mg cost less per mg than the 50mg
- Packaging does not align with the typical 21-day treatment cycle creating a potential safety issue as patients my take therapy without recommended follow up

Creation Date: 11/2021
Effective Date: 01/2024
Reviewed Date: 9/2023
Revised Date:

TYROSINE KINASE INHIBITORS (TKIS) 2ND/LATTER GENERATION

Generic	Brand	HICL	GCN/GPID	Other
ASCIMINIB	SCEMBLIX	47647		Nonformulary, Latter generation TKI

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA

A. Patient is new to KPCO within the past 90 days, and the medication has been prescribed by an Oncologist

If met, approve x 2 years.
If not met, then use Initial Criteria.

INITIAL CRITERIA: Must meet the following criteria based on drug and diagnosis below:

A. Asciminib (Scemblix) for Chronic Myeloid Leukemia (CLL)
B. All other indications

A. **Asciminib (Scemblix) for chronic phase CML: Must meet all the following:**
   1. Must be prescribed by a CPMG or affiliated oncologist
   2. Patient must NOT have any of the following BCR-ABL1 mutations: A337T or P465S
   3. Patient must have Philadelphia Chromosome (aka BCR-ABL) and one of the following criteria, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. Patient must have a documented intolerance not alleviated by dose reductions [noted below], or patient has inadequate response/treatment failure that is not due to patient nonadherence, to at least two (per FDA labeling) of the following agents:
         i. Imatinib (Gleevec) [≤200 mg/day]
         ii. Ponatinib (Iclusig) [15mg/day. If patient developed cardiac AE during treatment with ponatinib (Iclusig) at any dose, or is at high risk for developing cardiac AE during treatment with ponatinib (Iclusig) per provider assessment, patient may be deemed “intolerant”]
         iii. Bosutinib (Bosulif) [≤300mg/day]
         iv. Nilotinib (Tasigna) [400mg/day]
         v. Dasatinib (Sprycel) [70mg/day. If patient developed pulmonary arterial hypertension (PAH) during treatment with dasatinib (Sprycel) at any dose, patient may be deemed “intolerant”]
      b. Patient must have one of the following BCR-ABL1 mutations: T315I AND one of the following criteria:
         i. Patient has tried and failed ponatinib (Iclusig) with an inadequate response that is not due to patient nonadherence

ii. Patient must have a documented intolerance to ponatinib (Iclusig) not alleviated by dose reductions (15mg/day) [If patient developed serious cardiac AE during treatment with ponatinib (Iclusig) at any dose, patient may be deemed "intolerant"]

If criteria are met, approve x2 years with quantity limit of 10 tabs/day.
If criteria are not met, do not approve.

B. **If for any other diagnosis (e.g., hypereosinophilic syndrome, eosinophilic leukemia, dermatofibrosarcoma, chordoma): Must meet all the following:**
   1. Prescribed by an oncology specialist
   2. Use must meet the Medicare Compendia criteria as detailed in the following policy: Medicare Benefit Policy Manual Chapter 15 - Covered Medical and Other Health Services Section 50.4.5 - Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

If criteria are met, approve x 1 year.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet the following:
A. Patient has been on the TKI for greater than 3 months and one of the following criteria:
   1. Disease progression or relapse are not noted in the chart
   2. Patient has experienced improvement in disease symptoms since starting the medication

If criteria are met, approve x 2 years.
If criteria are not met, do not approve.

RATIONALE

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology Chronic Myeloid Leukemia v.2.2023 www.nccn.org
2. NCCN Clinical Practice Guidelines in Oncology Acute Lymphoblastic Leukemia v.1.2022 www.nccn.org
3. NCCN Clinical Practice Guidelines in Oncology Gastrointestinal Stromal Tumors (GISTs) v.1.2023 www.nccn.org

Creation Date: 11/2019
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

STELARA (USTEKINUMAB)

Generic	Brand	HICL	GCN	Exception/Other
USTEKINUMAB	STELARA	36187		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:

A. Patient is new to KPCO with the past 90 days, is currently stable on Stelara, Medication is not being used in combination with another biologic for the same indication, and has one of the following indications prescribed by the appropriate specialist as noted below:
   1. Patient has a diagnosis of Psoriatic Arthritis (PsA) and is being prescribed by a CPMG or affiliated rheumatologist.
   2. Patient has a diagnosis of Psoriasis and is being prescribed by a CPMG or affiliated dermatologist.
   3. Patient has a diagnosis of Ulcerative Colitis or Crohn's Disease or Unclassified IBD with Crohn's or Ulcerative Colitis Features and is being prescribed by a CPMG or affiliated gastroenterology specialist.

If met, approve indefinitely, based on indication:
   1. PsA: max 1 syringe per 84 days [max qty: 1, min ds: 84]
   2. Psoriasis: max 1 syringe per 84 days [max qty: 1, min ds: 84]
   3. Ulcerative Colitis or Crohn's Disease: 1 syringe per 56 days [max qty: 1, min ds: 56]

If not met, use Initial Criteria for review.

INITIAL CRITERIA: Must have one of the following indications, and must meet all indication-specific criteria below:

A. Psoriatic Arthritis (PsA)
B. Psoriasis
C. Crohn's Disease or Unclassified IBD with Crohn's Features
D. Ulcerative Colitis or Unclassified IBD with Ulcerative Colitis Features

A. Psoriatic Arthritis: All the following must be met:
   1. Patient has a diagnosis of PsA, and medication is prescribed by a rheumatologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response, intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. at least two DMARDs (including methotrexate), or the patient has high disease activity in which traditional DMARDs would not be suitable treatment
      b. at least 1 TNF inhibitor (e.g., infliximab-dyyb (Inflectra)-preferred [F], adalimumab-atto (Amjevita)-preferred [F, PA], etanercept (Enbrel) [F, PA])
      c. secukinumab (Cosentyx) [F]
      d. guselkumab (Tremfya) [NF, PA]

If initial criteria are met, approve at HICL x 1 month, max 1 syringe per 28 days (loading dose) [max qty: 1, min ds: 28], then 1 syringe per 84 days (maintenance dose) indefinitely [max qty: 1, min ds: 84].
If initial criteria are not met, do not approve.

B. Psoriasis: All the following must be met:
   1. Patient has a diagnosis of moderate to severe psoriasis, and medication is prescribed by a dermatology provider.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced inadequate response, intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      e. A topical corticosteroid or topical calcineurin inhibitor (pimecrolimus, tacrolimus), or the patient is reported as having very high disease activity (ex: > 50% BSA, erythrodermic, pustular psoriasis), disease affecting critical areas (ex: genitals, face), or prior biologic therapy within the past 4 months, skip and proceed to step 3c]
      f. Inadequate response (after at least 2 months) or intolerance to at least one OR contraindication to at least two of the following therapies: Acitretin, Cyclosporine, Methotrexate, Apremilast (Otezla), Phototherapy or narrow-band short wave ultraviolet B (NB-UVB) light therapy
      g. At least one TNF inhibitor (adalimumab (Amjevita) - preferred [F, PA], infliximab (Inflectra)- preferred [F], etanercept (Enbrel) [F, PA])
      h. At least one IL-17 inhibitor (secukinumab (Cosentyx) - preferred [F])
      i. At least one IL-23 inhibitor (guselkumab (Tremfya) - preferred [NF, PA], risankizumab-rzaa (Skyrizi) [NF, PA])

If initial criteria are met, approve at HICL x 1 month, max 1 syringe per 28 days (loading dose) [max qty: 1, min ds: 28], then 1 syringe per 84 days (maintenance dose) indefinitely [max qty: 1, min ds: 84].
If initial criteria are not met, do not approve.

C. Crohn's Disease or Unclassified IBD with Crohn's Features: All the following must be met:
   1. Patient has a diagnosis of Crohn's Disease or Unclassified IBD with Crohn's Features, and the medication is prescribed by a gastroenterologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response, intolerance, or has a contraindication to at least 1 TNF inhibitor (e.g. adalimumab (Amjevita) - preferred [F, PA], infliximab (Inflectra)- preferred [F], or certolizumab (Cimzia) [NF, PA]), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If initial criteria are met, then approve indefinitely, max 1 syringe per 56 days [max qty: 1, min ds: 56].
If initial criteria are not met, do not approve.

D. Ulcerative Colitis or Unclassified IBD with Ulcerative Colitis Features: All the following must be met:
   1. Patient has a diagnosis of ulcerative colitis or unclassified IBD with ulcerative colitis features, and the medication is prescribed by a gastroenterologist.
   2. Medication is not being used in combination with another biologic for the same indication.
   3. Patient has experienced an inadequate response, intolerance, or has a contraindication to all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
      a. At least 1 TNF inhibitor (e.g. adalimumab (Amjevita) - preferred [F, PA], infliximab (Inflectra)- preferred [F], or golimumab (Simponi) [NF, PA])
      b. A JAK-inhibitor (e.g. tofacitinib (Xeljanz) – [F], upadacitinib (Rinvoq) [NF, PA])

If initial criteria are met, then approve indefinitely, max 1 syringe per 56 days [max qty: 1, min ds: 56].
If initial criteria are not met, do not approve.

ESCALATION CRITERIA/QTY LIMIT OVERRIDES: Patient must meet New Member, Initial, or Renewal PA Criteria prior to review for Quantity Overrides. Escalation Criteria review only the quantities authorized upon PA approval.

A. Patient diagnosis of Ulcerative Colitis or Crohn's disease
   1. For requests to start on escalated frequencies (1 syringe per less than 56 days):
      Provider states patient requires escalation based on medical necessity. Patient must have objective signs of disease activity as demonstrated on colonoscopy or with elevated inflammatory markers (fecal calprotectin or C-reactive protein).

      If met, approve at HICL x1 year, max 1 syringe per 28 days [max qty: 1, min ds: 28].
      If not met, then deny and offer maximum 1 syringe per 56 days indefinitely [max qty: 1, min ds: 56].

   2. For requests to continue escalated frequencies (1 syringe per less than 56 days):
      Patient must have been assessed by a gastroenterologist in the last 1 year, and the gastroenterologist evaluated if the frequency can be de-escalated and determined that the escalated frequency continues to be medically necessary.

      If met, approve at HICL x2 years, max 1 syringe per 28 days [max qty: 1, min ds: 28].
      If not met, deny and offer max 1 syringe per 56 days indefinitely [max qty: 1, min ds: 56].

RATIONALE
"Currently stable on medication," means patient is tolerating well, medication appears to be effective, and provider wishes to continue therapy.

Trial and failure of 2 DMARDs is required, as the DMARD classification is not representative of a specific pharmacological class and these medications are pharmacologically unrelated in terms of mechanism of action.

FDA APPROVED INDICATIONS

1. Treatment of patients 6 years of age or older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.
2. Treatment of patients 6 years of age with active psoriatic arthritis, with or without concurrent methotrexate.
3. Treatment of moderately to severely active Crohn disease in adults
4. Treatment of moderately to severely active ulcerative colitis in adults
5. Treatment of refractory inflammatory bowel disease in children and adolescents ≥12 years old (off label)

Treatment	Relative Contraindications for Psoriasis
Phototherapy or NVU-UB	*Past/current melanoma or non-melanoma skin cancer, concomitant cyclosporine, predominant symptoms on genitals or face, type I skin (highly sensitive skin), erythroderma, preexisting photodermatoses (ex: systemic lupus, porphyria)*
Cyclosporine	*Uncontrolled hypertension, impaired renal function, prior PUVA or radiation therapy, drug hypersensitivity, and malignancy. Due to side effect profile, cyclosporine is not used chronically for psoriasis.*
Methotrexate	*Pregnancy, breastfeeding, actively trying to conceive, alcoholism or history of heavy alcohol use, chronic liver disease, immunodeficiency syndrome, preexisting blood dyscrasias, persistent liver or renal abnormalities, active malignancy, and hypersensitivity*
Acitretin	*Women of child potential (cannot consider pregnancy up to 3 years after completion of treatment), pregnancy, lactation, severe hepatic or renal dysfunction, chronically abnormal elevated lipid values, and hypersensitivity*

Creation date: 09/26/2018
Effective date: 01/01/2024
Revised date: 11/2023
Reviewed date: 11/2023

VAGINAL ESTROGEN CREAM

Generic name	Brand name	HICL	GPID	Comments
CONJUGATED ESTROGENS VAGINAL CREAM	PREMARIN		28410	

GUIDELINES FOR COVERAGE

Criteria for all requests: Review based on drug requested (listed below in preferential order).
Must meet the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

1. Patient has tried and failed, or has a contraindication to, estradiol vaginal cream (Estrace) and/or estradiol vaginal tablet (Yuvafem)

   If met, approve indefinitely.
   If not met, do not approve.

RATIONALE

- Current practice guidelines, including those from the North American Menopause Society, state that vaginal estrogen is safe and effective for most patients. These guidelines do not make preference for one vaginal product over another.
- A Cochrane 2016 systematic review of 19 randomized trials including over 4000 patients investigated local estrogen treatment and found that creams, tablets/inserts, and rings were all similarly effective in relieving symptoms of vaginal atrophy.
- KPCO preferred, formulary vaginal estrogen treatment is estradiol vaginal cream (Estrace) for all patients, including those with a history of breast cancer who fail lifestyle modifications and non-hormonal treatment options.

FDA APPROVED INDICATIONS

Vulvar and vaginal atrophy associated with menopause: Treatment of moderate to severe vulvar and vaginal atrophy associated with menopause

Note: The International Society for the Study of Women's Sexual Health and The North American Menopause Society have endorsed the term genitourinary syndrome of menopause (GSM) as new terminology for vulvovaginal atrophy. The term GSM encompasses all genital and urinary signs and symptoms associated with a loss of estrogen due to menopause.

REFERENCES

1. Per Health Plan
2. North American Menopause Society (NAMS), Genitourinary Syndrome of Menopause, 2020
3. Suckling JA, Kennedy R, Lethaby A, Roberts H. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database of Systematic Reviews 2006, Issue 4
4. KPCO FAQ: Management of Urogenital Symptoms in Women with a History of Breast Cancer

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date:05/2023
Revised Date:

VAGINAL ESTROGEN RING

Generic name	Brand name	HICL	GPID	Comments
ESTRADIOL VAGINAL RING	ESTRING		10773	

GUIDELINES FOR COVERAGE

Criteria for all requests: Review based on drug requested (listed below in preferential order).
Must meet the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

1. Estradiol vaginal ring (Estring) - must meet one of the following:
   a. Patient has tried and failed, or has a contraindication to, estradiol vaginal cream (Estrace) and/or estradiol vaginal tablet (Yuvafem)
   b. Patient is physically or mentally unable to apply or insert vaginal estrogen cream/tablet

   If met, approve indefinitely.
   If not met, do not approve.

RATIONALE

- Current practice guidelines, including those from the North American Menopause Society, state that vaginal estrogen is safe and effective for most patients. These guidelines do not make preference for one vaginal product over another.
- A Cochrane 2016 systematic review of 19 randomized trials including over 4000 patients investigated local estrogen treatment and found that creams, tablets/inserts, and rings were all similarly effective in relieving symptoms of vaginal atrophy.
- KPCO preferred, formulary vaginal estrogen treatment is estradiol vaginal cream (Estrace) for all patients, including those with a history of breast cancer who fail lifestyle modifications and non-hormonal treatment options.

FDA APPROVED INDICATIONS

Vulvar and vaginal atrophy associated with menopause: Treatment of moderate to severe vulvar and vaginal atrophy associated with menopause

Note: The International Society for the Study of Women's Sexual Health and The North American Menopause Society have endorsed the term genitourinary syndrome of menopause (GSM) as new terminology for vulvovaginal atrophy. The term GSM encompasses all genital and urinary signs and symptoms associated with a loss of estrogen due to menopause.

REFERENCES

1. Per Health Plan
2. North American Menopause Society (NAMS), Genitourinary Syndrome of Menopause, 2020
3. Suckling JA, Kennedy R, Lethaby A, Roberts H. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database of Systematic Reviews 2006, Issue 4
4. KPCO FAQ: Management of Urogenital Symptoms in Women with a History of Breast Cancer

Creation Date: 05/2022
Effective Date: 01/2024
Reviewed Date:05/2023
Revised Date:

VAGINAL ESTROGEN TABLET

Generic name	Brand name	HICL	GPID	Comments
ESTRADIOL VAGINAL TABLET	YUVAFEM		28107	

GUIDELINES FOR COVERAGE

Criteria for all requests: Review based on drug requested (listed below in preferential order).
Must meet the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:

1. Patient has tried and failed, or has a contraindication to estradiol vaginal cream (Estrace)

   If met, approve indefinitely.
   If not met, do not approve.

RATIONALE

- Current practice guidelines, including those from the North American Menopause Society, state that vaginal estrogen is safe and effective for most patients. These guidelines do not make preference for one vaginal product over another.
- A Cochrane 2016 systematic review of 19 randomized trials including over 4000 patients investigated local estrogen treatment and found that creams, tablets/inserts, and rings were all similarly effective in relieving symptoms of vaginal atrophy.
- KPCO preferred, formulary vaginal estrogen treatment is estradiol vaginal cream (Estrace) for all patients, including those with a history of breast cancer who fail lifestyle modifications and non-hormonal treatment options.

FDA APPROVED INDICATIONS

Vulvar and vaginal atrophy associated with menopause: Treatment of moderate to severe vulvar and vaginal atrophy associated with menopause

Note: The International Society for the Study of Women's Sexual Health and The North American Menopause Society have endorsed the term genitourinary syndrome of menopause (GSM) as new terminology for vulvovaginal atrophy. The term GSM encompasses all genital and urinary signs and symptoms associated with a loss of estrogen due to menopause.

REFERENCES

1. Per Health Plan
2. North American Menopause Society (NAMS), Genitourinary Syndrome of Menopause, 2020
3. Suckling JA, Kennedy R, Lethaby A, Roberts H. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database of Systematic Reviews 2006, Issue 4
4. KPCO FAQ: Management of Urogenital Symptoms in Women with a History of Breast Cancer

Creation Date: 05/2022
Effective Date: 01/2024
Revised: 3/29/2024

Reviewed Date:05/2023
Revised Date:

VENCLEXTA MD RESTRICTION

Generic	Brand	HICL	GCN	Exception/Other
VENETOCLAX	VENCLEXTA	43284		Formulary - Specialty tier

GUIDELINES FOR COVERAGE for Commercial plans

1. The requesting provider is a CPMG or affiliated network Oncologist or Oncology specialist, with appropriate referral, if needed.

   If yes, approve the MD restriction at HICL x 1 year. [specialty tier drug]
   If no, do not approve.

RATIONALE
Venetoclax is formulary, however it should only be prescribed by Oncologists.

FDA APPROVED INDICATIONS

REFERENCES
Creation Date: 11/2022
Effective Date: 12/2022
Reviewed Date:
Revised Date:

VERQUVO (VERICIGUAT)

Generic	Brand	HICL	GCN	Exception/Other
VERICIGUAT	VERQUVO	47075		

GUIDELINES FOR COVERAGE
NEW MEMBER CRITERIA: Must meet the following:
1. Patient is new to KPCO within the past 90 days and is currently stable on Verquvo

If met, approve at HICL indefinitely.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following criteria:
1. Medication is prescribed by a CPMG or affiliated cardiologist
2. Not currently taking PDE-5 inhibitor (e.g., tadalafil, sildenafil, vardenafil) or another soluble guanyl cyclase (sGC) stimulator (e.g., riociguat)
3. GFR >15mL/min
4. Heart failure with previous or current LVEF less than or equal to 45%
5. NYHA Class II-IV
6. Hospitalization for heart failure or received outpatient IV diuretics within past 6 months during which BNP was >300 pg/mL or NT-proBNP was >1000 pg/mL
7. Has contraindications to, is currently using, OR has failed all the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:
   i. ARNI (Entresto)
   ii. Beta blocker
   iii. Aldosterone antagonist (e.g., spironolactone, eplerenone)
   iv. SGLT2 inhibitor

If criteria met, approve at HICL indefinitely.
If criteria are not met, do not approve.

RATIONALE

FDA APPROVED INDICATIONS

REFERENCES

Creation Date: 07/2021
Effective Date: 01/01/2024
Reviewed Date:05/2023
Revised Date: 05/2023

VIBEGRON (GEMTESA)

Generic	Brand	HICL	GCN	Exception/Other
VIBEGRON	GEMTESA TABLETS	47040	49009	Nonformulary with max daily dose of 1/day

GUIDELINES FOR COVERAGE

Review based on diagnoses noted in section A or B:

A. PATIENTS WITH A DIAGNOSIS OF OVERACTIVE BLADDER AND MYASTHENIA GRAVIS: Must meet all of the following criteria:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm.
   2. Patient has a diagnosis of myasthenia gravis.
   3. Meets the drug-specific criteria as noted:
      a. Vibegron (Gemtesa): Patient has tried and failed or has an intolerance or a contraindication to mirabegron (Myrbetriq), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

   If criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.
   If criteria are not met, do not approve.

B. PATIENTS WITH A DIAGNOSIS OF OVERACTIVE BLADDER <u>WITHOUT</u> A DIAGNOSIS OF MYASTHENIA GRAVIS: Must meet all the following criteria:
   1. Patient has a diagnosis of overactive bladder, urge incontinence, urgency, urinary frequency or bladder spasm.
   2. Patient has a history of trial and failure, inadequate response, or intolerance/contraindication to at least one of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception [listed in preferential order]: oxybutynin IR/ER, solifenacin, trospium IR and tolterodine IR/ER.
   3. Meets the drug-specific criteria as noted:
      a. Vibegron (Gemtesa): Patient has tried and failed or has an intolerance or a contraindication to mirabegron (Myrbetriq), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) is/(are) contraindicated or will likely cause an adverse reaction or harm; ii) the required drug(s) is/(are) ineffective based on known clinical characteristics of the patient or drug(s); iii) the patient has tried and failed the required drug(s) or another drug in the same

pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If criteria are met, approve at HICL indefinitely, max daily dose of 1 tablet.
If criteria are not met, do not approve.

RATIONALE

Per Health Plan.

- An adequate response is defined as one less episode of frequency or incontinence per day after an adequate trial of 4-6 weeks. Patients with a diagnosis of myasthenia gravis should avoid the use of anticholinergic agents.
- Preferred formulary agents, in order: oxybutynin ER, oxybutynin IR, solifenacin, trospium IR and oxybutynin syrup.
- Oral oxybutynin is not preferred in patients with dementia or cognitive impairment. Darifenacin is a preferred non-formulary option for patients with history of cognitive issues after solifenacin and trospium IR.
- Preferred nonformulary agents in order: tolterodine IR, tolterodine ER, darifenacin, fesoterodine, trospium ER, mirabegron and vibegron, Oxybutynin gel (Gelnique) and oxybutynin patch (Oxytrol) are excluded from coverage.
- Mirabegron granules are FDA approved for pediatric patients 3 to 17 years of age for neurogenic detrusor overactivity. Both oxybutynin (ER formulation) and solifenacin are FDA approved for neurogenic detrusor overactivity.

FDA APPROVED INDICATIONS

See individual medication.

REFERENCES

Creation Date: 9/26/2019
Effective Date: 01/2024
Reviewed Date: 09/2023
Revised Date: 09/2023

VILOXAZINE (QELBREE)

Generic	Brand	HICL	GCN	Exception/Other
VILOXAZINE	QELBREE	07345		

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA: Must meet all the following:
1. Patient is new to KPCO within the past 90 days and stable on therapy with Qelbree.

If met, approve x3 months.
If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient is at least 6 years of age
2. Patient has a diagnosis of ADHD or ADD
3. Patient has failed or has a contraindication to atomoxetine, or the patient has difficulty swallowing oral capsules

If initial criteria are met, approve at HICL x3 months, max daily dose (MDD) of 3.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Patient has shown improvement of symptoms since starting on the drug

If renewal criteria are met, approve at HICL indefinitely, max daily dose (MDD) of 3.
If renewal criteria are not met, do not approve.

RATIONALE
Viloxazine is a Brand non-stimulant (SNRI) treatment option for ADHD in patients 6 years and older. Atomoxetine represents a generic, non-stimulant (SNRI) treatment option for the same diagnosis and age group without significant differences in efficacy or safety. As such, trial of atomoxetine should be required prior to viloxazine approval/trial. The only exception will be for patients unable to swallow capsules whole as atomoxetine capsules should not be opened (atomoxetine is an ocular irritant) whereas viloxazine capsules may be opened and contents sprinkled on applesauce or pudding for consumption.

FDA APPROVED INDICATIONS
Viloxazine is indicated for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older.

REFERENCES
1. Qelbree [package insert]. Rockville, MD: Supernus Pharmaceuticals, Inc; April 2022.
2. Wolraich ML. et. al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Pediatrics. Oct. 2019, 144 (4) 2019-2528.

Creation Date: 6/7/2023
Effective Date: 01/2024
Reviewed Date:
Revised Date:

VISMODEGIB (ERIVEDGE)

Generic Name	Brand Name	HICL	GPID	Comments
VISMODEGIB	ERIVEDGE 150MG CAPSULE	38455	31307	Nonpreferred for BCC

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
Patient is new to KPCO in the past 90 days and stable on therapy.

If new member criteria are met, approve x1 year.
If new member criteria are not met, proceed to Initial Criteria.

INITIAL CRITERIA: Must have all of the criteria below:

A. Medication is prescribed by a CPMG or affiliated Dermatologist or Oncologist
B. Patient has a diagnosis of Basal Cell Carcinoma (BCC) and one of the following: metastatic disease, recurrence of BCC following surgery or radiation therapy, locally advanced disease and medication is being used to shrink tumor to allow the patient to become a surgical candidate, or the patient is not a candidate for surgery or radiation therapy
C. Must meet all of the following or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug is contraindicated or likely will cause an adverse reaction or harm; ii) based on supporting clinical documentation provided, the required drug is ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the drug was discontinued due to lack of efficacy or effectiveness, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and a received step therapy exception:
    a. Patient has failed sonidegib (Odomzo) due to intolerability even after appropriate dose reductions
    b. Patient's disease has not progressed on sonidegib (Odomzo)

    If initial criteria above are met, approve x2 years.
    If initial criteria above are not met, do not approve.

RENEWAL CRITERIA:
Patient's disease has not progressed since treatment initiation as assessed by treating physician OR treating physician believes patient is deriving significant clinical benefit to justify treatment continuation.

If renewal criteria above are met, then approve x1 year.
If renewal criteria are not met, do not approve.

RATIONALE
Per KPCO treatment guidelines

- Sonidegib is the preferred hedgehog inhibitor per KP National guidelines.
- Sonidegib and vismodegib are accepted as equal in terms of efficacy.
- If patient has contraindication to either sonidegib or vismodegib, they would be considered to have a contraindication to the other.
- A patient may have intolerable toxicities with sonidegib that might not occur with vismodegib.

- If a patient has progression of disease with sonidegib, there is no value in trying vismodegib based on currently available data.

FDA APPROVED INDICATIONS
ODOMZO™ (sonidegib) is a hedgehog pathway inhibitor indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.

ERIVEDGE™ (vismodegib) is a hedgehog pathway inhibitor indicated for the treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and not candidates for radiation.

REFERENCES
Ekim Ekinci, Stephanie Cho

Creation Date: 3/8/2019
Effective Date: 1/2024
Reviewed Date: 1/2024
Revised Date: 1/2024

VMAT2-INHIBITORS
DEUTETRABENAZINE (AUSTEDO)

Generic	Brand	HICL	GCN/GPID	Formulary Status
DEUTETRABENAZINE	AUSTEDO	44192		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
1. Patient is new to KPCO with the past 90 days and is stable on therapy with deutetrabenazine (Austedo)

   If met, approve x3 months to allow time for consideration of formulary alternatives.
   If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient must be age 18 years or older
2. Medication must be prescribed by a CPMG Neurologist or Psychiatrist or an affiliated network Neurologist or Psychiatrist with active referral
3. Must meet the diagnosis/drug specific criteria below:
   a. For Tardive Dyskinesia
      i. Patient must have a diagnosis of tardive dyskinesia, neuroleptic induced tardive dyskinesia or orofacial dyskinesia
      ii. Patient must have Abnormal Involuntary Movement Scale (AIMS) score of at least 6
      iii. Patient has had persistent symptoms of tardive dyskinesia despite trial of dose reduction or discontinuation of [suspected] offending medication or the patient is not a candidate for dose reduction or discontinuation of [suspected] offending medication
      iv. Patient has had persistent symptoms of tardive dyskinesia despite discontinuation of anticholinergics or is not a candidate for discontinuation of anticholinergics
      v. Patient has an intolerance to, contraindication to, or failed a 12-week trial of tetrabenazine, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

   If initial criteria are met, approve x3 months at HICL with the following quantity limit of a max daily dose of 4 tablets.
   If initial criteria are not met, do not approve.

   b. For Chorea associated with Huntington's Disease
      i. Diagnosis of Huntington's Disease must be confirmed by genetic testing
      ii. Patient must have a diagnosis of Chorea associated with Huntington's Disease
      iii. Patient has a contraindication to, intolerance to, or failed a 12-week trial of tetrabenazine, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same

pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If initial criteria are met, approve x 1 year at HICL with the following quantity limit of a max daily dose of 4 tablets.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Medication continues to be prescribed by a CPMG or an affiliated network Neurologist or Psychiatrist with active referral
2. For Tardive Dyskinesia: patient has shown improvement by retaining or decreasing baseline AIMS score since starting the medication
3. For Chorea associated with Huntington's Chorea: patient has demonstrated improvement in symptoms based on clinical assessment

If renewal criteria are met, approve indefinitely at HICL, max 4/day for deutetrabenazine.
If renewal criteria are not met, do not approve.

Medication	Dosage Strengths	Maximum Dose	Quantity Limit for 30 Days
Deutetrabenazine	6 mg, 9 mg, 12 mg	48 mg	#120 tablets
Valbenazine	40 mg, 60 mg, 80 mg	80 mg	#30 capsules

RATIONALE

For New Member Criteria

Deutetrabenazine has 3 month initial approval to allow for a tetrabenazine trial for which there are dose equivalencies guidance and a direct switch option, minimizing risk for uncontrolled abnormal movement related disability. Unfortunately, valbenazine does not have any guidance re: tetrabenazine dose equivalencies or switching strategies so if new member is stable and their cost share is affordable, valbenazine continuation is recommended.

For Tardive Dyskinesia

When treating tardive dyskinesia (TD), guidelines recommend to first evaluate whether dopamine receptor blockers (e.g., antipsychotics, metoclopramide) or anticholinergics (e.g., benztropine, trihexyphenidyl) can be discontinued, dose reduced, or changed as these agents contribute to or may worsen TD. Notably, anticholinergics may be mistakenly prescribed for TD treatment. In general, if a patient is taking a first-generation antipsychotic, changing to a second-generation antipsychotic (SGA) with a lower risk can be considered. If the patient is already taking an SGA, changing to either quetiapine or clozapine is largely considered in clinical practice, though a 2018 meta-analysis also supports changing to aripiprazole or olanzapine. Even with these changes, distressing and disabling TD may persist requiring the use of adjunctive treatment strategies.

If adjustment of the existing medication regimen described above is clinically inappropriate or failed, then adjunctive therapies for TD management can be considered. Tetrabenazine, deutetrabenazine, and valbenazine are all vesicular monoamine transporter 2 (VMAT2) inhibitors. VMAT2 inhibitors have been studied for treatment of moderate-severe TD. Although tetrabenazine has only been approved in the US for the symptomatic management of chorea associated with Huntington's disease, it is reasonable to consider a trial prior to deutetrabenazine and valbenazine as:

- Tetrabenazine is approved for TD management in other countries (e.g., United Kingdom).
- Tetrabenazine has been used off-label with success for the symptomatic management of other hyperkinetic movement disorders including tardive dyskinesia.
- Clinical experience suggests that the drug is effective in TD, including in some severe and/or refractory cases.
- Based on American Academy of Neurology (AAN) guidelines, tetrabenazine is possibly effective and may be considered in the treatment of patients with TD.
- While deutetrabenazine and valbenazine are established as effective for the treatment of TD per AAN guidelines, there are no randomized controlled trials of tetrabenazine for TD nor are there head-to-head studies comparing tetrabenazine to any other active treatment, including deutetrabenazine to valbenazine.
- Tetrabenazine remains the most cost-effective VMAT2 inhibitor option for tardive dyskinesia without known quantifiable comparisons in safety and efficacy relative to deutetrabenazine and valbenazine.
- The only known advantage of deutetrabenazine over tetrabenazine is the need for less frequent dosing (BID instead of TID) at the higher end of the dosing range.

All VMAT2 inhibitors should be used with caution in patients with active suicidal ideation or untreated depression. While tetrabenazine and deutetrabenazine have boxed warnings for depression and suicidality, this is specific to their indication for chorea treatment. Patients with Huntington's disease have a higher risk of depression and suicidality at baseline. In a large longitudinal prospective observational study, tetrabenazine treatment was not found to be associated with an increased risk of depression and suicidality. Even though deutetrabenazine and valbenazine lack this boxed warning for increased depression and suicidality when used for TD, clinical trials have excluded patients with a significant risk of suicidal behavior so no comparisons can be made for differences in depression or suicidality risk amongst VMAT2 inhibitors at this time.

For Chorea associated with Huntington's Disease
According to the American Academy of Neurology (AAN) guidelines on the treatment of chorea of Huntington's disease (2012), if Huntington's disease chorea requires treatment, clinicians should prescribe tetrabenazine (≤ 100 mg/day), amantadine (300 to 400 mg/day), or riluzole (200 mg/day) [Level B] for varying degrees of expected benefit. Deutetrabenazine is not addressed in the guidelines.

FDA APPROVED INDICATIONS

Deutetrabenazine:	Treatment of patients with tardive dyskinesia and chorea associated with Huntington's Disease
Valbenazine:	Treatment of patients with tardive dyskinesia and chorea associated with Huntington's Disease

APPENDIX A. Antipsychotics

First-generation antipsychotics	Second-generation antipsychotics
Chlorpromazine	Aripiprazole
Fluphenazine	Asenapine
Haloperidol	Brexpiprazole
Loxapine	Cariprazine
Molindone	Clozapine
Perphenazine	Iloperidone
Pimozide	Lumateperone
Thioridazine	Lurasidone
Thiothixene	Olanzapine
Trifluoperazine	Paliperidone
	Quetiapine
	Risperidone
	Ziprasidone

APPENDIX B. Anticholinergics commonly prescribed by psychiatry and neurology for drug-induced movement disorders.

- Benztropine
- Diphenhydramine
- Hydroxyzine
- Trihexyphenidyl

REFERENCES

1. Tetrabenazine monograph. Facts and Comparisons online. (www.fco-factsandcomparisons-com.kaiserpermanente.idm.oclc.org), Wolters Kluwer Health, St. Louis, MO. Last updated 5/15/21.
2. Sweetman S (Ed), Martindale: The Complete Drug Reference. London: The Royal Pharmaceutical Society of Great Britain. Electronic version, IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (cited: *5/19/21*).
3. Bhidayasiri R, Fahn S, Weiner WJ, et al. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology.* 2013;81(5):463-469. doi: 10.1212/WNL.0b013e31829d86b6
4. Austedo [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; August 2017.
5. Ingrezza [prescribing information]. San Diego, CA: Neurocrine Biosciences, Inc.; April 2017.
6. Fernandez HH, Factor SA, Hauser RA, et al. Randomized controlled trial of deutetrabenazine for tardive dyskinesia. The ARM-TD study. *Neurology.* 2017;88(21):2003-2010. doi: 10.1212/WNL.0000000000003960
7. Anderson KE, Stamler D, Davis MD, et al. Deutetrabenazine for treatment of involuntary movements in patients with tardive dyskinesia (AIM-TD): a double-blind, randomized, placebo-controlled, phase 3 trial. *Lancet Psychiatry.* 2017;4(8):595-604. doi: 10.1016/S2215-0366(17)30236-5
8. Hauser RA, Factor SA, Marder SR, et al. KINECT 3: a phase 3 randomized, double-blind, placebo-controlled trial of valbenazine for tardive dyskinesia. *Am J Psychiatry.* 2017;174(5):476-484. doi: 10.1176/appi.ajp.2017.16091037
9. Bhidayasiri R, Jitkritsadakul O, Friedman JH and Fahn S. Updating the recommendations for treatment of tardive syndromes: a systematic review of new evidence and practical treatment algorithm. *J Neurol Sci.* 2018;389:67-75. doi: 10.1016/j.jns.2018.02.010

10. Dorsey ER, Brocht AFD, Nichols PE, et al. Depressed mood and suicidality in individuals exposed to tetrabenazine in a large Huntington disease observational study. *J Huntingtons* Dis. 2013;2(4):509-515. doi: 10.3233/JHD-130071
11. American Hospital Formulary Service (AHFS). Drug Information 2021 [STAT!Ref Web site]. Available at: http://online.statref.com. [via subscription only]
12. Sweetman S (Ed), Martindale: The Complete Drug Reference. London: The Royal Pharmaceutical Society of Great Britain. Electronic version, IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (cited: May 26, 2021)
13. American Psychiatric Association (APA). The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia, 3rd ed. Washington, DC: APA, 2021.
14. Bhidayasiri R, Fahn S, Weiner W, et al. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. 2013;81(22): 1968.
15. Carbon M, Kane JM, Leucht S, et al. Tardive dyskinesia risk with first- and second-generation antipsychotics in comparative randomized controlled trials: a meta-analysis. World Psychiatry 2018;17:330-40.
16. Armstrong MJ, Miyasaki JM. Evidence-based guideline: pharmacologic treatment of chorea in Huntington disease: report of the guideline development subcommittee of the American Academy of Neurology. Neurology. 2012;79:597-603. (last reaffirmed 2015)

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VMAT2-INHIBITORS
VALBENAZINE (INGREZZA)

Generic	Brand	HICL	GCN/GPID	Formulary Status
VALBENAZINE TOSYLATE	INGREZZA	44202		Nonformulary

GUIDELINES FOR COVERAGE

NEW MEMBER CRITERIA:
1. Patient is new to KPCO with the past 90 days and is stable on therapy valbenazine (Ingrezza)

   If met, approve indefinitely at HICL, max 1 per day.
   If not met, review by Initial Criteria.

INITIAL CRITERIA: Must meet all the following:
1. Patient must be age 18 years or older
2. Medication must be prescribed by a CPMG Neurologist or Psychiatrist or an affiliated network Neurologist or Psychiatrist with active referral
3. Must meet the diagnosis/drug specific criteria below:
   a. For Tardive Dyskinesia
      i. Patient must have a diagnosis of tardive dyskinesia, neuroleptic induced tardive dyskinesia or orofacial dyskinesia
      ii. Patient must have Abnormal Involuntary Movement Scale (AIMS) score of at least 6
      iii. Patient has had persistent symptoms of tardive dyskinesia despite trial of dose reduction or discontinuation of [suspected] offending medication or the patient is not a candidate for dose reduction or discontinuation of [suspected] offending medication
      iv. Patient has had persistent symptoms of tardive dyskinesia despite discontinuation of anticholinergics or is not a candidate for discontinuation of anticholinergics
      v. Patient has an intolerance to, contraindication to, or failed a 12-week trial of tetrabenazine, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

      If initial criteria are met, approve x3 months at HICL with the following quantity limit of a max daily dose of 1 capsule.
      If initial criteria are not met, do not approve.

   b. For Chorea associated with Huntington's Disease
      i. Diagnosis of Huntington's Disease must be confirmed by genetic testing
      ii. Patient must have a diagnosis of Chorea associated with Huntington's Disease
      iii. Patient has a contraindication to, intolerance to, or failed a 12-week trial of tetrabenazine, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was

discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception

If initial criteria are met, approve x 1 year at HICL with the following quantity limit of a max daily dose of 1 capsule.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. Medication continues to be prescribed by a CPMG or an affiliated network Neurologist or Psychiatrist with active referral
2. For Tardive Dyskinesia: patient has shown improvement by retaining or decreasing baseline AIMS score since starting the medication
3. For Chorea associated with Huntington's Chorea: patient has demonstrated improvement in symptoms based on clinical assessment

If renewal criteria are met, approve indefinitely at HICL, max 1/day.
If renewal criteria are not met, do not approve.

Medication	Dosage Strengths	Maximum Dose	Quantity Limit for 30 Days
Deutetrabenazine	6 mg, 9 mg, 12 mg	48 mg	#120 tablets
Valbenazine	40 mg, 60 mg, 80 mg	80 mg	#30 capsules

RATIONALE

For New Member Criteria

Deutetrabenazine has 3 month initial approval to allow for a tetrabenazine trial for which there are dose equivalencies guidance and a direct switch option, minimizing risk for uncontrolled abnormal movement related disability. Unfortunately, valbenazine does not have any guidance re: tetrabenazine dose equivalencies or switching strategies so if new member is stable and their cost share is affordable, valbenazine continuation is recommended.

For Tardive Dyskinesia

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FDA APPROVED INDICATIONS

Deutetrabenazine:	Treatment of patients with tardive dyskinesia and chorea associated with Huntington's Disease
Valbenazine:	Treatment of patients with tardive dyskinesia and chorea associated with Huntington's Disease

APPENDIX A. Antipsychotics

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Perphenazine	Iloperidone
Pimozide	Lumateperone
Thioridazine	Lurasidone
Thiothixene	Olanzapine
Trifluoperazine	Paliperidone
	Quetiapine
	Risperidone
	Ziprasidone

APPENDIX B. Anticholinergics commonly prescribed by psychiatry and neurology for drug-induced movement disorders.

- Benztropine
- Diphenhydramine
- Hydroxyzine
- Trihexyphenidyl

REFERENCES

1. Tetrabenazine monograph. Facts and Comparisons online. (www.fco-factsandcomparisons-com.kaiserpermanente.idm.oclc.org), Wolters Kluwer Health, St. Louis, MO. Last updated 5/15/21.
2. Sweetman S (Ed), Martindale: The Complete Drug Reference. London: The Royal Pharmaceutical Society of Great Britain. Electronic version, IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (cited: *5/19/21*).
3. Bhidayasiri R, Fahn S, Weiner WJ, et al. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology.* 2013;81(5):463-469. doi: 10.1212/WNL.0b013e31829d86b6
4. Austedo [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; August 2017.
5. Ingrezza [prescribing information]. San Diego, CA: Neurocrine Biosciences, Inc.; April 2017.
6. Fernandez HH, Factor SA, Hauser RA, et al. Randomized controlled trial of deutetrabenazine for tardive dyskinesia. The ARM-TD study. *Neurology.* 2017;88(21):2003-2010. doi: 10.1212/WNL.0000000000003960
7. Anderson KE, Stamler D, Davis MD, et al. Deutetrabenazine for treatment of involuntary movements in patients with tardive dyskinesia (AIM-TD): a double-blind, randomized, placebo-controlled, phase 3 trial. *Lancet Psychiatry.* 2017;4(8):595-604. doi: 10.1016/S2215-0366(17)30236-5
8. Hauser RA, Factor SA, Marder SR, et al. KINECT 3: a phase 3 randomized, double-blind, placebo-controlled trial of valbenazine for tardive dyskinesia. *Am J Psychiatry.* 2017;174(5):476-484. doi: 10.1176/appi.ajp.2017.16091037
9. Bhidayasiri R, Jitkritsadakul O, Friedman JH and Fahn S. Updating the recommendations for treatment of tardive syndromes: a systematic review of new evidence and practical treatment algorithm. *J Neurol Sci.* 2018;389:67-75. doi: 10.1016/j.jns.2018.02.010

10. Dorsey ER, Brocht AFD, Nichols PE, et al. Depressed mood and suicidality in individuals exposed to tetrabenazine in a large Huntington disease observational study. *J Huntingtons* Dis. 2013;2(4):509-515. doi: 10.3233/JHD-130071
11. American Hospital Formulary Service (AHFS). Drug Information 2021 [STAT!Ref Web site]. Available at: http://online.statref.com. [via subscription only]
12. Sweetman S (Ed), Martindale: The Complete Drug Reference. London: The Royal Pharmaceutical Society of Great Britain. Electronic version, IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (cited: May 26, 2021)
13. American Psychiatric Association (APA). The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia, 3rd ed. Washington, DC: APA, 2021.
14. Bhidayasiri R, Fahn S, Weiner W, et al. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. 2013;81(22): 1968.
15. Carbon M, Kane JM, Leucht S, et al. Tardive dyskinesia risk with first- and second-generation antipsychotics in comparative randomized controlled trials: a meta-analysis. World Psychiatry 2018;17:330-40.
16. Armstrong MJ, Miyasaki JM. Evidence-based guideline: pharmacologic treatment of chorea in Huntington disease: report of the guideline development subcommittee of the American Academy of Neurology. Neurology. 2012;79:597-603. (last reaffirmed 2015)

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VORTIOXETINE (TRINTELLIX)

Generic	Brand	HICL	GCN	Exception/Other
VORTIOXETINE HYDROBROMIDE	TRINTELLIX	40637	35346, 35347, 35349	

GUIDELINES FOR COVERAGE
Must meet either 1, or 2-5 of the following, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception:

1. Patient is new to KPCO within the past 90 days and is stable on vortioxetine
2. Patient must have a diagnosis of major depressive disorder (MDD)
3. Patient has tried and failed treatment with vilazodone
4. Patient has tried and failed treatment or has an intolerance or contraindication to treatment with at least 2 SSRIs/SNRIs, with at least one SSRI (fluoxetine, citalopram, escitalopram, sertraline, paroxetine) and at least one SNRI (venlafaxine or duloxetine)
5. Patient has tried and failed treatment with at least 1 atypical antidepressant (bupropion, nefazodone, or mirtazapine)

If above criteria (either #1 or 2-5) are met, approve indefinitely at HICL, max 1 unit per day
If above criteria are not met, do not approve.

Criteria for overriding quantity limits: Must meet one of the following:

1. Dose is above FDA-labeled maximum when prescribed by a CPMG or affiliated behavioral health provider.
2. Request is due to patient needing doses other than those of the current available strengths (i.e. vortioxetine 15 mg daily).
3. One time approval for titration sig at the start of therapy

If criteria 1 or 2 are met, approve indefinitely for max number of units needed per day.
If criteria 3 is met, approve x1 fill (30 days) for max number of units needed per day.
If criteria are not met, do not approve.

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ePA Questions

1. Is the patient stable on therapy with vortioxetine?
2. For patients noted stable on therapy, start date of therapy (MMDDYY):
3. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
4. Is there reasoning why alternatives (citalopram tablets/solution, escitalopram tablets, fluoxetine capsules/solution, paroxetine IR tablets, sertraline tablets/susp; venlafaxine ER capsules (37.5 mg, 75 mg, 150 mg), duloxetine capsules (20 mg, 30 mg, 60 mg); vilazodone tablets; bupropion XL tablets (150 mg, 300 mg), bupropion IR tablets (75 mg); mirtazapine tablets) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

RATIONALE
Ensure appropriate criteria are used for the management of requests for vortioxetine according to approved indication, dosing, and national treatment guidelines.

FDA APPROVED INDICATIONS
Treatment of major depressive disorder

HOW SUPPLIED
Vortioxetine is supplied as 5 mg, 10 mg and 20 mg tablets

REFERENCES
Creation date: 07/2020
Effective date: 04/2024
Reviewed date: 03/2024
Revised date: 03/2024

VOSORITIDE (VOXZOGO)

Generic	Brand	HICL	GPID	Comments
VOSORITIDE	VOXZOGO	47677		Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Prescriber must be a Pediatric Endocrinologist or Geneticist
2. Bone age is either females less than 14 or males less than 16
3. Diagnosis of achondroplasia documented and genetic testing confirming FGFR3 mutation associated with achondroplasia

If initial criteria are met, approve at HICL x 12 months.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following criteria:
1. Individual's condition responded while on therapy (example: improved limb proportion/anthropometric criteria) as provided by pediatric endocrinologist or geneticist
2. Open epiphyses or bone age is either females less than 14 or males less than 16

If renewal criteria are met, approve at HICL x 12 months.
If renewal criteria are not met, do not approve.

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ePA Questions
Initial Review Questions
1. Current bone age of the patient:
2. Has the patient completed genetic testing that confirms FGFR3 mutation associated with achondroplasia?

Renewal Review Questions
1. Current bone age of the patient:
2. Has the patient's condition improved while on therapy?

REFERENCES

Specialty drug to be dispensed by Accredo Specialty Pharmacy, Memphis, TN

Creation Date: 05/2022
Effective Date: 04/2024
Reviewed Date: 03/2024
Revised Date: 11/2023

ZILUCOPLAN (ZILBRYSQ)

Generic	Brand	HICL	GCN	Exception/Other
ZILUCOPLAN	ZILBRYSQ	49273	54876, 54877, 54878	

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. The patient is 18 years of age or older
2. Prescribed by a neurologist
3. Positive serologic test for anti-acetylcholine receptor (AChR) antibodies[§]
4. Patient must have a diagnosis of Generalized Myasthenia Gravis (gMG)
5. No history of thymic neoplasms or a thymectomy within 12 months prior to treatment initiation
6. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV
7. Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) total score of at least 6 at baseline
8. Patient is currently taking chronic corticosteroid with pyridostigmine as prescribed unless there is an intolerance or contraindication to one or both, and the patient has tried and failed, or has contraindication to, all of the following therapies, or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception
    a. ONE nonsteroidal immunosuppressive therapy (NSIST): azathioprine[¥], cyclophosphamide[¥], mycophenolate mofetil[¥], cyclosporine[¥], methotrexate[¥]
    b. TWO biologic therapies: rituximab or its biosimilar, chronic IVIG, efgartigimod (Vyvgart) [requires authorization], ravulizumab (Ultomiris) [requires authorization]

If criteria are met, approve x6 months.
If criteria are not met, do not approve.

RENEWAL CRITERIA: Must meet all the following:
1. The patient has at least a 2-point improvement in the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) from baseline

If renewal criteria are met, authorize for 12 months.
If renewal criteria are not met, do not approve.

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ePA Questions
Initial Review Questions
1. Does the patient have a positive serologic test for anti-acetylcholine receptor (AChR) antibodies?
2. Does the patient have history in the last 12 months of thymic neoplasms or a thymectomy?
3. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of this patient (1-5):
4. Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) score prior to treatment with zilucoplan:

5. Date of MG-ADL score:
6. Has the patient failed other treatments for this indication? If yes, must list the medication, strength, dates of treatment, and reason for discontinuation in Provider Comment section below or attach applicable chart notes.
7. Is there reasoning why alternatives (chronic corticosteroid with pyridostigmine, azathioprine tablets (50 mg), cyclosporine capsules (25 mg, 100 mg), methotrexate 2.5 mg tablets or 25mg/ml vials, mycophenolate mofetil 250 mg capsules or 500 mg tablets, cyclophosphamide capsules) are not suitable? If yes, must list reasoning in Provider Comment section below or attach applicable chart notes.

Renewal Review Questions

1. Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) since starting treatment with zilucoplan:
2. Date of MG-ADL score:

RATIONALE

Treatment – Refractory Myasthenia Gravis

Summary of current biological therapies for gMG.

- Complement C5 inhibitors:
  - Eculizumab (Soliris) for IV infusion– approved 2017
  - Ravulizumab (Ultomiris) for IV infusion – approved 4/2022
  - Zilucoplan (Zilbrysq) for SC self-administration – approved 10/2023
- FcRn inhibitors (aka neonatal Fc receptor inhibitors- halts IgG recycling):
  - Efgartigimod (Vyvgart) for IV infusion – approved 12/2021
  - Efgartigimod and Hyaluronidase (Vyvgart-Hytrulo for SC injection by health care professional) – approved 12/2021
  - Rozanolixizumab (Rystiggo) (for SC infusion by health care professional) – approved 6/2023

Both 2020 treatment guidelines, lack of comparative clinical trial data, and side effect profile indicate that zilucoplan and other complement inhibitors should be used as 3rd line treatments, specifically when first and second-line therapies fail. Though low utilization is expected, given its high cost, exceedingly judicious prescribing with the guidance of PA guidelines is warranted. The KP ETSP treatment guidelines recommend that rituximab +/- oral immunosuppressants be used prior to the newer agents. Off-label use of rituximab is supported by a CMS-approved Compendia resource. LexiComp categorizes off-label rituximab for use in Myasthenia Gravis (refractory) with level of evidence [B,G] and Micromedex categorizes off-label use of rituximab for Myasthenia Gravis (refractory); Strength of recommendation Adult, Class1. Strength of evidence, Adult Category B.

FDA APPROVED INDICATIONS:
Generalized Myasthenia gravis

APPENDIX

¥ Peer-Reviewed Evidence-Based and CMS Compendia Approved Therapies: rituximab, azathioprine, mycophenolate

§Positive antibody status does NOT include anti-muscle-specific receptor tyrosine kinase (MuSK) or anti-low-density lipoprotein receptor-related protein (LRP4) antibodies.

REFERENCES

1. Zilbrysq subcutaneous injection [prescribing information]. Symra, GA: UCB: October 2023.

2. National Institute of Neurological Disorders and Stroke (NINDS). Myasthenia Gravis Fact Sheet. National Institutes of Health (NIH) Publication No. 17-768. Publication last updated: March 2020. Available at: https://www.ninds.nih.gov/sites/default/files/migratedocuments/myasthenia_gravis_e_march_2020_508c.pdf. Accessed on February 12, 2024.
3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. Neurology. 2016;87:419–425.
4. Howard JF, Bresch S, Genge A, et al on behalf of the RAISE study team. Safety and efficacy of zilucoplan in patients with generalized myasthenia gravis (RAISE): a randomized, double-blind, placebo-controlled, phase 3 study. Lancet Neurology. 2023;22:395-406.
5. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. Neurology. 2021;96(3):114-122.

Creation Date: 03/2024
Effective Date: 04/2024
Reviewed Date:
Revised Date:

ZOLMITRIPTAN NASAL SPRAY - STEP THERAPY

Generic	Brand	HICL	GCN	Exception/Other
ZOLMITRIPTAN NASAL SPRAY	ZOMIG		18972	Generic - Formulary

Step Therapy Criteria

Patient has tried and failed, or had an intolerance/allergy to any sumatriptan product (oral, nasal or injection - HICL 12779), or the provider has submitted justification and supporting clinical documentation that states one of the following: i) the required drug(s) will likely cause an adverse reaction or harm; ii) the required drug(s) is/are ineffective based on known clinical characteristics of the patient or drug; iii) the patient has tried and failed the required drug(s) or another drug in the same pharmacological class or with the same mechanism of action, and the use of the drug was discontinued due to lack of efficacy, diminished effect or an adverse event; iv) the patient is stable on the requested drug after undergoing step therapy or after having sought and received a step therapy exception.

If met, override restriction only for generic zolmitriptan nasal spray at GPID-g indefinitely
If not met, do not approve.

RATIONALE
Per Health Plan

REFERENCE
Note: this product does have a quantity limit per fill applied to it. The claims will look for the quantity limit first and if that is met will begin the step therapy look back for HICL 12779 in the claim history.

Since Zomig nasal spray is available as a generic, the brand will remain non-formulary.

Creation date: 01/2022
Effective date: 02/2024
Reviewed date: 01/2024
Revised date: 01/2024

ZONISAMIDE 100 MG/5 ML SUSPENSION - AGE RESTRICTION CRITERIA

Generic	Brand	HICL	GCN	Exception/Other
ZONISAMIDE SUSPENSION 100 MG/5 ML	ZONISADE		52582	

GUIDELINES FOR COVERAGE

INITIAL AND RENEWAL CRITERIA: ONE of the following criteria must be met:
1. Patient is less than or equal to 10 years old
2. Patient is using an alternative administration route, such as a gastrostomy tube
3. Dose cannot be administered by using a combo of the zonisamide capsules
4. Patient cannot swallow capsules whole

If any criterion is met, approve x1 year.
If no criteria are met, do not approve, and suggest changing to capsule strengths that can be used in combination to achieve desired dose.

RATIONALE
Per Health Plan.

General Clinical Criteria for solutions/suspension
1. Age is less than or equal to 10 years old
2. Presence of gastrostomy
3. Dose does not allow use of halved, whole or combo of tablet
4. Dose does not use whole capsule (cannot “cut” capsules in half)
5. Clinical condition where unable to swallow crushed/opened tablets/capsules (i.e., esophageal stricture)

FDA APPROVAL
1. Adjunctive therapy in the treatment of focal (partial) onset seizures in adolescents > 16 years of age and adults

REFERENCES
Per Health Plan

Creation date: 09/2023
Effective date: 03/2024
Reviewed date: 12/2023
Revised date: 12/2023

ZURANOLONE (ZURZUVAE)

Generic	Brand	HICL	GCN	Exception/Other
ZURANOLONE	ZURZUVAE	49127	43601, 45723, 48261	Nonformulary

GUIDELINES FOR COVERAGE

INITIAL CRITERIA: Must meet all the following:
1. Patient must be between 18 and 45 years of age.
2. Patient has a diagnosis of postpartum depression (PPD).
3. Moderately severe to severe depression which correlates to a Patient Health Questionnaire-9 (PHQ-9) score of at least 15.
4. Treatment initiated within 12 months postpartum.
5. Patient must not have active psychosis, bipolar disorder, schizophrenia, schizoaffective disorder, or alcohol or drug use disorders.
6. Patient must not have received a full 14-day course of past treatment in current episode of PPD (typically conceptualized as onset no earlier than third trimester of pregnancy and up to 12 months postpartum)

If initial criteria are met, approve x 2 weeks only.
If initial criteria are not met, do not approve.

RENEWAL CRITERIA:
This drug is not eligible for renewal. Zuranolone use beyond 14 days in a single treatment course for PPD has not been studied and is not recommended.

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ePA Questions
1. Current Patient Health Questionnaire-9 (PHQ-9) score:
2. Date of completion of Current PHQ-9 (MMDDYY):
3. How many months postpartum is this patient?
4. Does the patient have any of the following (Check all that apply):
    a. active psychosis
    b. bipolar disorder
    c. schizophrenia
    d. schizoaffective disorder
    e. alcohol or drug use disorders
5. Has the patient completed a 14-day course of zuranolone treatment at any time during this episode of PPD?

RATIONALE
Criteria for drug approval closely matches clinical trial criteria and KP emerging therapeutics strategy program (ETSP) interregional practice recommendations. A full course of treatment is defined as a 14-d course of zuranolone at any dose.

Zuranolone is the only FDA approved *oral* treatment option for postpartum depression as brexanolone requires IV continuous administration x 60hr in an inpatient setting with an associated FDA Risk Evaluation and Mitigation Strategy (REMS) program. Zuranolone offers a novel mechanism of action as a neuroactive steroid that is fast acting (e.g. symptom improvement noted as early as Day 3) with a 14-

d treatment course yielding lasting effects up to 4 weeks after last zuranolone dose (has not been studied longer). However, zuranolone, should not be used if pregnant, caution warranted if breastfeeding*, has a boxed warning regarding impaired ability to drive or engage in other potentially hazardous activities due to CNS depressant effects for up to 12 hours after administration during the 14-day treatment course**, must be taken with 400-1,000 calories, has clinically significant interactions with CYP3A4 inducers and inhibitors, and is not known to treat other comorbid psychiatric conditions (e.g. GAD, PTSD) or depressive illness e.g. bipolar depression. Zuranolone has not been studied head-to-head with traditional treatment options. Updated ACOG guidelines for the treatment of depression during pregnancy and postpartum recommend off-label SSRIs as first line with serotonin norepinephrine reuptake inhibitors as reasonable alternatives for moderate-severe PPD. For milder PPD symptoms, cognitive behavioral therapy has been shown to be effective.

*Data suggests <1% zuranolone enters breastmilk but its boxed warning re: CNS depressant effects and impaired driving ability urges caution even with small amount of infant exposure. Conversely, many antidepressants are considered safe in breastfeeding.

**Clinical trials suggest zuranolone is generally well-tolerated with common adverse events reported as somnolence, dizziness, and sedation. 1 patient receiving zuranolone 30mg dose experienced a confusional state. Nonetheless it does have the associated boxed warning re: impaired driving ability and CNS depressant effects. Conversely, brexanolone, a neuroactive steroid available/administered as an IV formulation, does have a REMS program related to the boxed warning of “excessive sedation and sudden loss of consciousness” that requires continuous pulse oximetry monitoring and patients to be accompanied during interactions with their children.

FDA APPROVED INDICATIONS

1. **Depression, postpartum.** Treatment of postpartum depression in adults.

REFERENCES

1. ACOG clinical practice guideline: treatment and management of mental health conditions during pregnancy and postpartum. Obstetrics and Gynecology; June 2023:141(5):1262-1288.
2. ETSP Interregional Practice Recommendations: Brexanolone (Zulresso) and Zuranolone (Zurzuvae) for Treatment of Postpartum Depression. November 2023.
3. Zurzuvae. Package Insert. Biogen MA Inc. November, 1, 2023.
4. Deligiannidis KM, et al. Effect of zuranolone vs placebo in postpartum depression. JAMA Psychiatry. 2021;78(9):951-959.
5. Deligiannidis KM, et al. Effect of zuranolone on concurrent anxiety and insomnia symptoms in women with postpartum depression. J Clin Psychiatry. 2023;84(1):22m14475.
6. Deligiannidis KM, et al. Zuranolone for the treatment of postpartum depression. Am J Psychiatry. 2023;180:668-675.

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