DICHLORPHENAMIDE

Generic	Brand	HICL	GCN	Exception/Other
DICHLORPHENAMIDE	KEVEYIS	03642		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of primary hypokalemic periodic paralysis and have all of the following criteria been met?
   - The patient has tried acetazolamide AND a potassium-sparing diuretic (i.e., spironolactone, triamterene)
   - The patient is at least 18 years old
   - The prescription is written by or currently supervised by a neurologist
   - The patient does not have hepatic insufficiency, pulmonary obstruction, or a health condition that warrants concurrent use of high-dose aspirin

   If yes, **approve for two months by HICL with a quantity limit of #4 tablets per day.**
   If no, continue to #2.

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INITIAL CRITERIA (CONTINUED)

2. Does the patient have a diagnosis of primary hyperkalemic periodic paralysis or Paramyotonia Congenita and have all of the following criteria been met?
   - The patient has tried acetazolamide AND a thiazide diuretic (i.e., hydrochlorothiazide)
   - The patient is at least 18 years old
   - The prescription is written by or currently supervised by a neurologist
   - The patient does not have hepatic insufficiency, pulmonary obstruction, or a health condition that warrants concurrent use of high-dose aspirin

   If yes, **approve for two months by HICL with a quantity limit of #4 tablets per day.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **DICHLORPHENAMIDE** requires that the patient has a diagnosis of primary hypokalemic periodic paralysis, primary hyperkalemic periodic paralysis, or Paramyotonia Congenita and meets all of the following criteria:
   - patient age of at least 18 years
   - prescription written by or currently supervised by a neurologist
   - patient does not have hepatic insufficiency, pulmonary obstruction, or a health condition that warrants concurrent use of high-dose aspirin.

   Additional guideline requirements apply.
   - **For patient with primary hypokalemic periodic paralysis**, a trial of acetazolamide AND a potassium-sparing diuretic (i.e., spironolactone, triamterene) is required.
   - **For patient with primary hyperkalemic periodic paralysis or Paramyotonia Congenita**, a trial of acetazolamide AND a thiazide diuretic (i.e., hydrochlorothiazide) is required.

RENEWAL CRITERIA

1. Has the patient experienced at least two fewer attacks per week from their baseline?

   If yes, **approve for 12 months by HICL with a quantity limit of #4 tablets per day.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **DICHLORPHENAMIDE** renewal requires that the patient experiences at least two fewer attacks per week from their baseline.

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RATIONALE

Promote appropriate utilization of dichlorphenamide based on FDA approved indication, dosing, and contraindications. A step therapy has been implemented to promote cost-effective therapies based on previously available agents. A specialist edit has also been implemented to promote appropriate diagnosis and on-label use due to rare neuromuscular condition.

Keveyis is the first FDA approved treatment for primary hyperkalemic and primary hypokalemic periodic paralysis. The only clinical trials demonstrating a benefit for treatment in periodic paralysis involve the carbonic anhydrase inhibitor, dichlorphenamide. Dichlorphenamide was initially approved in 1958 as the branded drug Daranide for the treatment of elevated intraocular pressure but was discontinued in May 2003. In 2015, it was reintroduced as Keveyis as an orphan drug.

Affecting almost 5,000 people in the United States, periodic paralysis is a rare neuromuscular disorder related to a defect in muscle ion channels, characterized by episodes of painless but debilitating muscle weakness or paralysis (lasting minutes to an hour or two), which may be precipitated by heavy exercise, fasting, or high-carbohydrate meals. Periodic paralysis (PP) is classified as hypokalemic when episodes occur in association with low potassium blood levels or as hyperkalemic when episodes can be induced by elevated potassium. Most cases of periodic paralysis are hereditary, usually with an autosomal dominant inheritance pattern. Acquired cases of hypokalemic PP have been described in association with hyperthyroidism. When there is an established family history, episodes of periodic paralysis often require no further diagnostic evaluation. Otherwise, the diagnosis of PP is suggested by documentation of hypo/hyperkalemia during a typical attack of weakness. Even when this is demonstrated, diagnosis is not as easily accomplished as other testing is required to rule out alternative diagnoses. Genetic testing is available for most, but not all of the mutations underlying hypokalemic PP. Evidence of myotonia (seen in up to 80% with this subtype) during electromyographic (EMG) examination can help support the diagnosis of hyperkalemic PP.

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RATIONALE (CONTINUED)
Nonpharmacologic interventions that may be effective for preventing attacks include a low-carbohydrate diet and refraining from vigorous exercise. When attacks continue to be disabling, prophylactic treatment is indicated to avoid morbidity, even mortality, which can be associated with hospitalization and acute treatment. When lifestyle changes are not sufficiently effective, symptomatic potassium supplementation, diuretics, and medications such as carbonic anhydrase inhibitors are used. The mechanism whereby carbonic anhydrase inhibitors are effective in PP is not clear, but appears to be independent of carbonic anhydrase inhibition. Studies in animal models suggest that these agents trigger calcium-activated potassium channels on skeletal muscle. Acetazolamide, another carbonic anhydrase inhibitor, is also commonly reported to be effective in reducing attacks when dosed at 250mg twice daily. However, one retrospective study found that only half of patients respond to acetazolamide therapy. The subset of patients who might find acetazolamide treatment helpful are those who experience mild, fluctuating weakness between attacks. For hypokalemic PP, potassium-sparing diuretics such as spironolactone (100mg daily) or triamterene (150mg daily) can be used as a supplement or as an alternative to a carbonic anhydrase inhibitor in patients who experience worsening or intolerance. For hyperkalemic PP, thiazide diuretics (i.e. hydrochlorothiazide 25-50mg daily) have been reported as helpful in controlling attacks in some patients.

DOSAGE
Initiate dosing at 50 mg twice daily. The initial dose may be increased or decreased based on individual response, at weekly intervals (or sooner in case of adverse reaction). The maximum total daily dose is 200 mg.

Primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants are a heterogeneous group of conditions, for which the response to Keveyis may vary. Therefore, prescribers should evaluate the patient's response after 2 months of treatment to decide whether Keveyis should be continued.

FDA APPROVED INDICATION
Keveyis is an oral carbonic anhydrase inhibitor indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.

AVAILABLE STRENGTHS
- 50 mg tablet

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REFERENCES

- Keveyis [Prescribing Information]. Hawthorne, NY: Taro Pharmaceuticals; August 2015.
- UpToDate, Inc. Hypokalemic periodic paralysis. UpToDate [database online]. Waltham, MA. Available at: http://www.uptodate.com/home/index.html. Updated July 23, 2014.
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- Jeffrey S. FDA Nod for Keveyis in Primary Periodic Paralysis. Available at: http://www.medscape.com/viewarticle/850050 Updated August 25, 2015.
- Periodic paralysis international. Available at: http://hkpp.org/patients/hyperkpp-FAQ Updated June 25, 2011.

Library	Commercial	NSA
Yes	Yes	No

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Commercial Effective: 01/01/16

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