SIMEPREVIR

Generic	Brand	HICL	GCN	Exception/Other
SIMEPREVIR	OLYSIO	40771		

***********Customer Service/PAC Alert************
(For Internal Use Only)

THIS IS A HIGH-IMPACT MEDICATION. DO NOT OVERRIDE OR APPROVE WITHOUT SUBMITTING FOR PHARMACIST REVIEW.

GUIDELINES FOR USE

1. Does the patient meet ALL of the following?
   - A diagnosis of chronic hepatitis C, genotype 1
   - Patient has a recent HCV infection documented by one detectable HCV RNA level within the past 6 months
   - Age of at least 18 years old
   - This medication is prescribed by or in consultation with a gastroenterologist, infectious disease specialist, physician specializing in the treatment of hepatitis (for example, a hepatologist), or a specially trained group such as ECHO (Extension for Community Healthcare Outcomes) model

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Has the patient completed a prior full course of therapy with 1) any HCV protease inhibitor [for example, telaprevir (Incivek), simeprevir (Olysio), or boceprevir (Victrelis)] OR 2) regimen containing an NS5A inhibitor (e.g., Harvoni, Epclusa, Technivie, Viekira Pak or Viekira XR, Zepatier, or Daklinza-containing regimen) and has not achieved a sustained virologic response (SVR)?

   If yes, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #3.

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GUIDELINES FOR USE (CONTINUED)

3. Does the patient meet at least **ONE** of the following criteria?
   - Decompensated or compensated cirrhosis
   - Limited life expectancy (less than 12 months) due to non-liver related comorbid conditions
   - The requested medication is being used with ribavirin **AND** peginterferon alfa
   - Patient is taking any of the following medications that are not recommended for concurrent use with Olysio:
     - Amiodarone, carbamazepine, phenytoin, phenobarbital, oxcarbazepine, rifampin, rifabutin, rifapentine, erythromycin (does not include topical formulations), clarithromycin, telithromycin, itraconazole, ketoconazole, posaconazole, fluconazole (does not include topical formulations), voriconazole, dexamethasone, cisapride, cyclosporine, rosuvastatin (dose above 10mg), or atorvastatin (dose above 40mg)
     - Any of the following HIV medications:
       - A cobicistat-containing medication (e.g., Stribild or Genvoya [elvitegravir/cobicistat/ emtricitabine/tenofovir], Evotaz, Prezcobix, or Tybost)
       - An HIV protease inhibitor (e.g., atazanavir, fosamprenavir, lopinavir, indinavir, nelfinavir, saquinavir, tipranavir, ritonavir, or darunavir/ritonavir)
       - Delavirdine, etravirine, nevirapine, or efavirenz

   If yes, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #4.

4. Is the request for a combination regimen with Sovaldi plus Olysio for 12 weeks?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

5. Does the patient meet **ONE** of the following?
   - The patient has contraindications to Epclusa, Harvoni and Mavyret
   - The patient has previously failed a short trial with Epclusa, Harvoni or Mavyret (e.g., inability to tolerate, adverse effect early in therapy); [**NOTE:** An individual who has completed a full course of therapy with Epclusa, Harvoni or Mavyret that did not achieve SVR will not be approved]

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

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GUIDELINES FOR USE (CONTINUED)

6. Does the patient meet **ONE** of the following?
   - Treatment naïve
   - Treatment experienced with prior treatment with peginterferon/ribavirin

   If yes, **approve for 12 weeks by HICL for #1 capsule per day.**
   CLINICAL PHARMACISTS: Please review Sovaldi prior authorization guideline, member history, and hepatitis C MRF if available to ensure appropriate length of approval.
   APPROVAL TEXT: Regimen approved: Sovaldi + Olysio for 12 weeks.

   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: The guideline named **SIMEPREVIR (Olysio)** requires a diagnosis of chronic hepatitis C, genotype 1. The following criteria must also be met:
- Concurrent use of Olysio with Sovaldi
- Patient is 1) treatment naïve or 2) treatment-experienced with prior treatment with peginteferon/ ribavirin
- Patient is at least 18 years old
- Patient is currently supervised by a gastroenterologist, infectious disease specialist, physician specializing in the treatment of hepatitis (for example, a hepatologist), or a specially trained group such as ECHO (Extension for Community Healthcare Outcomes) model
- Patient must have documentation of recent HCV infection by at least one detectable HCV RNA level within the past 6 months
- Patient must have had a short trial of Harvoni, Mavyret or Epclusa (e.g., adverse effect or intolerance early in therapy) **OR** contraindications to ALL three agents; [an individual who has completed a full course of therapy that did not achieve sustained virologic response (SVR) will not be approved]

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GUIDELINES FOR USE (CONTINUED)

Olysio will not be approved for the following patients:

- Patients who have failed a full course of treatment with 1) any HCV protease inhibitor (for example, simeprevir [Olysio], telaprevir [Incivek] or boceprevir [Victrelis]) **OR** 2) a regimen containing an NS5A inhibitor (e.g., Harvoni, Epclusa, Technivie, Viekira Pak or Viekira XR, Zepatier, or Daklinza-containing regimen)
- Patients with compensated cirrhosis or decompensated cirrhosis
- Patients with a limited life expectancy (less than 12 months) due to non-liver related comorbid conditions
- Patients who are using Olysio with ribavirin and peginterferon alfa
- Patients who are taking any of the following medications that are not recommended for concurrent use with Olysio:
  - Amiodarone, carbamazepine, phenytoin, phenobarbital, oxcarbazepine, rifampin, rifabutin, rifapentine, erythromycin, clarithromycin, telithromycin, itraconazole, ketoconazole, posaconazole, fluconazole, voriconazole, dexamethasone, cisapride, cyclosporine, rosuvastatin (dose above 10mg), or atorvastatin (dose above 40mg)
  - Any cobicistat-containing medication (e.g., Stribild or Genvoya [elvitegravir/cobicistat/emtricitabine/tenofovir], Evotaz, Prezcobix, or Tybost)
  - Delavirdine, etravirine, nevirapine, or efavirenz
  - Any HIV protease inhibitor (e.g., atazanavir, fosamprenavir, lopinavir, indinavir, nelfinavir, saquinavir, tipranavir, ritonavir, or darunavir/ritonavir)

RATIONALE

Ensure appropriate utilization of Olysio based on FDA approved indication.

FDA APPROVED INDICATIONS

For the treatment of chronic hepatitis C infection as a component of a combination antiviral treatment regimen.

Limitations:

- Olysio with peginterferon alfa (IFN) and ribavirin (RBV): Screening patients with HCV genotype 1a infection for the presence of virus with the NS3 Q80K polymorphism at baseline is strongly recommended. Alternative therapy should be considered for patients infected with HCV genotype 1a containing the Q80K polymorphism.
- Olysio must not be used as monotherapy
- Olysio is not recommended in patients who have previously failed a regimen that included Olysio or any other HCV protease inhibitor.

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FDA APPROVED INDICATIONS (CONTINUED)

FDA APPROVED DOSAGE

Olysio 150mg once daily is added to peginterferon alfa and ribavirin for the first twelve weeks of therapy for genotype 1 or genotype 4 infection. Olysio is a component of triple therapy with peginterferon and ribavirin that will require a total treatment duration of 24 or 48 weeks.

- All treatment-naïve and prior relapser patients not co-infected with HIV, with or without cirrhosis, should receive an additional 12 weeks of peginterferon alfa and ribavirin after completing 12 weeks of treatment with Olysio, peginterferon alfa and ribavirin; (total treatment duration of peginterferon/ribavirin is 24 weeks).
- All treatment-naïve and prior relapser patients *co-infected with HIV with cirrhosis*, should receive an additional 36 weeks of peginterferon alfa and ribavirin after completing 12 weeks of treatment with Olysio, peginterferon alfa and ribavirin; (total treatment duration of peginterferon/ribavirin is 24 weeks).
- All prior non-responder patients (including partial and null-responders), with or without cirrhosis and with or without HIV should receive an additional 36 weeks of peginterferon alfa and ribavirin after completing 12 weeks of treatment with Olysio, peginterferon alfa and ribavirin (total treatment duration of peginterferon/ribavirin is 48 weeks).

Olysio 150mg once daily can also be used with sofosbuvir 400mg once daily in an all-oral regimen for patients with genotype 1 infection. This regimen is administered for a duration of 12 or 24 weeks:

Duration of therapy:	
Treatment naïve or treatment experienced, without cirrhosis	12 weeks
Treatment naïve or treatment experienced, with cirrhosis	24 weeks

For peginterferon alfa/ribavirin and Sovaldi (sofosbuvir) specific dosage instructions, refer to their respective prescribing information.

No dosage recommendations can be made for patients of East Asian ancestry or for patients with severe hepatic impairment.

OTHER INFORMATION

Olysio is FDA-approved to treat HCV genotypes 1 and 4, but AASLD recommends use of Olysio only for genotype 1 infection. See **hcvguidelines.org for most recent recommendations.**

SAFETY

Common adverse reactions (incidence in greater than 20% of clinical trial participants and at least 3% higher frequency than those receiving placebo with ribavirin and peginterferon alfa) occurring in those receiving Olysio in combination with ribavirin and peginterferon alfa include rash (including photosensitivity), pruritus, and nausea.

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FDA APPROVED INDICATIONS (CONTINUED)

SAFETY
Concurrent use of Olysio with another agent such as Sovaldi and amiodarone may increase the risk of symptomatic bradycardia.

Patients should be counseled regarding the risk of photosensitivity reactions while taking Olysio. Patients must use sun protection measures and limit sun exposure during Olysio therapy. Consider discontinuation of therapy if a photosensitivity reaction occurs.

Contraindications include all contraindications known for peginterferon alfa and ribavirin since Olysio is administered in combination with these agents.

Patients with genotype 1a NS3 Q80K polymorphism are likely to experience a significant reduction in efficacy and/or treatment failure when taking Olysio. Patients with genotype 1a should be screened at baseline for the NS3 Q80K polymorphism, and alternative therapy should be considered for any patient infected with a virus that contains the NS3 Q80K polymorphism.

Strong CYP 3A4 inducers and inhibitors may affect Olysio serum levels, and should be avoided when possible in patients taking Olysio. CYP3A4 inducers, including phenytoin, carbamazepine, oxcarbazepine, phenobarbital and rifampin may increase serum levels, while CYP3A4 inhibitors, including erythromycin, clarithromycin, itraconazole, ketoconazole, posaconazole, fluconazole, voriconazole, darunavir/ritonavir and ritonavir, may decrease Olysio serum levels. Olysio may increase levels of HMG CoA reductase inhibitors, including rosuvastatin, atorvastatin, and simvastatin and others, and may require statin dose reduction. Olysio may increase digoxin levels and affect serum levels of certain immunosuppressants, including cyclosporine, tacrolimus, and sirolimus. See prescribing information for a full description of all significant drug interactions.

Olysio is pregnancy category C; however, when administered in regimens with peginterferon alfa and ribavirin (pregnancy category X), avoid use during pregnancy in females receiving therapy and female partners of males receiving therapy. Patients must have a negative pregnancy test before starting therapy, use two methods of contraception during therapy, and have a monthly pregnancy test.

The safety and efficacy of Olysio has not been studied in liver transplant patients or patients with severe renal impairment, end-stage renal disease, or those requiring dialysis.

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FDA APPROVED INDICATIONS (CONTINUED)

SAFETY
Concurrent Sovaldi and Olysio therapy +/- ribavirin (12 or 24 week treatment)

- Results from the COSMOS trial showed excellent SVR rates from an all-oral combination of Olysio 150 mg once daily plus Sovaldi 400 mg once daily when used for patients infected with HCV genotype 1. Patients were randomized to 12 or 24 weeks of the Olysio plus Sovaldi combination, with or without ribavirin. Results were similar in groups treated with or without ribavirin. Results were similar for 12 or 24 weeks of treatment, and high SVR rates were seen regardless of Metavir fibrosis stage or status of previous treatment (prior null responders to peginterferon/ribavirin versus treatment naïve).
- Patients were either treatment experienced (prior null responders to peginterferon/ribavirin) with Metavir fibrosis stage of 0 or 2 (n=80, Cohort 1)) or a treatment naïve or prior null responders with Metavir fibrosis stage of 3 or 4 (n=87, Cohort 2).
- The two-drug combination treatment for 12 weeks showed an SVR12 rate of 93% in previously treated patients (Cohort 1) , and SVR of 96% when used in combination with ribavirin as triple therapy. The two-drug combination treatment for 24 weeks showed an SVR12 rate of 79% and 93%, with and without ribavirin, respectively. Cohort 1 had no viral breakthrough during therapy, although 3 patients with genotype 1a and Q80K polymorphism experienced viral relapse after completing therapy.
- Cohort 2 has SVR4 results available at the time of AASLD/IDSA guideline publication. The 12-week treatment group demonstrated a 100% SVR in treatment naïve patients with and without ribavirin. The prior null responders in cohort 2 also showed excellent SVR rates with 100% and 93% with or without ribavirin, respectively. Again, no viral breakthrough was observed during treatment and after therapy one patient with genotype 1a and Q80K polymorphism experienced viral relapse after completing therapy.

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REFERENCES

- Guidance from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) Recommendations for Testing, Managing, and Treating hepatitis C. Available online at http://www.hcvguidelines.org/full-report-view Accessed November 3, 2017.
- Jacobson I. SVR results of a once-daily regimen of simeprevir (TMC-438) plus sofosbuvir (GS-7977) with or without ribavirin in cirrhotic and non-cirrhotic HCV genotype 1 treatment-naïve and prior null responder patients: the COSMOS study. Program and abstracts of American Association for the Study of Liver Diseases The Liver Meeting® 2013; November 1-5, 2013. Abstract LB-3.
- Lawitz E, Sulkowski M, Ghalib R, Rodriguez-Torres M, Younossi Z, et al. Simeprevir plus sofosbuvir with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naïve patients: the COSMOS randomized study. Lancet 2014; Jul 26. pii: S0140-6736(14)61036-9. doi: 10.1016/S0140-6736(14)61036-9. [Epub ahead of print]
- Olysio [Prescribing Information]. Titusville, NJ: Janssen Pharmaceuticals; November 2014.
- Sovaldi [Prescribing Information]. Foster City, CA: Gilead Sciences; December 2013.

Library	Commercial	NSA
Yes	Yes	No

Part D Effective: N/A
Commercial Effective: 01/01/18

Created: 02/14
Client Approval: 12/17

P&T Approval: 10/17