VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Hepatitis C – Olysio® (simeprevir capsules –Janssen [obsolete 05/25/2018])

REVIEW DATE: 10/10/2018

OVERVIEW

Olysio is a hepatitis C virus (HCV) NS3/4A protease inhibitor (PI) indicated for the treatment of chronic HCV infection as a component of a combination antiviral treatment regimen.[1] The following points should be considered when initiating Olysio for treatment of chronic HCV:

- Olysio must not be used as monotherapy;
- The efficacy of Olysio in combination with peginterferon and ribavirin (PR) is substantially reduced in patients infected with genotype 1a chronic HCV with an NS3 Q80K polymorphism at baseline compared with patients infected with HCV genotype 1a without the Q80K polymorphism. Screening patients with 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; and
- The efficacy of Olysio has not been studied in patients who have previously failed therapy with a treatment regimen that includes Olysio or other HCV protease inhibitors (PIs) [i.e., Incivek® (telaprevir tablets) and Victrelis® (boceprevir capsules)].

The prescribing information notes that prior to initiation of treatment with Olysio with Sovaldi® (sofosbuvir tablets) screening patients infected with HCV genotype 1a for the presence of virus with the NS3 Q80K polymorphism is not strongly recommended but may be considered.[1]

There are no data directly comparing the clinical efficacy of Olysio with the other NS3/4A PIs. However, efficacy (sustained virologic response [SVR]) has been established in treatment-naïve adults with genotype 1 HCV as well as prior treatment-failure (null responders and partial responders) and relapse patients.[2-6] The approval of Olysio in combination with Sovaldi represents the second approved all-oral (interferon-free) regimen approved for patients with genotype 1 chronic HCV.

Dosing

Olysio + PR

Olysio Food and Drug Administration (FDA)-approved for once-daily (QD) dosing administered in combination with PR (as triple-therapy) for 12 weeks.[1] To prevent treatment failure, the dose of Olysio must not be reduced or interrupted. In all patients, treatment with Olysio should be initiated in combination with PR and should be administered for 12 weeks. All *treatment-naïve* and *prior relapse patients*, including those with cirrhosis, should receive an additional 12 weeks of PR after completing 12 weeks of triple-therapy with Olysio PR (total treatment duration of 24 weeks). All *prior non-responder patients* (including partial and null responders), including those with cirrhosis, should receive an additional 36 weeks of PR after completing 12 weeks of treatment with Olysio PR (total duration of treatment 48 weeks).

Olysio + Sovaldi

In patients without cirrhosis who are treatment-naïve or have previously been treated with PR the recommended treatment regimen is Olysio + Sovaldi for 12 weeks; in patients with cirrhosis who are treatment-naïve or have previously been treated with PR the recommended treatment regimen is Olysio + Sovaldi for 24 weeks.[1]

Q80K Polymorphism

The Division of Anti-viral Products (DAVP) recommends that all genotype 1a patients be screened for the Q80K polymorphism given the high frequency of the Q80K polymorphism in the US population and its significant impact on rates of sustained viral response 12 weeks after the end of treatment (SVR12).[2] Alternative treatment options for patients with this polymorphism should be considered. No Q80K-related reduction in efficacy was observed during the pivotal trials with Incivek or Victrelis. The HCV GenoSure® NS3/4A drug resistance test has been approved to screen for the Q80K polymorphism.[6] It also provides a comprehensive sequence-based analysis of drug resistance for HCV protease inhibitors.

The Q80K polymorphism is a common polymorphism found in patients with Genotype 1a in the US.[2] In an analysis pooling patients from the Phase III and Phase IIb trials with Olysio, of the 298 patients with CHC genotype 1a from the US with sequencing data, 48% had the Q80K polymorphism at baseline. None of the genotype 1b patients in the US with sequencing data had the Q80K polymorphism at baseline. The observed prevalence of the Q80K polymorphism was 30% in patients with genotype 1a and 0.5% in patients with genotype 1b in the Phase IIb and III trials.[1]

In the pooled analysis of the Phase III trials with Olysio + PR (QUEST-1, QUEST-2, and PROMISE), the efficacy of Olysio in combination with PR was substantially reduced in patients infected with HCV genotype 1a with the NS3 Q80K polymorphism at baseline.[1] The difference was noted in both of the pooled treatment-naïve studies and the relapser study (SVR rates of 84% vs. 43%, respectively [treatment-naïve] and 78% vs. 24%, respectively [relapse study]).[3] The overall SVR in the subgroup of patients with baseline Q80K polymorphism was no better than that in the placebo group. In contrast to the other studies, in prior non-responder patients (including null, partial, and relapse patients) in the Phase IIb ASPIRE[4] trial rates of SVR did not differ between patients with and without the Q80K polymorphism. However, prescribing information still supports the use of the test prior to initiating Olysio and does not support use in patients with the polymorphism.[1] If used in combination with Sovaldi, baseline resistance testing for the Q80K polymorphism may be considered in patients with genotype 1a HCV.[5]

Clinical Efficacy

For efficacy information with Olysio see the *Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary*.

Guidelines

Please refer to the *Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary* for a summary of the American Association for the Study of Liver Diseases (AASLD) guidelines. For the most up-to-date information always visit the guidelines.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Olysio. Criteria are based on the guidance issued by American Association for the Study of Liver Diseases (AASLD)/International Antiviral Society-USA (IAS-USA), FDA-approved indications, clinical data, and expert review. Approval durations differ by baseline characteristics. Because of the specialized skills required for evaluation and diagnosis of patients treated with Olysio as well as the monitoring required for adverse events (AEs) and efficacy, approval requires Olysio to be prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or liver transplant physician.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Olysio is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Chronic Hepatitis C Virus (HCV) Genotype 1.** Approve Olysio for the specified duration in patients that meet the all of following criteria (A, B, C, and D):
   - **A)** The patient is ≥ 18 years of age; AND
   - **B)** Olysio is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
   - **C)** For patients with genotype 1a, the patient does not have the Q80K polymorphism (Note: testing for the Q80K polymorphism is not required for patients with genotype 1b); AND
   - **D)** The patient meets ONE of the following conditions (i or ii):
     - **i. Approve for 12 weeks** if Olysio will be prescribed in combination with Sovaldi AND the patient does not have cirrhosis; OR
     - **ii. Approve for 24 weeks if** Olysio will be prescribed in combination with Sovaldi AND the patient has cirrhosis.

   In the opinion of a specialist reviewing the data, we have adopted these criteria.

Other Uses with Supportive Evidence

2. **Recurrent Hepatitis C Virus (HCV) Post-Liver Transplantation, Genotype 1.** Approve Olysio for 12 weeks in patients who meet all of the following criteria (A, B, C, and D):
   - **A)** The patient is ≥ 18 years of age; AND
   - **B)** The patient has genotype 1 recurrent hepatitis C virus (HCV) after a liver transplantation; AND
   - **C)** Olysio is prescribed by or in consultation with one of the following prescribers who is affiliated with a liver transplant center[14], a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
   - **D)** If the patient has genotype 1a, the patient does not have the Q80K polymorphism (Note: testing for the Q80K polymorphism is not required for patients with genotype 1b); AND
   - **E)** Olysio is prescribed in combination with Sovaldi.

AASLD guidelines offer Olysio as an alternative regimen in patients with genotype 1 recurrent HCV post liver transplantation with compensated disease (Sovaldi + Olysio ± weight-based ribavirin [WBR] for 12 weeks [Class I, Level B]).[3] There are limited data assessing the combination of Olysio and Sovaldi ± ribavirin in the post-transplant setting.[7]

In the opinion of a specialist reviewing the data, we have adopted these criteria.

3. **Patient Has Been Started on Olysio.** Approve Olysio for an indication or condition addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indications) or other use with supportive evidence to complete a course of therapy. Authorization for Olysio should not exceed 24 weeks of therapy. For example if a patient is eligible for 12 weeks of therapy and has received 3 weeks of therapy, approve 9 weeks of therapy to complete the 12-week course.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Olysio has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Life Expectancy Less Than 12 Months Due to Non-Liver Related Comorbidities.** Patients with limited life expectancy for whom HCV therapy would not improve symptoms or prognosis do not require treatment.[3] According to AASLD guidance, the panel continues to recommend treatment for all patients with chronic HCV infection, *except* those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. For these patients, the benefits of HCV treatment are unlikely to be realized, and palliative care strategies should take precedence.

2. **Monotherapy with Olysio.** Olysio must not be used as monotherapy.[1,3]

3. **Pediatric Patients (Age < 18 years).** The safety and efficacy of Olysio have not been established in pediatric patients. Olysio is indicated for use in *adult* patients with genotype 1 chronic HCV.[1] Guidelines from the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Practice (NASPGHAN) for the diagnosis and management of hepatitis C infection in infants, children, and adolescents state that the PIs should only be used in children in the context of a clinical trial as they have not been studied in children nor are there published pharmacokinetic or safety data in the pediatric population.[5] In the opinion of a specialist physician reviewing the data we have adopted this criterion.

4. **Patient Has Failed Therapy with Olysio or Another NS3/4A Protease Inhibitor for Hepatitis C Virus [HCV] (i.e., Incivek [telaprevir tablets] or Victrelis [boceprevir capsules]). [Note: this does not include patients who have discontinued Incivek or Victrelis due to an adverse reaction to Incivek or Victrelis. Failure includes prior null response, partial response, or relapse]** The efficacy of Olysio has not been studied in patients who have previously failed therapy with a treatment regimen that includes Olysio or other HCV protease inhibitors.[1]

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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4. Zeuzem S, Berg T, Gane E, et al. Simeprevir increases rate of sustained virologic response among treatment-experienced patients with HCV genotype-1 infection: a phase IIb trial. *Gastroenterology*. 2014;146(2):430-441.
5. Mack CL, Gonzalez-Peralta RP, Gupta N, et al. North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Practice Guidelines: Diagnosis and Management of Hepatitis C Infection in Infants, Children and Adolescents. *J Pediatr Gastroenterol Nutr*. 2012;54(6):838-55.
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7. Pungpapong S, Aqel B, Leise M, et al. Multicenter experience using simeprevir and sofosbuvir with or without ribavirin to treat hepatitis C genotype 1 after liver transplant. Hepatology. 2015 Jun;61(6):1880-1886.