Clinical Policy: Simeprevir (Olysio)

Reference Number: CP.PHAR.280
Effective Date: 09.16
Last Review Date: 02.20
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Simeprevir (Olysio™) is an inhibitor of the hepatitis C virus (HCV) nonstructural protein 3/4A (NS3/4A) protease.

FDA Approved Indication(s)

Olysio is indicated for the treatment of adults with chronic HCV infection:

- In combination with sofosbuvir in patients with HCV genotype 1 without cirrhosis or with compensated cirrhosis
- In combination with peginterferon alfa (Peg-IFN-alfa) and ribavirin (RBV) in patients with HCV genotype 1 or 4 without cirrhosis or with compensated cirrhosis

Limitation(s) of use:

- Efficacy of Olysio in combination with Peg-IFN-alfa and RBV is substantially reduced in patients infected with HCV genotype 1a with an NS3 Q80K polymorphism.
- Olysio is not recommended in patients who have previously failed therapy with a treatment regimen that included Olysio or other HCV protease inhibitors.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Olysio is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Hepatitis C Infection (must meet all)**:**

1. Diagnosis of chronic HCV infection as evidenced by detectable serum HCV RNA levels by quantitative assay in the last 6 months;
2. Confirmed HCV genotype 1;
   **Chart note documentation and copies of lab results are required*
3. Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease specialist, or provider who has expertise in treating HCV based on a certified training program (*see Appendix F*);
4. Age ≥ 18 years;
5. Member must use sofosvubir/velpatasvir (Epclusa®) (*authorized generic preferred*) or Mavyret™ unless both are contraindicated or clinically significant adverse effects are experienced;

6. Life expectancy ≥ 12 months with HCV treatment;
7. Member agrees to participate in a medication adherence program including both of the following components (a and b):
   a. Medication adherence monitored by pharmacy claims data or member report;
   b. Member's risk for non-adherence identified by adherence program or member/prescribing physician follow-up at least every 4 weeks;
8. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
9. Dose does not exceed 150 mg (1 capsule) per day.

Approval duration: 12 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration; The AASLD/IDSA HCV guidance updated May 2018 no longer recommends use of simeprevir for the treatment of genotype 1 with compensated cirrhosis for 24 weeks)*

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Chronic Hepatitis C Infection (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Both of the following (i and ii):
      i. Documentation supports that member is currently receiving Olysio for chronic HCV infection and has recently completed at least 60 days of treatment with Olysio;
      ii. Confirmed HCV genotype 1;
2. Member is responding positively to therapy;
3. Dose does not exceed 150 mg (1 capsule) per day.

Approval duration: up to a total of 12 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration; The AASLD/IDSA HCV guidance updated May 2018 no longer recommends use of simeprevir for the treatment of genotype 1 with compensated cirrhosis for 24 weeks)*

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
FDA: Food and Drug Administration
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
NS3/4A, NS5A/B: nonstructural protein
PegIFN: pegylated interferon
RBV: ribavirin
RNA: ribonucleic acid

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Epclusa® (sofosbuvir/ velpatasvir)	Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis: **Genotype 1** One tablet PO QD for 12 weeks	Epclusa: sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-naïve chronic HCV infection: **Genotype 1** Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 8 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-experienced with pegIFN/RBV: **Genotype 1** Without cirrhosis: Three tablets PO QD for 8 weeks With compensated cirrhosis: Three tablets PO QD for 12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): Because Olysio is used only in combination with other antiviral drugs (including Peg-IFN-alfa and RBV) for the treatment of chronic HCV infection, the contraindications to other drugs also apply to the combination regimen.
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfected with HCV and HBV.

Appendix D: Direct-Acting Antivirals for Treatment of HCV Infection

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
Daklinza	Daclatasvir				
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

Appendix E: General Information

- Hepatitis B Virus Reactivation (HBV) is a Black Box Warning for all direct-acting antiviral drugs for the treatment of HCV. HBV reactivation has been reported when treating HCV for patients co-infected with HBV, leading to fulminant hepatitis, hepatic failure, and death, in some cases. Patients should be monitored for HBV reactivation and hepatitis flare during HCV treatment and post-treatment follow-up, with treatment of HBV infection as clinically indicated.

Appendix F: Healthcare Provider HCV Training

Acceptable HCV training programs and/or online courses include, but are not limited to the following:

- Hepatitis C online course (https://www.hepatitisc.uw.edu/): University of Washington is funded by the Division of Viral Hepatitis to develop a comprehensive, online self-study course for medical providers on diagnosis, monitoring, and management of hepatitis C virus infection. Free CME and CNE credit available.
- Fundamentals of Liver Disease (https://liverlearning.aasld.org/fundamentals-of-liver-disease): The AASLD, in collaboration with ECHO, the American College of Physicians (ACP), CDC, and the Department of Veterans Affairs, has developed Fundamentals of Liver Disease, a free, online CME course to improve providers' knowledge and clinical skills in hepatology.
- Clinical Care Options: http://www.clinicaloptions.com/hepatitis.aspx
- CDC training resources: https://www.cdc.gov/hepatitis/resources/professionals/trainingresources.htm

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1: Treatment-naive or treatment-experienced patients without cirrhosis	Sovaldi 400 mg plus Olysio 150 mg PO QD for 12 weeks	Olysio: 150 mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Genotype 1 or 4: Treatment-naïve and treatment-experienced liver transplant patients with or without compensated cirrhosis	Sovaldi 400 mg plus Olysio 150 mg PO QD with or without weight-based RBV for 12 weeks	Olysio: 150 mg/day	AASLD-IDSA (updated May 2018)

AASLD/IDSA treatment guidelines for chronic hepatitis C infection are updated at irregular intervals; refer to the most updated AASLD/IDSA guideline for most accurate treatment regimen.
Treatment-experienced refers to previous treatment with peginterferon/RBV unless otherwise stated
The use of Olysio in combination with peginterferon and ribavirin for the treatment of chronic HCV GT1 or 4 is no longer recommended by the AASLD/IDSA guidelines.
AASLD/IDSA HCV guidance updated May 2018 no longer recommends use of simeprevir for the treatment of genotype 1 with compensated cirrhosis or for the treatment of genotype 4.

VI. Product Availability

Capsule: 150 mg

VII. References

1. Olysio Prescribing Information. Titusville, NJ: Janssen Therapeutics.; November 2017. Available at https://www.olysio.com/shared/product/olysio/prescribing-information.pdf. Accessed May 1, 2019.
2. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). HCV guidance: recommendations for testing, managing, and treating hepatitis C. Last updated May 24, 2018. Available at: https://www.hcvguidelines.org/. Accessed May 1, 2019.
3. Platt L, Easterbrook P, Gower E, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. Lanet Infect Dis 2016;16:797-808. http://dx.doi.org/10.1016/
4. Centers for Disease Control and Prevention. HIV and viral hepatitis: fact sheet. June 2017. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/hiv-viral-hepatitis.pdf. Accessed May 1, 2019.
5. Wolitski R. When it comes to curing hepatitis c, your health care provider may not need to be a specialist. U.S. Department of Health & Human Services. Last updated September 20, 2017. Available at: https://www.hhs.gov/hepatitis/blog/2017/09/20/study-calls-for-expansion-of-hepatitis-c-treatment.html. Accessed October 30, 2019.

6. CDC. Viral hepatitis: Q&As for health professionals. Last updated July 2, 2019. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed October 30, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created, split from CP.PHAR.17 Hepatitis C Therapies. HCV RNA levels over six-month period added to confirm infection is chronic. Life expectancy "≥12 months if HCC and awaiting transplant" is modified to indicate "≥12 months with HCV therapy." Testing criteria reorganized by "no cirrhosis"/"cirrhosis" consistent with the regimen tables; HCC population is included under "cirrhosis" and broadened to incorporate HCC amenable to curative measures (resection, ablation, transplant). Methods to diagnose fibrosis/cirrhosis are modified to require presence of HCC, liver biopsy or a combination of one serologic and one radiologic test. Serologic and radiologic tests are updated and correlated with METAVIR per Appendix B. Removed creatinine clearance restriction. Criteria added excluding post-liver transplantation unless regimens specifically designate. Dosing regimens are presented in Appendix D and E per AASLD guidelines and FDA-approved indications. The initial approval is shortened to 8 weeks.	08.16	09.16
Policy converted to new template. Deleted references to peg-IFN as Olysio/RBV/peg-IFN is not recommended by AASLD; added requirement for prevention of HBV reactivation. Consolidated appendix D and E into dosing and administration in section V; added maximum dose requirement; initial approval duration expanded to full 24 weeks, limited continued therapy approval duration to 24 weeks, deleted viral load and adherence requirement in continued, added documentation of positive response to therapy and continuity of care, and removed CIs in section II, added reference column in section V. Added preferencing information requiring Mavyret for FDA-approved indications. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Exception made to require Hep B screening.	08.17	09.17
Removed the following language: "If a lower cost alternative regimen carries an equal or higher AASLD-IDSA rating, a clinical contraindication or intolerance must be present for the alternative regimen prior to approval."	09.17	
3Q 2018 annual review: removed requirement for HBV verification; expanded duration of tx required for COC from 30 days to 60 days; required verification of genotype for COC; removed conditional requirement for RBV CI; reduced maximum approval duration from	05.22.18	08.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
24 weeks to 12 weeks per AASLD/IDSA guidance updated September 2017; references reviewed and updated.		
Removed advanced liver disease requirement to align with 2018 AASLD/IDSA hepatitis C treatment guidelines.	04.18.19	05.19
3Q 2019 annual review: removed documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy; references reviewed and updated.	06.26.19	08.19
RT4: updated Mavyret dosing recommendations to 8 weeks total duration of therapy for treatment-naïve HCV with compensated cirrhosis across all genotypes (1-6).	10.03.19	
Added new prescriber requirement to include a "provider who has expertise in treating HCV based on a certified training program"; added preferencing for AG Epclusa, Mavyret, or AG Harvoni (8 weeks only); removed redirection to Mavyret based on contraindications criteria; Appendix F (Healthcare Provider HCV Training) added.	12.17.19	02.20
Removed redirection to Harvoni AG per March SDC and prior clinical guidance.	03.03.20	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a

discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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