Clinical Policy: Simeprevir (Olysio)

Reference Number: OH.PHAR.PPA.11
Effective Date: 01.19
Last Review Date: 12.18
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 90 days;
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 other hepatitis specialist. Consult must be within the past year with documentation of recommended regimen;
4. Age ≥ 18 years;
5. Member has at least one of the following contraindications to Mavyret (a or b):
   a. Decompensated cirrhosis (Child-Pugh B or C) confirmed by lab findings and clinical notes;

b. Receiving treatment with efavirenz or atazanavir;
**See Appendix F for additional details on acceptable contraindications*

6. Member does not have limited life expectancy (less than 12 months) due to non-liver-related comorbid conditions;
7. Documentation in provider notes (**must be submitted**) showing that member has had no abuse of alcohol and drugs for the previous 6 months. **MUST submit** urine drug screen for members with history of abuse of drugs other than alcohol. Counseling **MUST** be provided and documented regarding non-abuse of alcohol and drugs as well as education on how to prevent HCV transmission;
8. Documentation of Metavir Fibrosis score, documentation of the method used and date fibrosis score was obtained;
9. Prescriber has discussed the importance of adherence to office visits, lab testing, imaging, procedures and to taking requested regimen as prescribed. Prescriber attests that member will be adherent to treatment plan;
10. If prescribed regimen includes ribavirin, the following criteria must be met (must meet all):
    a. Member or member's partner(s) is NOT pregnant and is NOT planning to become pregnant during treatment or within 6 months of stopping;
    b. Agreement that member and their partner(s) will use two forms of effective contraception during treatment and for at least 6 months after stopping;
    c. Verification that monthly pregnancy tests will be performed throughout treatment;
    d. Members with CrCl <50 ml/min (moderate or severe renal dysfunction, ESRD, HD) should have dosage reduced;
    e. At the time of request, member does NOT meet any of the following:
        1) History of severe or unstable cardiac disease
        2) Diagnosis of hemoglobinopathy (e.g., thalassemia major, sickle cell anemia)
        3) Hypersensitivity to ribavirin
        4) Baseline platelet count <70,000 cells/mm3
        5) ANC <1500 cells/mm3
        6) Hb <12 g/dl in women or <13 g/dl in men
11. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
12. 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 September 2017 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. Must meet 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 September 2017 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
APRI: AST to platelet ratio
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
IQR: interquartile range
MRE: magnetic resonance elastography
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
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-naïve or treatment-experienced with pegIFN/RBV: **Genotype 1** Without cirrhosis:	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Three tablets PO QD for 8 weeks With compensated cirrhosis: Three tablets PO QD for 12 weeks	

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

- 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.

Appendix D: Approximate Scoring Equivalencies using METAVIR F3/F4 as Reference

Fibrosis/ Cirrhosis	Serologic Tests*				Radiologic Tests†		Liver Biopsy‡	
	Fibro Test	FIBRO Spect II	APRI	FIB-4	FibroScan (kPa)	MRE (kPa)	METAVIR	Ishak
Advanced fibrosis	≥0.59	≥42	>1.5	>3.25	≥9.5	≥4.11	F3	F4-5
Cirrhosis	≥0.75	≥42	>1.5	>3.25	≥12.0	≥4.71	F4	F5-6

*Serologic tests:
FibroTest (available through Quest as FibroTest or LabCorp as FibroSure)
FIBROSpect II (available through Prometheus Laboratory)
APRI (AST to platelet ratio index)
FIB-4 (Fibrosis-4 index: includes age, AST level, platelet count)
†Radiologic tests:
FibroScan (transient elastography)
MRE (magnetic resonance elastography)
‡Liver biopsy (histologic scoring systems):
METAVIR F3/F4 is equivalent to Knodell, Scheuer, and Batts-Ludwig F3/F4 and Ishak F4-5/F5-6
METAVIR fibrosis stages: F0 = no fibrosis; F1 = portal fibrosis without septa; F2 = few septa; F3 = numerous septa without cirrhosis; F4 = cirrhosis

Appendix E: 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

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

Appendix F: 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.
- Acceptable medical justification for inability to use Mavyret (preferred product):
  - Severe hepatic disease (Child-Pugh C): use of Mavyret is not recommended due to higher exposures of glecaprevir and pibrentasvir.
  - Moderate hepatic disease (Child-Pugh B): although not an absolute contraindication, use of Mavyret is not recommended in patients with moderate hepatic disease (Child-Pugh B) due to lack of safety and efficacy data.
    - Following administration of Mavyret in HCV infected subjects with *compensated* cirrhosis (Child-Pugh A), exposure of glecaprevir was approximately 2-fold and pibrentasvir exposure was similar to non-cirrhotic *HCV infected* subjects.
    - At the clinical dose, compared to *non-HCV infected* subjects with *normal hepatic function*, glecaprevir AUC was 100% higher in Child-Pugh B subjects, and increased to 11-fold in Child-Pugh C subjects. Pibrentasvir AUC was 26% higher in Child-Pugh B subjects, and 114% higher in Child-Pugh C subjects.
  - Drug-drug interactions with one or more the following agents:
    - Atazanavir
    - Efavirenz
- Unacceptable medical justification for inability to use Mavyret (preferred product):
  - Black Box Warning (BBW): currently or previously infected with hepatitis B virus. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Therefore it is not a valid clinical reason not to use Mavyret.
  - Concurrent anticoagulant therapy: Fluctuations in International Normalized Ratio (INR) have been observed in warfarin recipients who were also receiving treatment for HCV infections. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Although caution is advised when using Mavyret while receiving concurrent anticoagulant therapy, specifically warfarin, this is not an absolute

contraindication as long as patient is adequately monitored and educated during therapy.
- Drug-drug interactions with one or more of the following agents:
  - Rifampin, carbamazepine, or St. John's wort:
  - These drug-drug interactions are not unique to Mavyret, and they apply across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection.

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 September 2017)
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 September 2017)

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 September 2017 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, 2018.
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 September 21, 2017. Available at: https://www.hcvguidelines.org/. Accessed May 1, 2018.
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 2016. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/hiv-viral-hepatitis.pdf. Accessed March 13, 2018.

5. Bonder A, Afdhal N. Utilization of FibroScan in clinical practice. Curr Gastroenterol Rep. 2014; 16(372): 1-7. DOI 10.1007/s11894-014-0372-6.
6. Halfon P, Bourliere M, Deydier R, et al. Independent prospective multicenter validation of biochemical markers (Fibrotest–Actitest) for the prediction of liver fibrosis and activity in patients with chronic hepatitis C: The Fibropaca study. Am J Gastroenterol. 2006; 101: 547-555. DOI: 10.1111/j.1572-0241.2006.0411.x
7. Hepatitis C Virus (HCV) FibroSure. Laboratory Corporation of America Holdings and Lexi-Comp, Inc. Available at https://www.labcorp.com. 2016. Accessed May 1, 2018.
8. Hepatitis C Virus (HCV) FibroTest-ActiTest Panel. Nichols Institute/Quest Diagnostics. Available at http://education.questdiagnostics.com/physician_landing_page. 2017. Accessed May 1, 2018.
9. Hepatitis C Virus (HCV) FIBROSpect II. Prometheus Therapeutics and Diagnostics. Available at http://www.prometheuslabs.com/Resources/Fibrospect/Fibrospect_II_Product_Detail_Sheet_FIB16005_04-16.pdf. April 2016. Accessed May 1, 2018.
10. Hsieh YY, Tung SY, Lee K, et al. Routine blood tests to predict liver fibrosis in chronic hepatitis C. World J Gastroenterol. February 28, 2012; 18(8): 746-53. doi: 10.3748/wjg.v18.i8.746.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created.	12.18	N/A

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.