Clinical Policy: Simeprevir (Olysio)

Reference Number: OH.PHAR.PPA.11
Effective Date: 07/17
Last Review Date: 09/17 Revision Log
Line of Business: Medicaid

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
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

Limitations 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 (including office chart notes and lab results) 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 HCV ribonucleic acid (RNA) levels in the last 6 months;
2. Confirmed HCV genotype is 1;
3. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
4. Age ≥ 18 years;
5. Life expectancy ≥ 12 months with HCV treatment;
6. Documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy, if applicable;
7. Moderate to Advanced liver disease defined as a or b:
   a. Moderate to Advanced fibrosis indicated by i or ii:

i. Liver biopsy showing a METAVIR score of F2 or equivalent (Knodell, Scheuer, Batts-Ludwig – F2; Ishak – F3);
ii. One serologic test and one radiologic test showing an equivalent score to METAVIR F2 per Appendix C;

b. Cirrhosis indicated by i, ii or iii:
i. Hepatocellular carcinoma (HCC) - and the HCC is amenable to resection, ablation or transplant;
ii. Liver biopsy showing a METAVIR score of F4 or equivalent (Knodell, Scheuer, Batts-Ludwig – F4; Ishak - F5/6);
iii. Both of the following:
a) One serologic test showing an equivalent score to METAVIR F4 per Appendix C;
b) One radiologic test showing an equivalent score to METAVIR F4 per Appendix C or other radiologic test showing evidence of cirrhosis (e.g., portal hypertension);

8. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
9. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A): contraindication or intolerance to Mavyret;
10. Member agrees to participate in a medication adherence program meeting both of the following components:
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;
11. Member is hepatitis B virus (HBV) negative, or if positive, documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
12. If prescribed with ribavirin, at the time of request, member has none of the following contraindications:
a. Pregnancy;
b. For Rebetol: creatinine clearance < 50 mL/min;
13. Dose does not exceed 150 mg (1 capsule) per day.

Approval duration: up to 24 weeks*
*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

B. Other diagnoses/indications
1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Olysio for chronic hepatitis C virus infection and has received this medication for at least 30 days;
2. Member is responding positively to therapy (e.g. decreased HCV RNA level, no unacceptable toxicity);
3. Dose does not exceed 150mg (1 capsule) per day.

Approval duration: up to a total of 24 weeks*
*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALT: alanine aminotransferase
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBeAg: hepatitis B virus envelope antigen
HBV: hepatitis B virus
HIV-1: human immunodeficiency virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
IDSA: Infectious Diseases Society of America
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
Peg-IFN: pegylated interferon
PI: protease inhibitor
RBV: ribavirin
RNA: ribonucleic acid

Appendix B: General Information

- Hepatitis B Reactivation is a black box warning for all direct-acting antiviral drugs for the treatment of HCV. The provider must provide either:
  - Documentation of absence of concurrent HBV infection as evidenced by laboratory values showing absence of hepatitis B virus envelope antigen (HBeAg) and HBV DNA;
  - Documentation that HBV co-infected patient may not be candidates for therapy as evidenced by one of the following:
    - Absence of HBeAg, HBV DNA less than 2,000 international units/mL, and alanine aminotransferase (ALT) level within 1 to 2 times the upper limit of normal;
    - HBeAg-positive and HBV DNA greater than 1,000,000 international units/mL and ALT level within 1 to 2 times the upper limit of normal;

  - Documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced
- The 2016 AASLD/IDSA treatment guideline for HBV consider ALT levels <30 U/L for men and <19 U/L for women as upper limits of normal.
- The 2016 AASLD/IDSA treatment guideline for HBV recommend adults with compensated cirrhosis, even with low levels of viremia (<2,000 IU/mL) be treated with antiviral therapy to reduce the risk of decompensation, regardless of ALT level. The recommendation extends to adults with decompensated cirrhosis be treated with antiviral therapy indefinitely regardless of HBV DNA level, HBeAg status, or ALT level to decrease the risk of worsening liver-related complications.
- The 2017 AASLD/IDSA treatment guideline for HCV no longer recommend use of simeprevir in treatment of chronic HCV genotype 4.

Appendix C: Approximate Scoring Equivalencies using METAVIR F2/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
Moderate fibrosis	0.48 - 0.58	≥42	0.7 – 1.4	> 3.25	≥7.0	>3.2	F2	F3
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 F2 is equivalent to Knodell, Scheuer, and Batts-Ludwig F2 and Ishak F3
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 D: Direct-Acting Antivirals for Treatment of HCV Infection

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

*Combination drugs

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1 CHC: Treatment-naive or treatment-experienced with peg-IFN/RBV patients without cirrhosis	Sovaldi 400 mg by mouth daily plus Olysio150 mg by mouth daily for 12 weeks	Olysio: 150mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated April, 2017)
Genotype 1 CHC: Treatment-naive or treatment-experienced with peg-IFN/RBV patients with compensated cirrhosis:	Sovaldi 400 mg by mouth daily plus Olysio150 mg by mouth daily with‡ or without weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) for 24 weeks	Olysio: 150mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated April, 2017)
Genotype 1 CHC: Liver transplant patients including those with compensated cirrhosis	Sovaldi 400 mg by mouth daily plus Olysio150 mg by mouth daily with or without weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) for 12 weeks	Olysio: 150mg/day	AASLD-IDSA (updated April, 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.*

**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.*

V. Product Availability

Capsule: 150 mg

VI. References

1. Olysio Prescribing Information. Titusville, NJ: Janssen Therapeutics.; May 2016. Available at https://www.olysio.com/shared/product/olysio/prescribing-information.pdf. Accessed May 11, 2017.
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9. PegIntron Prescribing Information. Whitehouse Station, NJ: Merck Sharp and Dohme Corp.; February 2016. Available at https://www.merck.com/product/usa/pi_circulars/p/pegintron/pegintron_pi.pdf. Accessed July 25, 2016.
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Reviews, Revisions, and Approvals	Date	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	08/16	09/16

Reviews, Revisions, and Approvals	Date	Approval Date
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.		
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	

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.