

## Clinical Policy: Simeprevir (Olysio)

Reference Number: CP.CPA.289

Effective Date: 11.01.16

Last Review Date: 08.19

Line of Business: Commercial

[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 or infectious disease specialist;
4. Age ≥ 18 years;
5. Member must use Harvoni® (*authorized generic or brand for 8 weeks only*), sofosbuvir/velpatasvir (Epclusa®) (*authorized generic preferred*), Mavyret™, or Zepatier® unless all are contraindicated or clinically significant adverse effects are experienced;

6. Prescribed regimen is consistent with an FDA or AASLD-IDSAs recommended regimen (see Section V Dosage and Administration for reference);
7. 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.CPA.09 for commercial.

**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 more than three quarters of the full regimen 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 CP.CPA.09 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.CPA.09 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

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
Harvoni <sup>®</sup> (sofosbuvir/ ledipasvir)	Without cirrhosis, treatment-naïve, whose HCV viral load is less than 6 million IU/mL: <b>Genotypes 1</b>  One tablet PO QD for 8	Harvoni: sofosbuvir 400 mg/ ledipasvir 90 mg (1 tablet) per day
Epclusa <sup>®</sup> (sofosbuvir/ velpatasvir)	Treatment-naïve or treatment-experienced with pegIFN/RBV with or without compensated cirrhosis: <b>Genotype 1</b>  One tablet PO QD for 12 weeks	Epclusa: sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Mavyret <sup>™</sup> (glecaprevir/ pibrentasvir)	Treatment-naïve or treatment-experienced with pegIFN/RBV: <b>Genotype 1</b>  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
Zepatier <sup>®</sup> (grazoprevir / elbasvir)	<b>Genotype 1a:</b> Treatment-naïve or pegIFN/RBV-experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93  One tablet PO QD for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier <sup>®</sup> (grazoprevir / elbasvir)	<b>Genotype 1a:</b> Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93  One tablet PO QD plus weight-based RBV for 16 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier <sup>®</sup> (grazoprevir / elbasvir)	<b>Genotype 1b:</b> Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	One tablet PO QD for 12 weeks	
Zepatier® (grazoprevir / elbasvir)	<b>Genotype 1a or 1b:</b> pegIFN/RBV/NS3 PI*† -experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93  One tablet PO QD plus weight-based RBV for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir / elbasvir)	<b>Genotype 1a or 1b:</b> pegIFN/RBV/NS3 PI*† -experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93  One tablet PO QD plus weight-based RBV for 16 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) 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 coinfecting 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	

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
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.
- Child-Pugh Score:

	1 Point	2 Points	3 Points
Bilirubin	Less than 2 mg/dL Less than 34 umol/L	2-3 mg/dL 34-50 umol/L	Over 3 mg/dL Over 50 umol/L
Albumin	Over 3.5 g/dL Over 35 g/L	2.8-3.5 g/dL 28-35 g/L	Less than 2.8 g/dL Less than 28 g/L
INR	Less than 1.7	1.7 - 2.2	Over 2.2
Ascites	None	Mild / medically controlled	Moderate-severe / poorly controlled
Encephalopathy	None	Mild / medically controlled Grade I-II	Moderate-severe / poorly controlled. Grade III-IV

Child-Pugh class is determined by the total number of points: A = 5-6 points; B = 7-9 points; C = 10-15 points.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1: Treatment-naïve 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.oly시오.com/shared/product/oly시오/prescribing-information.pdf>. Accessed April 30, 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 April 30, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy converted to new template from “Olysio NATL 07.22.16.docx”. Annual review – removed approval for GT 4 per 2017 AASLD guideline; added requirement for GT, tx status, and cirrhosis status for consistency; added trial of Epclusa for those not a candidate for Harvoni; added re-direction to Epclusa if >12 week request for Harvoni.	06.17	11.17
Added redirection to Mavyret for FDA-approved indications and as an option in addition to Epclusa for Harvoni requests >12 weeks. Safety criteria were applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Exception made to require Hep B screening for all patients prior to treatment to ensure that proper risk reduction measures are taking, though this is not specifically addressed in boxed warning.	09.05.17	11.17
3Q 2018 annual review: removed requirement for HBV verification; added age limit; removed redirection to Epclusa or Mavyret if treatment duration is greater than 12 weeks since parity and redirections no longer shorten duration of tx; added requirement that prescribed regimen should be consistent with FDA or AASLD recommendations; removed requirement for documentation of treatment and cirrhosis status since it does not change treatment duration; expanded duration of tx required for COC from 30 days to three quarters of the full regimen; required verification of genotype for COC; reduced maximum approval duration from 24 weeks to 12 weeks per AASLD/IDSA guidance updated September 2017; removed prior tx hx with DAA, acute HCV infection, and monotherapy from section III since addressed throughout policy; references reviewed and updated.	05.22.18	08.18
Removed requirement for advanced fibrosis or other candidacy for therapy following approved clinical guidance; combined with and retired CP.CPA.EX.289 for HNAZ exchange lines of business.	09.03.18	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
No clinically significant changes: revised preferencing from Harvoni, Epclusa, and Mavyret to Harvoni (Brand/AG) for 8 weeks only, Epclusa AG only, Mavyret, and Zepatier in line with previously approved clinical guidance.	01.07.19	
3Q 2019 annual review: no clinically significant changes; references reviewed and updated.	05.13.19	08.19

**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.

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