Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)

Reference Number: HIM.PA.SP1
Effective Date: 08.16
Last Review Date: 08.22
Line of Business: HIM*

Revision Log

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

Description

Sofosbuvir/velpatasvir (Epclusa®) is a combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor.

**These criteria do NOT apply to California Commercial Exchange Plans.*

FDA Approved Indication(s)

Epclusa is indicated for the treatment of adult and pediatric patients 3 years of age and older with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection:

- Without cirrhosis or with compensated cirrhosis
- With decompensated cirrhosis for use in combination with ribavirin (RBV)

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 Epclusa 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 is 1, 2, 3, 4, 5 or 6;
   **Chart note documentation and copies of lab results are required*
3. For genotype 3: One of the following (a or b):
   a. Laboratory testing for the presence or absence of NS5A resistance-associated substitution (RAS) Y93H for velpatasvir if member meets one of the following scenarios (i and ii):
      i. Member is treatment-naïve and has cirrhosis;
      ii. Member has had previous HCV treatment and has no cirrhosis;
   b. Member does not meet one of the above scenarios in 3a;
4. One of the following (a or b):
   a. If **request is from Florida**, member must use Epclusa **authorized generic**, unless contraindicated or clinically significant adverse effects are experienced;
   b. For **all other** requests, member must use **brand** version of Epclusa, unless contraindicated or clinically significant adverse effects are experienced;

5. Documentation of the treatment status of the member (treatment-naive or treatment-experienced);
6. Documentation of cirrhosis status of the member (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
7. 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*);
8. Age ≥ 3 years;
9. Life expectancy ≥ 12 months with HCV treatment;
10. Member agrees to participate in a medication adherence program meeting 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;
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 one of the following (a, b, or c):
    a. Adult and pediatric members with body weight ≥ 30 kg: sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day;
    b. Pediatric members 3 years of age and older with body weight < 17 kg: sofosbuvir/velpatasvir 150 mg/37.5 mg per day;
    c. Pediatric members 3 years of age and older with body weight 17 kg to < 30 kg: sofosbuvir/velpatasvir 200 mg/50 mg 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 (must meet all)**:**
1. Member meets one of the following (a or b):
    a. If **request is from Florida**, member must use Epclusa **authorized generic**, unless contraindicated or clinically significant adverse effects are experienced;
    b. For **all other** requests, member must use **brand** version of Epclusa, unless contraindicated or clinically significant adverse effects are experienced;
2. Must meet one of the following (a or b):
    a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
        i. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
        ii. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
    b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

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

1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
   c. Documentation supports that member is currently receiving Epclusa for chronic HCV infection and has recently completed at least 60 days of treatment with Epclusa;
2. Member is responding positively to therapy;
3. Dose does not exceed one of the following (a, b, or c):
   a. Adult and pediatric members with body weight ≥ 30 kg: sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day;
   b. Pediatric members 3 years of age and older and body weight < 17 kg: sofosbuvir/velpatasvir 150 mg/37.5 mg per day;
   c. Pediatric members 3 years of age and older and body weight 17 kg to < 30 kg: sofosbuvir/velpatasvir 200 mg/50 mg 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 (must meet all)**:**

1. Member meets one of the following (a or b):
   a. If **request is from Florida**, member must use Epclusa **authorized generic**, unless contraindicated or clinically significant adverse effects are experienced;
   b. For **all other** requests, member must use **brand** version of Epclusa, unless contraindicated or clinically significant adverse effects are experienced;
2. Must meet one of the following (a or b):
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
      i. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
      ii. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
   b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

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 – HIM.PA.154 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
RAS: resistance-associated substitution
RNA: ribonucleic acid

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): Epclusa and RBV combination regimen is contraindicated in patients for whom RBV is contraindicated. Refer to the RBV prescribing information for a list of contraindications for RBV.
- Boxed warning(s): risk of hepatitis B virus (HBV) 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
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Sovaldi		Sofosbuvir			
Viekira Pak*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

**Combination drugs*

Appendix E: General Information

- HBV reactivation 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

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 1-6: Without cirrhosis or with compensated cirrhosis, treatment-naïve or treatment-experienced* patient	One tablet PO QD for 12 weeks	Adult/Peds ≥ 30 kg: sofosbuvir 400 mg /velpatasvir 100 mg (one tablet) per day; Peds 17 to < 30 kg: sofosbuvir 200 mg /velpatasvir 50 mg per day;	FDA-approved labeling
Genotype 1-6: With decompensated cirrhosis treatment-naïve	One tablet PO QD with weight-based RBV for 12 weeks		

Indication	Dosing Regimen	Maximum Dose	Reference
or treatment-experienced* patient	(RBV-ineligible patients patients may use: one tablet PO QD for 24 weeks)‡	Peds < 17 kg: sofosbuvir 150 mg /velpatasvir 37.5 mg per day	
Genotype 1-6: Treatment-naïve and treatment-experienced patients, post-liver transplant with compensated cirrhosis or without cirrhosis	One tablet PO QD for 12 weeks		
Genotype 1-6: With decompensated cirrhosis in whom prior sofosbuvir- or NS5A inhibitor-based treatment experienced failed	One tablet PO QD with weight-based RBV for 24 weeks‡	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated September 2021)
Genotype 1-6: Treatment-naïve and treatment-experienced patients, post-liver transplant with decompensated cirrhosis	One tablet PO QD with RBV (starting at 600 mg and increased as tolerated) for 12 weeks (treatment naïve) or 24 weeks (treatment experienced)‡	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated September 2021)
Genotype 3 with NS5A Y93H polymorphism: Treatment-naïve with compensated cirrhosis or treatment-experienced* without cirrhosis patient	One tablet PO QD with weight-based RBV for 12 weeks‡	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated September 2021)

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.
**From clinical trials, treatment-experienced refers to previous treatment with NS3/4A protease inhibitor (telaprevir, boceprevir, or simeprevir) and/or peginterferon/RBV unless otherwise stated*
‡ *Off-label, AASLD-IDSA guideline-supported dosing regimen*

VI. Product Availability

- Tablets: sofosbuvir 400 mg with velpatasvir 100 mg, sofosbuvir 200 mg with velpatasvir 50 mg
- Oral pellets: sofosbuvir 200 mg with velpatasvir 50 mg, sofosbuvir 150 mg with velpatasvir 37.5 mg

VII. References

1. Epclusa Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; April 2022. Available at http://www.gilead.com/~/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf . Accessed May 1, 2022.

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 29, 2021. Available at: https://www.hcvguidelines.org/. Accessed August 23, 2022.
3. CDC. Hepatitis C Q&As for health professionals. Last updated August 7, 2020. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed May 1, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.05.19	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.	07.02.19	08.19
Via CP.PCH.21: HIM.PA.SP1 retired and combined with Commercial to CP.PCH.21; added requirement that life expectancy ≥ 12 months with HCV treatment and participation in a medication adherence program; added new prescriber requirement to include a "provider who has expertise in treating HCV based on a certified training program"; Appendix F (Healthcare Provider HCV Training) added.	12.03.19	02.20
Via CP.PCH.21: RT4: updated FDA indication and dosing for pediatric extension to age 6 years or weight ≥ 17 kg.	04.02.20	
3Q 2020 annual review: CP.PCH.21 retired; HIM.PA.SP1 unretired per June SDC and prior clinical guidance; no clinically significant changes; references reviewed and updated.	06.10.20	08.20
RT4: added updated FDA-labeled dosing for post-liver transplant setting.	08.20.20	
3Q 2021 annual review: revised medical justification language for not using brand version of Eplcusa to "must use" language; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; updated Section V table with AASLD recommended regimens; RT4: updated criteria for Epclusa pediatric age expansion to 3 years and older along with pediatric dosing and new oral pellet dosage formulation; references reviewed and updated.	07.12.21	08.21
3Q 2022 annual review: no significant changes; references reviewed and updated.	05.05.22	08.22
Added criterion for NS5A RAS test for specific genotype 3 scenarios per AASLD recommendation. Template changes applied to other diagnoses/indications and continued therapy section.	08.30.22	
Per SDC, revised redirection for Florida only to require use of Epclusa authorized generic; all other requests continue to require use of brand Epclusa.	01.12.23	

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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