Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)

Reference Number: IL.PHAR.268
Effective Date: 1.1.20
Last Review Date: 9.22.22
Line of Business: Medicaid

Revision Log

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

Description

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

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 Hepatitis C infection genotype 1, 2, 3, 4, 5 or 6 confirmed by lab documentation and quantitative baseline HCV-RNA.
2. Patient's Metavir/fibrosis score must be documented in the request for prior approval. The patient's Metavir/fibrosis score can be determined based on Liver Biopsy, Transient Elastography (FibroScan ®), FibroTest®/FibroSure®, or FibroMeter™.
3. Prescriber must provide a copy of the following lab test reports, completed within 3 months prior to the request for prior approval, unless otherwise noted:
   - **a.** Baseline quantitative HCV RNA level (within 1 year of request for prior approval)
   - **b.** ALT and AST
   - **c.** CBC
   - **d.** GFR
   - **e.** INR, albumin, and bilirubin, for stage 4 fibrosis only
   - **f.** Negative HBV screen; **or evidence of immunity due to vaccination or previous natural infection**, and if member is **acutely or chronically infected,** must provide quantitative HBV DNA and verification of treatment

regimen (Interpretation of Hepatitis B Serologic Test Results: https://www.cdc.gov/hepatitis/hbv/pdfs/serologicchartv8.pdf

4. Age ≥ 3 years;,
5. Member must use authorized generic version of Epclusa, unless contraindicated or clinically significant adverse effects are experienced;
6. In the opinion of the prescriber, the patient is able to make appropriate decisions about treatment and comply with dosing and other instructions, and is capable of completing therapy as prescribed. The prescriber must provide a copy of a signed patient commitment letter for all hepatitis C treatment regimens.
7. The treatment regimen prescribed is not for an indication outside of the FDA approved labeling, and no contraindications or significant drug interactions to treatment exist as specified in the product labeling.
8. The patient has no history of an incomplete course of treatment with DAAs. (Prior treatment with telaprevir, boceprevir, and DAA regimens used in combination with interferons is not taken into consideration for purposes of this criterion.) HFS will review requests and pertinent clinical information for an additional course of DAA, after previous such therapy, on a case-by-case basis, considering whether the person has received counseling for or otherwise addressed the cause of non-adherence, where applicable.
9. 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*);
10. Non-adherence with the regimen (> 7 days) or patient's failure to obtain refills in a timely manner may result in discontinuation of current prior approval. Non-adherence or failure to obtain refills that result from situations that are beyond the patient's control will not result in discontinuation of a prior approval.
11. The prescriber agrees to submit HCV RNA levels to HFS for patients prescribed DAAs within 8 weeks after beginning treatment, 12 weeks post treatment, and 24 weeks post treatment. If at any point the patient's viral load is undetectable, the prescriber is not required to submit any subsequent test. Prescriber's failure to submit a lab report in a timely fashion due to patient's non-cooperation may result in denial of retreatment, should that situation arise. However, situations beyond the control of the prescriber or the patient will not result in a denial of re-treatment under this criteria.
12. Requests for exceptions to these criteria can be made when the services are medically necessary to meet the medical needs of the patient. Requests for exceptions to these criteria can be made on the prior approval form itself and will be reviewed on a case-by-case basis.
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

1. Member must use authorized generic 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):

1. For drugs on the PDL: CP.PMN.255; or
2. For drugs NOT on the PDL: CP.PMN.16 ; 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 2 above does not apply, refer to the off-label use policy CP.PMN.53

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. Member must use authorized generic version of Epclusa, unless contraindicated or clinically significant adverse effects are experienced;
4. 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 must use **authorized generic version of Epclusa**, unless contraindicated or clinically significant adverse effects are experienced;
2. 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: CP.PMN.255 for Medicaid; 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: CP.PMN.16 for Medicaid; 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 2a above does not apply, refer to the off-label use policy for the relevant line of business: 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
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 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			

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

- 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.

- AASLD-IDSA simplified treatment recommendations: In their October 2022 HCV guidance, AASLD-IDSA updated treatment recommendations to recommend two simplified regimens for adults with chronic hepatitis C (*any genotype*) who do not have cirrhosis and have not previously received hepatitis C treatment: either Mavyret x8 weeks or Epclusa x12 weeks. With the advent of pangenotypic HCV treatment regimens, HCV genotyping is no longer required prior to treatment initiation for all individuals. In those with evidence of cirrhosis and/or past unsuccessful HCV treatment, treatment regimens may differ by genotype and thus pretreatment genotyping is recommended. For noncirrhotic treatment-naive patients, although genotyping may impact the preferred treatment approach, it is not required if a pangenotypic regimen is used.

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

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; Peds < 17 kg: sofosbuvir 150 mg /velpatasvir 37.5 mg per day	FDA-approved labeling
Genotype 1-6: With decompensated cirrhosis, treatment-naïve or treatment-experienced* patient	One tablet PO QD with weight-based RBV for 12 weeks (RBV-ineligible patient may use: one tablet PO QD for 24 weeks)‡		
Genotype 1-6: Treatment-naïve and treatment-experienced patients, post-liver	One tablet PO QD for 12 weeks		

transplant with compensated cirrhosis or without cirrhosis			
Genotype 1-6: With decompensated cirrhosis in whom prior sofosbuvir- or NS5A inhibitor-based treatment failed	One tablet PO QD with weight-based RBV for 24 weeks‡	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated March 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 March 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 March 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.
**Treatment-experienced refers to previous treatment with NS3 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?la=en. Accessed July 9, 2021.
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 March 12, 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 2, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created, adapted from CP.PHAR.268 Velpatasvir (Epclusa)	11.21.19	1.7.20
2Q 2021 annual review – **Updated** FDA approved indication; **added** authorized generic version of Epclusa; ; **Added** new prescriber requirement to include a "provider who has expertise in treating HCV based on a certified training program"; Dosage and Administration tables updated; **Added** Appendix F (Healthcare Provider HCV Training); **Added** Child-Pugh Score in Appendix E; **updated** Age ≥ 6 years or weight ≥ 17 kg; **updated** criteria for dosage;; **removed** medical justification for ability to use Mavyret from Appendix F; Updated *Appendix B: Therapeutic Alternatives*; references reviewed and updated	6.14.21	
Revised medical justification language for not using authorized generic version of Eplcusa to "must use" language; 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.	9.14.21	
3Q 2022 annual review: Updated initial criteria to reflect HFS criteria.Template changes applied to other diagnoses/indications and continued therapy section; references reviewed and updated.	9.30.22	
2Q2024 annual review: corrected formatting, updated appendix E, reviewed references	3.5.24	

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.