Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)

Reference Number: ERX.SPA.133
Effective Date: 10.01.16
Last Review Date: 08.21
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 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. Member must use brand version of Epclusa, unless contraindicated or clinically significant adverse effects are experienced;
4. Documentation of the treatment status of the member (treatment-naive or treatment-experienced);
5. Documentation of cirrhosis status of the member (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
6. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist, or provider who has expertise in treating HCV based on a certified training program (*see Appendix F)*;
7. Age ≥ 3 years;
8. Life expectancy ≥ 12 months with HCV treatment;
9. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
10. 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. Refer to ERX.PA.01 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. Member meets one of the following (a or b):
   a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
   b. 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
1. Refer to ERX.PA.01 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 – ERX.PA.01 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
IDSA: Infectious Diseases Society of America
NS3/4A, NS5A/B: nonstructural protein
PegIFN: pegylated interferon
RBV: ribavirin
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 (DAAs) 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

- 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.

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; 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	One tablet PO QD for 12 weeks		

Indication	Dosing Regimen	Maximum Dose	Reference
patients, post-liver 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.
**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 / 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.; June 2021. 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 April 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Modified diagnosis requirement for HCV RNA levels from over a six-month period to within the last 6 months; consolidated appendix D and E into dosing and administration in section V, added maximum dose requirement, initial approval duration expanded to full 12 weeks, limited continued therapy approval duration to 12 weeks, deleted viral load and adherence requirement in continued therapy section since appropriate full regimen is provided through initial approval duration per specialist feedback to prevent barriers to adherence, added documentation of positive response to therapy and continuity of care, and removed CIs in section II, added reference column in section V. Safety criteria was applied according to the safety guidance discussed at CPAC and per EPS.PHARM.31. Exception made to require hep B screening	07.17	08.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
for all patients prior to treatment to ensure that proper risk reduction measures are taking, though this is not specifically addressed in boxed warning.		
Removed direction to Harvoni & Sovaldi per 2018 formulary status	03.20.18	
3Q 2018 annual review: removed requirement for HBV verification; added requirement for documentation of treatment and cirrhosis status; expanded duration of treatment required for COC from 30 days to 60 days; references reviewed and updated.	05.22.18	08.18
3Q 2019 annual review: removed advanced liver disease requirement to align with 2018 AASLD/IDSA hepatitis C treatment guidelines; references reviewed and updated.	05.01.19	08.19
RT4: updated FDA indication and dosing for pediatric extension to age 6 years or weight ≥ 17 kg.	04.02.20	
3Q 2020 annual review: 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; references reviewed and updated. RT4: added updated FDA-labeled dosing for post-liver transplant setting.	07.22.20	08.20
3Q 2021 annual review: added criterion that prescribed agent be brand version Epclusa as this is the preferred formulary agent; removed criterion for sobriety documentation as AASLD recommends to treat all patients with HCV except those with short life expectancy; 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

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.