Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)

Reference Number: PA.CP.PHAR.268
Effective Date: 01/18
Last Review Date: 09/17 Revision Log

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
Epclusa is indicated for the treatment of adult patients 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

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness ® that Epclusa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
*** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria ***

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

1. Age ≥ 18 years;
2. Diagnosis of chronic hepatitis C virus (HCV) infection as evidenced by detectable HCV ribonucleic acid (RNA) levels
3. Confirmed HCV genotype is 1, 2, 3, 4, 5 or 6;
4. If actively abusing alcohol or IV drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse and an offer of a referral for substance use disorder treatment.
5. Has all of the following:
   a. Documented quantitative HCV RNA at baseline that was tested within the past 3 months.
   b. Dose not have a life expectancy of less than 12 months due to non-liver-related comorbid conditions.
   c. Has correct or addressed the causes of non-adherence to a previously prescribed Hepatitis C treatment regimen if the recipient has a history of failed treatment due to non-adherence.
   d. Had all potential drug interactions addressed by the prescriber
6. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see section V Dosage and Administration for reference)*;
7. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A): contraindication or intolerance to Mavyret or Mavyret is not AASLD recommended;
8. Has a documented commitment to adherence with the planned course of treatment
9. Has documented completion of

a. Hepatitis B immunization series or Hepatitis B screening (sAb/sAg and cAb/cAg) AND
b. If there is detectable HBV DNA, will be treated for Hepatitis B or if negative for hepatitis BsAb, is being vaccinated against Hepatitis B.AND
c. Has a documented HIV screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay: Is being treated for HIV or is not being treated for HIV and the medical record documents the rationale for not being treated

10. Dose does not exceed sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) 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: Refer to PA.CP.PHAR.57 - Global Biopharm Policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Approval

*** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria ***

A. Chronic Hepatitis C Infection (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of care policy (PA.LTSS.PHAR.01) applies;
2. Dose does not exceed sofosbuvir/velpatasvir 400mg/100mg (1 tablet) per day.

Approval duration: up to a total of 24 weeks*
*(*Approved duration should be consistent with a regimen in Appendix D)*

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy 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 – PA.CP.PHAR.57 or evidence of coverage documents.

Appendices

Appendix A: Abbreviation Key

ALT: alanine aminotransferase
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
CTP: Child Turcotte Pugh
CrCl: creatinine clearance
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBV: hepatitis B 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.

Appendix C: 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			
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
.Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs
**Additional PIs no longer recommended: Victrelis (boceprevir), Incivek (telaprevir)

IV. Dosage and Administration

A. **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.*

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1-6 CHC: Without cirrhosis or with compensated cirrhosis, treatment-naïve or treatment-experienced patient	One tablet PO QD for 12 weeks (GT 2 or 3 with compensated cirrhosis for Peg-IFN/RBV or sofosbuvir-based treatment-experienced patient may use: one tablet PO QD with weight-based ribavirin for 12 weeks) ǂ	One tablet (sofosbuvir 400mg /velpatasvir 100mg) per day	1) FDA-approved labeling 2) AASLD-IDSAhttps://www.hcvguidelines.org/
Genotype 1-6 CHC : With decompensated cirrhosis treatment-naïve or treatment-experienced patient	One tablet PO QD plus weight-based RBV for 12 weeks (GT 1, 4, 5, or 6 with decompensated cirrhosis and RBV ineligible may use: one tablet PO QD for 24 weeks) ǂ	One tablet (sofosbuvir 400mg /velpatasvir 100mg) per day	1) FDA-approved labeling 2) AASLD-IDSA (updated 04/17)

**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.*

V. Product Availability
Tablet: sofosbuvir 400 mg / velpatasvir 100 mg

References

1. Epclusa Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; June 2016. Available at http://www.gilead.com/~/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf?la=en. Accessed July 8, 2016.
2. AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed July 12, 2016.
3. Curry MP, Nezam AH. Noninvasive assessment of hepatic fibrosis: Overview of serologic and radiographic tests. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed July 15, 2016.
4. Fiel MI. Histologic scoring system for chronic liver disease. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed July 15, 2016.
5. Bonder A, Afdhal N. Utilization of FibroScan in clinical practice. *Curr Gastroenterol Rep.* 2014; 16(372): 1-7. DOI 10.1007/s11894-014-0372-6.
6. Halfon P, Bourliere M, Deydier R, et al. Independent prospective multicenter validation of biochemical markers (Fibrotest–Actitest) for the prediction of liver fibrosis and activity in patients with chronic hepatitis C: The Fibropaca study. Am J Gastroenterol. 2006; 101: 547-555. DOI: 10.1111/j.1572-0241.2006.0411.x
7. Hepatitis C Virus (HCV) FibroSure. Laboratory Corporation of America Holdings and Lexi-Comp, Inc. Available at https://www.labcorp.com. 2016. Accessed July 15, 2016.
8. Hepatitis C Virus (HCV) FibroTest-ActiTest Panel. Nichols Institute/Quest Diagnostics. Available at http://education.questdiagnostics.com/physician_landing_page. 2016. Accessed July 15, 2016.
9. Hepatitis C Virus (HCV) FIBROSpect II. Prometheus Therapeutics and Diagnostics. Available at http://www.prometheuslabs.com/Resources/Fibrospect/Fibrospect_II_Product_Detail_Sheet_FIB16005_04-16.pdf. April 2016. Accessed July 15, 2016.
10. Hsieh YY, Tung SY, Lee K, et al. Routine blood tests to predict liver fibrosis in chronic hepatitis C. World J Gastroenterol. February 28, 2012; 18(8): 746-53. doi: 10.3748/wjg.v18.i8.746.
11. Bruix J and Sherman M. Management of hepatocellular carcinoma: An update. AASLD Practice Guideline. *Hepatology*. 2011; 53(3): 1020-22.
12. Ribavirin (systemic): Drug information. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed July 11, 2016.