

<b>Clinical Policy Title:</b>	sofosbuvir/velpatasvir
<b>Policy Number:</b>	RxA.369
<b>Drug(s) Applied:</b>	Epclusa®
<b>Original Policy Date:</b>	09/14/2020
<b>Last Review Date:</b>	09/14/2021
<b>Line of Business Policy Applies to:</b>	All lines of business

## Background

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. It is indicated for the treatment of adult patients and pediatric patients 6 years of age and older or weighing at least 17 kg 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)

## Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 1-6: Without cirrhosis or with compensated cirrhosis, treatment-naïve or pegIFN/ RBV-experienced patient	One tablet orally once daily for 12 weeks  (GT 3 with compensated cirrhosis for pegIFN/RBV experienced patient may use: one tablet orally once daily with weight-based RBV for 12 weeks) ‡	One tablet (sofosbuvir 400 mg /velpatasvir 100 mg) per day
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 1-6: With decompensated cirrhosis treatment-naïve or treatment-experienced* patient	One tablet orally once daily with weight-based RBV for 12 weeks  (GT 1, 4, 5, or 6 with decompensated cirrhosis and RBV-ineligible may use: one tablet orally once daily for 24 weeks) ‡	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 1-6: With decompensated cirrhosis in whom prior sofosbuvir- or NS5A-based treatment experienced failed	One tablet orally once daily with weight-based RBV for 24 weeks	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

Sofosbuvir/velpatasvir (Epclusa®)	Genotype 1b: With compensated cirrhosis or without cirrhosis and nonNS5A inhibitor, sofosbuvir-containing regimen-experienced	One tablet orally once daily for 12 weeks	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 2: With or without compensated cirrhosis, sofosbuvir + RBV-experienced	One tablet orally once daily for 12 weeks	One tablet (sofosbuvir 400mg/velpatasvir 100 mg) per day
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 2 or 3: Treatment-naïve and treatment-experienced patients, post-liver transplant with compensated cirrhosis or decompensated cirrhosis	One tablet orally once daily with weight-based RBV for 12 weeks	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 3 with NS5A Y93H polymorphism: Treatment-naïve with cirrhosis or treatment experienced* patient	One tablet orally once daily with weight-based RBV for 12 weeks	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day

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

## Dosage Forms

- Tablet: sofosbuvir 400 mg with velpatasvir 100 mg, sofosbuvir 200 mg with velpatasvir 50 mg

## Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

### 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. Must try and fail generic sofosbuvir-velpatasvir 400-100 mg tablets prior to receiving brand Eplusa® 400-100 mg tablets; unless medical justification supports inability to use the brand (e.g., contraindications to excipients in the generic);
4. Documentation of the treatment status of the patient (treatment-naive or treatment-experienced);
5. Documentation of cirrhosis status of the patient (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  $\geq$  6 years or weight  $\geq$  17 kg;
  
8. Life expectancy  $\geq$  12 months with HCV treatment;
9. 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;
10. Prescribed regimen is consistent with an FDA or AASLD-IDSAs recommended regimen (see Section V Dosage and Administration for reference);
11. Dose does not exceed one of the following (a or b):
  - a. Adult and pediatric members with body weight  $\geq$  30 kg: sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day;
  - b. Pediatric members with body weight 17 to 29 kg: sofosbuvir/velpatasvir 200 mg/50 mg (1 tablet) per day.

**Approval duration**

**Commercial:** 168 days\*

\*Approved duration should be consistent with a regimen in Dosing Information section above.

**II. Continued Therapy Approval**

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

1. Member meets one of the following (a or b):
  - a. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
  - b. Documentation supports that member is currently receiving Eplusa for chronic HCV infection and has recently completed at least 60 days of treatment with Eplusa
2. Member is responding positively to therapy;
3. Dose does not exceed sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day.
4. Adult and pediatric members with body weight  $\geq$  30 kg: sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day;
5. Pediatric members with body weight 17 to 29 kg: sofosbuvir/velpatasvir 200 mg/50 mg (1 tablet) per day.

**Approval duration**

**Commercial:** 168 days\*

\*Approved duration should be consistent with a regimen in Dosing Information section above.

**III. Appendices**

**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**

- Not applicable.

**APPENDIX C: Contraindications/Boxed Warnings**

- Contraindication(s):
  - Eplclusa and RBV combination regimen is contraindicated in patients for whom RBV 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 coinfectd 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				
Eplclusa*	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	
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.

#### APPENDIX E: 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-liverdisease>): 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>

#### References

1. Epclusa Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; July 2020. Available at [http://www.gilead.com/~media/files/pdfs/medicines/liverdisease/epclusa/epclusa\\_pi.pdf?la=en](http://www.gilead.com/~media/files/pdfs/medicines/liverdisease/epclusa/epclusa_pi.pdf?la=en). Accessed November 24, 2020.
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 August 27, 2020. Available at: <https://www.hcvguidelines.org/>. Accessed November 24, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: <ol style="list-style-type: none"> <li>1. Policy title table was updated.</li> <li>2. Line of business 'Policy Applies to' was updated to all lines of business.</li> <li>3. Background: Added pediatric patient to FDA approved indication.</li> <li>4. Dosages form: One more strength added</li> <li>5. Initial therapy age criteria updated to ≥ 6 years and age 6 years or ≥ 17 kg.</li> <li>6. Initial therapy Dose Criteria further divided for adult and pediatric members.</li> <li>7. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..."</li> <li>8. Reference reviewed and updated.</li> </ol>	07/20/2020	09/14/2020
Policy was reviewed: <ol style="list-style-type: none"> <li>1. Policy title table was updated.</li> <li>2. Initial approval criteria I.A.3 updated to reflect use of brand over generic due to rebates available.</li> <li>3. References updated.</li> </ol>	11/24/2020	12/07/2020
Policy was reviewed. <ol style="list-style-type: none"> <li>1. Dosing Information table was updated to remove "References" column.</li> <li>2. Statement about provider sample "The provision of provider samples does not guarantee coverage..." was added to Clinical Policy.</li> <li>3. Initial Approval Criteria I.A.3 was updated to member to try generic " sofosbuvir-velpatasvir 400-100 mg tablets before brand Epclusa® 400-100 mg tablets".</li> </ol>	08/24/2021	09/14/2021

<p>4. Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration.</p> <p>5. Initial Approval Criteria and Continued Therapy Approval Criteria approval duration footnote was updated from “*Approved duration should be consistent with a regimen in Section V Dosage and Administration” to “*Approved duration should be consistent with a regimen in Dosing Information section above”.</p>		
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