RXADVANCE
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Clinical Policy Title:	sofosbuvir/velpatasvir
Policy Number:	RxA.369
Drug(s) Applied:	Epclusa®
Original Policy Date:	09/14/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	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	Reference
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 1-6: Without cirrhosis or with compensated cirrhosis, treatment-naïve or pegIFN/ RBV-experienced patient	One tablet PO once daily for 12 weeks (GT 3 with compensated cirrhosis for pegIFN/RBV experienced patient may use: one tablet PO once daily with weight-based RBV for 12 weeks) ‡	One tablet (sofosbuvir 400 mg /velpatasvir 100 mg) per day	1) FDA approved labeling 2) AASLD-IDSA (updated May 2018)
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 1-6: With decompensated cirrhosis treatment-naïve or treatment-experienced* patient	One tablet PO 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 PO once daily for 24 weeks) ‡	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	1) FDA approved labelling 2) AASLD-IDSA (updated May 2018)

Drug Name	Indication	Dosing Regimen	Maximum Dose	Reference
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 1-6: With decompensated cirrhosis in whom prior sofosbuvir- or NS5A-based treatment experienced failed	One tablet PO once daily with weight-based RBV for 24 weeks	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated May 2018)
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 1b: With compensated cirrhosis or without cirrhosis and nonNS5A inhibitor, sofosbuvir-containing regimen-experienced	One tablet PO once daily for 12 weeks	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated May 2018)
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 2: With or without compensated cirrhosis, sofosbuvir + RBV-experienced	One tablet PO once daily for 12 weeks	One tablet (sofosbuvir 400mg/velpatasvir 100 mg) per day	AASLD-IDSA (updated May 2018)
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 2 or 3: Treatment-naïve and treatment-experienced patients, post-liver transplant with compensated cirrhosis or decompensated cirrhosis	One tablet PO once daily with weight-based RBV for 12 weeks	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated May 2018)
Sofosbuvir/velpatasvir (Epclusa®)	Genotype 3 with NS5A Y93H polymorphism: Treatment-naïve with cirrhosis or treatment experienced* patient	One tablet PO once daily with weight-based RBV for 12 weeks	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated May 2018)

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 ǂ 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.

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 brand product prior to receiving an authorized generic version of Epclusa®, unless medical justification supports inability to use the brand (e.g., contraindications to excipients in the brand);
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 (S*ee Appendix F*);
7. Age ≥ 6 years or weight ≥ 17 kg;
8. Life expectancy ≥ 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-IDSA 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 ≥ 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*
HIM: 168 days*
*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

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 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 sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day.
   a. Adult and pediatric members with body weight ≥ 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*
HIM: 168 days*
*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

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):
  - Epclusa 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 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
Daklinza	Daclatasvir				
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Olysio				Simeprevir	

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
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. 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: 1. Policy title table was updated. 2. Line of business 'Policy Applies to' was updated to all lines of business. 3. Background: Added pediatric patient to FDA approved indication. 4. Dosages form: One more strength added 5. Initial therapy age criteria updated to ≥ 6 years and age 6 years or ≥ 17 kg. 6. Initial therapy Dose Criteria further divided for adult and pediatric members. 7. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 8. Reference reviewed and updated.	07/20/2020	09/14/2020
Policy was reviewed: 1. Policy title table was updated. 2. Initial approval criteria I.A.3 updated to reflect use of brand over generic due to rebates available. 3. References updated.	11/24/2020	12/07/2020