RXADVANCE
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Clinical Policy Title:	sofosbuvir-velpatasvir-voxilaprevir
Policy Number:	RxA.558
Drug(s) Applied:	Vosevi®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Sofosbuvir-velpatasvir-voxilaprevir (Vosevi®) is a fixed-dose combination oral tablet. Sofosbuvir is a nucleotide analog hepatitis C virus (HCV) NS5B polymerase inhibitor, velpatasvir is an NS5A inhibitor, and voxilaprevir is an NS3/4A protease inhibitor.

It is indicated for the treatment of adult patients with chronic HCV infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have:

- Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor*;
- Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor**.
    - Additional benefit of Vosevi® over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.

* In clinical trials, prior NS5A inhibitor experience included daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir.

** In clinical trials, prior treatment experience included sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (boceprevir, simeprevir or telaprevir).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Sofosbuvir-velpatasvir-voxilaprevir (Vosevi®)	Genotype 1-6: Treatment experienced with NS5A inhibitor* with or without compensated cirrhosis	One tablet PO once daily with food for 12 weeks	One tablet (sofosbuvir 400 mg-velpatasvir 100 mg-voxilaprevir 100 mg) per day
	Genotype 1a or 3: Treatment experienced with a sofosbuvir-containing regimen without NS5A inhibitor* with or without compensated cirrhosis	One tablet PO once daily with food for 12 weeks	
Sofosbuvir-velpatasvir-voxilaprevir (Vosevi®)	Genotype 3‡:	One tablet PO once daily with food for 12	One tablet (sofosbuvir 400 mg- velpatasvir 100

Drug Name	Indication	Dosing Regimen	Maximum Dose
	Treatment-naïve with compensated cirrhosis or pegIFN/RBV experienced without cirrhosis with Y93H presence	weeks	mg-voxilaprevir 100 mg) per day
	Genotype 3‡: Treatment experienced with pegIFN/RBV with compensated cirrhosis	One tablet PO once daily with food for 12 weeks	

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.
‡ Off-label, AASLD-IDSA guideline-supported dosing regimen * See Appendix E

Dosage Forms

- Tablet: sofosbuvir 400 mg-velpatasvir 100 mg-voxilaprevir 100 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. Member meets one of the following (a or b):
   a. HCV genotype is 1, 2, 3, 4, 5 or 6, and member has previously been treated with an HCV regimen containing one of the following NS5A inhibitors: daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir;
   b. HCV genotype is 1a or 3, and member has previously been treated with an HCV regimen containing sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (boceprevir, simeprevir or telaprevir);
   **Chart note documentation and copies of lab results are required*
3. Member must use Epclusa®(brand preferred over generic) unless contraindicated or clinically significant adverse effects are experienced (*see Appendix F)*;
4. Prescribed by or in consultation with a gastroenterologist, hepatologist or infectious disease specialist;
5. Age ≥ 18 years;
6. If cirrhosis is present, confirmation of Child-Pugh A status;
7. Member has received ≥ 8 weeks of the prior direct-acting antiviral agent (DAA) regimen from 2a or 2b above, unless virologic failure was determined prior to 8 weeks of therapy;
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 Dosing Information)
11. Dose does not exceed Vosevi® (sofosbuvir 400 mg-velpatasvir 100 mg-voxilaprevir 100 mg) 1 tablet per day.

Approval Duration
Commercial: 84 days *
Medicaid: 84 days *
(*Approved duration should be consistent with a regimen in Dosing Information)

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 Vosevi® for chronic HCV infection and has recently completed at least 60 days of treatment with Vosevi®;
2. Member is responding positively to therapy;
3. Dose does not exceed Vosevi® (sofosbuvir 400 mg-velpatasvir 100 mg-voxilaprevir 100 mg)1 tablet per day.

Approval Duration
Commercial: Up to a total treatment duration of 84 days *
Medicaid: Up to a total treatment duration of 84 days *
(*Approved duration should be consistent with a regimen in Dosing Information)

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
PO: by mouth

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Mavyret® (glecaprevir /pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection: **Genotypes 1, 2, 4, 5, or 6** Without cirrhosis: Three tablets PO once daily for 8 weeks With compensated cirrhosis: Three tablets PO once daily for 12 weeks	glecaprevir 300 mg-pibrentasvir 120 mg (3 tablets) per day
	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection: **Genotype 3** Without cirrhosis or with compensated cirrhosis: Three tablets PO once daily for 16 weeks	
	Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor CHC infection: **Genotype 1** Without cirrhosis or with compensated cirrhosis: Three tablets PO once daily for 16 weeks	
Mavyret® (glecaprevir /pibrentasvir)	Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor CHC infection: **Genotype 1** Without cirrhosis or with compensated cirrhosis: Three tablets PO once daily for 12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Epclusa® (sofosbuvir/ velpatasvir)	With decompensated cirrhosis in whom prior sofosbuvir- or NS5A-based treatment experienced failed: **Genotype 1-6:** One tablet PO once daily with weight-based RBV for 24 weeks	One tablet (sofosbuvir 400 mg/ velpatasvir 100 mg) per day
	With compensated cirrhosis or without cirrhosis and non-NS5A inhibitor, sofosbuvir containing regimen-experienced: **Genotype 1b:** One tablet PO once daily for 12 weeks	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):

- Coadministration with rifampin.

- Boxed Warning(s):
  - Risk of hepatitis B virus reactivation in patients coinfected with HCV and HBV.

APPENDIX D: 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: 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			
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Sovaldi		Sofosbuvir			
Viekira PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir

Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

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-liverdisease): The AASLD, in collaboration with ECHO, the American College of Physician (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.html

References

1. Vosevi® Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; November 2019. Available at: www.vosevi.com. 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.
3. Bourliere M, et al. Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection. NEJM 2017;376:2134-46.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title table was updated. 2. Line of business policy applies to was updated to "All lines of business". 3. Dosing Information table updated to remove Reference column. 4. Initial approval duration was updated for "12 weeks" to "84 days" for both commercial and Medicaid and Continued approval duration update from "Up to a total treatment duration of 12 weeks" to "84 days" for both commercial and Medicaid. 5. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 6. APPENDIX B: Was rephrased to "Below	08/2020	12/07/2020

Review/Revision History	Review/Revision Date	P&T Approval Date
are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements". 7. References were updated.		
Policy was reviewed: 1. Policy title table was updated. 2. Initial approval criteria I.A.3 updated to prefer Epclusa® and reflect use of brand over generic due to rebates available. 3. Continued therapy approval criteria II.A.1.b updated to simplify and align with updated initial approval criteria. 4. References updated.	12/2020	12/07/2020