

Clinical Policy: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)

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Line of Business: Illinois Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

Vosevi 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).

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 Vosevi 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. 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, pibrentasvir, 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. 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*);
 4. Age ≥ 18 years;

5. Member must use Mavyret® (as a single agent or in combination as indicated below) if member meets one of the following (a, b, or c), unless contraindicated or clinically significant adverse effects are experienced:
 - a. HCV genotype is 1, and member has previously been treated with an HCV regimen containing an NS5A inhibitor without an NS3/4A protease inhibitor (i.e., Daklinza®, Epclusa®, Harvoni®);
 - 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);
 - c. For HCV genotype 1 through 6 and member previously treated with Vosevi, Mavyret must be used in combination with Sovaldi® and RBV;
6. If cirrhosis is present, confirmation of Child-Pugh A status;
7. Life expectancy ≥ 12 months with HCV treatment;
8. 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;
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 sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 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

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. Both of the following (i and ii):
 - i. Documentation supports that member is currently receiving Vosevi for chronic HCV infection and has recently completed at least 60 days of treatment with Vosevi;
 - ii. Member meets one of the following (1 or 2):
 - 1) 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, pibrentasvir, or velpatasvir;
 - 2) 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);
2. Member is responding positively to therapy;
3. Dose does not exceed sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg (1 tablet) per day.

Approval duration: Up to a total treatment duration 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Mavyret® (glecaprevir /pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir: Genotypes 1, 2, 4, 5, or 6 Without cirrhosis: Three tablets PO QD for 8 weeks With compensated cirrhosis: Three tablets PO QD for 12 weeks	Adults/Peds age ≥ 12 years or with body weight ≥ 45 kg: glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day; Peds age 3 years to < 12 years of age with body weight < 20 kg: glecaprevir 150 mg/pibrentasvir 60 mg per day;
Mavyret® (glecaprevir /pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir: Genotype 3 Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks	Peds age 3 years to < 12 years of age with body weight < 20 kg: glecaprevir 150 mg/pibrentasvir 60 mg per day;
Mavyret® (glecaprevir /pibrentasvir)	Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor: Genotype 1 Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks	Peds age 3 years to < 12 years of age with body weight 20 kg to < 30 kg: glecaprevir 200 mg/pibrentasvir 80 mg per day;
Mavyret® (glecaprevir /pibrentasvir)	Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor: Genotype 1 Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 12 weeks	Peds age 3 years to < 12 years of age with body weight 30 kg to < 45 kg: glecaprevir 250 mg/pibrentasvir 100 mg per day
Mavyret® (glecaprevir /pibrentasvir) + RBV	With prior sofosbuvir/velpatasvir/voxilaprevir treatment failure, with or without compensated cirrhosis Genotypes 1-6[‡]: Sovaldi 400 mg + Mavyret 300 mg/120 mg + weight-based RBV for 16 weeks	Three tablets (glecaprevir 300 mg/ pibrentasvir 120 mg) per day AASLD-IDSA (updated March 2021)

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.

‡ Off-label, AASLD-IDSA guideline-supported dosing regimen

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): coadministration with rifampin
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfecting 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

- Per the Vosevi package labeling, Vosevi is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C).

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: Treatment-experienced with NS5A inhibitor* with or without compensated cirrhosis	One tablet PO QD for 12 weeks	One tablet (sofosbuvir 400 mg/ velpatasvir 100 mg/ voxilaprevir 100 mg) per day	FDA-approved labeling
Genotype 1a or 3: Treatment-experienced with a sofosbuvir-containing regimen without NS5A inhibitor* with or without compensated cirrhosis	One tablet PO QD for 12 weeks		FDA-approved labeling
Genotype 1-6:	One tablet PO QD with weight-based RBV for 24 weeks		AASLD-IDSA (updated March 2021)

Indication	Dosing Regimen	Maximum Dose	Reference
Treatment-experienced with Vosevi® with or without compensated cirrhosis			

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.

* See appendix D

VI. Product Availability

Tablet: sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg

VII. References

1. Vosevi Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; November 2019. Available at: www.vosevi.com. Accessed April 15, 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.
3. Bourliere M, et al. Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection. NEJM 2017;376:2134-46.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	04.27.21	05.21
3Q 2021 annual review: removed criterion for sobriety documentation as AASLD recommends to treat all patients with HCV except those with short life expectancy; updated Appendix B: Therapeutic Alternatives and Section V dosing; references reviewed and updated.	07.16.21	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.

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