Clinical Policy: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)

Reference Number: GA.PMN.25
Effective Date: 9/17
Last Review Date: 7/2020 Revision Log
Line of Business: Medicaid

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 oral tablet. Sofosbuvir is a nucleotide analog HCV NS5B polymerase inhibitor, velpatasvir is an NS5A inhibitor, and voxilaprevir is an NS3/4A protease inhibitor.

FDA Approved Indication(s)
Vosevi is indicated for the treatment of adult patients with chronic hepatitis C virus (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.

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Vosevi is **medically necessary** when the following criteria are met:

I. 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. Diagnosis of chronic HCV infection as evidenced by detectable HCV RNA (ribonucleic acid) levels in the last 6 months;
2. Age ≥ 18 years;
3. Member meets one of the following (a or b):
    a. If HCV genotype 1, 2, 3, 4, 5 or 6, member has previously been treated with an HCV regimen containing one of the following NS5A inhibitors: daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir;
    b. If HCV genotype is 1a or 3, 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);

4. 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;
5. Member must use Mavyret™ if member meets one of the following (a or b), 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. Life expectancy ≥ 12 months with HCV treatment;
7. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Appendix D Dosage*);
8. Member is hepatitis B virus (HBV) negative, or if positive, documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced (*see Appendix E*);
9. Prescribed dose does not exceed one tablet (sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg) daily.

Approval duration: up to a total of 24 weeks*
*(*Approved duration should be consistent with a regimen in Appendix D FDA approved dosages and Treatment Duration)*

B. Other diagnoses/indications: Refer to CP.PMN.53 – No Coverage Criteria/Off-Label Use Policy if diagnosis is NOT specifically listed under section I.

II. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
APRI: AST to platelet ratio
CTP: Child Turcotte Pugh
CrCl: creatinine clearance
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
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: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-experienced with IFN/pegIFN+RBV+/- sofosbuvir chronic HCV infection: **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 wee	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-experienced with IFN/pegIFN+RBV+/- sofosbuvir chronic HCV infection: **Genotypes 3** Without cirhhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor chronic HCV infection: **Genotype 1** Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (3 tablets) per day
Mavyret™ (glecaprevir/pibrentasvir)	Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor chronic HCV infection: **Genotype 1** Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 12 weeks	Mavyret: glecaprevir 300mg/pibrentasvir 120mg (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 QD with weight-based RBV for 24 weeks	One tablet (sofosbuvir 400mg/velpatasvir 100mg) per day

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
Epclusa® (sofosbuvir/velpatasvir)	With compensated cirrhosis or without cirrhosis and non-NS5A inhibitor, sofosbuvir-containing regimen-experienced: **Genotype 1b** One tablet PO QD for 12 weeks	One tablet (sofosbuvir 400mg/velpatasvir 100mg) per day

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

Appendix C: Contraindications

- Coadministration with rifampin

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

*Combination drugs

Appendix E: General Information

- Hepatitis B Virus (HBV) Reactivation 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.
- Acceptable medical justification for inability to use Mavyret (preferred product):

- Severe hepatic disease (Child-Pugh C): use of Mavyret is not recommended due to higher exposures of glecaprevir and pibrentasvir.
- Moderate hepatic disease (Child-Pugh B): although not an absolute contraindication, use of Mavyret is not recommended in patient with moderate hepatic disease (Child-Pugh B) due to lack of safety and efficacy data.
  - Following administration of Mavyret in HCV infected subjects with *compensate*d cirrhosis (Child-Pugh A), exposure of glecaprevir was appromiately 2-fold and pibrentasvir exposure was similar to non-cirrhotic *HCV infected* subjects
  - At the clinical dose, compared to *non-HCV infected* subjects with *normal hepatic function*, glecaprevir AUC was 100% higher in Child-Pugh B subjects, and increased to 11-fold in Child-Pugh C subjects. Pibrentasvir AUC was 26% higher in Child-Pugh B subjects, and 114% higher in Child-Pugh C subjects
- Drug-drug interactions with one or more of the following agents:
  - Atazanavir
  - Efavirenz

- <u>Unacceptable medical justification for inability to use Mavyret (preferred product):</u>
  - Black Box warning (BBW): currently or previously infected with hepatitis B virus. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Therefore it is not a valid clinical reason not to use Mavyret.
  - Concurrent anticoagulant therapy: Fluctuations in International Normalized Ration (INR) have been observed in warfarin recipients who were also receibing treatment for HCV infections. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection..
  - Drug-drug interactions with one or more of the following agents:
    - Rifampin, carbamazepine, or St. John's wort:
    - These drug-drug interactions are not unique to Mavyret, and they apply across the entire therapeutic class of direct-acting antivirals for the treatment of HCV infection.

III. 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	1) FDA-approved labeling 2) AASLD-IDSA (updated November 2019)
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		1) FDA-approved labeling 2) AASLD-IDSA (updated November 2019)
Genotype 1-6: Treatment-experienced with Vosevi® with or without compensated cirrhosis	Vosevi one tablet PO QD with weight-based RBV for 24 weeks		AASLD-IDSA (updated November 2019)

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 E*

IV. Product Availability

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

V. References

1. Vosevi Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; November 2019. Available at: www.vosevi.com. Accessed April 30, 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 November 6, 2019. Available at: https://www.hcvguidelines.org/. Accessed April 30, 2020.
3. Bourliere M, et al. Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection. NEJM 2017;376:2134-46.
4. Platt L, Easterbrook P, Gower E, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. Lanet Infect Dis 2016;16:797-808. http://dx.doi.org/10.1016/
5. Centers for Disease Control and Prevention. HIV and viral hepatitis: fact sheet. June 2017. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/hiv-viral-hepatitis.pdf. Accessed May 1, 2019.

6. Wolitski R. When it comes to curing hepatitis C, your health care provider may not need to be a specialist. U.S. Department of Health & Human Services. Last updated September 20, 2017. Available at: https://www.hhs.gov/hepatitis/blog/2017/09/20/study-calls-for-expansion-of-hepatitis-c-treatment.html. Accessed October 30, 2019.
CDC. Viral hepatitis: Q&As for health professionals. Last updated July 2, 2019. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed October 30, 2019.

Reviews, Revisions, and Approvals	Date	Approval Date
Policy created	09/17	9/17
Changed current Georgia policy templates to corporate standard templates for drug coverage criteria to meet corporate compliance. Changes/revisions included; new formatting, font size, use of standard policy language for each section of policy, and rearranged order of certain steps in criteria and sections. Added new preferred treatment tables that includes dosage and frequency based on genotype for Mavyret. Removed background sections. Updated general information and contraindication section to be consistent with corporate HCV policies.	2/21/19	2/19
Annual review. Updated wording of approval criteria for meeting use of preferential Mavyret.	10/19	10/19
Added Epclusa to Appendix B. Removed Appendix D for Metavir scoring. Removed dosing for Mavyret treatment-naïve. Updated order of all other Appendices. Updated references.	4/2020	4/2020
Added preferred re-direction for off-label Mavyret + Sovaldi + RBV after Vosevi failure; modified initial and continued approval durations up to 24 weeks to allow for post Vosevi failure off-label indication dosing per per AASLD/IDSA guideline; references reviewed and updated.	7/2020	7/2020

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a

contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.