CENTENE Corporation

Clinical Policy: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)

Reference Number: LA. PHAR.347
Effective Date: 09/17
Last Review Date 05/18
Line of Business: 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 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

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.

* 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 (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® 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 multiple detectable HCV RNA (ribonucleic acid) levels in the last 6 months;
2. Age ≥ 18 years;
3. Life expectancy ≥ 12 months with HCV treatment;
4. Prescriber and patient must attest that the patient is not actively participating in illicit IV drug use and/or alcohol use;;
5. Advanced liver disease defined as a or b:
   a. Advanced fibrosis indicated by i, ii or iii;

i. Liver biopsy showing a METAVIR score of F3 or equivalent (Knodell, Scheuer, Batts-Ludwig – F3; Ishak – F4/5);
ii. One serologic test showing an equivalent score to METVIR F3 per Appendix C
iii. One radiologic test showing an equivalent score to METAVIR F3 per Appendix C;

b. Cirrhosis indicated by i, ii, iii, iv or v:
i. Hepatocellular carcinoma (HCC) - and the HCC is amenable to resection, ablation or transplant;
ii. Liver biopsy showing a METAVIR score of F4 or equivalent (Knodell, Scheuer, Batts-Ludwig – F4; Ishak - F5/6);
iii. One serologic test showing an equivalent score to METAVIR F4 per Appendix C;
iv. One radiologic test showing an equivalent score to METAVIR F4 per Appendix C;
v. Other radiologic test showing evidence of cirrhosis (e.g., portal hypertension);

c. If member is HIV/HCV co-infected, there shall be no METAVIR score requirements.

6. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference*);
7. If cirrhosis is present, confirmation of Child-Pugh A status;
8. 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);
9. Member has received ≥ 8 weeks of the prior direct-acting antiviral agent (DAA) regimen from 9a or 9b above, unless virologic failure was determined prior to 8 weeks of therapy;
10. Member has a contraindication or intolerance to Mavyret and meets one of the following (a or b):
    a. Member has genotype 1 without cirrhosis or with compensated cirrhosis (Child-Pugh A) and has previously been treated with an HCV regimen containing an NS5A inhibitor;
    b. Member has genotype 1a or 3 and 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);

11. Member agrees to participate in a medication adherence program meeting both of the following components:
    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;
12. 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 B*);
13. Prescribed dose does not exceed one tablet (sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg) daily.

Approval duration: 12 weeks

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 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. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Vosevi for treatment of chronic HCV infection and has received this medication for at least 30 days;
2. Member is responding positively to therapy (e.g., decreased HCV RNA level, no unacceptable toxicity);
3. Dose does not exceed one tablet (sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg) daily.

Approval duration: Up to a total treatment duration of 12 weeks

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 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 – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DAA: direct-acting antiviral agent
DNA: deoxyribonucleic acid
FDA: Food and Drug Administration
HBeAg: hepatitis B virus envelope antigen
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
RNA: ribonucleic acid

Appendix B: General Information

- Hepatitis B reactivation is a black box warning for all direct-acting antiviral drugs for the treatment of HCV. The provider must provide either 1, 2, or 3:
  1. Documentation of absence of concurrent HBV infection as evidenced by laboratory values showing absence of hepatitis B virus envelope antigen (HBeAg) and HBV DNA;
  2. Documentation that HBV co-infected patient may not be candidates for therapy as evidenced by:
     - Absence of HBeAg, HBV DNA (deoxyribonucleic acid) < 2,000 international units/mL, and alanine aminotransferase (ALT) level within 1 to 2 times the upper limit of normal;
     - HBeAg-positive and HBV DNA greater than 1,000,000 international units/mL and ALT level within 1 to 2 times the upper limit of normal;
  3. Documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced.
- Per the Vosevi package labeling, Vosevi is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C).
- Approximate scoring equivalencies using METAVIR F3/F4 as reference are below:

Appendix C: Approximate scoring equivalencies using METAVIR F3/F4 as reference

Fibrosis/ Cirrhosis	Serologic Tests*				Radiologic Tests†		Liver Biopsy‡	
	Fibro Test	FIBRO Spect II	APRI	FIB-4	FibroScan (kPa)	MRE (kPa)	METAVIR	Ishak
Advanced fibrosis	≥0.59	≥42	>1.5	>3.25	≥9.5	≥4.11	F3	F4-5
Cirrhosis	≥0.75	≥42	>1.5	>3.25	≥12.0	≥4.71	F4	F5-6

*Serologic tests:
FibroTest (available through Quest as FibroTest or LabCorp as FibroSure)
FIBROSpect II (available through Prometheus Laboratory)
APRI (AST to platelet ratio index)
FIB-4 (Fibrosis-4 index: includes age, AST level, platelet count)

†Radiologic tests:
FibroScan (transient elastography)
MRE (magnetic resonance elastography)

‡Liver biopsy (histologic scoring systems):
METAVIR F3/F4 is equivalent to Knodell, Scheuer, and Batts-Ludwig F3/F4 and Ishak F4-5/F5-6
METAVIR fibrosis stages: F0 = no fibrosis; F1 = portal fibrosis without septa; F2 = few septa; F3 = numerous septa without cirrhosis; F4 = cirrhosis

Appendix D: Direct-Acting Antivirals for Initial 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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chronic HCV Infection	1 tablet by mouth daily	1 tablet/day

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.; July 2017. Available at: www.vosevi.com. Accessed July 19, 2017.
2. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). Retreatment of persons in whom prior therapy has failed. http://www.hcvguidelines.org. Last update April 12, 2017. Accessed July 19, 2017.
3. Bourliere M, et al. Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection. NEJM 2017;376:2134-46.

Reviews, Revisions, and Approvals	Date	Approval Date
Policy created	08/17	09/17
Due to State requirements, removed prescriber restrictions regarding who can prescribe Hepatitis C DAA agents; Removed the abstinence period of 6 months and added documentation required that member is not actively participating in alcohol and/or illicit IV drugs use,; Added statement that NO Fibrosis score is required for HIV/HCV co-infected members	05/18	05/18

Reviews, Revisions, and Approvals	Date	Approval Date
Changed language to one serologic test OR one radiologic test from one serologic test and one radiologic test	5/18	5/18

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.

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.