Clinical Policy: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)

Reference Number: PA.CP. PHAR.347
Effective Date: 01/18
Last Review Date 09/17
Line of Business: Medicaid

Revision Log

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 Pennsylvania Health and Wellness ® 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
2. Age ≥ 18 years;
3. If actively abusing alcohol or IV drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse and an offer of a referral for substance use disorder treatment.
4. Has all of the following:
   a. Documented quantitative HCV RNA at baseline that was tested within the past 3 months.
   b. Does not have a life expectancy of less than 12 months due to non-liver-related comorbid conditions.

c. Has correct or addressed the causes of non-adherence to a previously prescribed Hepatitis C treatment regimen if the recipient has a history of failed treatment due to non-adherence.
d. Had all potential drug interactions addressed by the prescriber

5.
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 or meets one of the following (a, b, or c):
    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);
    c. Mavyret is not AASLD recommended for the condition
11. Has a documented commitment to adherence with the planned course of treatment
12. Has documented completion of
    a. Hepatitis B immunization series or Hepatitis B screening (sAb/sAg and cAb/cAg) AND
    b. If there is detectable HBV DNA, will be treated for Hepatitis B or if negative for hepatitis BsAb, is being vaccinated against Hepatitis B.AND
    c. Has a documented HIV screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay: Is being treated for HIV or is not being treated for HIV and the medical record documents the rationale for not being treated
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 PA.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 Pennsylvania Health and Wellness benefit, or documentation supports that member is currently receiving Vosevi for treatment of chronic HCV infection;or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. 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 PA.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 – PA.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

A. **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.*

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.
