Clinical Policy: sofosbuvir-velpatasvir-voxilaprevir (Vosevi)

Reference Number: NM.CP.PPA.05
Effective Date: 1/1/19
Last Review Date: 1/11/23
Revision Log

Description and FDA Approved Indication(s)
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.

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).

Black Box Warning
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.

Product Availability
Oral tablet
Brand: (Vosevi) sofosbuvir-velpatasvir-voxilaprevir 400 mg-100 mg-100 mg

Policy/Criteria

It is the policy of Western Sky Community Care (WSCC) 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 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);
3. Age ≥ 18 years;
4. If cirrhosis is present, confirmation of Child-Pugh A status ***(see appendix E);***
5. Life expectancy ≥ 12 months with HCV treatment;
6. ****Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see appendix C and D*);
7. ****Dose does not exceed sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg (1 tablet) per day.

Approval duration: 12 weeks*

*(*Approved duration should be consistent with guidelines, see appendix C and D)*

****If treatment regimen varies in dosing or interval from FDA or AASLD-IDSA guideline recommendations but it is documented on PA request/office chart notes that requested regimen in consultation with Project ECHO—please approve regimen.**

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.
2. **If denial is likely please make attempt to contact prescriber's office for peer-to-peer.**

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 or member has previously met initial approval criteria;
   b. Must meet 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, or velpatasvir;
         2. 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);

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 12 weeks*
*(*Approved duration should be consistent with guidelines, see appendices C and D)* ****If treatment regimen varies in dosing or interval from FDA or AASLD-IDSA guideline recommendations but it is documented on PA request/office chart notes that requested regimen in consultation with Project ECHO—please approve regimen.**

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.
2. **If denial is likely please make attempt to contact prescriber's office for peer-to-peer.**

Appendices

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
APRI: AST to platelet ratio
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
IQR: interquartile range
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
PegIFN: pegylated interferon
RBV: ribavirin
RNA: ribonucleic acid

***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 B: 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			
Mavyret*	Pibrentasvir			Glecaprevir	
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie**	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/Pak**	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs***Additional PIs no longer recommended that have been discontinued:*

Appendix C: Vosevi treatment duration

Genotype	Liver status	Treatment-Experienced Adult Patients	Duration
1, 2, 3, 4, 5, 6	No Cirrhosis	Treatment-experienced with an NS5A inhibitor†	12 wk
	Compensated Cirrhosis*	Treatment-experienced with an NS5A inhibitor†	12 wk
1a or 3	No Cirrhosis	Treatment-experienced with sofosbuvir **without** an NS5A inhibitor‡	12 wk
	Compensated Cirrhosis*	Treatment-experienced with sofosbuvir **without** an NS5A inhibitor‡	12 wk

*Child-Pugh A
† 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).

Appendix D: AASLD-IDSA Recommended Regimens and Treatment Durations
https://www.hcvguidelines.org/

Appendix E:
Any of the following meet the definition for cirrhosis per NM state directives:

- APRI >= 1.0
- Fib-4 >= 3.25
- Transient Elastography Score >= 12.5 dP3 (F4 equivalent)
- Fibrotest >= 0.73 (f4 equivalent) OR Fibrometer with F4 predominance

- Radiographic imaging or physical exam findings consistent with cirrhosis
- Liver biopsy confirming a METAVIR score of F4

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 F: 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.

- <u>Acceptable medical justification for inability to use Mavyret (preferred product):</u>
  - 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 patients with moderate hepatic disease (Child-Pugh B) due to lack of safety and efficacy data.
    - Following administration of Mavyret in HCV infected subjects with *compensated* cirrhosis (Child-Pugh A), exposure of glecaprevir was approximately 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 the following agents:
    - Atazanavir
    - Efavirenz

- Unacceptable medical justification for inability to use Mavyret (preferred product):
  - 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 Ratio (INR) have been observed in warfarin recipients who were also receiving 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. Although caution is advised when using Mavyret while receiving concurrent anticoagulant therapy, specifically warfarin, this is not an absolute contraindication as long as patient is adequately monitored and educated during therapy.
  - 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 treatment of HCV infection.

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Revision Log

Reviews, Revisions, and Approvals	Date	Approval Date
New clinical policy created for WSCC based on New Mexico requirements	11/18	11/18
Added provision for approval of drug dosing and interval (despite not meeting AASLD and IDSA recommended guidelines) if regimen is recommended/requested after consultation with Project ECHO; added Project ECHO to references;	1/25/19	1/25/19
Renamed clinical policy per corporate guidelines; Changed from NM.CP.PHAR.05 to NM.CP.PPA.05; Name presented at WSCC P&T Committee;	3/20/19	3/20/19
Annual Review. References updated. Reviewed and approved by WSCC P&T Committee.	1/29/20	1/29/20
Edited criteria to match updated directive from NM HSD, MAD Supplement 20-13 to include updated forms. Updated references to reflect this change in NM Medicaid direction.	1/12/21	
Annual review. Reviewed and approved by WSCC P&T Committee.		1/20/21
Edited references and links to NM HCV Uniform HCV checklist.	1/7/22	

Reviews, Revisions, and Approvals	Date	Approval Date
Annual review. Reviewed and approved by WSCC P&T Committee.		1/12/22
Removing trial of Mavyret prior to trial of Vosevi based on current HCV guidelines recommendation which show Mavyret as an alternative regimen for 16 weeks (longer duration than the recommended regimen, per HCV guidelines, of Vosevi x 12 weeks) for sofosbuvir-based and elbasvir/grazoprevir treatment failures. Removed "Member has received ≥ 8 weeks of the prior direct-acting antiviral agent (DAA) regimen" as difficult to determine based on records that member received exactly that length of therapy. Completed prior therapy to be assumed based on provider visit notes.	7/11/22	
Reviewed and approved by WSCC P&T Committee.		7/13/2022
Annual Review. Updated References. Removed requirement for Drug Authorization Form and Uniform New Mexico HCV Checklist. Reviewed and approved by WSCC P&T Committee.	1/9/23	1/11/23