# Clinical Policy: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)

Reference Number: PA.CP. PHAR.347
Effective Date: 01/18
Last Review Date: 07/17/19
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 hepatitis C virus (HCV) infection with documented genotyping;
2. 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;
3. Has a Metavir fibrosis score documented by a recent noninvasive test such as a blood test or imaging, a Fibroscan, or findings on physical examination;
4. Has documented completion of the following (a or b, c, d, and e):
   a. Hepatitis B immunization series; or
   b. Hepatitis B screening (sAb/sAg and cAb);
   c. If positive for hepatitis B sAg, quantitative HBV DNA results;
   d. If there is detectable HBV DNA, a treatment plan for hepatitis B consistent with AASLD recommendations; and

e. If negative for hepatitis B sAb, a hepatitis B immunization plan or counseling to receive the hepatitis B immunization series;

5. Has a documented HIV screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay meets the following (a or b):
   a. Is being treated for HIV or is not being treated for HIV; or
   b. The medical record documents the rationale for not being treated;
6. Has documentation of AASLD-recommended resistance- associated substitution (RAS) testing and is prescribed a drug regimen in accordance with AASLD guidance;
7. If genotype 1a, or had a previous treatment failure with a direct-acting antiretroviral (DAA) regimen, is prescribed an AASLD recommended drug regimen based on the documented results of a NS5A RAS screening;
8. Does not have a life expectancy of less than 12 months due to non-liver-related comorbid conditions;
9. Has a documented quantitative HCV RNA at baseline that was tested within the past 3 months;
10. Has corrected or addressed the causes of non-adherence to a previously prescribed Hepatitis C treatment regimen if the member has a history of failed treatment due to non-adherence;
11. Had all potential drug interactions addressed by the prescriber;
12. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
    a. If a lower cost alternative regimen carries an equal or higher AASLD-IDSA rating, a clinical contraindication or intolerance must be present for the alternative regimen prior to the approval of a Vosevi-based regimen;
13. If prescribed with ribavirin, no changes will be required of therapy;
14. Has a documented commitment to adherence with the planned course of treatment and appropriate monitoring;
15. Prescribed dose does not exceed one tablet (sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg) daily;
    a. If request exceeds limit, refer to PA.CP.PMN.53.

**Approval duration: 12 weeks**

**B. Other diagnoses/indications**

1. Refer to PA.CP.PMN.53 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.PMN.53 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.PMN.53 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.*

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## 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.

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| Updated policy to incorporate DUR Memo dated 12.10.18. | 1.7.2019 | |
| 3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020 | 07/17/19 | |