Clinical Policy: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)

Description
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.

*This criteria does NOT apply to California Commercial Exchange Plans.

FDA Approved Indication(s)
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).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) 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 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);

*Chart note documentation and copies of lab results are required

3. Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease specialist, or provider who has expertise in treating HCV based on a certified training program (see Appendix F);

4. Age ≥ 18 years;

5. If cirrhosis is present, confirmation of Child-Pugh A status;

6. 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;

7. Life expectancy ≥ 12 months with HCV treatment;

8. Member agrees to participate in a medication adherence program meeting both of the following components (a and b):
   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;

9. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (see Section V Dosage and Administration for reference);

10. Dose does not exceed Vosevi (sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir) 100 mg (1 tablet) per day.

Approval duration: up to 24 weeks*

(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)

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): HIM.PHAR.21 for health insurance marketplace.

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 via Centene benefit 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 Vosevi (sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir) 100 mg (1 tablet) per day.

**Approval duration: Up to a total treatment duration of 24 weeks**
(*Approved duration should be consistent with a regimen in Section V Dosage and Administration*)

**B. Other diagnoses/indications** (must meet 1 or 2):
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): HIM.PHAR.21 for health insurance marketplace.

**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 – HIM.PHAR.21 for health insurance marketplace, or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

<table>
<thead>
<tr>
<th>Abbreviation/Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AASLD</td>
<td>American Association for the Study of Liver Diseases</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>HBV</td>
<td>hepatitis B virus</td>
</tr>
<tr>
<td>HCV</td>
<td>hepatitis C virus</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>IDSA</td>
<td>Infectious Diseases Society of America</td>
</tr>
<tr>
<td>NS3/4A, NS5A/B</td>
<td>nonstructural protein</td>
</tr>
<tr>
<td>PegIFN</td>
<td>pegylated interferon</td>
</tr>
<tr>
<td>RBV</td>
<td>ribavirin</td>
</tr>
<tr>
<td>RNA</td>
<td>ribonucleic acid</td>
</tr>
</tbody>
</table>

*Appendix B: Therapeutic Alternatives*

*Not applicable.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): coadministration with rifampin
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfected with HCV and HBV

*Appendix D: Direct-Acting Antivirals for Treatment of HCV Infection*

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>NS5A Inhibitor</th>
<th>Nucleotide Analog NS5B Polymerase Inhibitor</th>
<th>Non-Nucleoside NS5B Palm Polymerase Inhibitor</th>
<th>NS3/4A Protease Inhibitor (PI)</th>
<th>CYP3A Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daklinza</td>
<td>Daclatasvir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epclusa*</td>
<td>Velpatasvir</td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harvoni*</td>
<td>Ledipasvir</td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mavyret*</td>
<td>Pibrentasvir</td>
<td></td>
<td></td>
<td></td>
<td>Gledcaprevir</td>
</tr>
<tr>
<td>Sovaldi</td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### CLINICAL POLICY
Sofosbuvir/Velpatasvir/Voxilaprevir

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Drug Class</th>
<th>NS5A Inhibitor</th>
<th>Nucleotide Analog NS5B Polymerase Inhibitor</th>
<th>Non-Nucleoside NS5B Palm Polymerase Inhibitor</th>
<th>NS3/4A Protease Inhibitor (PI)</th>
<th>CYP3A Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viekira PAK*</td>
<td>Ombitasvir</td>
<td>Dasabuvir</td>
<td>Paritaprevir</td>
<td>Ritonavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vosevi*</td>
<td>Velpatasvir</td>
<td>Sofosbuvir</td>
<td></td>
<td>Voxilaprevir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zepatier*</td>
<td>Elbasvir</td>
<td></td>
<td></td>
<td></td>
<td>Grazoprevir</td>
<td></td>
</tr>
</tbody>
</table>

*Combination drugs

### Appendix E: 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.
- 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 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.

- Child-Pugh Score:

<table>
<thead>
<tr>
<th>Condition</th>
<th>1 Point</th>
<th>2 Points</th>
<th>3 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>Less than 2 mg/dL</td>
<td>2-3 mg/dL</td>
<td>Over 3 mg/dL</td>
</tr>
<tr>
<td></td>
<td>Less than 34 umol/L</td>
<td>34-50 umol/L</td>
<td>Over 50 umol/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>Over 3.5 g/dL</td>
<td>2.8-3.5 g/dL</td>
<td>Less than 2.8 g/dL</td>
</tr>
<tr>
<td></td>
<td>Over 35 g/L</td>
<td>28-35 g/L</td>
<td>Less than 28 g/L</td>
</tr>
<tr>
<td>INR</td>
<td>Less than 1.7</td>
<td>1.7 - 2.2</td>
<td>Over 2.2</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild / medically controlled</td>
<td>Moderate-severe / poorly controlled</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Mild / medically controlled</td>
<td>Moderate-severe / poorly controlled.</td>
</tr>
<tr>
<td></td>
<td>Grade I-II</td>
<td>Grade III-IV</td>
<td></td>
</tr>
</tbody>
</table>

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: Healthcare Provider HCV Training
Acceptable HCV training programs and/or online courses include, but are not limited to the following:

- Hepatitis C online course (https://www.hepatitisc.uw.edu/): University of Washington is funded by the Division of Viral Hepatitis to develop a comprehensive, online self-study course for medical providers on diagnosis, monitoring, and management of hepatitis C virus infection. Free CME and CNE credit available.
- Fundamentals of Liver Disease (https://liverlearning.aasld.org/fundamentals-of-liver-disease): The AASLD, in collaboration with ECHO, the American College of Physicians (ACP), CDC, and the Department of Veterans Affairs, has developed Fundamentals of Liver Disease, a free, online CME course to improve providers’ knowledge and clinical skills in hepatology.
- Clinical Care Options: http://www.clinicaloptions.com/hepatitis.aspx
- CDC training resources: https://www.cdc.gov/hepatitis/resources/professionals/trainingresources.htm

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1-6: Treatment-experienced with NS5A inhibitor* with or without compensated cirrhosis</td>
<td>One tablet PO QD for 12 weeks</td>
<td>One tablet (sofosbuvir 400 mg/ velpatasvir 100 mg/ voxilaprevir 100 mg) per day</td>
<td>1) FDA-approved labeling 2) AASLD-IDSA (updated November 2019)</td>
</tr>
<tr>
<td>Genotype 1a or 3: Treatment-experienced with a sofosbuvir-</td>
<td>One tablet PO QD for 12 weeks</td>
<td></td>
<td>1) FDA-approved labeling</td>
</tr>
</tbody>
</table>
Indication | Dosing Regimen | Maximum Dose | Reference |
---|---|---|---|
containing regimen without NS5A inhibitor* with or without compensated cirrhosis | Vosevi one tablet PO QD with weight-based RBV for 24 weeks | 2) AASLD-IDSA (updated November 2019) |
Genotype 1-6: Treatment-experienced with Vosevi® with or without compensated cirrhosis | | 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.

VI. Product Availability
Tablet: sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg

VII. References

Reviews, Revisions, and Approvals
| Date | P&T Approval Date |
---|---|
Policy created (adapted from CP.PCH.22 which is being retired) per June SDC and prior clinical guidance. | 06.04.20 | 08.20 |

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.

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