Clinical Policy: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)
Reference Number: CP.CPA.290
Effective Date: 07.26.17
Last Review Date: 08.19
Line of Business: Commercial

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 hepatitis C virus (HCV) NS5B polymerase inhibitor, velpatasvir is an NS5A inhibitor, and voxilaprevir is an NS3/4A protease inhibitor.

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. Member must use Mavyret™ if member meets one of the following (a or b), unless contraindicated or clinically significant adverse effects are experienced (see Appendix F):
   a. HCV genotype 1 and member has previously been treated with an HCV regimen containing an NS5A inhibitor without an NS3/4A protease inhibitor (i.e., Daklinza®, Epclusa®, Harvoni®);
   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);

4. Prescribed by or in consultation with a gastroenterologist, hepatologist or infectious disease specialist;

5. Age ≥ 18 years;

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

7. 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;

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

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

**Approval duration: 12 weeks***
(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)

B. Other diagnoses/indications

1. Refer to CP.CPA.09 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. 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 12 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): CP.CPA.09 for commercial.

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.CPA.09 for commercial or evidence of coverage documents.

IV. **Appendices/General Information**

   **Appendix A: Abbreviation/Acronym Key**
   
   AASLD: American Association for the Study of Liver Diseases
   FDA: Food and Drug Administration
   HBV: hepatitis B virus
   HCV: hepatitis C virus
   HIV: human immunodeficiency virus
   IDSA: Infectious Diseases Society of America
   NS3/4A, NS5A/B: nonstructural protein
   PegIFN: pegylated interferon
   RBV: ribavirin
   RNA: ribonucleic acid

   **Appendix B: Therapeutic Alternatives**
   *This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
</table>
| Mavyret™ (glecaprevir/pibrentasvir) | Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection: Genotypes 1, 2, 4, 5, or 6
Without cirrhosis:
Three tablets PO QD for 8 weeks
With compensated cirrhosis:
Three tablets PO QD for 12 weeks | Mavyret: glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day |
<p>| Mavyret™ (glecaprevir/pibrentasvir) | Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection: Genotype 3 | Mavyret: glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day |</p>
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks</td>
<td></td>
</tr>
</tbody>
</table>
| Mavyret™ (glecaprevir/pibrentasvir) | Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor CHC infection: **Genotype 1**  
Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks | Mavyret: glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day                     |
| Mavyret™ (glecaprevir/pibrentasvir) | Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor CHC infection: **Genotype 1**  
Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 16 weeks | Mavyret: glecaprevir 300 mg/pibrentasvir 120 mg (3 tablets) per day                     |
| Epclusa® (sofosbuvir/velpatasvir) | With decompensated cirrhosis in whom prior sofosbuvir- or NS5A-based treatment experienced failed: **Genotype 1-6:**  
One tablet PO QD with weight-based RBV for 24 weeks | One tablet (sofosbuvir 400mg/velpatasvir 100 mg) per day                             |
| Epclusa® (sofosbuvir/velpatasvir) | With compensated cirrhosis or without cirrhosis and non-NS5A inhibitor, sofosbuvir-containing regimen-experienced: **Genotype 1b:**  
One tablet PO QD for 12 weeks | One tablet (sofosbuvir 400mg/velpatasvir 100 mg) per day                             |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

**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>Glecaprevir</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Olysio</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Sovaldi</td>
<td></td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technivie*</td>
<td>Ombitasvir</td>
<td>Paritaprevir</td>
<td>Ritonavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viekira XR/PAK*</td>
<td>Ombitasvir</td>
<td>Dasabuvir</td>
<td>Paritaprevir</td>
<td>Ritonavir</td>
<td></td>
</tr>
<tr>
<td>Vosevi*</td>
<td>Velpatasvir</td>
<td>Sofosbuvir</td>
<td></td>
<td>Voxilaprevir</td>
<td></td>
</tr>
<tr>
<td>Zepatier*</td>
<td>Elbasvir</td>
<td></td>
<td>Grazoprevir</td>
<td></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.
- Child-Pugh Score:

<table>
<thead>
<tr>
<th></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 Grade I-II</td>
<td>Moderate-severe / poorly controlled Grade III-IV</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.
### 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 May 2018)</td>
</tr>
<tr>
<td>Genotype 1a or 3: Treatment-experienced with a sofosbuvir-containing regimen without NS5A inhibitor* with or without compensated cirrhosis</td>
<td>One tablet PO QD for 12 weeks</td>
<td></td>
<td>1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)</td>
</tr>
<tr>
<td>Genotype 3(^1): Treatment-naïve with compensated cirrhosis or pegIFN/RBV-experienced without cirrhosis with Y93H presence</td>
<td>One tablet PO QD for 12 weeks</td>
<td></td>
<td>AASLD-IDSA (updated May 2018)</td>
</tr>
<tr>
<td>Genotype 3(^1): Treatment-experienced with pegIFN/RBV with compensated cirrhosis</td>
<td>One tablet PO QD for 12 weeks</td>
<td></td>
<td>AASLD-IDSA (updated May 2018)</td>
</tr>
</tbody>
</table>

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.

\(^1\) Off-label, AASLD-IDSA guideline-supported dosing regimen

* See appendix E

### VI. Product Availability

Tablet: sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg

### VII. References

## Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created. Safety criteria were applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Exception made to require Hep B screening for all patients prior to treatment to ensure that proper risk reduction measures are taking, though this is not specifically addressed in boxed warning.</td>
<td>07.26.17</td>
<td>08.17</td>
</tr>
<tr>
<td>Added redirection to Mavyret or Eplusa for FDA-approved indications. None applicable for Harvoni.</td>
<td>09.05.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Removed redirection to Eplucsa for GT3 and GT1a for sofosbuvir-experienced pts per updated AASLD guidelines (updated September 21, 2017)</td>
<td>09.25.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Clarified redirection to Mavyret for GT1 only if previously treated with an HCV regimen containing an NS5A inhibitor without an NS3/4A protease inhibitor (i.e., Daklinza, Eplusa, Harvoni)</td>
<td>09.29.17</td>
<td></td>
</tr>
<tr>
<td>3Q 2018 annual review: removed requirement for HBV verification; added requirement that member had received at least 8 weeks of prior tx unless virologic failure before 8 weeks; added requirement that prescribed regimen should be consistent with FDA or AASLD recommendations; expanded duration of tx required for COC from 30 days to 60 days; required verification of genotype for COC; references reviewed and updated.</td>
<td>05.22.18</td>
<td>08.18</td>
</tr>
<tr>
<td>Removed requirement for advanced fibrosis or other candida cy for therapy following approved clinical guidance; combined with and retired CP.CPA.EX.290 for HNAZ exchange lines of business.</td>
<td>09.03.18</td>
<td></td>
</tr>
<tr>
<td>No clinically significant changes: modifications made to update template.</td>
<td>01.07.19</td>
<td></td>
</tr>
<tr>
<td>3Q 2019 annual review: no clinically significant changes; references reviewed and updated.</td>
<td>05.24.19</td>
<td>08.19</td>
</tr>
</tbody>
</table>

### 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
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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
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This clinical policy is effective as of the date determined by the Health Plan. The date of posting
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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
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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
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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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