Clinical Policy: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)
Reference Number: GA.PMN.25
Product: Medicaid
Effective Date: 9/17
Last Review Date: 9/17

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for sofosbuvir/velpatasvir/voxilaprevir (Vosevi®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Vosevi is medically necessary when the following criteria are met:

I. Approval Criteria
   **Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria**

   A. Chronic Hepatitis C Infection (must meet all):
      1. Diagnosis of chronic HCV infection as evidenced by detectable HCV RNA (ribonucleic acid) levels in the last 6 months;
      2. Age ≥ 18 years;
      3. 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);
      4. 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;
      5. Member has a contraindication or intolerance to Mavyret and meets one of the following (a or b):
         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);
      6. Life expectancy ≥ 12 months with HCV treatment;
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Simeprevir

7. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (see Appendix D Dosage);
8. Member is hepatitis B virus (HBV) negative, or if positive, documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced (see Appendix E);
9. Prescribed dose does not exceed one tablet (sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg) daily.

Approval duration: up to a total of 12 weeks*
(*Approved duration should be consistent with a regimen in Appendix D FDA approved dosages and Treatment Duration)

B. Other diagnoses/indications
Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section II (Diagnoses/Indications for which coverage is NOT authorized). (*Approved duration should be consistent with a regimen in Appendix D)

II. 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.PHAR.57 or evidence of coverage documents.

Background
Description/Mechanism of Action:
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.

Vosevi Formulations
- Tablet, Oral
  Vosevi: 400/100/100 mg

FDA Approved Indications:
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**.
  o 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.
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* 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).

**Appendices**

**Appendix A: Abbreviation 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: Approximate Scoring Equivalencies using METAVIR F3/F4 as Reference**

<table>
<thead>
<tr>
<th>Fibrosis/Cirrhosis</th>
<th>Serologic Tests*</th>
<th>Radiologic Tests†</th>
<th>Liver Biopsy‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FibroTest</td>
<td>FIBRO Spect II</td>
<td>APRI</td>
</tr>
<tr>
<td>Advanced fibrosis</td>
<td>≥0.59</td>
<td>≥42</td>
<td>&gt;1.5</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>≥0.75</td>
<td>≥42</td>
<td>&gt;1.5</td>
</tr>
</tbody>
</table>

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 (ultrasound-based 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 C: 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>Olysio</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<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>Vickira XR/PAK*</td>
<td>Ombitasvir</td>
<td>Dasabuvir</td>
<td>Paritaprevir</td>
<td>Ritonavir</td>
<td></td>
</tr>
<tr>
<td>Zepatier*</td>
<td>Elbasvir</td>
<td></td>
<td></td>
<td></td>
<td>Grazoprevir</td>
</tr>
</tbody>
</table>
Appendix D: FDA-Approved Regimens and Treatment Durations

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic HCV Infection</td>
<td>1 tablet by mouth daily</td>
<td>1 tablet/day</td>
</tr>
</tbody>
</table>

Appendix E: 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 META VIR F3/F4 as reference are below:

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References


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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members**, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at [http://www.cms.gov](http://www.cms.gov) for additional information.

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