Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)
Reference Number: CP.CPA.286
Effective Date: 11.01.16
Last Review Date: 08.18
Line of Business: Commercial

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

Description
Sofosbuvir/velpatasvir (Epclusa®) is a fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor.

FDA Approved Indication(s)
Epclusa is indicated for the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection:
- Without cirrhosis or with compensated cirrhosis
- With decompensated cirrhosis for use in combination with ribavirin (RBV)

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 Epclusa 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. Confirmed HCV genotype is 1, 2, 3, 4, 5, or 6;
         *Chart note documentation and copies of lab results are required
      3. Authorized generic version of Epclusa is prescribed, unless medical justification supports inability to use the authorized generic (e.g., contraindications to excipients in the authorized generic);
      4. Documentation of the treatment status of the patient (treatment-naive or treatment-experienced);
      5. Documentation of cirrhosis status of the patient (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
      6. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
      7. Age ≥ 18 years;
      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 sofosbuvir/velpatasvir 400mg/100mg (1 tablet) per day.
   Approval duration: up to a total of 24 weeks*
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(*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): CP.CPA.09 for commercial.

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. Documentation supports that member is currently receiving Epclusa for chronic HCV infection and has recently completed at least 60 days of treatment with Epclusa;
   2. Member is responding positively to therapy;
   3. Dose does not exceed sofosbuvir/velpatasvir 400mg/100mg (1 tablet) per day.
   Approval duration: up to a total of 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): 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 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
Not applicable

Appendix C: Contraindications/Boxed Warnings
• Contraindication(s): Epclusa and RBV combination regimen is contraindicated in patients for whom RBV is contraindicated in patients for whom RBV is contraindicated. Refer to the RBV prescribing information for a list of contraindications for RBV.
• 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>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>Daklinza</td>
<td>Daclatasvir</td>
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<td></td>
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<tr>
<td>Epclusa*</td>
<td>Velpatasvir</td>
<td>Sofosbuvir</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Harvoni*</td>
<td>Ledipasvir</td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mavyret*</td>
<td>Pibrentasvir</td>
<td></td>
<td></td>
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<tr>
<td>Olysio</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Simeprevir</td>
<td></td>
</tr>
<tr>
<td>Sovaldi</td>
<td></td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
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<tr>
<td>Technivie*</td>
<td>Ombitasvir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Paritaprevir</td>
</tr>
<tr>
<td>Viekira</td>
<td>Ombitasvir</td>
<td>Dasabuvir</td>
<td>Paritaprevir</td>
<td>Ritonavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XR/PAK*</td>
<td></td>
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</tr>
<tr>
<td>Vosevi*</td>
<td>Velpatasvir</td>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
<td>Voxilaprevir</td>
</tr>
<tr>
<td>Zepatier*</td>
<td>Elbasvir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Grazoprevir</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</td>
<td>Moderate-severe / poorly controlled</td>
</tr>
<tr>
<td></td>
<td>Grade I-II</td>
<td>Grade III-IV</td>
<td>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>
</table>
| Genotype 1-6: Without cirrhosis or with compensated cirrhosis, treatment-naïve or pegIFN/RBV-experienced patient | One tablet PO QD for 12 weeks (GT 3 with compensated cirrhosis for pegIFN/RBV-experienced patient may use: one tablet PO QD with weight-based RBV for 12 weeks) ‡ | One tablet (sofosbuvir 400 mg /velpatasvir 100 mg) per day | 1) FDA-approved labeling  
2) AASLD-IDSA (updated September 2017) |
| Genotype 1-6: With decompensated cirrhosis treatment-naïve or treatment-experienced* patient | One tablet PO QD with weight-based RBV for 12 weeks (GT 1, 4, 5, or 6 with decompensated cirrhosis and RBV-ineligible may use: one tablet PO QD for 24 weeks) ‡ | One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day | 1) FDA-approved labeling  
2) AASLD-IDSA (updated September 2017) |
| Genotype 1-6: With decompensated cirrhosis in whom prior sofosbuvir- or NS5A-based treatment experienced failed | One tablet PO QD with weight-based RBV for 24 weeks | One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day | AASLD-IDSA (updated September 2017) |
| Genotype 1b: With compensated cirrhosis or without cirrhosis and non-NS5A inhibitor, sofosbuvir-containing regimen-experienced | One tablet PO QD for 12 weeks | One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day | AASLD-IDSA (updated September 2017) |
| Genotype 2: With or without compensated cirrhosis, sofosbuvir + RBV-experienced | One tablet PO QD for 12 weeks | One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day | AASLD-IDSA (updated September 2017) |
| Genotype 2 or 3: Treatment-naïve and treatment-experienced patients, post-liver transplant with compensated cirrhosis | One tablet PO QD with weight-based RBV for 12 weeks | One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day | AASLD-IDSA (updated September 2017) |
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<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>or decompensated cirrhosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 3 with NS5A Y93H polymorphism: Treatment-naïve with cirrhosis or treatment-experienced* patient</td>
<td>One tablet PO QD with weight-based RBV for 12 weeks</td>
<td>One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day</td>
<td>AASLD-IDSA (updated September 2017)</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.

*Treatment-experienced refers to previous treatment with NS3 protease inhibitor (telaprevir, boceprevir, or simeprevir) and/or peginterferon/RBV unless otherwise stated

† Off-label, AASLD-IDSA guideline-supported dosing regimen

VI. Product Availability
Tablet: sofosbuvir 400 mg with velpatasvir 100 mg

VII. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy converted to new template from “Epclusa NATL 04.03.17.docx&quot;. Annual Review – added requirement for GT, tx status, and cirrhosis status for consistency; added prescriber requirement.</td>
<td>06.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Removed redirection to Harvoni for 12-week therapy. 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>09.05.17</td>
<td>11.17</td>
</tr>
<tr>
<td>3Q 2018 annual review: removed requirement for HBV verification; 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; references reviewed and updated.</td>
<td>05.22.18</td>
<td>08.18</td>
</tr>
</tbody>
</table>
Sofosbuvir/Velpatasvir

Reviews, Revisions, and Approvals

| Removed requirement for advanced fibrosis or other candidacy for therapy following approved clinical guidance; combined with and retired CP.CPA.EX.286 for HNAZ exchange lines of business. | 09.03.18 |
| No clinically significant changes: added redirection to authorized generic in line with previously approved clinical guidance. | 01.07.19 |

**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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