Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)
Reference Number: CP.PCH.21
Effective Date: 01.01.20
Last Review Date: 02.20
Line of Business: Commercial, HIM

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, infectious disease specialist, or provider who has expertise in treating HCV based on a certified training program (see Appendix F);
      7. Age ≥ 18 years;
      8. Life expectancy ≥ 12 months with HCV treatment;
      9. 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;

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

11. 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 and 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. 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 and 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 – CP.CPA.09 for commercial and HIM.PHAR.21 for health insurance marketplace 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
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>
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<tbody>
<tr>
<td>Daklinza</td>
<td>Daclatasvir</td>
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<tr>
<td>Epclusa*</td>
<td>Velpatasvir</td>
<td>Sofosbuvir</td>
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<tr>
<td>Harvoni*</td>
<td>Ledipasvir</td>
<td>Sofosbuvir</td>
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<tr>
<td>Mavyret*</td>
<td>Pibrentasvir</td>
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<tr>
<td>Olysio</td>
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<tr>
<td>Sovaldi</td>
<td></td>
<td>Sofosbuvir</td>
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<tr>
<td>Technivie*</td>
<td>Ombitasvir</td>
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<td>Paritaprevir</td>
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<tr>
<td>Viekira XR/PAK*</td>
<td>Ombitasvir</td>
<td>Dasabuvir</td>
<td>Paritaprevir</td>
<td>Ritonavir</td>
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<tr>
<td>Vosevi*</td>
<td>Velpatasvir</td>
<td>Sofosbuvir</td>
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<td>Voxilaprevir</td>
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<tr>
<td>Zepatier*</td>
<td>Elbasvir</td>
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<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>
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</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: Without cirrhosis or with compensated cirrhosis, treatment-naïve or pegIFN/RBV-experienced patient</td>
<td>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) †</td>
<td>One tablet (sofosbuvir 400 mg /velpatasvir 100 mg) per day</td>
<td>1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)</td>
</tr>
<tr>
<td>Genotype 1-6: With decompensated cirrhosis treatment-naïve or treatment-experienced* patient</td>
<td>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) †</td>
<td>One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day</td>
<td>1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)</td>
</tr>
<tr>
<td>Indication</td>
<td>Dosing Regimen</td>
<td>Maximum Dose</td>
<td>Reference</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Genotype 1-6: With decompensated cirrhosis in whom prior sofosbuvir- or NS5A-based treatment experienced failed</td>
<td>One tablet PO QD with weight-based RBV for 24 weeks</td>
<td>One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day</td>
<td>AASLD-IDSA (updated May 2018)</td>
</tr>
<tr>
<td>Genotype 1b: With compensated cirrhosis or without cirrhosis and non-NS5A inhibitor, sofosbuvir-containing regimen-experienced</td>
<td>One tablet PO QD for 12 weeks</td>
<td>One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day</td>
<td>AASLD-IDSA (updated May 2018)</td>
</tr>
<tr>
<td>Genotype 2: With or without compensated cirrhosis, sofosbuvir + RBV-experienced</td>
<td>One tablet PO QD for 12 weeks</td>
<td>One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day</td>
<td>AASLD-IDSA (updated May 2018)</td>
</tr>
<tr>
<td>Genotype 2 or 3: Treatment-naïve and treatment-experienced patients, post-liver transplant with compensated cirrhosis or decompensated cirrhosis</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 May 2018)</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 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.
*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 created; per SDC and prior clinical guidance added HIM line of business to the existing Commercial policy (modified policy number to CP.PCH.21, retired HIM.PA.SP1 and CP.CPA.286); added requirement that life expectancy ≥ 12 months with HCV treatment and participation in a medication adherence program.</td>
<td>12.03.19</td>
<td>02.20</td>
</tr>
<tr>
<td>Added new prescriber requirement to include a “provider who has expertise in treating HCV based on a certified training program”; Appendix F (Healthcare Provider HCV Training) added.</td>
<td>11.07.19</td>
<td>02.20</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 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,
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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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