Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)
Reference Number: HIM.PA.SP1
Effective Date: 08/16
Last Review Date: 08/17
Line of Business: Health Insurance Marketplace

Coding Implications
Revision Log

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

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

**FDA approved indication**
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
- For the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection with decompensated cirrhosis for use in combination with ribavirin

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

**I. Initial Approval Criteria**

**A. Chronic Hepatitis C Infection** (must meet all)**:**

1. Diagnosis of chronic hepatitis C infection as evidenced by detectable HCV ribonucleic acid (RNA) levels over a six-month period;
2. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
3. Confirmed HCV genotype is 1, 2, 3, 4, 5 or 6;
4. Life expectancy ≥ 12 months with HCV treatment;
5. Documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy, if applicable;
6. Advanced liver disease defined as one of the following (a or b):
   a. Advanced fibrosis indicated by i or ii:
      i. Liver biopsy showing a METAVIR score of F3 or equivalent (Knodell, Scheuer, Batts-Ludwig – F3; Ishak – F4/5);
      ii. One serologic test and one radiologic test showing an equivalent score to METAVIR F3 per Appendix B;
   b. Cirrhosis indicated by i, ii or iii:
      i. Hepatocellular carcinoma (HCC) - and the HCC is amenable to resection, ablation or transplant;
      ii. Liver biopsy showing a METAVIR score of F4 or equivalent (Knodell, Scheuer, Batts-Ludwig – F4; Ishak - F5/6);
      iii. Both of the following (a and b):

a) One serologic test showing an equivalent score to METAVIR F4 per Appendix B;
b) One radiologic test showing an equivalent score to METAVIR F4 per Appendix B or other radiologic test showing evidence of cirrhosis (e.g., portal hypertension);

7. Prescribed regimen is consistent with an FDA or AASLD-IDSA regimen in Appendix D or E *(if regimens are applicable to post-liver transplantation they are specifically designated)*;
8. For genotype 1, 4, 5, 6 member has contraindications or clinically significant adverse effects to Harvoni , unless indicated treatment regimen with Harvoni is > 12 weeks;
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. Dose does not exceed 400/100 mg/day (1 tablet/day).

**Approval duration: 8 weeks**

**B. Other diagnoses/indications**

1. Refer to HIM.PHAR.21 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. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. Pharmacy claims support adherence to therapy;
4. If request is for a dose increase, new dose does not 400/100 mg/day (1 tablet/day).

**Approval duration: up to a total of 24 weeks***
*(*Approved duration should be consistent with a regimen in Appendix D)*

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 for specialty months (whichever is less)**; or
2. Refer to HIM.PA.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

## 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 or evidence of coverage documents

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
CTP: Child Turcotte Pugh
CrCl: creatinine clearance
DAA: direct-acting antiviral
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
IDSA: Infectious Diseases Society of America
IV: intravenous
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
Peg-IFN: pegylated interferon
PI: protease inhibitor
RBV: ribavirin
RNA: ribonucleic acid

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

| Fibrosis/ Cirrhosis | Serologic Tests* | | | | Radiologic Tests† | | Liver Biopsy‡ | |
|---|---|---|---|---|---|---|---|---|
| | Fibro Test | FIBRO Spect II | APRI | FIB-4 | FibroScan (kPa) | MRE (kPa) | METAVIR | Ishak |
| Advanced fibrosis | ≥0.59 | ≥42 | >1.5 | >3.25 | ≥9.5 | ≥4.11 | F3 | F4-5 |
| Cirrhosis | ≥0.75 | ≥42 | >1.5 | >3.25 | ≥12.0 | ≥4.71 | F4 | F5-6 |

*Serologic tests:
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 (DAAs) for Treatment of HCV Infection*

| Brand Name | Drug Class | | | | |
|---|---|---|---|---|---|
| | NS5A Inhibitor | Nucleotide Analog NS5B Polymerase Inhibitor | Non-Nucleoside NS5B Palm Polymerase Inhibitor | NS3/4A Protease Inhibitor (PI)** | CYP3A Inhibitor |
| Daklinza | Daclatasvir | | | | |
| Epclusa* | Velpatasvir | Sofosbuvir | | | |

| Brand Name | Drug Class | | | | |
|---|---|---|---|---|---|
| | NS5A Inhibitor | Nucleotide Analog NS5B Polymerase Inhibitor | Non-Nucleoside NS5B Palm Polymerase Inhibitor | NS3/4A Protease Inhibitor (PI)** | CYP3A Inhibitor |
| Harvoni* | Ledipasvir | Sofosbuvir | | | |
| Olysio | | | | Simeprevir | |
| Sovaldi | | Sofosbuvir | | | |
| Technivie* | Ombitasvir | | | Paritaprevir | Ritonavir |
| Viekira XR/PAK* | Ombitasvir | | Dasabuvir | Paritaprevir | Ritonavir |
| Zepatier* | Elbasvir | | | Grazoprevir | |

*Combination drugs
**Additional PIs no longer recommended: Victrelis (boceprevir), Incivek (telaprevir)

*Appendix D: FDA-Approved Regimens and Treatment Durations*

| Treatment Naive/Experienced | Genotype | Failed Treatment Regimen | Recommended Regimen *See footnotes for duration* |
|---|---|---|---|
| ***No Cirrhosis or Compensated Cirrhosis (CTP/Child-Pugh Class A)*** | | | |
| Treatment naive | 1a, 1b, 2, 3, 4 | None | Epclusa§ |
| | 5, 6 | None | Epclusa§ |
| Treatment experienced | 1* | NS3 PI/Peg-IFN/RBV** | Epclusa§ |
| | 1a, 1b, 2, 4 | Peg-IFN/RBV | Epclusa§ |
| | 2 | Sovaldi/RBV | Epclusa + RBV§ |
| | 3 | Peg-IFN/RBV | Epclusa§ |
| | | Sovaldi/RBV | Epclusa + RBV§ |
| | 5, 6 | Peg-IFN/RBV | Epclusa§ |
| ***Decompensated Cirrhosis (CTP/Child-Pugh Class B or C)*** | | | |
| Treatment experienced | 1*, 4 | Sovaldi/NS5A-based regimen | Epclusa + RBV† |
| Not specified | 1*, 2, 3, 4, 5, 6 | Not specified | Epclusa + RBV§ |
| | 1*, 4 | Not specified | Epclusa† *If RBV ineligible.* |

*Subtype a or b, or unknown subtype
**NS3 includes Victrelis (boceprevir), Incivek (telaprevir) or Olysio (simeprevir)
§Treatment duration - 12 weeks
†Treatment duration - 24 weeks

*Appendix E: AASLD-IDSA Recommended Regimens and Treatment Durations*

| Treatment Naive/Experienced | Genotype | Failed Treatment Regimen | Recommended Regimen *See footnotes for duration* |
|---|---|---|---|
| ***No Cirrhosis or Compensated Cirrhosis (CTP/Child-Pugh Class A)*** | | | |
| Treatment naive | 1a, 1b, 2, 3, 4 | None | Epclusa§ |
| | 5, 6 | None | Epclusa§ |
| Treatment experienced | 1* | NS3 PI/Peg-IFN/RBV** | Epclusa§ |
| | 1a, 1b, 2, 4 | Peg-IFN/RBV | Epclusa§ |
| | 2 | Sovaldi/RBV | Epclusa + RBV§ |
| | 3 | Peg-IFN/RBV | Epclusa§ |
| | | Sovaldi/RBV | Epclusa + RBV§ |

| Treatment Naive/Experienced | Genotype | Failed Treatment Regimen | Recommended Regimen *See footnotes for duration* |
|---|---|---|---|
| | 5, 6 | Peg-IFN/RBV | Epclusa§ |
| ***Decompensated Cirrhosis (CTP/Child-Pugh Class B or C)*** | | | |
| Treatment experienced | 1*, 4 | Sovaldi/NS5A-based regimen | Epclusa + RBV† |
| Not specified | 1*, 2, 3, 4 | Not specified | Epclusa + RBV§ |
| | 1*, 4 | Not specified | Epclusa† *If RBV ineligible.* |

*Subtype a or b, or unknown subtype
**NS3 includes Victrelis (boceprevir), Incivek (telaprevir) or Olysio (simeprevir)
§Treatment duration - 12 weeks
†Treatment duration - 24 weeks

## V. References

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| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| New policy created. | 08/16 | |
| Removed age, as age is not an absolute contraindication. | 04/17 | 08/17 |

**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.

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