Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)

Reference Number: GA.PMN.06
Effective Date: 12/16
Last Review Date: 7/2020 Revision Log
Line of Business: Medicaid

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 and pediatric patients 6 years of age and older or weighing at least 17 kg 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
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
*** 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 hepatitis C virus (HCV) infection as evidenced by detectable HCV ribonucleic acid (RNA) levels in the last 6 months;
2. Age ≥ 6 years or weight ≥ 17 kg;
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. Confirmed HCV genotype is 1, 2, 3, 4, 5 or 6;
   *Chart note documentation and copies of labs results are required
5. Documentation of the treatment status of the patient (treatment-naïve or treatment-experienced);
6. Documentation of cirrhosis status of the patient (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
7. Life expectancy ≥ 12 months with HCV treatment;
8. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section III Dosage and Administration for reference)*;

9. 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 B*);
10. If prescribed with ribavirin, member has none of the following contraindications:
    a. Pregnancy or possibility of pregnancy - member or partner;
    b. Hypersensitivity to ribavirin;
    c. Coadministration with didanosine;
    d. Significant/unstable cardiac disease;
    e. Hemoglobinopathy (e.g., thalassemia major, sickle cell anemia);
    a. Hemoglobin < 8.5 g/dL.
11. Dose does not exceed one of the following (a or b):
    a. Adult and pediatric members with body weight ≥ 30 kg: sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day;
    b. Pediatric members with body weight 17 to 29 kg: sofosbuvir/velpatasvir 200 mg/50 mg (1 tablet) per day.

Approval duration: up to a total of 24 weeks*
*(*Approved duration should be consistent with a regimen in Section III Dosage and Administration)*

B. Other diagnoses/indications: Refer to CP.PMN.53 – No Coverage Criteria/Off-Label Use Policy if diagnosis is NOT specifically listed under section I.

II. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

Appendix B: Contraindications

- Epclusa and RBV combination regimen is contraindicated in patients for whom RBV is contraindicated. Refer to the RBV prescribing information for a list of contraindications for RBV.

Appendix C: Direct-Acting Antivirals 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			
Harvoni*	Ledipasvir	Sofosbuvir			
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
.Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

Appendix D: General Information

- Hepatitis B Virus (HBV) Reactivation 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.

III. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
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 patients may use: one tablet PO QD for 12 weeks)ǂ	One tablet (sofosbuvir 400mg/velpatasvir 100mg) per day	1) FDA approved labeling 2) AASLDIDSA (updated May 2018)
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)ǂ	One tablet (sofosbuvir 400mg/velpatasvir 100mg) per day	1) FDA approved labeling 2) AASLDIDSA (updated May 2018)
Genotype 1-6: With decompensated cirrhosis in whom prior sofosbuvir-or NS5A treatment experienced failed	One tablet PO QD with weight-based RBV for 24 weeks	One tablet (sofosbuvir 400mg/velpatasvir 100mg) per day	AASLDIDSA (updated May 2018)
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 100mg) per day	AASLDIDSA (updated May 2018)
Genotype 2: With or without compensated cirrhosis, sofosbuvir +RBV-experienced	One tablet PO QD for 12 weeks	One tablet (sofosbuvir 400mg/velpatasvir 100mg) per day	AASLDIDSA (updated May 2018)
Genotype 2 or 3: Treatment-naïve and treatment-experienced patients, post-liver transplant with compensated cirrhosis or decompensated cirrhosis	One tablet PO QD with weight-based RBV for 12 weeks	One tablet (sofosbuvir 400mg/velpatasvir 100mg) per day	AASLDIDSA (updated May 2018)
Genotype 3 with NS5A Y93H polymorphism:	One tablet PO QD with weight-based RBV for 12 weeks	One tablet (sofosbuvir	AASLDIDSA (updated May 2018)

Indication	Dosing Regimen	Maximum Dose	Reference
Treatment-naïve with cirrhosis or treatment-experienced* patient		400mg/velpatasvir 100mg) per day	

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*
ǂ *Off-label, AASLD-IDSA guideline-supported dosing regimen*

IV. Product Availability

Tablet: sofosbuvir 400mg with velpatasvir 100mg

V. References

1. Epclusa Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; March 2020. Available at http://www.gilead.com/~/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf?la=en. Accessed April 30, 2020.
2. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). HCV guidance: recommendations for testing, managing, and treating hepatitis C. Last updated November 6, 2019. Available at: https://www.hcvguidelines.org/. Accessed April 30, 2020.
3. Platt L, Easterbrook P, Gower E, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. Lanet Infect Dis 2016;16:797-808. http://dx.doi.org/10.1016/
4. Centers for Disease Control and Prevention. HIV and viral hepatitis: fact sheet. June 2017. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/hiv-viral-hepatitis.pdf. Accessed May 1, 2019.
5. Wolitski R. When it comes to curing hepatitis c, your health care provider may not need to be a specialist. U.S. Department of Health & Human Services. Last updated September 20, 2017. Available at: https://www.hhs.gov/hepatitis/blog/2017/09/20/study-calls-for-expansion-of-hepatitis-c-treatment.html. Accessed October 30, 2019.
1. CDC. Viral hepatitis: Q&As for health professionals. Last updated July 2, 2019. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed October 30, 2019.

Reviews, Revisions, and Approvals	Date	Plan Approval Date
New policy created, split from CP.PHAR.17 Hepatitis C Therapies policy. HCV RNA levels over six-month period added to confirm infection is chronic.Life expectancy "≥12 months if HCC and awaiting transplant" is modified to indicate "≥12 months with HCV therapy." Methods to diagnose fibrosis/cirrhosis are modified to require a liver biopsy or a combination of one serologic and one radiologic test. Serologic and radiologic tests are	07/16	07/16

Reviews, Revisions, and Approvals	Date	Plan Approval Date
updated and correlated with METAVIR per Appendix C. Dosing regimens are presented in Appendix. Criteria is added requiring a verification of HCV RNA status at 4 weeks (and again at 6 weeks if present at 4) accordingly, the initial approval period is shortened to 8 weeks.		
Edited policy so congruent with the other HCV policies as follows: Testing criteria reorganized by cirrhosis status consistent with the regimen tables; HCC population broadened to incorporate those amenable to curative measures (resection, ablation, transplant). Fibrosure test that meets F3 requirement changed to ≥ 0.59. Criteria added excluding post-liver transplantation unless regimens specifically designate. Preferencing language edited for clarity. Removed creatinine clearance restriction. Under continuing approval, presence of HCV RNA is edited to remove specific timing of testing. Appendix B edited for clairity; Appendix C added. Appendix D – genotype "1" is footnoted to clarify possible subtypes. "Includes HCC" is removed from the decompensated cirrhosis. "Daily" is removed from the "recommended regimen" column; presentation of other data is abbreviated/short-handed.	08/16	09/16
Removed criteria regarding medication prescribed by a specialist Remove criteria regarding having HCC or advanced liver disease Removed criteria regarding medication adherence program Removed criteria regarding sobriety from alcohol/illicit drugs	9/16	9/2016
Added availability of full course of therapy as initial therapy consistent with appendix recommendation for initial criteria Removed continuation criteria	4/17	4/17
Added preferencing information requiring Mavyret for FDA-approved indications. Added information requiring Hep B screening for all patients prior to treatment to ensure that proper risk reduction measures are taken.	9/17	9/17
Annual review. No changes made.	3/18	3/18
Changed current Georgia policy templates to corporate standard templates for drug coverage criteria to meet corporate compliance. Changes/revisions included; new formatting, font size, use of standard policy language for each section of policy, and rearranged order of certain steps in criteria and sections. Added new preferred treatment tables that includes dosage and frequency based on genotype for Mavyret. Removed background sections. Updated general information and contraindication section to be consistent with corporate HCV policies.	2/21/19	2/19
Annual review. In the initial approval criteria, changed RNA detectable period from "over a 6 month period" to "in the last 6 months" for infection diagnosis.	10/19	10/19
Added preferencing for AG Epclusa; Removed redirection to Mavyret based on contraindications criteria and all other information relative to Mavyret.	4/2020	4/2020

Reviews, Revisions, and Approvals	Date	Plan Approval Date
Removed Appendix C for Metavir scoring. Updated order of all other Appendices. Updated references.		
Added pediatric indication and dosing. References reviewed and updated.	7/2020	7/2020

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.