

**Clinical Policy: Sofosbuvir/Velpatasvir (Epclusa)**

Reference Number: CP.CPA.286

Effective Date: 11.01.16

Last Review Date: 08.21

Line of Business: Commercial

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Sofosbuvir/velpatasvir (Epclusa<sup>®</sup>) 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 3 years of age and older 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<sup>®</sup> 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. Member must use brand version of Epclusa, unless contraindicated or clinically significant adverse effects are experienced;
4. Documentation of the treatment status of the member (treatment-naive or treatment-experienced);
5. Documentation of cirrhosis status of the member (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  $\geq$  3 years;
8. Life expectancy  $\geq$  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-IDSAs recommended regimen (*see Section V Dosage and Administration for reference*);
- 11. Dose does not exceed one of the following (a, b, or c):
  - a. Adult and pediatric members with body weight  $\geq 30$  kg: sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day;
  - b. Pediatric members 3 years of age and older with body weight  $< 17$  kg: sofosbuvir/velpatasvir 150 mg/37.5 mg per day;
  - c. Pediatric members 3 years of age and older with body weight 17 kg to  $< 30$  kg: sofosbuvir/velpatasvir 200 mg/50 mg 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.

**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 one of the following (a, b, or c):
  - a. Adult and pediatric members with body weight  $\geq 30$  kg: sofosbuvir/velpatasvir 400 mg/100 mg (1 tablet) per day;
  - b. Pediatric members 3 years of age and older and body weight  $< 17$  kg: sofosbuvir/velpatasvir 150 mg/37.5 mg per day;
  - c. Pediatric members 3 years of age and older and body weight 17 kg to  $< 30$  kg: sofosbuvir/velpatasvir 200 mg/50 mg 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. Refer to the RBV prescribing information for a list of contraindications for RBV.
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfecting with HCV and HBV

*Appendix D: 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
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Sovaldi		Sofosbuvir			
Viekira PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
Zepatier*	Elbasvir			Grazoprevir	

\*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:

	1 Point	2 Points	3 Points
Bilirubin	Less than 2 mg/dL Less than 34 umol/L	2-3 mg/dL 34-50 umol/L	Over 3 mg/dL Over 50 umol/L
Albumin	Over 3.5 g/dL Over 35 g/L	2.8-3.5 g/dL 28-35 g/L	Less than 2.8 g/dL Less than 28 g/L
INR	Less than 1.7	1.7 - 2.2	Over 2.2
Ascites	None	Mild / medically controlled	Moderate-severe / poorly controlled
Encephalopathy	None	Mild / medically controlled Grade I-II	Moderate-severe / poorly controlled. Grade III-IV

*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

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1-6: Without cirrhosis or with compensated cirrhosis, treatment-naïve or treatment-experienced* patient	One tablet PO QD for 12 weeks	Adult/Peds ≥ 30 kg: sofosbuvir 400 mg /velpatasvir 100 mg (one tablet) per day;	FDA-approved labeling
Genotype 1-6: With decompensated cirrhosis, treatment-naïve or treatment-experienced* patient	One tablet PO QD with weight-based RBV for 12 weeks  (RBV-ineligible patients may use: one tablet PO QD for 24 weeks) <sup>†</sup>	Peds 17 to < 30 kg: sofosbuvir 200 mg /velpatasvir 50 mg per day;  Peds < 17 kg: sofosbuvir 150 mg /velpatasvir 37.5 mg per day	
Genotype 1-6: Treatment-naïve and treatment-experienced	One tablet PO QD for 12 weeks		

Indication	Dosing Regimen	Maximum Dose	Reference
patients, post-liver transplant with compensated cirrhosis or without cirrhosis			
Genotype 1-6: With decompensated cirrhosis in whom prior sofosbuvir- or NS5A inhibitor-based treatment experienced failed	One tablet PO QD with weight-based RBV for 24 weeks <sup>‡</sup>	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated March 2021)
Genotype 1-6: Treatment-naïve and treatment-experienced patients, post-liver transplant with decompensated cirrhosis	One tablet PO QD with RBV (starting at 600 mg and increased as tolerated) for 12 weeks (treatment naïve) or 24 weeks (treatment experienced) <sup>‡</sup>	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated March 2021)
Genotype 3 with NS5A Y93H polymorphism: Treatment-naïve with compensated cirrhosis or treatment-experienced* without cirrhosis patient	One tablet PO QD with weight-based RBV for 12 weeks <sup>‡</sup>	One tablet (sofosbuvir 400mg /velpatasvir 100 mg) per day	AASLD-IDSA (updated March 2021)

*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.*

*\*From clinical trials, treatment-experienced refers to previous treatment with NS3/4A protease inhibitor (telaprevir, boceprevir, or simeprevir) and/or peginterferon/RBV unless otherwise stated*

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

## VI. Product Availability

- Tablets: sofosbuvir 400 mg with velpatasvir 100 mg, sofosbuvir 200 mg with velpatasvir 50 mg
- Oral pellets: sofosbuvir 200 mg with velpatasvir 50 mg, sofosbuvir 150 mg with velpatasvir 37.5 mg

## VII. References

1. Epclusa Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; June 2021. Available at [http://www.gilead.com/~media/files/pdfs/medicines/liver-disease/epclusa/epclusa\\_pi.pdf?la=en](http://www.gilead.com/~media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf?la=en). Accessed July 9, 2021.
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 March 12, 2021. Available at: <https://www.hcvguidelines.org/>. Accessed April 15, 2021.
3. CDC. Hepatitis C Q&As for health professionals. Last updated August 7, 2020. Available at: <https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm>. Accessed April 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy converted to new template from “Epclusa NATL 04.03.17.docx”. Annual Review – added requirement for GT, tx status, and cirrhosis status for consistency; added prescriber requirement.	06.17	11.17
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.	09.05.17	11.17
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.	05.22.18	08.18
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	
3Q 2019 annual review: no significant changes; references reviewed and updated.	04.30.19	08.19
Via CP.PCH.21: CP.CPA.286 retired and combined with HIM to CP.PCH.21; added requirement that life expectancy $\geq$ 12 months with HCV treatment and participation in a medication adherence program; 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.	12.03.19	02.20
Via CP.PCH.21: RT4: updated FDA indication and dosing for pediatric extension to age 6 years or weight $\geq$ 17 kg.	04.02.20	
3Q 2020 annual review: CP.PCH.21 retired and CP.CPA.286 unretired per June SDC and prior clinical guidance; no clinically significant changes; references reviewed and updated. RT4: added updated FDA-labeled dosing for post-liver transplant setting.	07.22.20	08.20
Per September SDC and prior clinical guidance for 1/1/21 effective, modified to redirect authorized generic Epclusa requests to brand Epclusa.	09.22.20	
3Q 2021 annual review: revised medical justification language for not using brand version of Epclusa to “must use” language; updated Section V table with AASLD recommended regimens; RT4: updated criteria for Epclusa pediatric age expansion to 3 years and older along with pediatric dosing and new oral pellet dosage formulation; references reviewed and updated.	07.12.21	08.21

**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.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene<sup>®</sup> and Centene Corporation<sup>®</sup> are registered trademarks exclusively owned by Centene Corporation.