Clinical Policy: Sofosbuvir (Sovaldi)

Reference Number: CP.CPA.176
Effective Date: 11.01.16
Last Review Date: 08.24
Line of Business: Commercial

Revision Log

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

Description

Sofosbuvir (Sovaldi®) is hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor.

FDA Approved Indication(s)

Sovaldi is indicated for the treatment of chronic HCV infection in:

- Adult patients without cirrhosis or with compensated cirrhosis:
  - Genotype 1 or 4 for use in combination with pegylated interferon and ribavirin (RBV).
  - Genotype 2 or 3 for use in combination with RBV.
- Pediatric patients 3 years of age and older with genotype 2 or 3 without cirrhosis or with compensated cirrhosis in combination with 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 Sovaldi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of HCV infection as evidenced by detectable serum HCV RNA levels by quantitative assay in the last 6 months;
2. 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*);
3. Confirmed HCV genotype is one of the following (a or b):
   a. For adults (age ≥ 18 years): Genotypes 1, 2, 3, 4, 5, or 6;
   b. For pediatrics (age ≥ 3 years): Genotypes 2 or 3;
   **Chart note documentation and copies of lab results are required*
4. Documentation of treatment status of the member (treatment-naïve or treatment-experienced);
5. Documentation of cirrhosis status of the member (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
6. Member must use **brand Epclusa®** or **Vosevi®**, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix E*);*
   **Coadministration with omeprazole up to 20 mg is not considered acceptable medical justification for inability to use Epclusa*

7. For pediatric patients (age ≥ 3 years) with genotype 2 or 3: Use is in combination with RBV;
8. Life expectancy ≥ 12 months with HCV treatment;
9. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
10. Dose does not exceed 400 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 (must meet all)**:**

1. Member must use **brand Epclusa** or **Vosevi**, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix E*);*
   **Coadministration with omeprazole up to 20 mg is not considered acceptable medical justification for inability to use Epclusa*
2. One of the following (a or b):
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
      i. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
      ii. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2a above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

II. Continued Therapy

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

1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
   c. Must meet both of the following (i and ii):
      i. Documentation supports that member is currently receiving Sovaldi for HCV infection and has recently completed at least 60 days of treatment with Sovaldi;
      ii. Confirmed HCV genotype is one of the following (1 or 2):
         1) For adults (age ≥ 18 years): Genotypes 1, 2, 3, 4, 5, or 6;
         2) For pediatrics (age ≥ 3 years): Genotypes 2 or 3;
2. Member is responding positively to therapy;
3. Dose does not exceed 400 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 for commercial or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
DAA: direct-acting antiviral
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
SVR12: sustained virologic response at 12 weeks

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
sofosbuvir/ velpatasvir (Epclusa®)	Without cirrhosis or with compensated cirrhosis, treatment naïve or treatment experienced*: **Genotypes 1 through 6** One tablet PO QD for 12 weeks	Adult/Peds ≥ 30 kg: sofosbuvir 400 mg /velpatasvir 100 mg (one tablet) per day; Peds 17 to < 30 kg: sofosbuvir 200 mg

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
		/velpatasvir 50 mg per day; Peds < 17 kg: sofosbuvir 150 mg /velpatasvir 37.5 mg per day
Vosevi® (sofosbuvir/ velpatasvir/ voxilaprevir) + RBV	Treatment-experienced with Vosevi with or without compensated cirrhosis: **Genotype 1 through 6** Vosevi one tablet PO QD with weight-based RBV for 24 weeks‡	Varies
Vosevi® (sofosbuvir/ velpatasvir/ voxilaprevir)	Treatment-experienced with Mavyret without cirrhosis: **Genotype 1 through 6** Vosevi one tablet PO QD for 12 weeks‡	
Vosevi® (sofosbuvir/ velpatasvir/ voxilaprevir) + RBV	Treatment-experienced with Mavyret with compensated cirrhosis: **Genotype 1 through 6** Vosevi one tablet PO QD with weight-based RBV for 12 weeks‡	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**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*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): when used in combination with peginterferon alfa/RBV or RBV alone, all contraindications to peginterferon alfa and/or RBV also apply to Sovaldi combination therapy.
- Boxed warning(s): risk of hepatitis B virus (HBV) reactivation in patients coinfected 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

- Unacceptable medical justification for inability to use Epclusa (preferred product):
  - Coadministration with omeprazole up to 20 mg is not considered acceptable medical justification for inability to use Epclusa.
    - Per the Epclusa Prescribing Information: "If it is considered medically necessary to coadminister, Epclusa should be administered with food and taken 4 hours before omeprazole 20 mg."
- 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.
- 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

Appendix G: Incomplete Adherence and AASLD-IDSA Recommended Management of Treatment Interruptions

- There are minimal data regarding the outcome of patients who have incomplete adherence to direct-acting antiviral (DAA) therapy or the threshold level of adherence below which the incidence of sustained virologic response at 12 weeks (SVR12) is significantly reduced. In general, a treatment interruption of < 7 days is unlikely to impact SVR12.
- There are few data on which to base recommendations regarding how to manage patients who have discontinued DAAs for several days to weeks. The below recommendations are applicable to treatment-naive patients with HCV, without cirrhosis or with compensated cirrhosis*, receiving either Mavyret or Epclusa*. Patients with prior DAA treatment, or receiving other DAA treatment regimens, or other populations (e.g., patients who are posttransplant or have decompensated cirrhosis) should be managed in consultation with an expert.
    - Interruptions during the first 28 days of DAA therapy:
        - If missed ≤ 7 days, restart DAA therapy immediately and complete therapy for originally planned duration (8 or 12 weeks).
        - If missed ≥ 8 days, restart DAA therapy immediately and obtain HCV RNA test as soon as possible. If HCV RNA is negative, complete originally planned DAA treatment course (8 or 12 weeks). Recommendation to extend DAA treatment for an additional 4 weeks for patients with genotype 3 and/or cirrhosis. If HCV RNA is positive or not obtained, extend DAA treatment for an additional 4 weeks.
    - Interruptions after receiving ≥ 28 days of DAA therapy:
        - If missed ≤ 7 days, restart DAA therapy immediately and complete therapy for originally planned duration (8 or 12 weeks).
        - If missed 8-20 consecutive days, restart DAA therapy immediately and obtain HCV RNA test as soon as possible. If HCV RNA is negative, complete originally planned DAA treatment course (8 or 12 weeks). Recommendation to extend DAA treatment for an additional 4 weeks for patients with genotype 3 and/or cirrhosis. If HCV RNA is positive or not obtained, stop treatment and

retreat according to the recommendations in the AASLD-IDSA Retreatment Section.

- If missed ≥ 21 consecutive days, stop DAA treatment and assess for SVR12. If SVR12 not achieved, retreat according to the recommendations in the AASLD-IDSA Retreatment Section.

V. Dosage and Administration

Indication: Adult patients with HCV infection			
Drugs	**Dosing Regimen**	**Maximum Dose**	**Reference**
Sovaldi + pegIFN + RBV	**Genotype 1 or 4** Treatment-naïve without cirrhosis or with compensated cirrhosis: Sovaldi 400 mg + pegIFN + weight-based RBV for 12 weeks	Sovaldi 400 mg/day	FDA-approved labeling
Sovaldi + RBV	**Genotype 2** Treatment-naïve and treatment-experienced*, without cirrhosis or with compensated cirrhosis: Sovaldi 400 mg + weight-based RBV for 12 weeks	Sovaldi 400 mg/day	FDA-approved labeling
Sovaldi + RBV	**Genotype 3** Treatment-naïve and treatment-experienced*, without cirrhosis or with compensated cirrhosis: Sovaldi 400 mg + weight-based RBV for 24 weeks	Sovaldi 400 mg/day	FDA-approved labeling
Sovaldi + Mavyret + RBV	**Genotypes 1 through 6** Patients with prior sofosbuvir/velpatasvir/voxilaprevir or glecaprevir/pibrentasvir treatment failure, with or without compensated cirrhosis‡ Sovaldi 400 mg + Mavyret 300 mg/120 mg + weight-based RBV for 16 weeks	Sovaldi 400 mg/day	AASLD/IDSA (updated December 2023)

AASLD/IDSA treatment guidelines for 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 pegIFN with or without RBV unless otherwise stated.*
‡ *Off-label, AASLD-IDSA guideline-supported dosing regimen*

Indication: Pediatric patients (age ≥ 3 years) with HCV infection			
Drugs	**Dosing Regimen**	**Maximum Dose**	**Reference**
Sovaldi + RBV	**Genotype 2** Treatment-naïve or treatment-experienced*, without cirrhosis or with compensated cirrhosis: • ≥ 35 kg: Sovaldi 400 mg + weight-based RBV for 12 weeks • 17 to < 35 kg: Sovaldi 200 mg + weight-based RBV for 12 weeks • < 17 kg: Sovaldi 150 mg + weight-based RBV for 12 weeks	Sovaldi 400 mg/day	FDA-approved labeling
Sovaldi + RBV	**Genotype 3** Treatment-naïve or treatment-experienced*, without cirrhosis or with compensated cirrhosis: • ≥ 35 kg: Sovaldi 400 mg + weight-based RBV for 24 weeks • 17 to < 35 kg: Sovaldi 200 mg + weight-based RBV for 24 weeks • < 17 kg: Sovaldi 150 mg + weight-based RBV for 24 weeks	Sovaldi 400 mg/day	FDA-approved labeling

AASLD/IDSA treatment guidelines for 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 peginterferon with or without RBV unless otherwise stated.*

VI. Product Availability

- Tablets: 400 mg, 200 mg
- Oral pellets: 200 mg, 150 mg

VII. References

1. Sovaldi Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; March 2020. Available at: https://www.gilead.com/-/media/8c41933bdd5d4e4691af495f40aa6016.ashx. Accessed May 6, 2024.
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 December 19, 2023. Available at: https://www.hcvguidelines.org/. Accessed May 20, 2024.
3. CDC. Clinical Overview of Hepatitis C. Last updated November 7, 2023. Available at: https://www.cdc.gov/hepatitis-c/hcp/clinical-overview. Accessed May 20, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2020 annual review: CP.PCH.20 retired and CP.CPA.176 unretired per June SDC and prior clinical guidance; removed coverage for Sovaldi + Daklinza as off-label combination is no longer recommended and added coverage for the combination of Sovaldi + Mavyret + ribavirin for patients experiencing treatment failure with Vosevi per updated AASLD/IDSA HCV guideline; references reviewed and updated.	06.10.20	08.20
Per June SDC and prior clinical guidance revised redirection to only include Epclusa authorized generic and Mavyret (Harvoni AG 8 weeks and Zepatier no longer preferred); Harvoni AG redirection retained only for age between 3 to 6 years with genotype 1 as Epclusa and Mavyret are not approvable in this population.	07.14.20	
Per September SDC and prior clinical guidance for 1/1/21 effective, revised redirection to require brand Epclusa or Vosevi.	09.22.20	
3Q 2021: updated criteria for age requirement of Epclusa use due to Epclusa's pediatric age expansion; added clarification that the brand version of Eplcusa is the preferred alternative; included reference to Appendix E with the addition of unacceptable rationale for bypassing preferred agents; updated Appendix B therapeutic alternatives; references reviewed and updated.	07.23.21	08.21
3Q 2022 annual review: no significant changes; added omeprazole coadministration as unacceptable rationale for not using preferred Epclusa in criteria and Appendix E; removed redundant rationale in Appendix E references; references reviewed and updated.	07.20.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.22.22	
3Q 2023 annual review: eliminated adherence program participation criterion since member is already being managed by an HCV-trained specialist and due to competitor analysis; added redirections to other diagnoses initial criteria section; references reviewed and updated.	04.17.23	08.23
3Q 2024 annual review: removed qualifier of "chronic" from HCV criteria as AASLD-IDSA recommends treatment of both acute and chronic HCV; removed the word "preferred" from Epclusa authorized generic redirection; added Appendix G for guidance on incomplete adherence and AASLD-IDSA recommended management of treatment interruptions; references reviewed and updated.	05.30.24	08.24

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.

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