Clinical Policy: Sofosbuvir (Sovaldi)

Reference Number: ERX.SPA.127
Effective Date: 10.01.16
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

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

Description

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

FDA Approved Indication(s)

Sovaldi is indicated for the treatment of chronic HCV 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Sovaldi 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 HCV RNA levels by quantitative assay in the last 6 months;
2. 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*
3. Documentation of treatment status of the member (treatment-naïve or treatment-experienced);
4. Documentation of cirrhosis status of the member (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
5. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist, or provider who has expertise in treating HCV based on a certified training program (*see Appendix F)*;
6. For members with no treatment failure with Vosevi: member has contraindication(s) or clinically significant adverse effects to both Harvoni and Epclusa® (*see Appendix E*):
7. For members age ≥ 18 years and treatment-experienced with Vosevi®: Member must use Vosevi in combination with RBV, unless contraindicated or clinically significant adverse effects are experienced;
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
1. Refer to ERX.PA.01 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. Member meets one of the following (a or b):
   a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
   b. Both of the following (i and ii):
      i. Documentation supports that member is currently receiving Sovaldi for chronic 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
1. Refer to ERX.PA.01 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 – ERX.PA.01 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
HCC: hepatocellular carcinoma
HCV: hepatitis C 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

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Harvoni® (ledipasvir/sofosbuvir)	**Genotype 1** Treatment-naïve without cirrhosis, who are HIV-uninfected, AND whose HCV viral load is less than 6 million IU/mL: One tablet PO QD for 8 weeks Treatment-naïve without cirrhosis (not meeting the 8 week treatment indication requirements above) or with compensated cirrhosis: for 12 weeks	1 tablet/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Treatment-experienced without cirrhosis: for 12 weeks **Genotype 4, 5, 6** Treatment naïve and treatment-experienced, without cirrhosis or with compensated cirrhosis: One tablet PO QD for 12 weeks	
Epclusa® (sofosbuvir/velpatasvir)	**Genotype 1 through 6** Without cirrhosis or with compensated cirrhosis, treatment naïve or treatment experienced: One tablet PO QD for 12 weeks	Varies
Vosevi® (sofosbuvir/velpatasvir/ voxilaprevir) + RBV	**Genotypes 1 through 6*** Without cirrhosis or with compensated cirrhosis, treatment in patients previously treated Vosevi: One tablet PO QD with weight-based RBV for 24 weeks	Varies

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.

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 reactivation in patients coinfected with HCV and HBV.

Appendix D: 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
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):
  - In patients indicated for co-administration of Epclusa with ribavirin: contraindications to ribavirin
- Unacceptable medical justification for inability to use Vosevi (preferred product):
  - In patients indicated for co-administration with amiodarone: serious symptomatic bradycardia in patients taking amiodarone, with cardiac monitoring recommended. All sofosbuvir-containing products carry this warning.
- Acceptable medical justification for inability to use Harvoni (preferred product):
  - In patients indicated for co-administration of Harvoni with ribavirin: contraindications to ribavirin

- 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.

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: Adult patients with chronic 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 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 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.
Treatment-experienced refers to previous treatment with peginterferon with or without RBV unless otherwise stated

Indication: Pediatric patients (age ≥ 3 years or weighing at least 35 kg) with chronic 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 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 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 http://www.sovaldi.com/. Accessed April 15, 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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy converted to new template. Modified diagnosis requirement for HCV RNA levels from over a six-month period to within the last 6 months; updated to reflect new pediatric indication; updated dosing and administration section per April 2017 AASLD/IDSA guideline; extended initial approval duration up to full regimen; deleted adherence requirement in continued therapy section since appropriate full regimen is provided through initial approval duration per specialist feedback to prevent barriers to adherence; added maximum dose requirement, added documentation of positive response to therapy and continuity of care. Safety criteria was applied according to the safety guidance discussed at CPAC and per EPS.PHARM.31. Exception made to require hep B screening for all patients prior to treatment to ensure that proper risk reduction	07.17	08.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
measures are taking, though this is not specifically addressed in boxed warning.		
Added redirection to Harvoni, Epclusa, and Vosevi per 2018 formulary status	03.20.18	
3Q 2018 annual review: removed requirement for HBV verification; expanded duration of treatment required for COC from 30 days to 60 days; required verification of genotype for COC; removed requirement for RBV CI; removed redirection to Vosevi due to different place in therapy; references reviewed and updated.	05.22.18	08.18
3Q 2019 annual review: removed advanced liver disease requirement to align with 2018 AASLD/IDSA hepatitis C treatment guidelines; references reviewed and updated.	05.13.19	08.19
3Q 2020 annual review: updated FDA-approved age of 3 years, dosage forms, pediatric dosing information, and criteria age limit; updated age limit for redirection to Harvoni & Epclusa based on FDA-approved age limits; 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; removed coverage for Sovaldi+Daklinza as off-label combination is no longer recommended by AASLD/IDSA HCV guideline; added requirement for Vosevi-treatment failures to use Vosevi + RBV per formulary preference and as recommended by AASLD/IDSA HCV guideline; references reviewed and updated.	05.20.20	08.20
3Q 2021 annual review: updated criteria for age requirement of Epclusa use due to Epclusa's pediatric age expansion; removed criterion for sobriety documentation as AASLD recommends to treat all patients with HCV except those with short life expectancy; included reference to Appendix E with the addition of un/acceptable rationale for bypassing preferred agents; updated Appendix B therapeutic alternatives and section V dosing tables; references reviewed and updated.	07.23.21	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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.