Clinical Policy: Sofosbuvir (Sovaldi)

Reference Number: GA.PMN.17
Effective Date: 12/16
Last Review Date: 4/2021 Revision Log

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

Description
Sofosbuvir (Sovaldi®) is an HCV nucleotide analog NS5B polymerase inhibitor. indicated for:

FDA Approved Indication(s)
Solvadi 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 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin (RBV).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Sovaldi is **medically necessary** when the following criteria are met:

I. 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 RNA (ribonucleic acid) levels in the last 6 months;
2. Confirmed HCV genotype is one of the following (a or b):
   *Chart note documentation and copies of labs results are required
   a. For adults (>18 years): Genotypes 1, 2, 3, 4, 5, 6;
   b. For pediatrics (age ≥ 3): Genotypes 2 or 3;
3. Documentation of the treatment status of the patient (treatment-naïve or treatment-experienced);
4. Documentation of cirrhosis status of the patient (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
5. Must meet one of the following (a, b, c, or d):
   a. If age ≥ 12 years or weight ≥ 45 kg: and member has not experienced treatment failure with Vosevi®: Member must use sofosbuvir/velpatasvir (Epclusa) (authorized generic preferred) or Mavyret®/™, unless both are contraindicated or clinically significant adverse effects are experienced;

b. If age ≥ 12 years or weight ≥ 45 kg and treatment-experienced with Vosevi®: Member must use Sovaldi in combination with Mavyret® and RBV, unless any individual agent is contraindicated or clinically significant adverse effects are experienced;
c. If age between 6 and 11 years, or weight 17 kg to 44 kg: Member must use sofosbuvir/velpatasvir (Epclusa) (*authorized generic preferred*), unless contraindicated or clinically significant adverse effects are experienced;
d. If age between 3 to 6 years with genotype 1: Member must use Harvoni (*authorized generic for 8 weeks only*), unless contraindicated or clinically significant adverse effects are experienced;

6. For pediatric patients (age ≥ 3 years) with genotype 2 or 3: use is in combination with RBV;
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 Administrationrence)*;
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 E*);
10. Creatinine clearance ≥ 50 mL/min if prescribed with peginterferon alfa-2b and ribavirin;
11. Member has none of the following contraindications:
    a. If Sovaldi is prescribed with ribavirin:
        i. Hypersensitivity to ribavirin;
        ii. Pregnancy or possibility of pregnancy - member or partner;
        iii. Significant/unstable cardiac disease;
        iv. Coadministration with didanosine;
        v. Hemoglobinopathy (e.g., thalassemia major, sickle cell anemia);
        vi. Hemoglobin < 8.5 g/dL;
    b. If Sovaldi is prescribed with peginterferon:
        i. Hypersensitivity to peginterferon alfa;
        ii. Pregnancy or possibility of pregnancy - member or partner;
        iii. Significant/unstable cardiac disease;
        iv. Autoimmune hepatitis;
        v. Decompensated hepatic disease (e.g., Child-Pugh class B or C);

Approval duration: up to a total of 48 weeks*
*(*Approved duration should be consistent with a regimen in Section III Dosage and AdministrationE)*

B. Other diagnoses/indications: Refer to CP.PHAR.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: 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/ ledipasvir (Harvoni®)	Without cirrhosis, treatment-naïve, HIV-uninfected, whose HCV viral load is less than 6 million IU/mL: **Genotype 1** One tablet PO QD for 8 weeks	*Weight ≥ 35 kg*: One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day *Weight ≥ 17 to < 35 kg*: One tablet (sofosbuvir 200 mg / ledipasvir 45 mg) per day *Weight < 17 kg*: One packet of pellets (sofosbuvir 150 mg / ledipasvir 33.75 mg) per day
Epclusa® (sofosbuvir/ velpatasvir)	Without cirrhosis or with compensated cirrhosis, treatment naïve or treatment experienced:	Epclusa: One tablet (Adult/Peds ≥ 30 kg: sofosbuvir 400 mg

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Genotypes 1 through 6 One tablet PO QD for 12 weeks	/velpatasvir 100 mg; Peds 17 to 29 kg: sofosbuvir 200 mg /velpatasvir 50 mg) per day
Epclusa® (sofosbuvir/ velpatasvir) plus RBV	With decompensated cirrhosis (Child-Pugh class B or C) treatment-naïve or treatment experienced: **Genotypes 1 through 6** One tablet PO QD plus weight-based RBV for 12 weeks	Epclusa: One tablet (Adult/Peds ≥ 30 kg: sofosbuvir 400 mg /velpatasvir 100 mg; Peds 17 to 29 kg: sofosbuvir 200 mg /velpatasvir 50 mg) per day
sofosbuvir/ velpatasvir (Epclusa®)	With decompensated cirrhosis in whom prior sofosbuvir- or NS5A-based treatment experienced failed: **Genotype 1 through 6** One tablet PO QD with weight-based RBV for 24 weeks‡	Epclusa: One tablet (Adult/Peds ≥ 30 kg: sofosbuvir 400 mg /velpatasvir 100 mg; Peds 17 to 29 kg: sofosbuvir 200 mg /velpatasvir 50 mg) per day
Mavyret™ (glecaprevir /pibrentasvir)	Treatment-naïve chronic HCV infection: **Genotypes 1, 2, 3, 4, 5, or 6** Without cirrhosis or with compensated cirrhosis: 3 tablets PO QD for 8 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir /pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir : **Genotypes 1, 2, 4, 5, or 6** Without cirrhosis: 3 tablets PO QD for 8 weeks With compensated cirrhosis: 3 tablets PO QD for 12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir /pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir **Genotype 3** Without cirrhosis or with compensated cirrhosis: 3 tablets PO QD for 16 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Mavyret™ (glecaprevir /pibrentasvir)	Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor : **Genotype 1** Without cirrhosis or with compensated cirrhosis: 3 tablets PO QD for 16 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir /pibrentasvir)	Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor : **Genotype 1** Without cirrhosis or with compensated cirrhosis: 3 tablets PO QD for 12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day

Theraputic 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.
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

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.

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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
Daklinza	Daclatasvir				
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Sovaldi		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
Viekira /PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Vosevi*	Velpatasvir	Sofosbuvir		Voxilaprevir	
.Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs

Appendix E: 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.
- Gane et al. studied 10 patients treated with Sovaldi monotherapy for 12 weeks who had genotype 2 or 3 disease. The primary efficacy (sustained virologic response (SVR) at 12 weeks after therapy stopped) was much lower (60%) on monotherapy versus 100% on combination therapy.

III. 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 November 2019)

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/RBV unless otherwise stated.
The use of Sovaldi in combination with pegIFN + RBV, Olysio, or Daklinza for the treatment of chronic HCV is no longer recommended by the AASLD/IDSA guidelines.

Indication: Pediatric patients (age ≥ 3 years) 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 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
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/RBV unless otherwise stated.
The use of Sovaldi in combination with pegIFN + RBV, Olysio, or Daklinza for the treatment of chronic HCV is no longer recommended by the AASLD/IDSA guidelines.

IV. Product Availability

Tablet: 400mg, 200mg
Oral pellets: 200 mg, 150 mg

V. References

1. Sovaldi Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; March 2020. Available at http://www.sovaldi.com/. 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.
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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.

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6. El-Shabrawi MH, Kamal NM. Burden of pediatric hepatitis C. World J Gastroenterol. 2013 Nov 28;19(44):7880-8. doi: 10.3748/wjg.v19.i44.7880.
7. Wirth S. Current treatment options and response rates in children with chronic hepatitis C. World J Gastroenterol 2012 Jan 14; 18(2): 99-104. doi:10.3748/wjg.v18.i2.99.
8. 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.
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Reviews, Revisions, and Approvals	Date	Approval Date
New policy created, split from CP.PHAR.17. 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." Testing criteria reorganized by "no cirrhosis"/"cirrhosis" consistent with the regimen tables; HCC population is included under "cirrhosis" and broadened to incorporate HCC amenable to curative measures (resection, ablation, transplant). Methods to diagnose fibrosis/cirrhosis are modified to require presence of HCC, liver biopsy or a combination of one serologic and one radiologic test. Serologic and radiologic tests are updated and correlated with METAVIR per Appendix B. Removed creatinine clearance restriction. Criteria added excluding post-liver transplantation unless regimens specifically designate. Dosing regimens are presented in Appendix D and E. The initial approval is shortened to 8 weeks.	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	10/16	10/2016
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 criteria for Pediatric Chronic Hepatitis C Infection.	6/17	6/17
Added preferencing information requiring Mavyret for FDA-approved indications. Added requirement for Hep B screening.	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	2/21/19	2/19

Reviews, Revisions, and Approvals	Date	Approval Date
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.		
Annual review. Added pediatric age to FDA Approved Indication Section. Added specification for Mavyret preferencing based on pediatric age or weight. Combined contraindication section to age/weight preferencing of Mavyret. 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
RT4: updated Sovaldi FDA-approved age (3 years), dosage forms, and pediatric dosing information; updated Mavyret dosing recommendations to 8 weeks total duration of therapy for treatment-naïve HCV with compensated cirrhosis across all genotypes (1-6). 2020 SDC decisions implemented added preferencing for AG Epclusa or Mavyret. emoved redirection to Mavyret based on contraindications criteria. Updated general information section. Updated order of all other Appendices. Updated references.Updated references	4/2020	4/2020
Removed coverage for Sovaldi + Daklinza as off-label combination is no longer recommended and added coverage for the combination of Sovaldi with Mavyret and ribavirin for patients experiencing treatment failure with Vosevi per updated AASLD/IDSA HCV guideline; references reviewed and updated.	7/2020	7/2020
Annual review. Added Vosevi treatment experience option as a part of initial criteria. Added Harvoni, an additional Epclusa dosing regimen, and treatment experience definition/reference to Appendix B: Therapeutic Alternatives Added Mayvret and Vosevi to Appendix D-Direct Acting Antivirals for Treatment of HCV infection and removed Olysio, Technivie, and Viekira XR as these were previously removed from the market. Changed Centene Logo to PSHP Logo.	4/2021	4/2021

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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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.