

Clinical Policy: Sofosbuvir (Sovaldi)

Reference Number: CP.PHAR.281

Effective Date: 09.16

Last Review Date: 08.19

Line of Business: Medicaid

[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:

- Adult patients with genotype 1, 2, 3 or 4 chronic HCV infection without cirrhosis or with compensated cirrhosis as a component of a combination antiviral treatment regimen
- Pediatric patients 12 years of age and older or weighing at least 35 kg with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis 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[®] 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 serum 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 (> 18 years): Genotypes 1, 2, 3, 4, 5, or 6;
 - b. For pediatrics (age ≥ 12 years or weight ≥ 35 kg): 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;
6. Age ≥ 12 years or weight ≥ 35 kg;
7. If age ≥ 12 years or weight ≥ 45 kg, member has at least one of the following contraindications to Mavyret[™] (a or b):
 - a. Decompensated cirrhosis (Child-Pugh B or C) confirmed by lab findings and clinical notes;
 - b. Receiving treatment with efavirenz or atazanavir;

**See Appendix E for additional details on acceptable contraindications*

8. Life expectancy \geq 12 months with HCV treatment;
9. Member agrees to participate in a medication adherence program including both of the following components:
 - 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 400 mg (1 tablet) per day.

Approval duration:

Adults: up to a total of 24 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

Pediatrics: 12 weeks for genotype 2; 24 weeks for genotype 3

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.PMN.53 for Medicaid.

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. Must meet 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 ($>$ 18 years): Genotypes 1, 2, 3, 4, 5, or 6;
 - 2) For pediatrics (age \geq 12 years or weight \geq 35 kg): Genotypes 2 or 3;
2. Member is responding positively to therapy;
3. Dose does not exceed 400 mg (1 tablet) per day.

Approval duration:

Adults: up to a total of 24 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

Pediatrics: up to 12 weeks for genotype 2; up to 24 weeks for genotype 3

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.PMN.53 for Medicaid.

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 policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases	IDSA: Infectious Diseases Society of America
FDA: Food and Drug Administration	NS3/4A, NS5A/B: nonstructural protein
HBV: hepatitis B virus	PegIFN: pegylated interferon
HCC: hepatocellular carcinoma	RBV: ribavirin
HCV: hepatitis C virus	RNA: ribonucleic acid
HIV: human immunodeficiency virus	

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
Mavyret™ (glecaprevir /pibrentasvir)	Treatment-naïve chronic hepatitis C (CHC) infection: Genotypes 1, 2, 3, 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 CHC infection: 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 CHC infection: 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 CHC infection: 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 CHC infection: 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

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 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
Daklinza	Daclatasvir				
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Mavyret*	Pibrentasvir			Glecaprevir	
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/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.
- 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.
- Acceptable medical justification for inability to use Mavyret (preferred product):
 - Severe hepatic disease (Child-Pugh C): use of Mavyret is not recommended due to higher exposures of glecaprevir and pibrentasvir.
 - Moderate hepatic disease (Child-Pugh B): although not an absolute contraindication, use of Mavyret is not recommended in patients with moderate hepatic disease (Child-Pugh B) due to lack of safety and efficacy data.
 - Following administration of Mavyret in HCV infected subjects with *compensated* cirrhosis (Child-Pugh A), exposure of glecaprevir was approximately 2-fold and pibrentasvir exposure was similar to non-cirrhotic HCV infected subjects.
 - At the clinical dose, compared to *non-HCV infected* subjects with *normal hepatic function*, glecaprevir AUC was 100% higher in Child-Pugh B subjects, and increased to 11-fold in Child-Pugh C subjects. Pibrentasvir AUC was 26% higher in Child-Pugh B subjects, and 114% higher in Child-Pugh C subjects.
 - Drug-drug interactions with one or more the following agents:
 - Atazanavir
 - Efavirenz
- Unacceptable medical justification for inability to use Mavyret (preferred product):
 - Black Box Warning (BBW): currently or previously infected with hepatitis B virus. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Therefore it is not a valid clinical reason not to use Mavyret.
 - Concurrent anticoagulant therapy: Fluctuations in International Normalized Ratio (INR) have been observed in warfarin recipients who were also receiving treatment for HCV infections. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Although caution is advised when using Mavyret while receiving concurrent anticoagulant therapy, specifically warfarin, this is not an absolute contraindication as long as patient is adequately monitored and educated during therapy.
 - Drug-drug interactions with one or more of the following agents:
 - Rifampin, carbamazepine, or St. John's wort:

- These drug-drug interactions are not unique to Mavyret, and they apply across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection.

V. Dosage and Administration

Indication: Adult patients with chronic HCV infection			
Drugs	Dosing Regimen	Maximum Dose	Reference
Sovaldi, Olysio	Genotype 1: Treatment-naïve or treatment-experienced with peg-IFN/RBV patients without cirrhosis: Sovaldi 400 mg plus Olysio 150 mg PO QD for 12 weeks	Sovaldi: 400 mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Sovaldi, Olysio	Genotype 1 or 4: Treatment-naïve or treatment-experienced, liver transplant patients with or without compensated cirrhosis: Sovaldi 400 mg plus Olysio 150 mg PO QD with or without weight-based RBV for 12 weeks	Sovaldi: 400 mg/day	AASLD-IDSA (updated May 2018)
Sovaldi, Daklinza	Genotype 1: Treatment-naïve or treatment-experienced without cirrhosis: Daklinza 60 mg plus Sovaldi 400 mg PO QD for 12 weeks	Sovaldi: 400 mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Sovaldi, Daklinza	Genotype 1, 2, 3, or 4: Decompensated cirrhosis (including those with hepatocellular carcinoma): Daklinza 60 mg plus Sovaldi 400 mg PO QD with low initial dose of RBV (600 mg) and increased as tolerated for 12 weeks	Sovaldi: 400 mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Sovaldi, Daklinza	Genotype 1, 2, 3, or 4: Decompensated cirrhosis (including those with hepatocellular carcinoma) and intolerant to RBV: Daklinza 60 mg plus Sovaldi 400 mg PO QD for 24 weeks	Sovaldi: 400 mg/day	AASLD-IDSA (updated May 2018)
Sovaldi, Daklinza	Genotype 1-6 [†] : Treatment-naïve or treatment-experienced, post-liver transplantation with or without compensated cirrhosis: Daklinza 60 mg plus Sovaldi 400 mg PO QD with low initial dose of RBV	Sovaldi: 400 mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)

Indication: Adult patients with chronic HCV infection			
Drugs	Dosing Regimen	Maximum Dose	Reference
	(600 mg) and increased as tolerated for 12 weeks		
Sovaldi, Daklinza	Genotype 2: Treatment-naïve or treatment-experienced without cirrhosis: Daklinza 60 mg plus Sovaldi 400 mg PO QD for 12 weeks	Sovaldi: 400 mg/day	AASLD-IDSA (updated May 2018)
Sovaldi, Daklinza	Genotype 2: Treatment-naïve or treatment-experienced with compensated cirrhosis: Daklinza 60 mg plus Sovaldi 400 mg PO QD for 16 to 24 weeks	Sovaldi: 400 mg/day	AASLD-IDSA (updated May 2018)
Sovaldi, Daklinza	Genotype 2 or 3: Treatment-naïve or treatment-experienced, post-liver transplantation with decompensated cirrhosis: Daklinza 60 mg plus Sovaldi 400 mg PO QD with low initial dose of RBV (600 mg) and increased as tolerated for 12 weeks	Sovaldi: 400 mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Sovaldi, Daklinza	Genotype 3: Treatment-naïve or treatment-experienced with peg IFN/RBV without cirrhosis: Daklinza 60 mg plus Sovaldi 400 mg PO QD for 12 weeks (If NS5A Y93H is present, weight-based RBV should be added)	Sovaldi: 400 mg/day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Sovaldi, Daklinza	Genotype 3: Treatment-naïve with compensated cirrhosis: Daklinza 60 mg plus Sovaldi 400 mg PO QD with or without weight-based RBV for 24 weeks	Sovaldi: 400 mg/day	AASLD-IDSA (updated May 2018)
Sovaldi, Zepatier [†]	Genotype 3: pegIFN/RBV-experienced with compensated cirrhosis: Sovaldi 400 mg PO QD plus Zepatier 1 tablet PO QD for 12 weeks	Sovaldi: 400 mg per day	AASLD-IDSA (updated May 2018)

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.

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

Treatment-experienced refers to previous treatment with peginterferon/RBV unless otherwise stated

The use of Sovaldi in combination with peginterferon and ribavirin for the treatment of chronic HCV is no longer recommended by the AASLD/IDSA guidelines.

Indication: Pediatric patients (age ≥ 12 years or weighing at least 35 kg) with chronic HCV infection			
Drugs	Dosing Regimen	Maximum Dose	Reference
Sovaldi, RBV	Genotype 2: Sovaldi 400 mg + RBV for 12 weeks	Sovaldi: 400 mg/day	FDA-approved labeling
Sovaldi, RBV	Genotype 3: Sovaldi 400 mg + RBV for 24 weeks	Sovaldi: 400 mg/day	FDA-approved labeling

VI. Product Availability

Tablet: 400 mg

VII. References

1. Sovaldi Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; November 2017. Available at <http://www.sovaldi.com/>. Accessed May 1, 2019.
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 May 24, 2018. Available at: <https://www.hcvguidelines.org/>. Accessed May 1, 2019.
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. *Lancet 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. Wirth et al. Sofosbuvir-Containing Regimens are Safe and Effective in Adolescents with Chronic hepatitis C Infection. 26th Annual Meeting of the Asian Pacific Association for the Study of the Liver (APASL) on February 15-19, 2017 in Shanghai, China [oral GT1-3].
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.

Reviews, Revisions, and Approvals	Date	P&T 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	08.16	09.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>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.</p>		
<p>Added criteria for Pediatric Chronic Hepatitis C Infection. Updated contraindications, removed hypersensitivity to drug and cardiac disease per PI;</p>	04.17	05.17
<p>Policy converted to new template. Added requirement for prevention of HBV reactivation; expanded genotypes to reflect AASLD/IDSA CHC tx guidelines. Consolidated appendix D and E into dosing and administration in section V, deleted “up to” in initial approval duration; deleted adherence requirement in continued, added documentation of positive response to therapy and continuity of care, and removed CIs in section II, added reference column in section V. Added preferencing information requiring Mavyret for FDA-approved indications. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Exception made to require Hep B screening.</p>	08.17	09.17
<p>Removed the following language: “If a lower cost alternative regimen carries an equal or higher AASLD-IDSA rating, a clinical contraindication or intolerance must be present for the alternative regimen prior to approval.”</p>	09.17	
<p>3Q 2018 annual review: removed requirement for HBV verification; added requirement for documentation of previous treatment and cirrhosis status; expanded duration of tx required for COC from 30 days to 60 days; required verification of genotype for COC; removed conditional requirement for RBV CI; references reviewed and updated.</p>	05.22.18	08.18
<p>Removed advanced liver disease requirement to align with 2018 AASLD/IDSA hepatitis C treatment guidelines.</p>	04.18.19	05.19
<p>3Q 2019 annual review: removed documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy; references reviewed and updated.</p>	06.26.19	08.19

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.

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