Clinical Policy: Sofosbuvir (Sovaldi)

Reference Number: CP.PHAR.281
Effective Date: 09/16
Last Review Date: 05/17 Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for sofosbuvir (Sovaldi®).

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. Initial 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. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
2. Age ≥ 12 years or body weight > 35kg;
3. Diagnosis of chronic hepatitis C virus (HCV) infection as evidenced by detectable HCV RNA (ribonucleic acid) levels over a six-month period;
4. Confirmed HCV genotype is one of the following (a or b):
   a. For adults (>18 years): Genotypes 1, 2, 3, or 4;
   b. For pediatrics (age ≥ 12 years or body weight > 35kg): Genotypes 2 or 3;
5. Life expectancy ≥ 12 months with HCV treatment;
6. Documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy, if applicable;
7. Advanced liver disease defined as a or b:
   a. Advanced fibrosis indicated by i or ii:
      i. Liver biopsy showing a METAVIR score of F3 or equivalent (Knodell, Scheuer, Batts-Ludwig – F3; Ishak – F4/5);
      ii. One serologic test and one radiologic test showing an equivalent score to METAVIR F3 per Appendix B;
   b. Cirrhosis indicated by i, ii or iii:
      i. Hepatocellular carcinoma (HCC) - and the HCC is amenable to resection, ablation or transplant;
      ii. Liver biopsy showing a METAVIR score of F4 or equivalent (Knodell, Scheuer, Batts-Ludwig – F4; Ishak - F5/6);
      iii. Both of the following:
         a) One serologic test showing an equivalent score to METAVIR F4 per Appendix B;

b) One radiologic test showing an equivalent score to METAVIR F4 per Appendix B or other radiologic test showing evidence of cirrhosis (e.g., portal hypertension);

8. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Appendix D and E for reference)*;
9. If member is ≥ 18 years of age, has a contraindication or intolerance to the following preferred medication(s)
   a. For genotype 1a, 1b and 4: Zepatier and Epclusa. *(Zepatier is the preferred agent; Eplcusa should be used if Zepatier is contraindicated);*
   b. For genotype 2 and 3: Epclusa;
10. Member agrees to participate in a medication adherence program meeting both of the following components:
    a. Medication adherence monitored by pharmacy claims data or member report;
    b. Member's risk for non-adherence monitored at least every 4 weeks;
11. Creatinine clearance ≥ 50 mL/min if prescribed with peginterferon alfa-2b and ribavirin;
12. Member has none of the following contraindications:
    a. If Sovaldi is prescribed with ribavirin:
       i. Pregnancy or possibility of pregnancy - member or partner;
       ii. Coadministration with didanosine;
       iii. Hemoglobinopathy (e.g., thalassemia major, sickle cell anemia);
       iv. Hemoglobin < 8.5 g/dL;
       v. Autoimmune hepatitis;
    b. If Sovaldi is prescribed with peginterferon:
       i. Autoimmune hepatitis;
       ii. Decompensated hepatic disease (e.g., Child-Pugh class B or C).

Approval duration: 8 weeks
Approval duration for Pediatrics: 12 weeks for genotype 2 and 24 weeks for genotype 3

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

*** 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. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Pharmacy claims support adherence to therapy;
3. Creatinine clearance ≥ 50 mL/min if prescribed with peginterferon alfa-2b and RBV;
4. Member has none of the following reasons to discontinue therapy:
   a. If Sovaldi is prescribed with ribavirin:
      i. Pregnancy or possibility of pregnancy - member or partner;
      ii. Coadministration with didanosine;

iii. Hemoglobinopathy (e.g., thalassemia major, sickle cell anemia);
iv. Hemoglobin < 8.5 g/dL;

b. If Sovaldi is prescribed with peginterferon:
i. Pregnancy or possibility of pregnancy - member or partner;
ii. Autoimmune hepatitis;
iii. Decompensated hepatic disease (e.g., Child-Pugh class B or C);
iv. Severe depression;
v. Platelets < 25 x 10^9/L;
vi. Development of typical colitis manifestations (abdominal pain, bloody diarrhea, fever);
vii. Pancreatitis;
viii. New or worsening ophthalmologic disorder.

5. If request is for a dose increase, new dose does not exceed 400 mg/day.

Approval duration: up to a total of 48 weeks*
*(*Approved duration should be consistent with a regimen in Appendix D or E)*
Approval duration for Pediatrics: up to 12 weeks for genotype 2 and up to 24 weeks for genotype 3

B. Other diagnoses/indications (1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

Background
Description/Mechanism of Action:
Sofosbuvir is a nucleotide analog HCV NS5B polymerase inhibitor and direct-acting antiviral (DAA) agent against the hepatitis C virus.

Sovaldi Formulations
Tablet, Oral
- Sovaldi: 400 mg of sofosbuvir

Ribavirin Formulations:
Capsule, Oral:
- Rebetol: 200 mg
- Ribasphere: 200 mg
- Generic: 200 mg

Solution, Oral:
- Rebetol: 40 mg/mL (100 mL)

Tablet, Oral:
- Copegus: 200 mg
- Moderiba (includes dose packs): 200 mg, 400 mg, 600 mg
- Ribasphere: 200 mg, 400 mg, 600 mg
- Ribasphere RibaPak (dose packs): 200 mg, 400 mg, 600 mg

- Generic: 200 mg

Peginterferon Alfa-2a Formulations:
Solution, Subcutaneous [preservative free]:
- Pegasys: 180 mcg/mL (1 mL); 180 mcg/0.5 mL (0.5 mL)
- Pegasys ProClick: 135 mcg/0.5 mL (0.5 mL)
- Pegasys ProClick: 180 mcg/0.5 mL (0.5 mL)

Peginterferon Alfa-2b Formulations:
Kit, Subcutaneous [preservative free]:
- Peg-Intron Redipen: 50 mcg/0.5 mL, 80 mcg/0.5 mL, 120 mcg/0.5 mL, 150 mcg/0.5 mL
- Peg-Intron Redipen Pak 4: 120 mcg/0.5 mL
- PegIntron: 50 mcg/0.5 mL, 80 mcg/0.5 mL, 120 mcg/0.5 mL, 150 mcg/0.5 mL
- Sylatron: 200 mcg, 300 mcg, 600 mcg

FDA Approved Indications:
Sovaldi is an HCV nucleotide analog NS5B polymerase inhibitor/oral tablet formulation indicated for:
- Treatment adult patients with genotype 1, 2, 3, or 4 chronic HCV infection as a component of a combination antiviral treatment regimen.
- Treatment of 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.

Appendices
Appendix A: Abbreviation Key
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
CTP: Child Turcotte Pugh
CrCl: creatinine clearance
DAA: direct acting antiviral
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

Appendix B: Approximate Scoring Equivalencies using METAVIR F3/F4 as Reference

Fibrosis/ Cirrhosis	Serologic Tests*				Radiologic Tests†		Liver Biopsy‡	
	Fibro Test	FIBRO Spect II	APRI	FIB-4	FibroScan (kPa)	MRE (kPa)	METAVIR	Ishak
Advanced fibrosis	≥0.59	≥42	>1.5	>3.25	≥9.5	≥4.11	F3	F4-5
Cirrhosis	≥0.75	≥42	>1.5	>3.25	≥12.0	≥4.71	F4	F5-6

*Serologic tests:
FibroTest (available through Quest as FibroTest or LabCorp as FibroSure)
FIBROSpect II (available through Prometheus Laboratory)
APRI (AST to platelet ratio index)

FIB-4 (Fibrosis-4 index: includes age, AST level, platelet count)
†Radiologic tests:
FibroScan (ultrasound-based elastography)
MRE (magnetic resonance elastography)
‡Liver biopsy (histologic scoring systems):
METAVIR F3/F4 is equivalent to Knodell, Scheuer, and Batts-Ludwig F3/F4 and Ishak F4-5/F5-6
METAVIR fibrosis stages: F0 = no fibrosis; F1 = portal fibrosis without septa; F2 = few septa; F3 = numerous septa without cirrhosis; F4 = cirrhosis

Appendix C: 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
Daklinza	Daclatasvir				
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs
**Additional PIs no longer recommended: Victrelis (boceprevir), Incivek (telaprevir)

Appendix D: FDA-Approved Regimens and Treatment Durations
Adult Patients:

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
Presence or Absence of Cirrhosis Not Specified			
Not specified	1*	Not specified	Sovaldi + RBV† *If Peg-IFN ineligible.*
	1*, 4	Not specified	Sovaldi + PEG-IFN alfa + RBV§
	2	Not specified	Sovaldi + RBV§
	3	Not specified	Sovaldi + RBV†
	Not specified	Not specified	Sovaldi + RBV‡ *If HCC and awaiting liver transplantation.*

*Subtype a or b, or unknown subtype
§Treatment duration - 12 weeks
†Treatment duration - 24 weeks
‡Treatment duration - up to 48 weeks or until liver transplantation

Pediatric Patients (>12 years or >35 kg):

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
Presence or Absence of Cirrhosis Not Specified			
	2	Not specified	Sovaldi + RBV§
	3	Not specified	Sovaldi + RBV†

§Treatment duration - 12 weeks
†Treatment duration - 24 weeks

Appendix E: AASLD-IDSA Recommended Regimens and Treatment Durations

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
No Cirrhosis			
Treatment naive	1*, 2, 3, 4	None	Sovaldi + Daklinza +RBV§ *If post-liver transplantation.*
	1a, 1b, 2, 3	None	Sovaldi + Daklinza§
			Sovaldi + Olysio§
	2	None	Sovaldi + RBV† *If post-liver transplantation.*
	2, 3	None	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
Treatment experienced	1*	NS3 PI/Peg-IFN/RBV**	Sovaldi + Daklinza§
	1*, 2, 3, 4	Not specified	Sovaldi + Daklinza + RBV§ *If post-liver transplantation.*
	1a, 1b	Peg-IFN/RBV	Sovaldi + Olysio§
	1a, 1b, 2, 3	Peg-IFN/RBV	Sovaldi + Daklinza§
	2	Not specified	Sovaldi + RBV† *If post-liver transplantation.*
	2, 3	Not specified	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
	3	Sovaldi/RBV	Sovaldi + Daklinza + RBV†
Not specified	1*, 4	Not specified	Sovaldi + Olysio +/- RBV§ *If post-liver transplantation.*
Compensated Cirrhosis (CTP/Child-Pugh Class A)			
Treatment naive	1*, 2, 3, 4	None	Sovaldi + Daklinza +RBV§ *If post-liver transplantation.*
	1*, 4	None	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
	1a	None	Sovaldi + Olysio +/-RBV†
	1a, 1b	None	Sovaldi + Daklinza +/- RBV†
	1b	None	Sovaldi + Olysio†
	2	None	Sovaldi + Daklinza◊
		None	Sovaldi + RBV† *If post-liver transplantation.*

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
	2, 3	None	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
	3	None	Sovaldi + Daklinza†
Treatment experienced	1*	NS3 PI/Peg-IFN/RBV**	Sovaldi + Daklinza + RBV†
		Olysio/Sovaldi	Sovaldi-based dual DAA therapy +/- RBV†
			Sovaldi-based triple/quadruple DAA therapy +/- RBV♦
		NS5A inhibitor	Sovaldi-based dual DAA therapy +/- RBV†
			Sovaldi-based triple/quadruple DAA therapy +/- RBV♦
	1*, 2, 3, 4	Not specified	Sovaldi + Daklinza + RBV§ *If post-liver transplantation.*
	1a	Peg-IFN/RBV	Sovaldi + Olysio +/- RBV† *If negative for the Q80K variant.*
	1a, 1b	Peg-IFN/RBV	Sovaldi + Daklinza +/- RBV†
	1b	Peg-IFN/RBV	Sovaldi + Olysio +/- RBV†
	2	Peg-IFN/RBV	Sovaldi + Daklinza◊
		Sovaldi/RBV	Sovaldi + Daklinza†
		Not specified	Sovaldi + RBV† *If post-liver transplantation.*
	2, 3	Not specified	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
	3	Sovaldi/RBV	Sovaldi + Daklinza + RBV†
		Peg-IFN/RBV	Sovaldi + Daklinza + RBV†
Not specified	1*, 4	Not specified	Sovaldi + Olysio +/- RBV§ *If post-liver transplantation.*
Decompensated Cirrhosis (CTP/Child-Pugh Class B or C)			
Treatment naive	1*, 4	None	Sovaldi + Daklinza +RBV§ *If post-liver transplantation.*
	2	None	Sovaldi + RBV† *If post-liver transplantation.*
Treatment experienced	1*, 4	Not specified	Sovaldi + Daklinza +RBV§ *If post-liver transplantation.*
	2	Not specified	Sovaldi + RBV† *If post-liver transplantation.*
Not specified	1*, 2, 3, 4	Not specified	Sovaldi + Daklinza + RBV§
	1*, 4	Not specified	Sovaldi + Daklinza† *If RBV ineligible.*

*Subtype a or b, or unknown subtype
**NS3 includes Victrelis (boceprevir), Incivek (telaprevir) or Olysio (simeprevir)
§Treatment duration - 12 weeks
♦Treatment duration – 12 to 24 weeks
◊Treatment duration – 16 to 24 weeks

†Treatment duration - 24 weeks

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
Added criteria for pediatric chronic hepatitis C infection. Updated contraindications, removed hypersensitivity to drug and cardiac disease per PI. Removed continued therapy requirement of HCV RNA not present or if present, has not increased by >10 fold per specialist.	04/17	05/17

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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.