Clinical Policy: Sofosbuvir (Sovaldi)

Reference Number: GA.PMN.17
Product: Medicaid
Effective Date: 12/16
Last Review Date: 3/18 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. 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 over a six-month period;
2. Confirmed HCV genotype is one of the following (a or b):
   a. For adults (>18 years): Genotypes 1, 2, 3, 4;
   b. For pediatrics (age ≥ 12 years or body weight > 35kg): Genotypes 2 or 3;
3. Life expectancy ≥ 12 months with HCV treatment;
4. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Appendix D and E for reference)*;
5. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A):
   a. Mavyret is preferred unless contraindication, intolerance, or pediatric age
6. 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 F*);
7. Creatinine clearance ≥ 50 mL/min if prescribed with peginterferon alfa-2b and ribavirin;
8. 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 Appendix D or E)*

B. Other diagnoses/indications: 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 of genotype 1, 2, 3, or 4 chronic HCV infection as a component of a combination antiviral treatment regimen.

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			

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)**	CYP3A Inhibitor
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

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

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§

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
	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.*
	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†

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
			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

Appendix F: General Information

- Hepatitis B Reactivation is a Black Box Warning for all direct-acting antiviral drugs for the treatment of HCV. The provider must provide either:
  - Documentation of absence of concurrent HBV infection as evidenced by laboratory values showing absence of hepatitis B virus envelope antigen (HBeAg) and HBV DNA (deoxyribonucleic acid);
  - Documentation that HBV co-infected patient may not be candidates for therapy as evidenced by one of the following:
    - Absence of HBeAg, HBV DNA less than 2,000 international units/mL, and alanine aminotransferase (ALT) level within 1 to 2 times the upper limit of normal;
    - HBeAg-positive and HBV DNA greater than 1,000,000 international units/mL and ALT level within 1 to 2 times the upper limit of normal;
  - Documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced.
- The 2016 AASLD/IDSA treatment guideline for HBV consider ALT levels <30 U/L for men and <19 U/L for women as upper limits of normal.
- The 2016 AASLD/IDSA treatment guideline for HBV recommend adults with compensated cirrhosis, even with low levels of viremia (<2,000 IU/mL) be treated with

antiviral therapy to reduce the risk of decompensation, regardless of ALT level. The recommendation extends to adults with decompensated cirrhosis be treated with antiviral therapy indefinitely regardless of HBV DNA level, HBeAg status, or ALT level to decrease the risk of worsening liver-related complications.

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	
Added criteria for Pediatric Chronic Hepatitis C Infection.	6/17	
Added preferencing information requiring Mavyret for FDA-approved indications. Added requirement for Hep B screening.	9/17	
Annual review. No changes made.	3/18	

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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

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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.

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