Clinical Policy: Sofosbuvir (Sovaldi)
Reference Number: HIM.PA.SP2
Effective Date: 08/16
Last Review Date: 08/17
Line of Business: Health Insurance Marketplace

Coding Implications
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
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
- For the 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

Policy/Criteria
Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

I. Initial Approval Criteria

A. Chronic Hepatitis C Infection (must meet all)**:**

1. Diagnosis of chronic HCV infection as evidenced by detectable HCV ribonucleic acid (RNA) levels over a six-month period;
2. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
3. Age ≥ 12 years or body weight > 35 kg;
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 one of the following (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 and b):
   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 regimen in Appendix D or E *(if regimens applicable to post-liver transplantation they are specifically designated)*;
9. If member is ≥ 18 years of age and has contraindication or clinically significant adverse effects to the following preferred medication(s):
   a. For genotype 1a, 1b and 4: Harvoni (Epclusa, if Harvoni is contraindicated or treatment duration with Harvoni is > 12 weeks);
   b. For genotype 2 and 3: Epclusa;
10. Member agrees to participate in a medication adherence program meeting both of the following components (a and b):
   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;
11. Dose does not exceed 400 mg/day (1 tablet/day).

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
1. Refer to HIM.PHAR.21 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. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Documentation of positive response to therapy;
3. Pharmacy claims support adherence to therapy;
4. If request is for a dose increase, new dose does not exceed 400 mg/day (1 tablet/day).

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 (must meet 1 or 2)**:**
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request 6 months (whichever is less); or

2. Refer to HIM.PA.21 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 – HIM.PHAR.21 or evidence of coverage documents;

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym 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
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
IDSA: Infectious Diseases Society of America
IV: intravenous
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
Peg-IFN: pegylated interferon
PI: protease inhibitor
RBV: ribavirin
RNA: ribonucleic acid

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*

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.*
	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♦

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

V. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created.	08/16	
Added pediatric chronic hepatitis C infection criteria; Removed HCV RNA is not present or, if present, has not increased by >10	04/17	08/17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
fold (>1 $\log_{10}$ IU/mL) per specialist feedback.		

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.