# Clinical Policy: sofosbuvir (Sovaldi)

Reference Number: NM.CP.PPA.06
Effective Date: 1/1/19
Last Review Date: 1/11/23
Revision Log

**Description and FDA Approved Indication(s)**
Sofosbuvir (Sovaldi®) is hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor. 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 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)

**Black Box Warning**
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.

**Product Availability**
Oral tablet
Brand: (Sovaldi) sofosbuvir 200 mg and 400 mg
Oral pellets/packet
Brand: (Sovaldi) sofosbuvir 150 mg and 200 mg

**Policy/Criteria**

It is the policy of Western Sky Community Care (WSCC) 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 ≥ 3 years): Genotypes 2 or 3;
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. If member is ≥ 18 years of age, 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 F for additional details on acceptable contraindications*
6. Life expectancy ≥ 12 months with HCV treatment;
7. ****Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see appendices C and D)*;
8. ****Dose as follows:
   a. **For Adults**: 400 mg (1 tablet) per day.
   b. For Pediatrics:
      i. Body weight at least 35 kg: 400 mg per day
      ii. Body weight 17 kg to < 35 kg: 200 mg per day
      iii. Body weight <17 kg: 150 mg per day (restricted to oral pellet formulation)

**Approval duration for Adults: up to a total of 24 weeks***
*(*Approved duration should be consistent with guidelines, see appendix C and D)*
**Approval duration for Pediatrics: 12 weeks for genotype 2; 24 weeks for genotype 3. ****If treatment regimen varies in dosing or interval from FDA or AASLD-IDSA guideline recommendations but it is documented on PA request/office chart notes that requested regimen in consultation with Project ECHO—please approve regimen.**

**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.
2. **If denial likely please make one attempt to reach prescriber's office for peer-to-peer.**

## 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 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):
         a. For adults (> 18 years): Genotypes 1, 2, 3, 4, 5, or 6;
         b. For pediatrics (age ≥ 3 years or older): Genotypes 2 or 3;
2. Member is responding positively to therapy;
3. ****Dose as follows:

a. **For Adults**: 400 mg (1 tablet) per day.
b. For Pediatrics:
    i. Body weight at least 35 kg: 400 mg per day
    ii. Body weight 17 kg to < 35 kg: 200 mg per day
    iii. Body weight <17 kg: 150 mg per day (restricted to oral pellet formulation)

**Approval duration for Adults: up to a total of 24 weeks***
*(*Approved duration should be consistent with guidelines- see appendices C and D)* ****If treatment regimen varies in dosing or interval from FDA or AASLD-IDSA guideline recommendations but it is documented on PA request/office chart notes that requested regimen in consultation with Project ECHO—please approve regimen.**

**Approval duration for 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.
2. **If denial is likely please make attempt to contact prescriber's office for peer-to-peer.**

## Appendices

### Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
APRI: AST to platelet ratio
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IDSA: Infectious Diseases Society of America
IQR: interquartile range
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
PegIFN: pegylated interferon
RBV: ribavirin
RNA: ribonucleic acid

***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 (transient 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 B: 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 ***Additional PIs no longer recommended that have been discontinued*

## Appendix C: Sovaldi Treatment Regimens

### Pediatrics

| Genotype | Pediatric Patients 3 Years of Age and Older | Treatment | Duration |
|---|---|---|---|
| **2** | Treatment-naïve and treatment-experienced‡ **without** cirrhosis OR with compensated cirrhosis* | Sovaldi +RBV† | 12 wk |
| **3** | Treatment-naïve and treatment-experienced‡ **without** cirrhosis OR with compensated cirrhosis* | Sovaldi +RBV† | 24 wk |

### Adults

| Genotype | Adult Patients | Treatment | Duration |
|---|---|---|---|
| **1 or 4** | Treatment-naïve **without** cirrhosis OR with compensated cirrhosis* | Sovaldi +IFN** +RBV† | 12 wk |
| **2** | Treatment-naïve and treatment-experienced‡ **without** cirrhosis OR with compensated cirrhosis* | Sovaldi +RBV† | 12 wk |
| **3** | Treatment-naïve and treatment-experienced‡ **without** cirrhosis OR with compensated cirrhosis* | Sovaldi +RBV† | 24 wk |

| Genotype | Adult Special populations | Treatment | Duration |
|---|---|---|---|
| 1 | Hepatocellular Carcinoma Awaiting Liver transplantation | Sovaldi +RBV† | 48 wk or until time of liver transplant if less than 48 wk |

*Child-Pugh A
**See peginterferon-alfa prescribing information for dosage recommendation for patients with genotype 1 or 4 HCV.
† Dosage of ribavirin is weight-based (<75 kg = 1000 mg and ≥75 kg = 1200 mg). The daily dosage of ribavirin is administered orally in two divided doses with food. Patients with renal impairment (CrCl ≤50 mL/min) require ribavirin dosage reduction; refer to ribavirin prescribing information.
‡ Treatment-experienced patients have failed an interferon based regimen with or without ribavirin.

**Appendix D: AASLD-IDSA Recommended Regimens and Treatment Durations**
https://www.hcvguidelines.org/

**Appendix E:**
**Any of the following meet the definition for cirrhosis per NM state directives:**

- APRI >= 1.0
- Fib-4 >= 3.25
- Transient Elastography Score >= 12.5 dP3 (F4 equivalent)
- Fibrotest >= 0.73 (f4 equivalent) OR Fibrometer with F4 predominance
- Radiographic imaging or physical exam findings consistent with cirrhosis
- Liver biopsy confirming a METAVIR score of F4

**Child-Pugh Score:**

| | 1 Point | 2 Points | 3 Points |
|---|---|---|---|
| Bilirubin | Less than 2 mg/dL<br>Less than 34 umol/L | 2-3 mg/dL<br>34-50 umol/L | Over 3 mg/dL<br>Over 50 umol/L |
| Albumin | Over 3.5 g/dL<br>Over 35 g/L | 2.8-3.5 g/dL<br>28-35 g/L | Less than 2.8 g/dL<br>Less than 28 g/L |
| INR | Less than 1.7 | 1.7 - 2.2 | Over 2.2 |
| Ascites | None | Mild / medically controlled | Moderate-severe / poorly controlled |
| Encephalopathy | None | Mild / medically controlled<br>Grade I-II | Moderate-severe / poorly controlled.<br>Grade III-IV |

Child-Pugh class is determined by the total number of points: A = 5-6 points; B = 7-9 points; C = 10-15 points

**Appendix F:**

- 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.

- <u>Acceptable medical justification for inability to use Mavyret (preferred product):</u>
  - 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

- <u>Unacceptable medical justification for inability to use Mavyret (preferred product):</u>
  - 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.

**References**


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## Revision Log

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| New clinical policy created for WSCC based on New Mexico requirements | 11/18 | 11/18 |
| Added provision for approval of drug dosing and interval (despite not meeting AASLD and IDSA recommended guidelines) if regimen is recommended/requested after consultation with Project ECHO; added Project ECHO to references; JJM | 1/25/19 | 1/25/19 |
| Renamed clinical policy per corporate guidelines; Changed from NM.CP.PHAR.06 to NM.CP.PPA.06; Name presented at WSCC P&T Committee | 3/20/19 | 3/20/19 |
| Edited indication to change pediatric age from “12” to “3” and removed weight requirement per new FDA indication. Added new formulary of oral pellets. Updated max dosing per weight based. Updated Appendix C with pediatric age “3”. Edited references. | 10/16/19 | |
| Reviewed and approved by WSCC P&T Committee | | 10/23/19 |
| Annual Review. References updated. Reviewed and approved by WSCC P&T Committee. | 1/29/20 | 1/29/20 |
| Edited criteria to match updated directive from NM HSD, MAD Supplement 20-13 to include updated forms. Updated references to reflect this change in NM Medicaid direction. | 1/15/21 | |
| Annual review. Reviewed and approved by WSCC P&T Committee. | | 1/20/21 |
| Edited references and links to NM HCV Uniform HCV checklist. | 1/7/22 | |
| Annual review. Reviewed and approved by WSCC P&T Committee. | | 1/12/22 |
| Updated dosing portion from “Dose does not exceed” to “Dose as follows” to prevent underdosing for pediatric members. | 10/10/22 | |
| Updated wording on dosage. Reviewed and approved by WSCC P&T Committee. | | 10/12/22 |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| Annual Review. Updated References. Removed requirement for Drug Authorization Form and Uniform New Mexico HCV Checklist. Reviewed and approved by WSCC P&T Committee. | 1/9/23 | 1/11/23 |