MEDICAL MUTUAL®

Drug Policy

Policy:	Sovaldi ® (sofosbuvir) tablets	Annual Review Date: 11/16/2023 Last Revised Date: 11/16/2023

OVERVIEW

Sovaldi is a hepatitis C virus (HCV) nucleotide analog non-serine (NS)5B polymerase inhibitor indicated for the treatment of genotype 1, 2, 3 or 4 chronic HCV infection as a component of a combination antiviral treatment.[1] Sovaldi is also indicated in pediatric patients ≥ 3 years of age with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin. Sovaldi is a direct acting antiviral agent (DAA) against HCV and an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is essential for viral replication.[1] Sovaldi is a nucleotide prodrug that undergoes intracellular metabolism to form the pharmacologically active uridine analog triphosphate (GS-461203), which can be incorporated into HCV RNA by the NS5B polymerase and acts as a chain terminator. The place in therapy for Sovaldi has greatly lessened or is non-existent in some cases due to the availability of other DAAs with greater efficacy for many genotypes. However, Sovaldi is the only DAA indicated in pediatric patients with genotype 2 or 3 chronic HCV.

Dosing

The recommended dose of Sovaldi tablets is one 400 mg tablet taken orally once daily (QD) with or without food. The recommended dosage of Sovaldi tablets or oral pellets in pediatric patients ≥ 3 years of age with genotype 2 or 3 HCV is based on weight, and is to be taken orally once daily in combination with ribavirin. Sovaldi should be used in combination with weight-based ribavirin (WBR) or peginterferon and ribavirin (PR) for the treatment of chronic HCV in adults. Regimens with Sovaldi + PR or Sovaldi + WBR are no longer recommended in treatment guidelines with the exception of pediatric patients due to inferior efficacy compared with other all-oral regimens for all genotypes. Sovaldi + WBR is indicated in pediatric patients with genotype 2 or 3 chronic HCV and has a unique role in such patients. Table 2 provides pediatric dosing.

Daklinza® (daclatasvir tablets) is indicated in combination with Sovaldi for the treatment of genotypes 1 and 3 HCV in adults.[12] Table 1 describes the approved regimens for Daklinza + Sovaldi in adults.

Table 1. Sovaldi Treatment Regimen in Pediatric Patients (≥ 3 years of age).[1]

	Patient Population	Treatment and Duration
Genotype 2	Treatment-naïve and treatment experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Sovaldi + ribavirin x 12 weeks
Genotype 3	Treatment-naïve and treatment experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Sovaldi + ribavirin x 24 weeks

Table 2. Daklinza + Sovaldi Treatment Regimens (Adults).[12]

	Patient Population	Treatment and Duration
Genotype 1	No Cirrhosis	Daklinza + Sovaldi x 12 weeks
	Compensated (Child-Pugh A) Cirrhosis	
	Post-Transplant	Daklinza + Sovaldi + ribavirin x 12 weeks
	Decompensated (Child-Pugh B or C) Cirrhosis	
Genotype 3	No Cirrhosis	Daklinza + Sovaldi x 12 weeks
	Compensated (Child Pugh A) Cirrhosis	Daklinza + Sovaldi + ribavirin x 12 weeks
	Decompensated (Child-Pugh B or C) Cirrhosis	
	Post-Transplant	

Guidelines

Please refer to the *Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary* for a summary of the American Association for the Study of Liver Diseases (AASLD) guidelines.[11] For the most up-to-date information always consult the guidelines. The guidelines generally prefer one of the many fixed-dose combinations in the majority of patients with HCV. Sovaldi still has a small role in combination with Daklinza in patients with Genotype 2 or 3 HCV with decompensated cirrhosis. Currently, Sovaldi + ribavirin remains the only FDA-approved DAA for children 3 through 11 years with genotype 2 or 3 infection. However, recent clinical trials evaluating weight-based dosing of Epclusa® (sofosbuvir/velpatasvir tablets) and Mavyret® (glecaprevir/pibrentasvir) are expected to lead to FDA approval for children aged 3 through 11 years. The HCV guidance panel recommends awaiting approval of a pangenotypic regimen unless there is a compelling need for immediate antiviral treatment of children aged 3 through 11 years with genotype 2 or 3 infection.

POLICY STATEMENT

This policy involves the use of Sovaldi. Prior authorization is recommended for pharmacy benefit coverage of Sovaldi. Criteria are based on the guidance issued by American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA)/International Antiviral Society-USA (IAS-USA), prescribing information, clinical data, and expert review. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Sovaldi as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Sovaldi be prescribed by or in consultation with a physician who specializes in the condition being treated. Sovaldi is subject to the Hepatitis C Virus Direct-Acting Antivirals Preferred Specialty Management Policy.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Sovaldi is recommended in those who meet the following criteria:

1. **Chronic Hepatitis C Virus (HCV) Genotype 2, Pediatric Patients.** Approve for 12 weeks if the patient meets the following criteria (A, B, C, and D):
   - **A)** Patient is ≥ 3 years of age and < 18 years of age; AND
   - **B)** Patient does not have decompensated cirrhosis (Child-Pugh B or C).

Note: Coverage is provided for patients without cirrhosis or for patients with compensated (Child-Pugh A) cirrhosis; AND

C) The medication will be prescribed in combination with ribavirin; AND

D) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

2. **Chronic Hepatitis C Virus (HCV) Genotype 3, Pediatric Patients.** Approve for 24 weeks if the patient meets the following criteria (A, B, C, and D):
   A) Patient is ≥ 3 years of age and < 18 years of age; AND
   B) Patient does not have decompensated cirrhosis (Child-Pugh B or C).
   Note: Coverage is provided for patients without cirrhosis or for patients with compensated (Child-Pugh A) cirrhosis; AND
   C) The medication will be prescribed in combination with ribavirin; AND
   D) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

Other Uses with Supportive Evidence

3. **Patient Has Been Started on Sovaldi.** Approve for an indication or condition addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indications or Other Uses with Supportive Evidence). Approve the duration described above to complete a course therapy (e.g., a patient who should receive 12 weeks, and has received 3 weeks should be approved for 9 weeks to complete their 12-week course).

Approval. See above criteria.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Sovaldi has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **HCV (any genotype), Combination use with Direct-Acting Antivirals (DAAs) Other than Daklinza or ribavirin.** In adults with genotype 3 chronic HCV with compensated cirrhosis who are peginterferon/ribavirin-experienced, Zepatier (elbasvir/grazoprevir tablets) + Sovaldi ± ribavirin is an alternative recommendation.[2] The C-ISLE study evaluated Zepatier + Sovaldi ± ribavirin, for 8 weeks to 16 weeks in treatment-naive or -experienced, genotype 3 patients with compensated cirrhosis (n = 100). The study included 53 patients with a history peginterferon/ribavirin failure. Treatment-experienced patients were randomized to 12 weeks of Zepatier + Sovaldi, 12 weeks of Zepatier + Sovaldi + weight-based ribavirin, or 16 weeks of Zepatier + Sovaldi. All three treatment arms had 100% SVR on the per protocol analysis, with 17 patients in each arm. Mavyret (glecaprevir/pibrentasvir tablets) and Vosevi (sofosbuvir/velpatasvir/voxilaprevir tablets) are recommended regimens in this setting; Mavyret is FDA-approved. In

adults with any genotype chronic HCV with or without compensated cirrhosis who have failed treatment with Mavyret, retreatment with Mavyret + Sovaldi + ribavirin is a recommended regimen based on data from an ongoing Phase IIIb study evaluating the safety and efficacy of Mavyret + Sovaldi + weight-based ribavirin as a 12- or 16-week retreatment regimen for patients who experienced virologic failure to Mavyret within the context of a previous clinical trial. Non-cirrhotic Mavyret non-responders with genotype 1, 2, 4, 5, or 6 who were naive to protease and NS5A inhibitors received 12 weeks Mavyret + Sovaldi and weight-based ribavirin. Patients with genotype 3, and/or compensated cirrhosis, and/or protease/NS5A experience (prior to their initial glecaprevir/pibrentasvir treatment) received 16 weeks of therapy with the same regimen. In a preliminary analysis, 96% (n = 22/23) of these patients achieved SVR12 with a single relapse in a cirrhotic patient with genotype 1a. Vosevi is also a recommended regimen in this instance and it is FDA-approved.

2. **Life Expectancy < 12 Months Due to Non-Liver Related Comorbidities.** According to AASLD guidance, little evidence exists to support initiation of HCV treatment in patients with limited life expectancy (< 12 months) due to non-liver-related comorbid conditions.[11] For these patients, the benefits of HCV treatment are unlikely to be realized, and palliative care strategies should take precedence.

3. **Monotherapy with Sovaldi.** Sovaldi is indicated as a component of a combination antiviral treatment regimen for HCV.

4. **Pediatric Patients (Age < 3 years).** The safety and efficacy of Sovaldi have not been established in pediatric patients < 3 years of age.[1]

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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