MEDICAL MUTUAL®

Drug Policy

Policy:	Epclusa® (sofosbuvir/velpatasvir tablets) & velpatasvir/sofosbuvir authorized generics	Annual Review Date: 07/18/2024 Last Revised Date: 07/18/2024

OVERVIEW

The fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor, is indicated for the treatment of **chronic HCV genotype 1 through 6** infection in patients ≥ 3 years of age.[1] In patients with decompensated cirrhosis (Child-Pugh B or C), sofosbuvir/velpatasvir is administered with weight-based ribavirin. The FDA-approved duration of therapy with sofosbuvir/velpatasvir is 12 weeks for all patients.

Guidelines

The American Association for the Study of Liver Diseases/Infectious Diseases Society of America (AASLD/IDSA) provide recommendations for testing, monitoring, and treating HCV (December 19, 2023).[2] Instances in which the guidelines provide recommendations for sofosbuvir/velpatasvir outside of the FDA-approved indications are outlined below.

With the availability of pangenotypic HCV treatment regimens, HCV genotyping is no longer required prior to treatment initiation for all individuals. Pretreatment genotyping is still recommended in patients with cirrhosis and/or past unsuccessful HCV treatment, because treatment regimens may differ by genotype. However, for treatment-naïve patients without cirrhosis, although genotyping may impact the preferred treatment approach, it is not required if a pangenotypic regimen is used. The recommendations provide a simplified treatment algorithm for treatment-naïve adults where genotyping is not required.[2] Treatment-naïve adults without cirrhosis are eligible for simplified treatment if they do not have hepatitis B virus (not hepatitis B serum antigen [HBsAg] positive), are not pregnant, do not have hepatocellular carcinoma, and have not had a liver transplantation. In treatment-naïve adults without cirrhosis, the recommended regimens are Mavyret® (glecaprevir/pibrentasvir tablets) for 8 weeks or sofosbuvir/velpatasvir for 12 weeks. Treatment-naïve adults with compensated cirrhosis are also eligible for simplified treatment; however, recommendations are genotype specific. In patients with compensated cirrhosis, the recommended regimen in patients with genotype 1 through 6 is Mavyret for 8 weeks; sofosbuvir/velpatasvir for 12 weeks is recommended in patients with genotype 1, 2, 4, 5, or 6 (patients with genotype 3 require baseline NS5A resistance-associated substitution testing. Those without Y93H can be treated with sofosbuvir/velpatasvir for 12 weeks).

In patients with decompensated cirrhosis, the guidelines offer a recommendation for patients who are ribavirin-ineligible to treat with sofosbuvir/velpatasvir for 24 weeks.[2] (Note: sofosbuvir/velpatasvir is FDA-approved in this setting in combination with ribavirin for 12 weeks for adult and pediatric patients). In pediatric patients with any genotype, sofosbuvir/velpatasvir with weight-based ribavirin is recommended in patients with prior exposure to an interferon-based regimen (± ribavirin) and/or sofosbuvir but no exposure to NS3/4A or NS5A protease inhibitors, with decompensated cirrhosis.

Although Vosevi® (sofosbuvir/velpatasvir/voxilaprevir tablets) is recommended in most instances for adults with no cirrhosis or compensated cirrhosis who have failed treatment with a sofosbuvir-containing regimen, sofosbuvir/velpatasvir is recommended in adults (genotypes 1 through 6) with decompensated cirrhosis who have failed therapy with a sofosbuvir-containing regimen. In this setting, sofosbuvir/velpatasvir is recommended for 24 weeks in combination with ribavirin. Data are limited to one Phase II study where sofosbuvir/velpatasvir was studied in patients with genotype 1, 2, and 3 who did not respond to velpatasvir-containing regimens including sofosbuvir/velpatasvir and Vosevi.[2,6] Retreatment with sofosbuvir/velpatasvir + ribavirin for 24 weeks yielded high overall response rates (sustained virologic response 12 weeks post-treatment [SVR12] 91% [n = 63/69]). Among patients with genotype 1 chronic HCV, 97% of patients (n = 36/37) achieved SVR12. In patients with genotype 2 chronic HCV, SVR12 was attained in 95% of patients (n = 13/14) and in patients with genotype 3 chronic HCV, SVR12 was attained in 78% of patients (n = 14/18). Baseline NS5A resistance associated substitutions did not appear to impact SVR rates. No breakdown of the proportion of patients with decompensated cirrhosis was provided in the study.

POLICY STATEMENT

This policy involves the use of Epclusa. Prior authorization is recommended for pharmacy benefit coverage of Epclusa. 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 Epclusa as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Epclusa be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of sofosbuvir/velpatasvir is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, No Cirrhosis or Compensated Cirrhosis (Child-Pugh A).** Approve for 12 weeks if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 3 years of age; AND
B) Patient meets ONE of the following (i or ii):
  i. Patient does not have cirrhosis; OR
  ii. Patient has compensated cirrhosis (Child-Pugh A); AND
C) Patient has not been previously treated with sofosbuvir/velpatasvir; 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 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Adult.** Approve for the duration below if the patient meets all of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has decompensated cirrhosis (Child-Pugh B or C); AND
   C) Patient meets ONE of the following (i or ii):
     i. Patient is ribavirin-eligible, according to the prescriber: Approve for 12 weeks, if the medication is prescribed in combination with ribavirin; OR
     ii. Patient is ribavirin-ineligible, according to the prescriber: Approve for 24 weeks; AND
   D) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

3. **Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Pediatric Patient.** Approve for 12 weeks if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 3 years of age and < 18 years of age; AND
   B) Patient has decompensated cirrhosis (Child-Pugh B or C); 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

4. **Chronic Hepatitis C Virus (HCV), Genotype Unknown/Undetermined.** Approve for 12 weeks if the patient meets ALL of the following (A, B, C, D, E, F, G, and H):
   A) Patient is ≥ 18 years of age; AND
   B) Patient does not have cirrhosis; AND
   C) Patient has not previously been treated for hepatitis C virus; AND
   D) Patient does not have hepatitis B virus; AND
   E) Patient is not pregnant; AND
   F) Patient does not have hepatocellular carcinoma; AND
   G) Patient has not had a liver transplantation; AND
   H) The medication will be prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

5. **Chronic Hepatitis C Virus (HCV), Genotype 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Prior Null Responder, Prior Partial Responder, and Prior Relapser to sofosbuvir/velpatasvir or Vosevi**. Approve for 24 weeks if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 3 years of age; AND
   - **B)** Patient has decompensated cirrhosis (Child-Pugh B or C); AND
   - **C)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has been previously treated with sofosbuvir/velpatasvir; OR
     - **ii.** Patient has previously been treated with Vosevi; AND
   - **D)** The medication will be prescribed in combination with ribavirin; AND
   - **E)** The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.

6. **Patient Has Been Started on sofosbuvir/velpatasvir.** 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).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of sofosbuvir/velpatasvir is not recommended in the following situations:

1. **Hepatitis C Virus (HCV) [any genotype], Combination with Any Other Direct-Acting Antivirals (DAAs) [Not Including Ribavirin].** Sofosbuvir/velpatasvir provides a complete antiviral regimen. Sofosbuvir/velpatasvir is not recommended to be used with other products containing sofosbuvir.

2. **Pediatric Patient (< 3 Years of Age).** The safety and efficacy of sofosbuvir/velpatasvir have not been established in pediatric patients < 3 years of age.[1]

3. 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

1. Epclusa® tablets and oral pellets [prescribing information]. Foster City, CA: Gilead; April 2022.
2. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Available at: http://www.hcvguidelines.org. Updated December 19, 2023. Accessed on March 26, 2024.
3. Gane EJ, Shiffman ML, Etzkorn K, et al. Sofosbuvir-velpatasvir with ribavirin for 24 weeks in HCV patients previously treated with a direct-acting antiviral regimen. Hepatology. 2017;66(4):1083-1089.