Drug Coverage Policy

Effective Date 07/01/2025
Coverage Policy Number.....IP0184
Policy Title.....Epclusa Prior Authorization Policy

Hepatitis C – Epclusa Prior Authorization Policy

- Epclusa® (sofosbuvir/velpatasvir tablets and oral pellets – Gilead)
- sofosbuvir/velpatasvir tablets (authorized generic to Epclusa – Asegua Therapeutics)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

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.

The European Society for Pediatric Gastroenterology, Hepatology and Nutrition recommendations on the treatment of hepatitis C (2024) describe the optimal therapeutic management of adolescents and children with HCV infection.[5] Direct-acting antiviral regimens are recommended for all treatment-naïve and treatment-experienced children ≥ 3 years of age with chronic HCV. When available, the regimen of choice should be one that has the shortest treatment duration and does not require concomitant ribavirin. In addition, to simplify treatment and avoid the need of genotyping and/or baseline resistance-associated substitutions assessment, pangenotypic regimens are preferred. In children and adolescents without cirrhosis, or with compensated cirrhosis, recommended regimens are Mavyret, sofosbuvir/velpatasvir, or ledipasvir/sofosbuvir. In children and adolescents with decompensated cirrhosis, treatment should follow adult guidelines.

Coverage Policy

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of sofosbuvir/velpatasvir. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with sofosbuvir/velpatasvir as well as the monitoring required for adverse events and efficacy, approval requires sofosbuvir/velpatasvir to be prescribed by or in consultation with a with a physician who specializes in the condition being treated.

NOTE: This product also requires the use of preferred products before approval of the requested product. Refer to the *Hepatitis C Virus Direct-Acting Antivirals Preferred Specialty Management Policy for Employer Plans (PSM025)* for additional preferred product criteria requirements and exceptions.

Sofosbuvir/velpatasvir products are considered medically necessary when ONE of the following is met (1, 2, 3, 4, 5, or 6):

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 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 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 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 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 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 above criteria sections (FDA-Approved Indications or Other Uses with Supportive Evidence). Approve the duration described above to complete a course of 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).

Sofosbuvir/velpatasvir products for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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]

References

1. Epclusa® tablets and oral pellets [prescribing information]. Foster City, CA: Gilead; April 2022.
2. sofosbuvir/velpatasvir tablets [prescribing information]. Foster City, CA: Asegua Therapeutics; June 2021.
3. 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 21, 2025.
4. 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.
5. Indolfi G, Gonzalez-Peralta RP, Jona MM, et al. ESPGHAN recommendations on treatment of chronic hepatitis C virus infection in adolescents and children including those living in resource limited settings. *J Pediatr Gastroenterol Nutr.* 2024;78:957-972.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	**Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, No Cirrhosis or Compensated Cirrhosis (Child-Pugh A).** **Updated** 'Has NOT been previously treated with sofosbuvir-containing or NS5A inhibitor-based therapy' TO 'Patient has not been previously treated with sofosbuvir/velpatasvir' **Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Adult.** **Removed** 'Has NOT been previously treated with sofosbuvir-containing or NS5A inhibitor-based therapy' **Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Pediatric Patient.** **Removed** 'Has NOT been previously treated with sofosbuvir-containing or NS5A inhibitor-based therapy' **Chronic Hepatitis C Virus (HCV), Genotype Unknown/Undetermined.** **Updated** as a stand-alone condition of approval [prior was included as part of Chronic HCV for all genotypes criteria]	8/1/2024

	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. **Updated** 'Has been previously treated with sofosbuvir-containing or NS5A inhibitor-based treatment' TO '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'	
Annual Revision	**Added** the following note to the policy, "NOTE: This product also requires the use of preferred products before approval of the requested product. Refer to the *Hepatitis C Virus Direct-Acting Antivirals Preferred Specialty Management Policy for Employer Plans (PSM025)* for additional preferred product criteria requirements and exceptions." **For Employer Plans:** removed and relocated the preferred product criteria to the *Hepatitis C Virus Direct-Acting Antivirals Preferred Specialty Management Policy for Employer Plans – (PSM025).*	07/01/2025

The policy effective date is in force until updated or retired.