

PRIOR AUTHORIZATION POLICY

POLICY: Hepatitis C – Epclusa

- Epclusa® (velpatasvir/sofosbuvir tablets – Gilead)
- velpatasvir/sofosbuvir tablets (authorized generic to Epclusa – Gilead)

TAC APPROVAL DATE: 06/12/2019; Selected revision 03/25/2020

OVERVIEW

Epclusa is a fixed-dose combination of velpatasvir, a hepatitis C virus (HCV) NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor, indicated for the treatment of chronic HCV genotype 1 through 6 infection in adult and pediatric patients ≥ 6 years of age or weighing ≥ 17 kg.¹ In patients without cirrhosis or with compensated cirrhosis, Epclusa is indicated alone. In patients with decompensated cirrhosis (Child-Pugh B or C), Epclusa is indicated in combination with ribavirin.

Dosing

The recommended dosage of Epclusa in adults is one tablet (400 mg velpatasvir/100 mg sofosbuvir) taken orally once daily (QD) with or without food.¹ In pediatric patients ≥ 6 years of age or weighing ≥ 17 kg to < 30 kg the recommended dosage of Epclusa is one tablet (200 mg velpatasvir/50 mg sofosbuvir) QD with or without food. In pediatric patients ≥ 6 years of age or weighing ≥ 30 kg the recommended dosage of Epclusa is one tablet (400 mg velpatasvir/100 mg sofosbuvir) or two tablets (200 mg velpatasvir/50 mg sofosbuvir) QD with or without food. In patients with decompensated cirrhosis (Child-Pugh B or C), Epclusa is administered with weight-based ribavirin (WBR). The FDA-approved duration of therapy is 12 weeks for all patients.

Clinical Efficacy

The efficacy of Epclusa for the treatment of genotypes 1 through 6 chronic HCV was established in four published, Phase III clinical trials (ASTRAL-1, -2, -3, and -4).³⁻⁵ In ASTRAL-1, -2, and -3, a total of 1,035 patients received 12 weeks of Epclusa; 21% of patients had compensated cirrhosis and 28% had failed prior therapies for HCV. In the ASTRAL-4 study, 267 patients with decompensated cirrhosis (Child-Pugh B) were randomized to receive 12 or 24 weeks of Epclusa \pm WBR. The primary endpoint for all four studies was sustained viral response 12 weeks after treatment completion (SVR12).

In ASTRAL-1 (n = 706), SVR12 was attained in 99% of patients overall with genotypes 1, 2, 4, 5, or 6 chronic HCV treated with Epclusa for 12 weeks. In ASTRAL-2 (n = 269), Epclusa was superior to Sovaldi + WBR in patients with genotype 2 chronic HCV. SVR12 was attained in 99% of patients treated for 12 weeks with Epclusa and in 94% of patients treated with Sovaldi + WBR for 12 weeks. In ASTRAL-3 (n = 558), Epclusa was superior to Sovaldi + WBR in patients with genotype 3 chronic HCV. SVR12 was attained in 95% of patients treated for 12 weeks with Epclusa and in 80% of patients treated with Sovaldi + WBR for 24 weeks.

In ASTRAL-4 (n = 268), Epclusa was administered in one of three regimens in patients with genotypes 1 through 6 chronic HCV with decompensated cirrhosis (Child-Pugh B). SVR12 was attained in 83%, 94%, and 86% of patients treated with Epclusa for 12 weeks, Epclusa + WBR for 12 weeks, and Epclusa for 24 weeks, respectively. The study was not designed to assess differences among treatment groups or

by genotype. However, numerically higher rates of SVR12 were generally observed for Epclusa + WBR vs. non-ribavirin containing arms.

For more detailed efficacy information with Epclusa see the [Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary](#).

Guidelines

A summary of the American Association for the Study of Liver Diseases (AASLD) recommendations can be found in the [Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary](#). For guideline recommendations see the [Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary](#). For the most up-to-date information always refer to the [guidelines](#).

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Epclusa (brand or generic). Criteria are based on the guidance issued by American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA, prescribing information, clinical data, and expert review. Because of the specialized skills required for evaluation and diagnosis of patients treated with Epclusa (brand or generic) as well as the monitoring required for adverse events (AEs) and efficacy, approval requires Epclusa (brand or generic) to be prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or liver transplant physician. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Epclusa (brand or generic) is recommended in those who meet 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 Epclusa (brand or generic) for 12 weeks if the patient meets all of the following criteria (A, B, C, and D):
 - A) The patient is ≥ 6 years of age or ≥ 17 kg; AND
 - B) Epclusa (brand or generic) is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
 - C) The patient has not been previously treated with Epclusa (brand or generic); AND
 - D) The patient does not have cirrhosis OR the patient has compensated cirrhosis (Child-Pugh A)
- 2. Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Adults.** Approve Epclusa (brand or generic) for the specified duration if the patient meets all of the following criteria (A, B, C, D, and E):
 - A) The patient is ≥ 18 years of age; AND
 - B) Epclusa (brand or generic) is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND

- C) The patient has not been previously treated with Epclusa (brand or generic) or Vosevi (*see Criterion 4*); AND
 - D) The patient has decompensated cirrhosis (Child-Pugh B or C); AND
 - E) The patient meets one of the following criteria:
 - i. The patient is ribavirin-eligible, according to the prescribing physician: Approve Epclusa (brand or generic) for **12 weeks**, if Epclusa (brand or generic) is prescribed **in combination with ribavirin**; OR
 - ii. The patient is ribavirin-ineligible, according to the prescribing physician: Approve Epclusa (brand or generic) for **24 weeks**.
- 3. Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 5, 6, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Pediatric Patients.** Approve Epclusa (brand or generic) for 12 weeks if the patient meets all of the following criteria (A, B, C, and D):
- A) The patient is ≥ 6 years of age or ≥ 17 kg; AND
 - B) Epclusa (brand or generic) is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
 - C) The patient has not been previously treated with Epclusa (brand or generic); AND
 - D) The patient has decompensated cirrhosis (Child-Pugh B or C); AND
 - E) Epclusa will be prescribed **in combination with ribavirin**.

Other Uses with Supportive Evidence

- 4. Chronic Hepatitis C Virus, Genotype 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Prior Null Responders, Prior Partial Responders, and Prior Relapsers to Epclusa (brand or generic) or Vosevi.** Approve Epclusa (brand or generic) for 24 weeks in patients who meet all of the following criteria (A, B, C, D, and E).
- A) The patient is ≥ 18 years of age; AND
 - B) Epclusa (brand or generic) is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
 - C) The patient has been previously treated with Epclusa (brand or generic) or Vosevi; AND
 - D) The patient has decompensated cirrhosis (Child-Pugh B or C); AND
 - E) Epclusa (brand or generic) will be prescribed in combination with ribavirin.

AASLD guidelines recommend Epclusa for 24 weeks in combination with ribavirin for patients with genotypes 1, 2, 3, 4, 5, or 6 chronic HCV who have not responded to treatment with an NS5A inhibitor or sofosbuvir (Level II, C).² Data are limited to one Phase II study where Epclusa was studied in patients with genotype 1, 2, and 3 who did not respond to velpatasvir-containing regimens including Epclusa and Vosevi.^{2,6} Retreatment with Epclusa + ribavirin for 24 weeks yielded high overall response rates (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 (RASs) did not appear to effect SVR rates. No breakdown of the proportion of patients with decompensated cirrhosis was provided in the study.

- 5. Patient Has Been Started on Epclusa (brand or generic).** 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

Eplusa (brand or generic) 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. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Hepatitis C Virus (HCV) [any genotype], Combination with Any Other Direct-Acting Antivirals (DAAs) [Not Including Ribavirin].** Eplusa (brand or generic) provides a complete antiviral regimen for patients with genotype 1 HCV. Eplusa (brand or generic) is not recommended to be used with other products containing sofosbuvir. In the opinion of a specialist physician reviewing the data we have adopted this criterion.
- 2. Life Expectancy Less Than 12 Months Due to Non-Liver Related Comorbidities.** Patients with a limited life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy do not require antiviral treatment. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert. Little evidence exists to support initiation of HCV treatment in patients with a limited life expectancy (< 12 months) owing to non-liver-related comorbid conditions. For these patients, the benefits of HCV treatment are unlikely to be realized and palliative care strategies should take precedence.
- 3. Pediatric Patients (Age < 6 Years or < 17 kg).** The safety and efficacy of Eplusa (brand or generic) have not been established in pediatric patients < 6 years of age or < 17 kg.¹
- 4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria.** Criteria will be updated as new published data are available.

REFERENCES

1. Eplusa® tablets [prescribing information]. Foster City, CA: Gilead; March 2020.
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 May 24, 2018. Accessed on June 6, 2018.
3. Feld JJ, Jacobson IM, Hezode C, et al; for the ASTRAL-1 Investigators. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5 and 6 infection. *N Engl J Med.* 2015;373(27):2599-2607.
4. Foster GR, Afdahl N, Roberts SK, et al; for the ASTRAL-2 and ASTRAL-3 Investigators. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. *N Engl J Med.* 2015; 31;373(27):2608-2617.
5. Curry MP, O’Leary JG, Bzowej N, et al; for the ASTRAL-4 Investigators. Sofosbuvir and velpatasvir for HCV in patients with decompensated cirrhosis. *N Engl J Med.* 2015;373(27):2618-2628.
6. 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. .

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New policy	New policy	06/29/2016
Selected revision	Removed requirement of a trial of another DAA for genotype 1	08/17/2016

	chronic HCV.	
Annual revision	<p>Criteria for patients with genotype 1, 2, or 3 chronic HCV with prior null response, prior partial response, or relapse to Epclusa with cirrhosis or advanced cirrhosis added as an approvable condition.</p> <p>The condition not recommended for approval of retreatment with Epclusa in patients who were prior null or partial responders or relapsers was removed. This is now addressed in separate criteria.</p>	06/14/2017
Annual revision	<p>Criteria for retreatment with Epclusa in patients with genotype 1, 2, or 3 chronic HCV was removed from the policy.</p> <p>Criteria for patients with decompensated cirrhosis updated to address ribavirin ineligible patients.</p> <p>Criteria for patients with decompensated cirrhosis previously treated with Vosevi or Epclusa added to other uses with supportive evidence.</p>	06/13/2018
DEU revision	Authorized generics to Epclusa added to targeting and applicable criteria	12/14/2018
Annual Revision	No criteria changes	06/12/2019
Selected Revision	<p>Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, No Cirrhosis or Compensated Cirrhosis (Child-Pugh A): Criteria were changed to approve for patients ≥ 6 years of age or ≥ 17 kg.</p> <p>Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Adults: The indication was updated to add “Adults”.</p> <p>Chronic Hepatitis C Virus (HCV) Genotype 1, 2, 3, 4, 5, or 6, Decompensated Cirrhosis (Child-Pugh B or C), Pediatric Patients: New criteria were created to approve for 12 weeks in pediatric patients ≥ 6 years of age or ≥ 17 kg not previously treated with Epclusa when the product is prescribed by a specialist and in combination with ribavirin.</p> <p>Pediatric Patients (< 18 years): Criteria for this Condition Not Recommended for Approval were changed to Pediatric Patients < 6 Years or < 17 kg).</p>	03/25/2020

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.