



## PRIOR AUTHORIZATION POLICY

**POLICY:** Hepatitis C – Vosevi® (sofosbuvir/velpatasvir/voxilaprevir tablets – Gilead)

**TAC APPROVAL DATE:** 08/01/2018

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### OVERVIEW

Vosevi is a direct-acting-antiviral (DAA) indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor and for patients with genotype 1a or 3 infection and who have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor. Additional benefit of Vosevi over Epclusa® (sofosbuvir/velpatasvir tablets) was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.

Vosevi contains sofosbuvir, a nucleotide analog NS5B polymerase inhibitor, velpatasvir, an HCV NS5A inhibitor, and voxilaprevir, a new HCV NS3/4A protease inhibitor. Sofosbuvir has previously been available as Sovaldi® (sofosbuvir tablets) and as part of Harvoni® (sofosbuvir/ledipasvir tablets) and Epclusa. Velpatasvir has previously been available as part of Epclusa.

### Dosing

The recommended dosage of Vosevi is one tablet, taken orally, once daily (QD) with food for 12 weeks.

### Clinical Efficacy

The efficacy of Vosevi was established in two, randomized, Phase III pivotal trials in adults with chronic HCV of any genotype with or without compensated cirrhosis who did not have a sustained viral response measured (SVR) with a prior DAA-based regimen.<sup>2</sup>

POLARIS-1 was a placebo-controlled study that enrolled patients with prior NS5A experience (n = 263).<sup>2</sup> At baseline in the Vosevi group, 50% of patients had genotype 1 chronic HCV (n = 57); 38% of patients had genotype 1a (n = 101) and 17% of patients had genotype 1b (n = 45). The remaining genotypes 2 through 6 included 2% of patients with genotype 2 (n = 5), 30% of patients with genotype 3 (n = 78), 8% of patients with genotype 4 (n = 22), < 1% of patients with genotype 5 (n = 1), and 2% of patients with genotype 6 (n = 2). There was one patient with an unknown genotype. Cirrhosis was present in 46% of patients at baseline. Prior HCV DAA therapy was NS5A inhibitor + NS3 inhibitor ± NS5B inhibitor in 32% of patients, NS5A inhibitor + NS5B inhibitor in 61% of patients, and NS5A inhibitor in 7% of patients. Most patients had previously been treated with one other HCV treatment regimen (61%), while just over one-third of patients (33%) had previously been treated with two or more treatment regimens. Regarding prior response to therapy, 8% of patients were prior null responders, 85% of patients had a prior relapse, and 7% of patients had some other form of non-response. **Results.** The overall rate of SVR measured 12 weeks after treatment completion (SVR12) in the Vosevi group was 96% (95% confidence interval [CI]: 93, 98), which was significantly superior to the prespecified performance goal of 85% (P < 0.001). SVR12 was high across all genotypes: genotype 1a (96%), genotype 1b (100%), genotype 2 (100%), genotype 3 (95%), genotype 4 (91%), genotype 5 (100%), and genotype 6 (100%).

POLARIS-4, was an open-label, active-controlled study in adults with chronic HCV of any genotype who did not attain SVR12 with prior non-NS5A-based DAA regimens (n = 333).<sup>2</sup> Patients with genotype 1, 2, or 3 chronic HCV were assigned in a 1:1 ratio to receive either Vosevi or Epclusa QD for 12 weeks. Patients who were infected with genotypes other than 1, 2, or 3 were assigned to receive Vosevi for 12 weeks. Genotype distribution was similar between Vosevi and Epclusa treatment arms. In the Vosevi arm 43% of patients were genotype 1 (30% genotype 1a and 13% genotype 1b), 17% of patients were genotype 2, 30% of patients were genotype 3, 10% of patients were genotype 4 and no patients with genotype 5 or 6 were enrolled. In the Epclusa arm, 44% of patients were genotype 1 (29% genotype 1a and 15% genotype 1b), 22% of patients were genotype 2, 34% of patients were genotype 3, and no patients with genotype 4, 5, or 6 were enrolled in the Epclusa arm. Cirrhosis was present in 46% of patients in both treatment arms. Prior treatment was similarly distributed in the Vosevi and Epclusa treatment arms. In the Vosevi arm 25% of patients were previously treated with an NS5B inhibitor + NS3 inhibitor, 74% of patients were previously treated with an NS5B inhibitor, and 1% of patients were previously treated with an NS3 inhibitor (enrolled in error). In the Epclusa group, 25% of patients were previously treated with an NS5B inhibitor + NS3 inhibitor, 72% of patients were previously treated with an NS5B inhibitor, and 2% of patients were previously treated with an NS3 inhibitor (enrolled in error). The proportion of patients who had previously been treated with two or more regimens for HCV were 39% and 40% in the Vosevi and Epclusa groups, respectively). **Results.** The overall rate of SVR12 was 98% (95% CI: 95, 99) among Vosevi-treated patients which was significantly superior to the prespecified performance goal of 85% (P < 0.001). Among Epclusa-treated patients SVR12 was 90% (95% CI: 84, 94), which was not significantly superior to the prespecified performance goal of 85%. In patients with genotype 1a or genotype 3 infection, the rates of SVR12 were higher with Vosevi vs. Epclusa (98% vs. 89% and 96% vs. 85%, respectively). For genotypes 1b and 2 the rates of SVR12 for Vosevi and Epclusa were similarly high (96% vs. 95% and 100% vs. 97%, respectively); no patients with genotype 4 enrolled in the Epclusa group (all patients in the Vosevi group with genotype 4 attained SVR12) and no patients with genotypes 5 or 6 were enrolled either the Vosevi or Epclusa arm.

For more detailed efficacy information with Vosevi see the [Vosevi Drug Evaluation](#).

## Guidelines

A summary of the AASLD recommendations can be found in the [Hepatitis C Virus Direct-Acting Antivirals Therapy Class Summary](#).<sup>3</sup> For the most up-to-date information always refer to the [guidelines](#). Vosevi is recommended in patients with genotype 1a HCV with or without compensated cirrhosis who are treatment-experienced with a sofosbuvir-containing regimen not containing an NS5A inhibitor for 12 weeks of treatment (Class I, Level A). In patients with genotype 1, 2, 3, 4, 5, or 6 HCV with or without compensated cirrhosis who are NS5A-experienced, Vosevi is recommended for 12 weeks (Class I, Level A [genotype 1, 3, 4], Class I, Level B [genotype 2], Class IIa, Level B [genotype 5, 6]). Vosevi is an alternative recommendation for patients with genotype 3 without compensated cirrhosis who are PR-experienced (Class IIb, Level B).

Although Vosevi is not approved in treatment-naïve patients with HCV, Guidelines do provide a recommendation for its use in this setting. In treatment-naïve patients with genotype 3 HCV with compensated cirrhosis, Vosevi is an alternative recommendation for 12 weeks of treatment (Class IIa, Level B).

## POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Vosevi. 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 Vosevi as well as the monitoring required for adverse events (AEs) and efficacy, approval requires Vosevi to be prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or liver transplant physician. All approvals are for 12 weeks.

**Automation:** None.

## **RECOMMENDED AUTHORIZATION CRITERIA**

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

### **FDA-Approved Indications**

- 1. Chronic Hepatitis C Virus (HCV) Genotype 1b, 2, 4, 5, or 6.** Approve for 12 weeks if the patient meets all of the following criteria (A, B, C, and D):
  - A)** The patient is  $\geq 18$  years of age; AND
  - B)** Vosevi is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
  - C)** The patient had a prior null response, prior partial response, or had relapse after prior treatment with an HCV direct-acting antiviral (DAA) regimen containing an NS5A inhibitor. [Note: DAAs that are, or contain, an NS5A inhibitor include: Daklinza<sup>®</sup> {daclatasvir tablets}, Epclusa {sofosbuvir/velpatasvir tablets brand or generics}, Harvoni {ledipasvir/sofosbuvir tablets brand or generics}, Technivie<sup>™</sup> {ombitasvir/paritaprevir/ritonavir tablets}, Viekira Pak<sup>™</sup> {ombitasvir/paritaprevir/ritonavir tablets; dasabuvir tablets, co-packaged}, Viekira XR<sup>™</sup> {dasabuvir/ombitasvir/paritaprevir/ritonavir extended-release tablets}, Zepatier<sup>™</sup> {elbasvir/grazoprevir tablets}]; AND
  - D)** The patient does not have cirrhosis OR the patient has compensated cirrhosis (Child-Pugh A).

Vosevi is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor.<sup>1</sup> The recommended duration of therapy with Vosevi is 12 weeks.

- 2. Chronic Hepatitis C Virus, Genotype 1a or 3.** Approve for 12 weeks if the patient meets the following criteria (A, B, C, and D):
  - A)** The patient is  $\geq 18$  years of age; AND
  - B)** Vosevi is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
  - C)** The patient meets ONE of the following conditions (i or ii):
    - i.** The patient had a prior null response, prior partial response, or had relapse after prior treatment with an HCV direct-acting antiviral (DAA) regimen containing an NS5A inhibitor. [Note: DAAs that are, or contain, an NS5A inhibitor include: Daklinza {daclatasvir tablets}, Epclusa {sofosbuvir/velpatasvir tablets brand or generics}, Harvoni {ledipasvir/sofosbuvir tablets brand or generics}, Technivie {ombitasvir/paritaprevir/ritonavir tablets}, Viekira Pak {ombitasvir/paritaprevir/ritonavir tablets; dasabuvir tablets, co-packaged}, Viekira XR {dasabuvir/ombitasvir/paritaprevir/ritonavir extended-release tablets}, Zepatier {elbasvir/grazoprevir tablets}]; OR
    - ii.** The patient had a prior null response, prior partial response, or had relapse after prior treatment with an HCV DAA regimen containing Sovaldi + a non-NS5A inhibitor. (Note:

regimens that contain Sovaldi + a non-NS5A inhibitor are Sovaldi + NS3 inhibitors [Olysio® {simeprevir capsules}, Victrelis® {boceprevir capsules}, or Incivek® {telaprevir tablets}] or Sovaldi + ribavirin ± pegylated interferon); AND

- D)** The patient does not have cirrhosis OR the patient has compensated cirrhosis (Child-Pugh A).

Vosevi is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor and for patients with genotype 1a or 3 infection and who have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor.<sup>1</sup> Additional benefit of Vosevi over Epclusa was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with Sovaldi without an NS5A inhibitor. The duration of Vosevi is 12 weeks.

### Other Uses with Supportive Evidence

- 3. Chronic Hepatitis C Virus (HCV) Genotype 1b, 2, 4, 5, or 6.** Approve for 12 weeks in patients who meet the following criteria (A, B, C, and D):

**A)** The patient is ≥ 18 years of age; AND

**B)** Vosevi is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND

**C)** The patient had a prior null response, prior partial response, or had relapse after prior treatment with an HCV DAA regimen containing Sovaldi + a non-NS5A inhibitor. (Note: regimens that contain Sovaldi + a non-NS5A inhibitor are Sovaldi + NS3 inhibitors [Olysio {simeprevir capsules}, Victrelis {boceprevir capsules}, or Incivek {telaprevir tablets}] or Sovaldi + ribavirin ± pegylated interferon); AND

**D)** The patient does not have cirrhosis OR the patient has compensated cirrhosis (Child-Pugh A).

Vosevi is a direct-acting-antiviral (DAA) indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor and for patients with genotype 1a or 3 infection and who have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor.<sup>1</sup> Additional benefit of Vosevi over Epclusa was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.

Although labeling notes that additional benefit of Vosevi over Epclusa was not shown in adults with genotype 1b, 2, 4, 5 or 6 chronic HCV in POLARIS-4 (patients previously treated with Sovaldi + a non-NS5A inhibitor DAA) the rates of SVR12 with Vosevi were high in patients with genotypes 1b (96%), 2 (100%), and 4 (100%).<sup>2</sup> There were no patients with genotypes 5 or 6 enrolled and these are rare genotypes. Epclusa is not indicated for retreatment in patients who have previously received treatment with Sovaldi + a non-NS5A inhibitor.

In the opinion of expert physicians reviewing the data, we have adopted these criteria.

- 4. Patient Has Been Started on Vosevi.** 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

Vosevi 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).** Vosevi provides a complete antiviral regimen. 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.** According to the AASLD guidelines, patients with a limited life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy do not require antiviral treatment.<sup>3</sup> Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert. Chronic HCV is associated with a wide range of comorbid conditions. 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 < 18 Years).** The safety and efficacy of Vosevi have not been established in pediatric patients < 18 years of age.<sup>1</sup> In the opinion of a specialist physician reviewing the data we have adopted this criterion.
- 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. Vosevi<sup>®</sup> tablets [prescribing information]. Foster City, CA: Gilead; November 2017.
2. Bourliere M, Gordon SC, Flamm SL, et al. Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection. *N Engl J Med.* 2017;376(22):214-2146.
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 May 24, 2018. Accessed on July 26, 2018.

### HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New policy	New policy	07/26/2017
Annual Revision	No criteria changes	08/01/2018
DEU revision	Addition of generics to Eplclusa and Harvoni	12/14/2018

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>.