

# Vosevi

## (sofosbuvir/velpatasvir/voxilaprevir)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Based on Genotype, Treatment status, Cirrhosis status or Polymorphism status.

Medication	Quantity Limit
Vosevi (sofosbuvir/velpatasvir/voxilaprevir)	1 tablet per day

### **APPROVAL DURATION**

Genotype and Status (HCV mono-infected or HCV/HIV-1 co-infected <sup>a</sup> )	Associated Treatment Regimens	Total Approval Duration of Vosevi (sofosbuvir/velpatasvir/voxilaprevir)
Genotype 1, 2, 3, 4, 5, or 6 (NS5A <sup>2a</sup> treatment-experienced, with compensated cirrhosis or without cirrhosis)	Vosevi	12 weeks
Genotype 1a or 3 (previous sofosbuvir-containing regimen without an NS5A <sup>2a</sup> , with compensated cirrhosis or without cirrhosis)	Vosevi	12 weeks
Genotype 1, 2, 4, 5, or 6 (treatment-experienced with sofosbuvir-containing direct- acting antiviral [DAA] regimen, or elbasvir/grazoprevir, with compensated cirrhosis or without cirrhosis)	Vosevi	12 weeks
Genotype 3 (treatment- experienced with sofosbuvir- containing DAA regimen, or elbasvir/grazoprevir without cirrhosis)	Vosevi	12 weeks
Genotype 3 (treatment- experienced with sofosbuvir- containing DAA regimen, or elbasvir/grazoprevir with compensated cirrhosis)	Vosevi + RBV	12 weeks
Genotype 3 (treatment naïve with compensated cirrhosis cirrhosis, with Y93H polymorphism)	Vosevi	12 weeks
Genotypes 1, 2, 3, 4, 5, or 6 (treatment failure with Mavyret)	Vosevi ± RBV <sup>b</sup>	12 weeks

monotherapy, with compensated cirrhosis)		
Genotype 1, 2, 3, 4, 5, or 6 (previous treatment failure with Vosevi [sofosbuvir/velpatasvir/voxilaprevir] or Sovaldi plus Mavyret [sofosbuvir/glecaprevir/pibrentasvir]) with compensated cirrhosis or without cirrhosis	Vosevi + RBV	24 weeks

## **APPROVAL CRITERIA**

Requests for Vosevi (sofosbuvir/velpatasvir/voxilaprevir) may be approved if the following criteria are met:

- I. Individual is 18 years of age or older; **AND**
- II. Documentation is provided for a diagnosis of chronic hepatitis C (CHC) infection<sup>a</sup>, which includes genotype and a positive HCV RNA result (AASLD/IDSA 2017, CDC 2013); **AND**
- III. Individual has received baseline evaluation for liver fibrosis to guide appropriate therapy; **AND**
- IV. Individual does not have a short life expectancy (less than 12 months owing to non-liver related comorbid conditions) that cannot be remediated by treating HCV, by transplantation or other directed therapy (AASLD/IDSA 2017); **AND**
- V. Individual has compensated<sup>1</sup> liver disease (with or without cirrhosis);

## **AND**

- VI. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to brand Epclusa (sofosbuvir/velpatasvir), unless one of the following conditions apply:
  - A. Individual is using in **one** of the following antiviral treatment regimens (Label, AASLD/IDSA 2021):
    1. As monotherapy for **one** of the following:
      - a. Individual is NS5A<sup>2a</sup> treatment-experienced with compensated<sup>1</sup> cirrhosis or without cirrhosis, and Genotype 1, 2, 3, 4, 5, or 6;
    - OR**
    - b. Individual is treatment experienced with a sofosbuvir-containing regimen without an NS5A<sup>2b</sup> inhibitor, with compensated<sup>1</sup> cirrhosis or without cirrhosis, and Genotype 1a or 3;
    - OR**
    - c. Individual is treatment-naïve, with compensated<sup>1</sup> cirrhosis, polymorphism present at the Y93H amino acid position, and Genotype 3; **AND**
    - d. Individual meets one of the following criteria:
      - i. Prior trial of brand Epclusa (sofosbuvir/velpatasvir) with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Vosevi; **OR**
      - ii. Individual is currently on and completing a course of therapy with Vosevi;
  - OR**

- iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
- iv. Individual is not a candidate for the brand Epclusa regimen when it contains ribavirin, due to being ribavirin ineligible (examples include individuals with hemoglobinopathies, significant cardiac disease, creatinine clearance less than 50 mL/min, documented severe allergic reaction, or pregnancy);

**OR**

- e. Individual is treatment-experienced with sofosbuvir-containing DAA regimen, or elbasvir/grazoprevir, with compensated cirrhosis or without cirrhosis, and Genotype 1, 2, 4, 5, or 6; **OR**
- f. Individual is treatment-experienced with sofosbuvir-containing DAA regimen, or elbasvir/grazoprevir, without cirrhosis, and Genotype 3;

**OR**

B. In combination with ribavirin for the following (AASLD/IDSA 2021):

- 1. Individual is treatment-experienced with sofosbuvir-containing DAA regimen, or elbasvir/grazoprevir, with compensated cirrhosis, and Genotype 3;  
**OR**
- 2. Individual had treatment failure with Mavyret (glecaprevir/pibrentasvir) monotherapy, with compensated cirrhosis and Genotype 1, 2, 3, 4, 5, or 6; **OR**
- 3. Individual had treatment failure with Vosevi (sofosbuvir/velpatasvir/voxilaprevir) or Sovaldi plus Mavyret (sofosbuvir/glecaprevir/pibrentasvir) with compensated cirrhosis or without cirrhosis, and Genotype 1, 2, 3, 4, 5, or 6.

Vosevi (sofosbuvir/velpatasvir/voxilaprevir) may **not** be approved for the following:

- I. Individual has decompensated<sup>1</sup> cirrhosis; **OR**
- II. Individual is requesting in concurrent therapy with contraindicated or not recommended agents, including but not limited to the following: amiodarone, atazanavir- or lopinavir containing regimens, tipranavir/ritonavir, efavirenz, etravirine, nevirapine, rosuvastatin, and pitavastatin, cyclosporine, poly glycoprotein (P-gp) inducers and moderate or strong cytochrome (CYP) 3A4 inducers (including but not limited to, phenytoin, St. John's Wort, phenobarbital, rifampin, rifabutin, rifapentine, carbamazepine, oxcarbazepine), or Breast Cancer Resistance Protein (BCRP) substrates (including but not limited to, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, sulfasalazine, topotecan); **OR**
- III. Individual is using in combination with a regimen containing a non-nucleoside NS5B polymerase inhibitor (such as dasabuvir) or another nucleotide NS5B polymerase inhibitor;  
**OR**
- IV. Individual is using in combination with a regimen containing another NS5A<sup>2a</sup> inhibitor; **OR**  
Individual is using in combination with a regimen containing another NS3/4A<sup>2c</sup> protease inhibitor.

#### **Notes:**

<sup>a</sup>Per AASLD/IDSA treatment guidance, Vosevi (sofosbuvir/velpatasvir/voxilaprevir) may be used in individuals who are co-infected with HIV-1. The AASLD/IDSA treatment guidance recommends that

concurrent use with tenofovir disoproxil fumarate (TDF) should be avoided with an eGFR below 60 mL/min.

<sup>b</sup>Per AASLD/IDSA treatment guidance, for patients with prior Mavyret failure and compensated cirrhosis, addition of weight-based ribavirin is recommended.

## 1. **Compensated Liver Disease:**

According to the American Association for the Study of Liver Diseases (AASLD/IDSA 2017), the specific criteria for compensated liver disease include all of the following: a total bilirubin; serum albumin; prothrombin time/INR; presence of ascites; and presence of hepatic encephalopathy. However, these criteria do not establish a comprehensive definition of compensated liver disease. The AASLD guidance refers to compensated liver disease as Class A based on the Child Pugh-Turcotte (CPT) classification scoring system.

**Moderate to Severe (Decompensated) Liver Disease:**

The AASLD guidance refers to decompensated (moderate to severe) liver disease as Class B or C based on the Child-Pugh Turcotte (CPT) classification scoring system.

### **Child Pugh Classification (AASLD/IDSA 2017)**

Parameters			
Points Assigned	1 point	2 points	3 points
Total Bilirubin (μmol/L)	<34	34-50	>50
Serum Albumin (g/L)	>35	28-35	<28
Prothrombin time/INR	<1.7	1.71-2.30	>2.30
Ascites	None	Mild	Moderate to Severe
Hepatic Encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)

### **Child Pugh Score Interpretation (AASLD/IDSA2017)**

Class A	5-6 points	Well compensated liver disease
Class B	7-9 points	Significant functional compromise (moderate hepatic impairment)
Class C	10-15 points	Uncompensated liver disease (severe hepatic impairment)

## 2. Past Treatment Exposure Definitions (AASLD/IDSA 2017):

- NS5A Inhibitor: includes daclatasvir, ledipasvir, elbasvir, ombitasvir, pibrentasvir, or velpatasvir-containing regimens
- P/R: includes peginterferon (or non-pegylated interferon) ± ribavirin
- NS3/4A Protease Inhibitor: includes simeprevir, grazoprevir, paritaprevir, glecaprevir, and voxilaprevir-containing regimens
- Triple therapy: includes NS3 protease inhibitor (simeprevir, boceprevir or telaprevir) plus peginterferon and ribavirin
- Direct Acting Antiviral (DAA): includes NS5A inhibitors, NS3/4A protease inhibitors, and NS5B polymerase inhibitors (sofosbuvir, dasabuvir)
- P/R/S: includes peginterferon (or non-pegylated interferon) ± ribavirin ± sofosbuvir

3. Chronic Kidney Disease (CKD) Definitions (AASLD/IDSA 2017):

Severe CKD (Stage 4): eGFR 15-29 mL/min

End-Stage CKD (Stage 5): eGFR < 15 mL/min

4. Metavir Scoring Systems for Fibrosis Staging (AASLD 2009):

Stage (F)	
0	No fibrosis
1	Periportal fibrotic expansion
2	Periportal septae 1 (septum)
3	Porto-central septae
4	Cirrhosis

5. Hepatitis C virus (HCV) direct acting antiviral (DAA) agents have a black box warning for risk of hepatitis B virus (HBV) reactivation in individuals with HCV-HBV co-infection. Individuals should be tested for evidence of current or prior HBV infection prior to initiation of DAA therapy. HBV reactivation has been reported in HCV/HBV co-infected individuals currently taking or previously completed DAA therapy and not concomitantly receiving HBV antiviral therapy. Some cases of HBV reactivation have led to fulminant hepatitis, hepatic failure, and death. Individuals should be monitored for hepatitis flare or HBV reactivation during and following HCV DAA therapy. Individuals should be appropriately managed for HBV infection as indicated.

**Key References:**

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2021. URL: <http://www.clinicalpharmacology.com>. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>. Accessed: June 12, 2021.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2021; Updated periodically.
5. American Association for the Study of Liver Diseases and the Infectious Disease Society of America, in collaboration with the International Antiviral Society-USA. Recommendations for testing, managing and treating hepatitis C. Available at <http://www.hcvguidelines.org/>. Published on: January 29, 2014. Updated on: January 21, 2021. Accessed on: January 27, 2021.
6. Centers for Disease Control and Prevention. Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians. *MMWR*. 2013; 62(18):362-365. Available from: <https://www.cdc.gov/mmwr/pdf/wk/mm6218.pdf>. Accessed on: January 13, 2021.
7. Kamal SM. Acute hepatitis C: a systematic review. *Am J Gastroenterol*. 2008;103(5):1283-1297.
8. U.S. Department of Health and Human Services AIDSinfo treatment guidelines. Considerations for Antiretroviral Use in Patients with Coinfections. Available at <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/26/hcv-hiv>. Accessed on: January 13, 2021.
9. Wyles D, Weiland O, Yao B, et al. Retreatment of patients who failed glecaprevir/pibrentasvir treatment for hepatitis C virus infection. *J Hepatol*. 2019;70(5):1019-1023.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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