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# Sofosbuvir/Velpatasvir

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## Related Coverage Resources

***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. 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

This policy supports medical necessity review for the following products:

- **Epclusa®** (sofosbuvir/velpatasvir tablets and oral pellets)
- **sofosbuvir/velpatasvir** tablets

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

Receipt of sample product does not satisfy any criteria requirements for coverage.

## Initial Approval Criteria

**Sofosbuvir/velpatasvir (Epclusa) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) for all genotypes or unknown genotype status when the individual meets ALL of the following criteria:**

1. Age 3 years or older
2. Does NOT have cirrhosis OR has compensated cirrhosis (Child-Pugh A)
3. Has NOT been previously treated with sofosbuvir-containing or NS5A inhibitor-based therapy (see Appendix for examples)
4. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
5. Non-Covered Product Criteria is met, refer to below table:

**Employer Group Non-Covered Products and Criteria:**

| Non-Covered Product | Criteria |
|---|---|
| **sofosbuvir/velpatasvir tablets** | Documentation of an inability to obtain Epclusa (the brand name product) due to market availability |

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**Sofosbuvir/velpatasvir (Epclusa) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 in an adult with decompensated cirrhosis (Child-Pugh B or C), when the individual meets ALL of the following criteria:**

1. Age 18 years or older
2. Has decompensated cirrhosis (Child-Pugh B or C)
3. Has NOT been previously treated with sofosbuvir-containing or NS5A inhibitor-based therapy (see Appendix for examples)
4. **ONE** of the following:
    a. Is ribavirin-eligible AND sofosbuvir/velpatasvir (Epclusa) will be prescribed in combination with ribavirin
    b. Is ribavirin-ineligible, according to the prescriber
5. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
6. Non-Covered Product Criteria is met, refer to below table:

**Employer Group Non-Covered Products and Criteria:**

| Non-Covered Product | Criteria |
|---|---|
| **sofosbuvir/velpatasvir tablets** | Documentation of an inability to obtain Epclusa (the brand name product) due to market availability |

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**Sofosbuvir/velpatasvir (Epclusa) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 in a pediatric individual with decompensated cirrhosis (Child-Pugh B or C), when ALL of the following criteria are met:**

1. Age 3 to 17 years old
2. Has decompensated cirrhosis (Child-Pugh B or C)
3. Has NOT been previously treated with sofosbuvir-containing or NS5A inhibitor-based therapy (see Appendix for examples)
4. Sofosbuvir/velpatasvir (Epclusa) will be prescribed in combination with ribavirin
5. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
6. Non-Covered Product Criteria is met, refer to below table:

**Employer Group Non-Covered Products and Criteria:**

| Non-Covered Product | Criteria |
|---|---|
| **sofosbuvir/velpatasvir tablets** | Documentation of an inability to obtain Epclusa (the brand name product) due to market availability |

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**Sofosbuvir/velpatasvir (Epclusa) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 with decompensated cirrhosis (Child-Pugh B or C) who are prior null responders, prior partial responders, or prior relapsers to sofosbuvir-containing or NS5A inhibitor-based treatment, when the individual meets ALL of the following criteria:**

1. Age 3 years or older
2. Has decompensated cirrhosis (Child-Pugh B or C)
3. **BOTH** of the following:
    a. Has been previously treated with sofosbuvir-containing or NS5A inhibitor-based treatment (see Appendix for examples)
    b. Sofosbuvir/velpatasvir (Epclusa) will be prescribed in combination with ribavirin
4. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
5. Non-Covered Product Criteria is met, refer to below table:

**Employer Group Non-Covered Products and Criteria:**

| Non-Covered Product | Criteria |
|---|---|
| **sofosbuvir/velpatasvir tablets** | Documentation of an inability to obtain Epclusa (the brand name product) due to market availability |

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**Sofosbuvir/velpatasvir (Epclusa) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) when the individual has already been started on the medication and will be completing a course of therapy.**

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When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

## Continuation of Therapy

Not applicable for continuation beyond initial approval duration.

## Authorization Duration

Initial approval duration:

1. **Chronic HCV Genotype 1, 2, 3, 4, 5, or 6, without Cirrhosis or with Compensated Cirrhosis (Child-Pugh A) or chronic Hepatitis C Virus, Genotype Unknown/Undetermined:** 12 weeks
2. **Adult Individual (age 18 or older) with Chronic HCV Genotype 1, 2, 3, 4, 5, or 6, with Decompensated Cirrhosis (Child-Pugh B or C):** 12 weeks in combination with ribavirin or 24 weeks if ribavirin ineligible

3. **Pediatric Individual (age 3 to 17 years) with Chronic HCV Genotype 1, 2, 3, 4, 5, or 6, with Decompensated Cirrhosis (Child-Pugh B or C):** 12 weeks in combination with ribavirin
4. **Chronic HCV Genotype 1, 2, 3, 4, 5, or 6, with Decompensated Cirrhosis (Child-Pugh B or C), Prior Null Responders, Prior Partial Responders, or Prior Relapsers to Sofosbuvir-Containing or NS5A Inhibitor-Based Treatment:** 24 weeks in combination with ribavirin

Reauthorization approval duration: not applicable

## Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

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

## Background

**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 (October 24, 2022).[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.

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.

**Appendix**

Examples of direct-acting antivirals that are, or contain, an NS5A inhibitor include: Daklinza (daclatasvir), Epclusa (sofosbuvir/velpatasvir), Harvoni (ledipasvir/sofosbuvir), Mavyret (glecaprevir/pibrentasvir), Viekira Pak (ombitasvir/paritaprevir/ritonavir; dasabuvir, co-packaged), Vosevi (sofosbuvir/velpatasvir/voxilaprevir), Zepatier (elbasvir/grazoprevir)

Examples of regimens that contain Sovaldi (sofosbuvir) + a non-NS5A inhibitor include: Sovaldi + NS3 inhibitors (Olysio [simeprevir], Victrelis [boceprevir], or Incivek [telaprevir]) or Sovaldi + ribavirin ± pegylated interferon

## 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 October 24, 2022. Accessed on March 24, 2023.
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.