Cigna National Formulary Coverage Policy

Effective Date..... 4/1/2023
Next Review Date..... 4/1/2024

Prior Authorization
Hepatitis C – Zepatier® (grazoprevir/elbasvir tablets)

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Product Identifier(s)

Effective 1/1/23 to 2/6/23: 111401

Effective 2/7/23: 65808

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.

National Formulary Medical Necessity

Cigna covers grazoprevir/elbasvir (Zepatier®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

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

FDA Indication(s)

1. **Chronic Hepatitis C Virus (HCV) Genotype 1a.** Approve for the duration noted if the individual meets the following criteria (A, B, and C):
   - **A)** Individual meets ONE of the following conditions (i or ii):
     - **i.** Individual is ≥ 12 years of age; OR
     - **ii.** Individual weighs ≥ 30 kg; AND

B) Individual meets ONE of the following criteria (i or ii):
- **i.** Approve for 12 weeks if the individual meets ONE of the following conditions (a or b):
  - **a)** Individual meets both of the following [(1) and (2)]:
    - **(1)** Individual is treatment-naïve, OR individual has previously been treated with pegylated interferon + ribavirin *only*; AND
    - **(2)** Individual does NOT have a baseline NS5A polymorphism at ONE (or more) of the following the amino acid positions: 28, 30, 31, or 93; OR
  - **b)** Individual meets both of the following [(1) and (2)]:
    - **(1)** Individual has previously been treated with pegylated interferon + ribavirin and an HCV protease inhibitor; AND
    - **(2)** The medication will be prescribed in combination with ribavirin; OR
- **ii.** Approve for 16 weeks if the individual meets the following criteria (a, b, and c):
  - **a)** Individual meets one of the following [(1) or (2)]:
    - **(1)** Individual is treatment-naïve; OR
    - **(2)** Individual has previously been treated with pegylated interferon + ribavirin *only*; AND
  - **b)** Individual has a baseline NS5A polymorphism at ONE (or more) of the following amino acid positions: 28, 30, 31, or 93; AND
  - **c)** The medication will be prescribed in combination with ribavirin; AND

C) 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 1b.** Approve for 12 weeks if the individual meets the following criteria (A, B, and C):

A) Individual meets ONE of the following conditions (i or ii):
- **i.** Individual is ≥ 12 years of age; OR
- **ii.** Individual weighs ≥ 30 kg; AND

B) Individual meets ONE of the following conditions (i or ii):
- **i.** Individual meets one of the following criteria (a or b):
  - **a)** Individual is treatment-naïve; OR
  - **b)** Individual has previously been treated with pegylated interferon + ribavirin *only*; OR
- **ii.** Individual meets the following criteria (a and b):
  - **a)** Individual has previously been treated with pegylated interferon + ribavirin + an HCV protease inhibitor; AND
  - **b)** The medication will be prescribed in combination with ribavirin; AND

C) 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 4**. Approve for the duration noted if the individual meets the following criteria (A, B, and C):

A) Individual meets ONE of the following criteria (i or ii):
- **i.** Individual is ≥ 12 years of age; OR
- **ii.** Individual weighs ≥ 30 kg; AND

B) Individual meets ONE of the following criteria (i or ii):
- **i.** Individual is treatment-naïve: Approve for 12 weeks; OR
- **ii.** Approve for 16 weeks if the individual meets both of the following (a and b):
  - **a)** Individual has previously been treated with pegylated interferon and ribavirin for HCV; AND
  - **b)** The medication will be prescribed in combination with ribavirin; AND

C) 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. **Individual is Currently Receiving Zepatier.** Approve for an indication or condition addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indications). Approve the duration described above to complete a course of therapy (e.g., an individual who should receive 12 weeks and has received 3 weeks should be approved for 9 weeks to complete their 12-week course).

Conditions Not Covered

Grazoprevir/elbasvir (Zepatier®) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Hepatitis C Virus (HCV), Child-Pugh Class B or Child-Pugh Class C Liver Disease (Moderate or Severe Hepatic Impairment).** Zepatier is contraindicated in individuals with moderate or severe hepatic impairment (Child-Pugh Class B or C).[1]

2. **Hepatitis C Virus (HCV) [Any Genotype], Combination with Any Other Direct-Acting Antivirals (Not Including Ribavirin).** Zepatier provides a complete antiviral regimen for individuals with genotype 1 and 4 chronic HCV.

3. **Life Expectancy Less Than 12 Months Due to Non-Liver Related Comorbidities.** According to AASLD guidance, little evidence exists to support initiation of HCV treatment in individuals with limited life expectancy (less than 12 months) due to non-liver-related comorbid conditions.[2] For these individuals, the benefits of HCV treatment are unlikely to be realized, and palliative care strategies should take precedence.

4. **Pediatric Individuals (Age < 12 Years or < 30 kg).** The safety and efficacy of Zepatier have not been established in pediatric individuals < 12 years of age or < 30 kg.[1] Guidelines recommend Harvoni (ledipasvir/sofosbuvir tablets) in pediatric individuals with genotypes 1 or 4 chronic HCV.[2]

5. **Retreatment with Zepatier in Individuals Who Have Previously Received Zepatier.** Zepatier is not recommended. This includes retreatment in prior null responders, prior partial responders, prior relapse individuals, and individuals who have not completed a course of therapy due to an adverse reaction or for other reasons.

Background

Overview

Zepatier, an oral fixed-dose combination tablet containing grazoprevir, a second generation protease inhibitor and elbasvir, an NS5A inhibitor, is indicated with or without ribavirin for the treatment of genotypes 1 and 4 **chronic hepatitis C virus** (HCV) in adults and pediatric patients ≥ 12 years of age or weighing at least 30 kg.[1]

Safety

Zepatier is contraindicated in patients with Child-Pugh B or C liver disease (decompensated cirrhosis). Zepatier is also contraindicated with inhibitors of organic anion transporting polypeptides 1B1/3 that are known or expected to significantly increase grazoprevir plasma concentrations, strong inducers of cytochrome P450 3A, and efavirenz.

Dosing

The duration of treatment is outlined below (Table 1) and is dependent on the patient population. Prior to initiating Zepatier in patients with genotype 1a infection, testing for the NS5A resistance associated polymorphism is recommended to guide treatment duration. In patients with genotype 1a and this polymorphism present at baseline, 12 weeks of treatment with Zepatier resulted in lower rates of sustained viral response 12 weeks after treatment completion relative to patients with genotype 1a without the presence of this baseline polymorphism.

Table 1. Recommended Zepatier Dosage Regimens for the Treatment of Genotype 1 or 4 Chronic HCV.[1]

Genotype	Treatment History	Baseline NS5A Polymorphism	Treatment Regimen	Treatment Duration
1a	TN/PR-experienced* without NS5A polymorphisms†	No†	Zepatier	12 weeks
1a	TN/PR-experienced* with baseline NS5A polymorphisms†	Yes†	Zepatier + ribavirin	16 weeks
1a§ or 1b	PR + HCV PI-experienced§	NA	Zepatier + ribavirin	12 weeks

1b	TN/TE*	NA	Zepatier	12 weeks
4	TN	NA	Zepatier	12 weeks
4	PR-experienced*	NA	Zepatier + ribavirin‡	16 weeks

HCV – Hepatitis C virus; TN – Treatment naïve; PR – Pegylated interferon/ribavirin; * Patients who have failed treatment with PR; † NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93;§ The optimal Zepatier-based treatment regimen and duration of therapy for PR + HCV protease inhibitor-experienced genotype 1a-infected patients with one or more baseline NS5A resistance-associated polymorphisms at positions 28, 30, 31, and 93 has not been established; PI – PI – Protease inhibitor; β Patients who have failed treatment with PR + and NS3/4A PI (i.e., Victrelis® [boceprevir capsules], Incivek® [telaprevir tablets], or Olysio® [simeprevir capsules]); TE – Treatment-experienced; NA – Not applicable.

Guidelines

According to the American Association for the Study of Liver Diseases (AASLD) [October 2022] NS5A RAS testing is recommended for genotype 1a-infected, treatment-naive or -experienced patients being considered for Zepatier.[2] If present, a different regimen should be considered. Zepatier is recognized as an alternative regimen in treatment-naïve patients with Genotype 1a with or without compensated cirrhosis, and a recommended treatment option in patients with genotype 1b or 4 chronic HCV with or without compensated cirrhosis in guidelines. It is also recognized as an alternative regimen in treatment-naïve and non-direct-acting antiviral-experienced kidney transplant patients with genotype 1 or 4 with or without compensated cirrhosis. The guidelines have not been updated to reflect the lower age indication approved with Zepatier.

References

1. Zepatier® tablets [prescribing information]. Whitehouse Station, NJ: Merck; December 2021.
2. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Updated October 24, 2022. Available at: http://www.hcvguidelines.org. Accessed on February 10, 2023.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	No criteria changes.	02/15/2023