Drug Coverage Policy

Effective Date.....07/01/2025
Coverage Policy Number.....IP0158
Policy Title..... Zepatier

Hepatitis C – Zepatier Prior Authorization Policy

- Zepatier® (grazoprevir/elbasvir tablets – Merck)

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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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
Zepatier is an oral fixed-dose combination tablet containing grazoprevir, a second-generation protease inhibitor and elbasvir, an NS5A inhibitor.[1] It is indicated with or without ribavirin for the

treatment of patients ≥ 12 years of age or weighing ≥ 30 kg with genotype 1 or 4 **chronic hepatitis C virus** (HCV).[1]
Zepatier is contraindicated in patients with Child-Pugh B or C liver disease (decompensated cirrhosis).[1]

Dosing
The duration of treatment is outlined below (Table 1). Prior to initiating Zepatier in patients with genotype 1a infection, testing for the NS5A resistance-associated polymorphism is recommended to guide treatment duration.[1] In patients with genotype 1a with the NS5A 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$^{\beta}$	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 patients with genotype 1a with one or more baseline NS5A resistance-associated polymorphisms at positions 28, 30, 31, and 93 has not been established; PI – PI – Protease inhibitor; $^{\beta}$ Patients who have failed treatment with PR + and NS3/4A PI (i.e., Victrelis® [boceprevir capsules], Incivek® [telaprevir tablets], or Olysio® [simeprevir capsules]); NA – Not applicable; TE – Treatment-experienced.

Guidelines
According to the American Association for the Study of Liver Diseases (AASLD) [December 2023], NS5A resistance-associated substitution testing is recommended for treatment-naïve or treatment-experienced patients with genotype 1a chronic HCV who are being considered for Zepatier.[2] If the NS5A polymorphism is present, a different regimen should be considered. Zepatier is recognized as an alternative regimen in treatment-naïve patients with genotype 1a chronic HCV with or without compensated cirrhosis, and a recommended treatment option in patients with genotype 1b or 4 chronic HCV with or without compensated cirrhosis. 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 chronic HCV with or without compensated cirrhosis. The pediatric portion of the guidelines have not been updated since the approval of the lower age indication approved with Zepatier.

The European Society for Pediatric Gastroenterology, Hepatology and Nutrition recommendations on the treatment of hepatitis C (2024) describe the optimal therapeutic management of adolescents and children with HCV infection.[3] Direct-acting antiviral regimens are recommended for all treatment-naïve and treatment-experienced children ≥ 3 years of age with chronic HCV. When available, the regimen of choice should be one that has the shortest treatment duration and does not require concomitant ribavirin. In addition, to simplify treatment and avoid the need of

genotyping and/or baseline resistance-associated substitutions assessment, pangenotypic regimens are preferred.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required 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 patients 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.

NOTE: This product also requires the use of preferred products before approval of the requested product. Refer to the *Hepatitis C Virus Direct-Acting Antivirals Preferred Specialty Management Policy for Individual and Family Plans (PSM026)* for additional preferred product criteria requirements and exceptions.

Zepatier is considered medically necessary when the following criteria are met:

FDA-Approved Indications

1. **Chronic Hepatitis C Virus (HCV) Genotype 1a.** Approve for the duration noted if the patient meets the following (A, B, and C):
   - **A)** Patient meets ONE of the following (i or ii):
     - **i.** Patient is ≥ 12 years of age; OR
     - **ii.** Patient weighs ≥ 30 kg; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Approve for 12 weeks if the patient meets ONE of the following (a or b):
       - **a)** Patient meets both of the following [(1) and (2)]:
         - **(1)** Patient is treatment-naïve, OR patient has previously been treated with pegylated interferon + ribavirin *only*; AND
         - **(2)** Patient 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)** Patient meets both of the following [(1) and (2)]:
         - **(1)** Patient 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 patient meets the following (a, b, and c):
       - **a)** Patient meets one of the following [(1) or (2)]:
         - **(1)** Patient is treatment-naïve; OR
         - **(2)** Patient has previously been treated with pegylated interferon + ribavirin *only*; AND
       - **b)** Patient 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; AND

2. **Chronic Hepatitis C Virus (HCV) Genotype 1b.** Approve for 12 weeks if the patient meets the following (A, B, and C):
   - **A)** Patient meets ONE of the following (i or ii):

i. Patient is ≥ 12 years of age; OR
ii. Patient weighs ≥ 30 kg; AND

B) Patient meets ONE of the following (i or ii):
i. Patient meets one of the following (a or b):
a) Patient is treatment-naïve; OR
b) Patient has previously been treated with pegylated interferon + ribavirin *only*; OR
ii. Patient meets the following (a and b):
a) Patient 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; AND

3. **Chronic Hepatitis C Virus (HCV) Genotype 4**. Approve for the duration noted if the patient meets the following (A, B, and C):
A) Patient meets ONE of the following (i or ii):
i. Patient is ≥ 12 years of age; OR
ii. Patient weighs ≥ 30 kg; AND

B) Patient meets ONE of the following (i or ii):
i. Patient is treatment-naïve: Approve for 12 weeks; OR
ii. Approve for 16 weeks if the patient meets both of the following (a and b):
a) Patient has previously been treated with pegylated interferon and ribavirin; 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; AND

Other Uses with Supportive Evidence

4. **Patient is Currently Receiving Zepatier.** Approve for an indication or condition addressed as an approval in the above criteria section (FDA-Approved Indications). Approve the duration described above to complete a course of 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).

Zepatier for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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 patients 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 patients with genotype 1 and 4 chronic HCV.

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

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

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 December 19, 2023. Available at: http://www.hcvguidelines.org. Accessed on February 5, 2025.
3. Indolfi G, Gonzalez-Peralta RP, Jona MM, et al. ESPGHAN recommendations on treatment of chronic hepatitis C virus infection in adolescents and children including those living in resource limited settings. *J Pediatr Gastroenterol Nutr.* 2024;78:957-972.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Conditions Not Recommended for Approval: Life Expectancy Less Than 12 Months Due to Non-Liver Related Comorbidities.** This condition was removed. **Medical Necessity Criteria: Does not have decompensated cirrhosis (Child-Pugh B or C).** This criterion was removed.	06/01/2024
Annual Revision	**Added** the following note to the policy: **"**NOTE: This product also requires the use of preferred products before approval of the requested product. Refer to the Hepatitis C Virus Direct-Acting Antivirals Preferred Specialty Management Policy for Individual and Family Plans (PSM026) for additional preferred product criteria requirements and exceptions." **For Employer Plans:** removed preferred product criteria requirements. **For Individual and Family Plans:** relocated the preferred product related criteria to *Hepatitis C Virus Direct-Acting Antivirals Preferred Specialty Management Policy for Individual and Family Plans – (PSM026).*	07/01/2025

The policy effective date is in force until updated or retired.