PRIOR AUTHORIZATION POLICY

POLICY: Hepatitis C – Zepatier Prior Authorization Policy
- Zepatier® (grazoprevir/elbasvir tablets – Merck)

REVIEW DATE: 02/14/2024; selected revision 02/28/2024

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]

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) [December 2023], NS5A resistance-associated substitution RAS testing is recommended for genotype 1a-infected, treatment-naïve 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 pediatric portion of the guidelines have not been updated since the approval of the lower age indication approved with Zepatier.

POLICY STATEMENT

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

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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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Zepatier is recommended in those who meet one of the following:

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.

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

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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 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.

Other Uses with Supportive Evidence

4. **Patient 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., 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

Coverage of Zepatier is not recommended in the following situations:

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.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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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 1, 2024.

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