PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 02/24/2021

OVERVIEW

Zepatier is an oral fixed-dose combination tablet containing grazoprevir, a second generation protease inhibitor and elbasvir, an NS5A inhibitor, indicated **with or without ribavirin for the treatment of genotypes 1 and 4 chronic hepatitis C virus in adults**.[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 (OATP1B1/3) that are known or expected to significantly increase grazoprevir plasma concentrations, strong inducers of cytochrome P450 (CYP)3A, and efavirenz.

Dosing

The recommended dosage of Zepatier is one co-formulated tablet containing 50 mg of grazoprevir and 100 mg of elbasvir once daily with or without food.[1] 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[β]	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; [‡] For patients with creatinine clearance (CrCl) > 50 mL/min, the recommended dose of ribavirin is weight-based. For patients with CrCl ≤ 50 mL/min, including patients receiving hemodialysis, refer to the ribavirin prescribing information for the correct ribavirin dosage; [§] The optimal Zepatier-based treatment regimen and duration of therapy for PR + HCV protease inhibitor (PI)-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]); NA – Not applicable

Guidelines

According to the American Association for the Study of Liver Diseases (AASLD) 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 a recommended treatment option in patients with genotype 1 or 4 chronic HCV in guidelines.

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 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 the following criteria:

FDA-Approved Indications

1. **Chronic Hepatitis C Virus (HCV) Genotype 1a.** Approve for the duration noted if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
   - **C)** Patient meets ONE of the following criteria (i or ii):
     - **i.** Approve for 12 weeks if the patient meets ONE of the following conditions (a or b):
       - **a)** Condition 1 (patient meets the following criteria [1] or [2], and [3]); OR
         - **(1)** Patient is treatment-naïve; OR
         - **(2)** Patient has previously been treated with pegylated interferon + ribavirin *only*. AND
         - **(3)** Patient does NOT have a baseline NS5A polymorphism at ONE (or more) of the following the amino acid positions: 28, 30, 31, or 93.
       - **b)** Condition 2 (patient meets the following criteria [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.
     - **ii.** Approve for 16 weeks if the patient meets the following criteria (a or b AND c and d):
       - **a)** Patient is treatment-naïve; OR
       - **b)** Patient has previously been treated with pegylated interferon + ribavirin *only*. AND
       - **c)** Patient has a baseline NS5A polymorphism at ONE (or more) of the following amino acid positions: 28, 30, 31, or 93; AND
       - **d)** The medication will be prescribed in combination with ribavirin.

2. **Chronic Hepatitis C Virus (HCV) Genotype 1b.** Approve for 12 weeks if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
   - **C)** Patient meets ONE of the following conditions (i or ii):
     - **i.** Condition 1 (patient meets the following criteria a or b):
       - **a)** Patient is treatment-naïve; OR
       - **b)** Patient has previously been treated with pegylated interferon + ribavirin *only*; OR
     - **ii.** Condition 2 (patient meets the following criteria 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.

3. **Chronic Hepatitis C Virus (HCV) Genotype 4**. Approve for the duration noted if the patient meets the following criteria (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
   C) Patient meets ONE of the following criteria (i or ii):
      i. Patient is treatment-naïve: Approve for 12 weeks; OR
      ii. Patient has previously been treated with pegylated interferon and ribavirin for HCV AND the medication will be prescribed in combination with ribavirin: Approve for 16 weeks.

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 or Other Uses with Supportive Evidence). 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 (DAAs) [Not Including Ribavirin].** Zepatier provides a complete antiviral regimen for patients 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 patients with limited life expectancy (less than 12 months) due to non–liver-related comorbid conditions.[2] For these patients, the benefits of HCV treatment are unlikely to be realized, and palliative care strategies should take precedence.

4. **Pediatric Patients (Age < 18 Years).** The safety and efficacy of Zepatier have not been established in pediatric patients < 18 years of age.[1] Guidelines recommend Harvoni (ledipasvir/sofosbuvir tablets) in pediatric patients with genotypes 1 or 4 chronic HCV.[2]

5. **Retreatment with Zepatier in Patients Who Have Previously Received Zepatier** (e.g., retreatment in prior null responders, prior partial responders, prior relapse patients, patients who have not completed a course of therapy due to an adverse reaction or for other reasons).

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

REFERENCES

1. Zepatier® tablets [prescribing information]. Whitehouse Station, NJ: Merck; December 2019.
2. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Updated January 21, 2021. Available at: http://www.hcvguidelines.org. Accessed on February 16, 2021.