MEDICAL MUTUAL®

Drug Policy

Policy:	Zepatier (elbasvir and grazoprevir)	Annual Review Date: 01/18/2024 Last Revised Date: 01/18/2024

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 (HCV) in adults.

POLICY STATEMENT

This policy involves the use of Zepatier. Prior authorization is recommended for pharmacy benefit coverage of Zepatier. Criteria are based on the guidance issued by American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA)/International Antiviral Society-USA (IAS-USA), prescribing information, clinical data, and expert review. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

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, initial approval requires Zepatier be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

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

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

2. **Chronic Hepatitis C Virus (HCV) Genotype 1b.** Approve for 12 weeks if patients meet the following criteria (A, B, and C):
A) Patient meets ONE of the following conditions (i or ii):
i. Patient is ≥ 12 years of age; OR
ii. Patient weighs ≥ 30 kg; AND
B) Zepatier is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician; AND
C) The patient meets ONE of the following conditions (i or ii):
i. Condition 1 (patients must meet a or b):
a) The patient is treatment-naïve; OR
b) The patient has previously been treated with pegylated interferon + ribavirin *only*; OR
ii. Condition 2 (patients must meet a and b):
c) The patient has previously been treated with pegylated interferon + ribavirin + an HCV protease inhibitor; AND
d) Zepatier will be prescribed in combination with ribavirin.

3. **Chronic Hepatitis C Virus (HCV) Genotype 4.** Approve for the duration specified below if patients meet the following criteria (A, B, and C):
A) Patient meets ONE of the following criteria (i or ii):
i. Patient is ≥ 12 years of age; OR
ii. Patient weighs ≥ 30 kg; AND
B) Zepatier is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician;
C) The patient meets ONE of the following conditions (i or ii):

i. Approve for 12 weeks if the patient is treatment-naïve; OR
ii. Approve for 16 weeks if the patient has previously been treated with pegylated interferon and ribavirin for HCV and Zepatier will be prescribed in combination with ribavirin.

Other Uses with Supportive Evidence

4. **Patient Has Been Started on 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 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).

Approval Duration. See above criteria.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Zepatier has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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.[5] For these patients, the benefits of HCV treatment are unlikely to be realized, and palliative care strategies should take precedence.

4. **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.

5. **Retreatment with Zepatier in Patients Who Have Previously Received Zepatier**. This includes 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.

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Drug Policy

Documentation Requirements:
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Zepatier ™ tablets [prescribing information]. Whitehouse Station, NJ: Merck; June 2018
2. Roth D, Nelson DR, Bruchfeld A, et al. Grazoprevir plus elbasvir in treatment-naïve and treatment-experienced patients with hepatitis C virus genotype 1 infection and stage 4-5 chronic kidney disease (the C-SURFER study): a combination phase 3 study. *Lancet*. 2015 Oct 6. [Epub ahead of print].
3. Zeuzem S, Ghalib R, Reddy R, et al. Grazoprevir-elbasvir combination therapy for treatment-naïve cirrhotic and non-cirrhotic patients with chronic hepatitis C virus genotype 1, 4, or 6 infection. *Ann Intern Med*. 2015;163:1-13.
4. Forns X, Gordon SC, Zuckerman E, et al. Grazoprevir and elbasvir plus ribavirin for chronic HCV genotype-1 infection after failure of combination therapy containing a direct-acting antiviral agent. *J Hepatol*. 2015;63:564-572.
5. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. Available at: http://www.hcvguidelines.org. Updated 21 September 2017. Accessed 19 December 2017
6. Forns X, Gordon SC, Zuckerman E, et al. Grazoprevir and elbasvir plus ribavirin for chronic HCV genotype-1 infection after failure of combination therapy containing a direct-acting antiviral agent. *J Hepatol*. 2015;63:564-572.
7. Rockstroh JR, Nelson M, Katlama C, et al. Efficacy and safety of grazoprevir (MK-5172) and elbasvir (MK-8742) in patients with hepatitis C virus and HIV co-infection (E-EDGE CO-INFECTION): a non-randomized, open-label trial. *Lancet HIV*. 2015;2(8):e319-327.
8. Brown A, Hezode C, Zuckerman E, et al. C-SCAPE: Efficacy and safety of 12 weeks of grazoprevir +/- elbasvir +/- ribavirin in patients with HCV GT2, 4, 5, or 6 infection P0771. *J Hepatology* . 2015; 62 (Suppl 2):S619.
9. Elbasvir/grazoprevir. In: DRUGDEX (online database). Truven Health Analytics: Greenwood Village, CO. Updated 1 December 2017. Accessed 19 December 2017