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| Reference number(s) |
| 2145-A, 2684-A |

SPECIALTY GUIDELINE MANAGEMENT

ZEPATIER (elbasvir and grazoprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Zepatier is indicated for the treatment of chronic hepatitis C virus (HCV) genotype 1 or 4 infection in adult and pediatric patients 12 years of age and older or weighing at least 30 kg.

Zepatier is indicated for use with ribavirin in certain patient populations.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber specializing in infectious disease, gastroenterology, hepatology, or transplant.

IV. CRITERIA FOR INITIAL APPROVAL

A. Hepatitis C virus infection, in combination with ribavirin (RBV)

1. Genotype 1a infection

- i. Authorization of up to 16 weeks total may be granted for members with baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section VII) who are either of the following:
 - a. Treatment-naïve
 - b. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)
- ii. Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section VII) who have failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

2. Genotype 1b infection

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Authorization of up to 12 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

3. Genotype 4 infection

Authorization of up to 16 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV.

B. Hepatitis C virus infection, without RBV

1. Genotype 1a infection

Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms who are either of the following:

- i. Treatment-naïve
- ii. Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

2. Genotype 1b infection

Authorization of up to 12 weeks total may be granted for members who are either of the following:

- i. Treatment-naïve
- ii. Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

3. Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members who are treatment-naïve.

4. Kidney transplant recipients

Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section VII) who have HCV genotype 1 or 4 infection and are treatment-naïve or who have not failed prior treatment with a direct-acting antiviral.

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. OTHER

- A. Member must be 12 years of age or older or weigh at least 30 kg.
- B. Some elements outlined in this policy may not be enforced for certain plans due to regulatory guidelines.
- C. The following information may be requested to support regulatory requirements and will not be used to decision individual requests:
 - 1. Treatment status (i.e., treatment-naïve or retreatment)
 - 2. For initial treatment: confirmation of member readiness
 - 3. For retreatment: reason for the need for retreatment (e.g., prior treatment failure, reinfection), confirmation of member readiness, and ability to adhere to proposed treatment plan
 - 4. Hepatitis B screening results
 - 5. Metavir/Fibrosis score

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VII. APPENDIX: NS5A RESISTANCE-ASSOCIATED SUBSTITUTIONS (POLYMORPHISMS)

NS5A resistance-associated substitutions (polymorphisms) at amino acid positions M28, Q30, L31 or Y93. Examples include M28A/T, Q30H/R, L31M/V, and Y93C/H/N.

VIII. REFERENCES

1. Zepatier [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; May 2022.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <https://www.hcvguidelines.org>. Last changes made October 5, 2021. Accessed August 9, 2022.