

Elbasvir-Grazoprevir (Zepatier)

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Drug Summary

Elbasvir-grazoprevir ([Figure 1](#)) and ([Figure 2](#)) provides a safe, effective, well-tolerated, one-pill once-daily option for the treatment-naïve and treatment-experienced persons with hepatitis C virus (HCV) genotype 1 or 4 infection. Individuals with HCV genotype 1a will need resistance testing prior to initiation of therapy. The presence of a substitution at amino acid positions 28, 30, 31, or 93 (seen in up to 10 to 15% of individuals with HCV genotype 1a (even those who are treatment-naïve) require the addition of ribavirin and extension of therapy from 12 to 16 weeks. This pretesting requirement and the potential need to use ribavirin has resulted in this regimen being less favored than others in persons with genotype 1a infection.

Adverse Effects

Based on pooled data from phase 2 and 3 trials (n = 834), the most common adverse reactions observed in persons receiving elbasvir-grazoprevir were fatigue (11%), headache (10%), and nausea (5%). Elevations in alanine aminotransferase levels (ALT) to greater than 5 times the upper limit of normal occurred in 1% of persons, typically occurring at or after 8 weeks of initiating therapy, with most resolving at or after the completion of therapy. To date, the rash and photosensitivity noted with earlier protease inhibitors has not been a problem in persons receiving elbasvir-grazoprevir.

Class and Mechanism

Elbasvir-grazoprevir is an oral fixed-dose combination of an NS5A replication complex inhibitor (elbasvir), and

a “later”-generation HCV NS3/4A protease inhibitor (grazoprevir). Elbasvir is a small-molecule inhibitor of nonstructural protein 5A and possesses in vitro activity against most major HCV genotypes and some viral variants resistant to earlier NS5A inhibitors. Grazoprevir is a macrocyclic compound that reversibly binds to the HCV NS3/4A protease, an enzyme responsible for cleaving and processing the HCV-encoded polyprotein.

Indications

The fixed-dose combination elbasvir-grazoprevir (50 mg/100 mg) is FDA-approved for the treatment of chronic hepatitis C genotypes 1 or 4 with the following specific requirements based on genotype, treatment experience, and presence of baseline polymorphisms at amino acid positions 28, 30, 31, or 93. It is recommended that patients with HCV genotype 1a infection undergo resistance testing prior to initiation of treatment with elbasvir-grazoprevir for the presence of virus with NS5A resistance-associated polymorphisms, as this will determine if ribavirin is added to the treatment regimen and the duration of therapy. For persons with HCV and HIV-1 coinfection, the dosage and duration are the same as listed below.

Elbasvir-Grazoprevir for Genotypes 1 or 4 (with or without cirrhosis)

- Genotype 1a, treatment-naïve or peginterferon/ribavirin-experienced* (without baseline NS5A polymorphisms[^]): Elbasvir-grazoprevir for 12 weeks
- Genotype 1a, treatment-naïve or peginterferon/ribavirin-experienced* (with baseline NS5A polymorphisms[^]): Elbasvir-grazoprevir plus ribavirin for 16 weeks
- Genotype 1b, treatment-naïve or peginterferon/ribavirin-experienced*: Elbasvir-grazoprevir for 12 weeks
- Genotype 1a[#] or 1b, peginterferon/ribavirin/protease inhibitor-experienced⁺: Elbasvir-grazoprevir plus ribavirin for 12 weeks
- Genotype 4, treatment-naïve: Elbasvir-grazoprevir for 12 weeks
- Genotype 4, peginterferon/ribavirin-experienced*: Elbasvir-grazoprevir plus ribavirin for 16 weeks

*Patients who have failed therapy with peginterferon alfa plus ribavirin

[^]One or more polymorphisms at the amino acid positions 28, 30, 31, or 93.

[#]The optimal treatment duration for peginterferon/ribavirin/protease inhibitor-experienced patients with genotype 1a and one or more baseline NS5A resistance-associated polymorphisms has not been established.

⁺Patients who have failed therapy with peginterferon alfa plus ribavirin plus an HCV NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir)

Dosing

Elbasvir-grazoprevir is available as a fixed-dose, coformulated tablet that contains 50 mg of elbasvir and 100 mg of grazoprevir.

- The recommended dose is one tablet taken orally once daily, with or without food.
- No dosage adjustment is recommended for elbasvir-grazoprevir in patients with renal insufficiency, including patients with end-stage renal disease or persons on hemodialysis.
- For patients with mild hepatic impairment (Child-Pugh Class A), no dose adjustment of elbasvir-grazoprevir is recommended. Elbasvir-grazoprevir is contraindicated for use in patients with moderate to severe hepatic impairment (Child-Pugh Class B or C).

- When ribavirin is used with elbasvir-grazoprevir in patients with a CrCl greater than 50 mL/min, it should be given as weight-based dosing in two divided doses with food (weight less than 66 kg=800 mg/day; 66 to 80 kg=1000 mg/day; 81 to 105 kg=1200 mg/day; greater than 105 kg=1,400 mg/day). For patients with CrCl less than 50 mL/min, the dose of ribavirin should be adjusted to be consistent with the recommendations in the ribavirin package insert.

Cost and Medication Access

- Merck has an active Patient Assistance Program for patients who cannot obtain or afford elbasvir-grazoprevir. Information on the program can be obtained at Merck Patient Assistance Program ([Merck Helps](#)) website or by calling 1-800-405-5810.
- Merck has also developed a copay assistance program. There are specific conditions that apply. Information to help patients get access and support to elbasvir-grazoprevir is available on the [Merck Access and Support Services](#) website.

Key Drug Interactions

For complete information on elbasvir-grazoprevir-related drug interactions, see the [Drug Interactions section in the Elbasvir-Grazoprevir \(Zepatier\) Prescribing Information](#).

Full Prescribing Information

Elbasvir-grazoprevir (Zepatier) [Full Prescribing Information](#).

Figures

[Figure 1. Pill - Elbasvir-Grazoprevir \(Zepatier\)](#)

Photograph courtesy of Merck & Co., Inc.

[Figure 2. Packaging - Elbasvir-Grazoprevir \(Zepatier\)](#)

Photograph courtesy of Merck & Co., Inc.

[Figure 3. Medication Contraindications](#)

Source: Elbasvir-Grazoprevir (*Zepatier*) Prescribing Information