Elbasvir-Grazoprevir (Zepatier)

Table of Contents

- Elbasvir-Grazoprevir Zepatier Editor's Summary
- Drug Summary
- Class and Mechanism
- Manufacturer for United States
- Cost and Medication Access
- Adverse Effects
- Key Drug Interactions

Drug Summary

Elbasvir-grazoprevir provides a safe, effective, well-tolerated, one-pill once-daily option for the treatment-naïve and treatment-experienced patients with genotype 1 or 4 infection. Patients with 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 10-15% of genotype 1a patients) requires the addition of ribavirin and extension of therapy from 12 to 16 weeks. Based on the C-SURFER data, this regimen is a particularly attractive option for patients with HCV and severe renal impairment (estimated Glomerular Filtration Rate [eGFR] less than 30 mL/min/1.73m2) for whom sofosbuvir-based regimens may not be optimal. The wholesale acquisition cost for elbasvir-grazoprevir ($54,600) is notably lower than other first-line regimens.

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 (formerly MK-8742) 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 (formerly MK-5172) is a macrocyclic compound that reversibly binds to the HCV NS3/4A protease, an enzyme responsible for cleaving and processing the HCV-encoded polyprotein. It is distinct from earlier-generation protease inhibitors in its potent in vitro activity against a broader array of HCV genotypes, as well activity against some of the major resistance-associated variants (R155K and D168Y) resulting from failure with a first-generation protease inhibitors.

Manufacturer for United States

Zepatier (ZEP-ah-teer) is a fixed-dose combination of elbasvir and grazoprevir (Figure 1) and (Figure 2). It is manufactured by Merck & Co., Inc.
Cost and Medication Access

Merck has established a list price of $54,600 for a 12-week treatment course. For patients needing a 16-week course, the list price is $72,800.

- 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 co-pay 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.

Adverse Effects

Using pooled data from phase 2 and 3 trials (N=834), the most common adverse observed in patients 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 subjects, typically occurring at or after 8 weeks of 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 patients receiving elbasvir-grazoprevir.

Key Drug Interactions

For complete information on elbasvir-grazoprevir-related drug interactions, see the Drug Interactions section in the Elbasvir-Grazoprevir (Zepatier) 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

<table>
<thead>
<tr>
<th>Drugs that are Contraindicated for Use with Elbasvir-Grazoprevir*</th>
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<tbody>
<tr>
<td><strong>Organic ion transporter polypeptide 1B (OATP1B) inhibitors</strong></td>
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<tr>
<td>Antimycobacterials</td>
<td>Rifampin</td>
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<tr>
<td>HIV medications</td>
<td>Atazanavir, Darunavir, Lopinavir, Saquinavir, Tipranavir</td>
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<tr>
<td>Immunosuppressants</td>
<td>Cyclosporine</td>
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<th><strong>Strong CYP3A Inducers</strong></th>
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<tr>
<td>Anticonvulsants</td>
<td>Phenytoin, Carbamazepine</td>
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<tr>
<td>Herbal products</td>
<td>St. John’s Wort (Hypericum perforatum)</td>
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<tr>
<td>HIV medications</td>
<td>Efavirenz*</td>
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*This is not a complete list of all drugs that inhibit OATP1B or strongly induce CYP3A

*Efavirenz is listed as a strong CYP3A inducer because it reduced grazoprevir exposure by ≥80%