

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 (*Zepatier*) ([Figure 1](#)) 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

The fixed-dose combination medication elbasvir and grazoprevir (*Zepatier*) 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.
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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

Concomitant use of elbasvir-grazoprevir with OATP1B inhibitors can cause significant increases in the plasma levels of grazoprevir; thus, these combinations are contraindicated. The concomitant use of elbasvir-grazoprevir with strong CYP3A inducers or efavirenz can result in significant lowering of elbasvir and grazoprevir plasma levels, which may result in reduced efficacy of elbasvir-grazoprevir; accordingly, these combinations are contraindicated. Use of elbasvir-grazoprevir is not recommended with moderate CYP3A inducers or with certain strong CYP3A inhibitors. For complete information on elbasvir-grazoprevir-related drug interactions, see the [Drug Interactions section in the Elbasvir-Grazoprevir \(Zepatier\) Prescribing Information](#).

Figures

Figure 1 Packaging - Elbasvir-Grazoprevir (Zepatier)

Photograph courtesy of Merck & Co., Inc.



Figure 2 Medication Contraindications

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

Drugs that are Contraindicated for Use with Elbasvir-Grazoprevir*	
Organic ion transporter polypeptide 1B (OATP1B) inhibitors	
Antimycobacterials	Rifampin
HIV medications	Atazanavir Darunavir Lopinavir Saquinavir Tipranavir
Immunosuppressants	Cyclosporine
Strong CYP3A Inducers	
Anticonvulsants	Phenytoin Carbamazepine
Herbal products	St. John's Wort (<i>Hypericum perforatum</i>)
HIV medications	Efavirenz [†]
<p>*This is not a complete list of all drugs that inhibit OAT1B or strongly induce CYP3A [†]Efavirenz is listed as a strong CYP3A inducer because it reduced grazoprevir exposure by ≥80%</p>	

Figure 3 Pill - Elbasvir-Grazoprevir (Zepatier)

Photograph courtesy of Merck & Co., Inc.



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<https://www.hepatitisc.uw.edu/page/treatment/drugs/elbasvir-grazoprevir>