Zepatier

(elbasvir, grazoprevir)

New Product
Slideshow

MPR

Introduction

- **Brand name:** Zepatier
- **Generic name:** Elbasvir, grazoprevir
- **Pharmacological class:** HCV NS5A inhibitor + HCV NS3/4A protease inhibitor
- **Strength and Formulation:** 50mg/100mg; tablets
- **Manufacturer:** Merck & Co.
- **How supplied:** Carton—2 x 14 dose packs
- **Legal Classification:** Rx

ZEPATIER


NDC 0006-3074-01
Zepatier™
(elbasvir and grazoprevir) tablets
50 mg/100 mg
Each tablet contains 50 mg elbasvir and 100 mg grazoprevir.
Usual Dosage: See Package Insert.
Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (between 59°F to 86°F).
Store in original blister package until use to protect from moisture.
Rx only
14 Tablets
770
Lift Here To Open

Indications

- Chronic HCV genotypes 1 or 4 infection with or without ribavirin (RBV)

Dosage & Administration

- ≥18 years: 1 tablet once daily
- **Genotype 1a:**
  - Treatment-naive or PegIFN/RBV-experienced without baseline NS5A polymorphisms: treat for 12 weeks
  - With baseline NS5A polymorphisms: take with RBV for 16 weeks
- **Genotype 1b:** treatment-naive or PegIFN/RBV-experienced: treat for 12 weeks

Dosage & Administration

- **Genotype 1a or 1b:** PegIFN/RBV/HCV NS3/4A protease inhibitor (PI)-experienced: take with RBV for 12 weeks
- **Genotype 4:**
  - Treatment-naive: treat for 12 weeks
  - PegIFN/RBV-experienced: take with RBV for 16 weeks
- HCV/HIV-1 co-infected with or without cirrhosis, renal impairment including hemodialysis: follow same dosage regimen
- See full labeling

Considerations for Special Populations

- **Pregnancy:** No adequate data available
- **Nursing mothers:** Consider benefits and adverse effects
- **Pediatric:** <18 years: not established
- **Geriatric:** Higher rate of ALT elevations observed
- **Hepatic impairment:** See Contraindications

Contraindications

- Moderate or severe hepatic impairment
- Concomitant atazanavir, carbamazepine, cyclosporine, darunavir, efavirenz, lopinavir, phenytoin, rifampin, saquinavir, St. John's wort, tipranavir
- When coadministered with ribavirin, its contraindications also apply to this combination regimen (eg, Pregnancy Category X)

Warnings/Precautions

- **HCV genotype 1a:** test for presence of virus with NS5A resistance-associated polymorphisms prior to initiation

- Monitor hepatic function prior to initiation, at Week 8, and as clinically indicated; perform additional testing at Week 12 for patients receiving 16 weeks of therapy

Warnings/Precautions

- Consider **discontinuing** if ALT persistently >10XULN
- **Discontinue** if ALT elevation is accompanied with liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR
- For **ribavirin** specific dosing and safety information, refer to the full prescribing label

Interactions

- See **Contraindications**
- Concomitant moderate CYP3A inducers or certain strong CYP3A inhibitors: not recommended
- May be antagonized by nafcillin, bosentan, etravirine, modafinil
- May be potentiated by ketoconazole, elvitegravir/cobicistat/emtricitabine/ tenofovir disoproxil fumarate or tenofovir alafenamide

Interactions

- Potentiates tacrolimus (monitor tacrolimus levels, changes in renal function), atorvastatin (limit maximum 20mg/day), rosuvastatin (limit maximum 10mg/day)
- May potentiate fluvastatin, lovastatin, simvastatin; use lowest effective dose of these drugs

Adverse Reactions

- Fatigue
- Headache
- Nausea
- Diarrhea
- Anemia

Mechanism of Action

- Zepatier combines two direct-acting antivirals with distinct mechanisms of action
- **Elbasvir** is an inhibitor of HCV NS5A, which is essential for viral RNA replication and virion assembly
- **Grazoprevir** is an inhibitor of the HCV NS3/4A protease which is necessary for the proteolytic cleavage of the HCV encoded polyprotein (into mature forms of the NS3, NS4A, NS4B, NS5A, and NS5B proteins) and is essential for viral replication

Pharmacokinetics

- **Distribution:**
  - Elbasvir: >99.9% bound to human plasma proteins
  - Grazoprevir: >98.8% bound to human plasma proteins
- **Metabolism:** CYP3A (major)
- **Elimination:** fecal (major)

Clinical Trials

- The efficacy of Zepatier was assessed in 2 placebo-controlled trials and 4 uncontrolled Phase 2 and 3 clinical trials in 1,401 subjects with genotype (GT) 1, 4, or 6 chronic hepatitis C virus infection with compensated liver disease (with or without cirrhosis)

Clinical Trials

- The 6 clinical studies (C-EDGE TN, C-EDGE COINFECTION, C-SURFER, C-SCAPE, C-EDGE TE, and C-SALVAGE), which enrolled a total of 1,373 patients, contributed to the assessment of efficacy in genotype 1 or 4
- The primary endpoint in all trials was sustained virologic response defined as HCV RNA
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the complete product monograph available at:

  http://www.empr.com/zepatier/drugproduct/408/