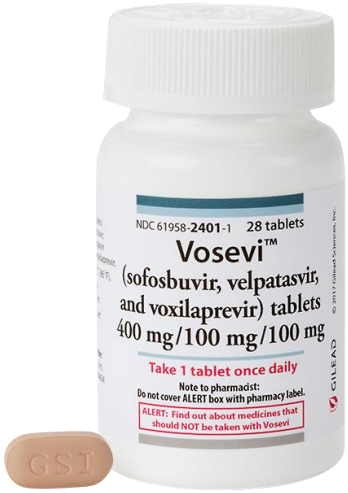
Vosevi

(sofosbuvir, velpatasvir, voxilaprevir)



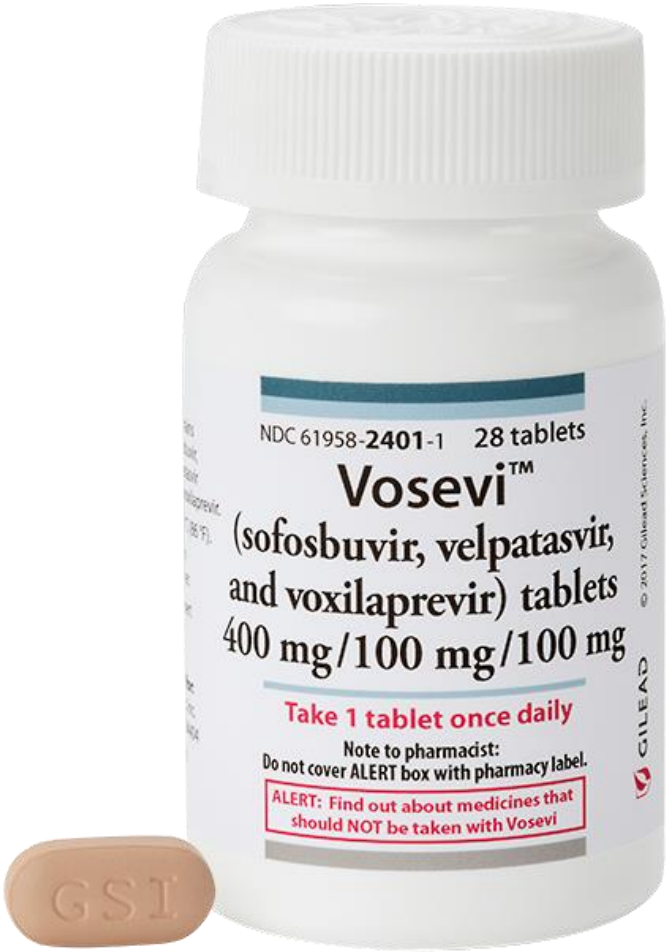
NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Vosevi
- **Generic name:** Sofosbuvir, velpatasvir, voxilaprevir
- **Pharmacological class:** HCV NS5B polymerase inhibitor + HCV NS5A inhibitor + HCV NS3/4A protease inhibitor
- **Strength and Formulation:** 400mg/100mg/100mg; tabs
- **Manufacturer:** Gilead
- **How supplied:** Bottle—28
- **Legal Classification:** Rx

VOSEVI


NDC 61958-2401-1 28 tablets
Vosevi™
(sofosbuvir, velpatasvir, and voxilaprevir) tablets
400 mg/100 mg/100 mg
Take 1 tablet once daily
Note to pharmacist:
Do not cover ALERT box with pharmacy label.
ALERT: Find out about medicines that should NOT be taken with Vosevi
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GSI

Indications

- Chronic **hepatitis C virus (HCV)** infection in adults without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have:
  - Genotype 1, 2, 3, 4, 5, or 6 and were previously treated with an NS5A inhibitor-containing regimen, or
  - Genotype 1a or 3 and were previously treated with a sofosbuvir-containing regimen without an NS5A inhibitor

Dosage & Administration

- Test for HBV infection prior to initiation
- Take with food
- 1 tab once daily for 12 weeks

Considerations for Special Populations

- **Pregnancy:** No adequate data to establish risk to pregnancy outcomes
- **Nursing mothers:** Consider benefits and potential adverse effects
- **Pediatric:** Not established
- **Elderly:** No dose adjustment needed
- **Hepatic impairment:** Moderate to severe impairment: not recommended
- **Renal impairment:** Severe impairment or ESRD requiring hemodialysis: not established

Contraindications

- Concomitant **rifampin**

Warnings/Precautions

- Risk of **HBV reactivation** in patients coinfected with HCV/HBV
- Test all patients for HBV infection by measuring HBsAg and anti-HBc
- If positive serologic evidence, monitor for hepatitis flare or HBV reactivation during and at post-treatment follow-up; treat if clinically indicated

Warnings/Precautions

- Increased risk of **symptomatic bradycardia** when concomitant amiodarone especially in patients also taking beta-blockers or with cardiac comorbidities and/or advanced liver disease

Interactions

- Concomitant **amiodarone**: not recommended; if no alternatives, monitor cardiac function (see full labeling)
- Concomitant certain immunosuppressants or chemotherapeutic agents: may increase risk of HBV reactivation

Interactions

- May potentiate P-gp, BCRP, OATP1B1, OATP1B3, or OATP2B1 substrates
- Concomitant BCRP substrates (eg, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, rosuvastatin, sulfasalazine, topotecan): not recommended

Interactions

- Concomitant P-gp and/or moderate to potent CYP2B6, CYP2C8, CYP3A4 inducers (eg, St. John's wort, carbamazepine), anticonvulsants (eg, phenytoin, phenobarbital, oxcarbazepine), rifabutin, rifapentine, tipranavir/ritonavir, atazanavir-, lopinavir-, or efavirenz-containing regimens, OATP inhibitors (eg, cyclosporine): not recommended

Interactions

- Separate dosing of antacids by 4hrs
- May give H_2-antagonists simultaneously or staggered from Vosevi (at a dose that does not exceed doses comparable with famotidine 40mg twice daily)
- May coadminister with omeprazole 20mg

Interactions

- May potentiate digoxin, dabigatran etexilate; monitor
- Concomitant tenofovir DF regimens; monitor
- May potentiate pravastatin (do not exceed 40mg dose), pitavastatin (not recommended), atorvastatin, fluvastatin, lovastatin, simvastatin; use lowest approved dose

Adverse Reactions

- Headache
- Fatigue
- Diarrhea
- Nausea
- Asthenia
- Insomnia
- Rash
- Depression
- Lab abnormalities

Mechanism of Action

- Vosevi is a fixed dose combination of sofosbuvir, velpatasvir, and voxilaprevir
- **Sofosbuvir** is an HCV NS5B RNA-dependent RNA polymerase inhibitor, a prodrug that acts as a chain terminator

Mechanism of Action

- **Velpatasvir** inhibits HCV NS5A, a protein required for viral replication
- **Voxilaprevir** is a noncovalent, reversible NS3/4A protease inhibitor, that blocks proteolytic cleavage of the HCV encoded polyproteins (into mature forms of NS3, NS4A, NS4B, NS5A, and NS5B proteins)

Clinical Studies

- Vosevi was evaluated in two Phase 3 trials in direct-acting antivirals (DAA)-experienced patients with genotype 1−6 HCV infection without cirrhosis or with compensated cirrhosis

Clinical Studies

- The **primary endpoint** in both trials was sustained virologic response (SVR12), defined as HCV RNA less than lower limit of quantification at 12 weeks after end of treatment

Clinical Studies

- **POLARIS-1** (N=415) was a randomized, double-blind, placebo-controlled trial that evaluated 12 weeks of Vosevi vs. placebo in patients with HCV genotypes 1−6 who previously failed an NS5A inhibitor-containing regimen
- SVR12 was achieved in **96%** of Vosevi-treated patients vs. **0%** of placebo patients

Clinical Studies

- **POLARIS-4** (N=333) was a randomized, open-label trial that evaluated 12 weeks of Vosevi vs. sofosbuvir/velpatasvir (SOF/VEL) in patients with HCV genotypes 1−4 who previously failed an HCV DAA-containing regimen that did not include an NS5A inhibitor

Clinical Studies

- Overall, SVR12 was achieved in **97%** of Vosevi-treated patients with genotypes 1−3 vs. **88%** of SOF/VEL-treated patients
- Patients with HCV genotype 4 (n=18) with prior SOF-containing regimen without an NS5A inhibitor were given Vosevi for 12 weeks
  - All patients achieved SVR12
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/vosevi/drug/34712/