

Sofosbuvir-Velpatasvir-Voxilaprevir (Vosevi)

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Drug Summary

Sofosbuvir-velpatasvir-voxilaprevir is the first pangenotypic fixed-dose tablet ([Figure 1](#)) that includes medications from three different HCV antiviral classes. In early development, sofosbuvir-velpatasvir-voxilaprevir held promise as the first pangenotypic agent that could be given for 8 weeks in nearly all cases, but results of the POLARIS-2 suggested that 8 weeks of a triple direct-acting antiviral (DAA) may not have the same efficacy as 12 weeks of dual therapy with sofosbuvir-velpatasvir in genotype 1A patients. Sofosbuvir-velpatasvir-voxilaprevir, however, fills an important role as a pangenotypic regimen for patients who have experienced treatment failure with DAA therapy. The presence of NS5A, NS3 or NS5B resistance-associated substitutions pre-treatment did not appear to influence the likelihood of SVR, and 12 weeks of monotherapy without ribavirin produced high SVR rates (96%) in DAA-experienced patients. Unfortunately, the presence of a HCV protease inhibitor in voxilaprevir does not make this an option for treatment-experienced patients who have moderate or severe liver disease (Child B or C cirrhosis).

Class and Mechanism

Sofosbuvir-velpatasvir-voxilaprevir (*Vosevi*) is an oral fixed-dose combination of sofosbuvir, a nucleotide analog NS5B polymerase inhibitor, velpatasvir, an NS5A replication complex inhibitor, and voxilaprevir, an NS3/4A protease inhibitor. Sofosbuvir is a nucleotide prodrug that is metabolized to form the pharmacologically active uridine analog triphosphate (GS-461203), and acts as a chain terminator for the NS5B polymerase. Velpatasvir (formerly GS-5816) has potent in vitro anti-HCV activity across all genotypes at the picomolar level. Voxilaprevir is a reversible inhibitor of the NS3/4A protease, which is necessary for the proteolytic cleavage of the HCV encoded polyprotein, and has been shown to have pangenotypic activity including activity against most resistance-associated substitutions.

Manufacturer for United States

Sofosbuvir-velpatasvir-voxilaprevir (Vosevi) is manufactured by Gilead Sciences. ([Figure 2](#))

Cost and Medication Access

The wholesale acquisition cost (WAC) for sofosbuvir-velpatasvir-voxilaprevir is \$890 per pill; the cost of 12-week course of therapy is \$74,760.

Adverse Effects

The most common adverse effects, observed in at least 10% of phase 3 trial participants, were headache, fatigue, diarrhea, and nausea.

Key Drug Interactions

For complete information on sofosbuvir-velpatasvir-voxilaprevir-related drug interactions, see the [Drug Interactions section in the Sofosbuvir-Velpatasvir-Voxilaprevir \(Vosevi\) Prescribing Information](#).

Figures

Figure 1 Sofosbuvir-Velpatasvir-Voxilaprevir (Vosevi) Pill

Photo: Andrew Karpenko, University of Washington



Figure 2 Sofosbuvir-Velpatasvir-Voxilaprevir (Vosevi) Bottle

Photo: Andrew Karpenko, University of Washington

