var drug_url = "epclusa";

Sofosbuvir-Velpatasvir *(Epclusa)*

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See also
Sofosbuvir
,
Ledipasvir-Sofosbuvir
,
Sofosbuvir-Velpatasvir-Voxilaprevir
.

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Drug Summary

Sofosbuvir-velpatasvir is the first available pangenotypic NS5A-NS5B inhibitor single-pill combination regimen, and is highly efficacious across HCV genotypes 1 to 6. It provides a much-needed interferon-free option for patients with genotype 3 infection that is more economical than sofosbuvir plus daclatasvir, and in patients who have compensated cirrhosis with genotype 3, this single-pill option provides an important ribavirin-free combination. Notably, unlike ledipasvir-sofosbuvir, an abbreviated duration of 8 weeks has not been studied with sofosbuvir-velpatasvir for any of the genotypes, except in conjunction with a third agent (voxilaprevir). Sofosbuvir-velpatasvir, like ledipasvir-sofosbuvir, will be susceptible to drug interactions with acid-reducing agents particularly proton-pump inhibitors and the impact of these agents on real-world clinical effectiveness remains to be determined.

Class and Mechanism

Sofosbuvir-Velpatasvir (*Epclusa*) is an oral fixed-dose combination of sofosbuvir, a nucleotide analog NS5B polymerase inhibitor and velapatasvir, an NS5A replication complex inhibitor. Sofosbuvir is currently approved in the United States for the treatment of genotype 1, 2, 3 and 4 HCV infection with different regimens and durations dependent on the HCV genotype. Velpatasvir (formerly GS-5816) is a novel NS5A inhibitor that has potent in vitro anti-HCV activity across all genotypes at the picomolar level. The combination of sofosbuvir-velpatasvir is the first once-daily single-tablet regimen with pangenotypic activity.

Manufacturer for United States

Sofosbuvir-velpatasvir (*Epclusa*) (Figure 1) is manufactured by Gilead Sciences.

Cost and Medication Access

The wholesale acquisition cost (WAC) for sofosbuvir-velpatasvir 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 and fatigue.

Key Drug Interactions

For complete information on sofosbuvir-velpatasvir-related drug interactions, see the Drug Interactions section in the Sofosbuvir-Velpatasvir (*Epclusa*) Prescribing Information.

Clinical Trials

Filter by Category

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ASTRAL-1

In this randomized, placebo-controlled phase 3 trial, treatment-naive and treatment-experienced patients with chronic hepatitis C genotype 1, 2, 4, 5, or 6 infection were randomized in a 5:1 ratio to receive either sofosbuvir-velpatasvir or placebo. In the treatment arm (n=624), 32% had compensated cirrhotic and 19% were treatment-experienced (except for prior NS5A or NS5B experience). The overall SVR12 rate was 99%, with a range of 97 to 100% across the genotypes.

Only two viral relapses occurred and these involved patients with genotype 1a and 1b. Among the 121 patients with cirrhosis, 99% achieved an SVR 12. The presence of baseline NS5A resistance-associated variants, present in 42% of evaluated patients, did not appear to influence SVR12. There was no significant difference in the rate of adverse events between the treatment and placebo arms.

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ASTRAL-2

The ASTRAL-2 trial was published in tandem with the similar trial involving patients with genotype 3 infection (ASTRAL-3). ASTRAL-2 was a randomized, open-label phase 3 trial that compared the safety and efficacy of the fixed-dose combination of sofosbuvir-velpatasvir for 12 weeks with sofosbuvir plus ribavirin for 12 weeks in patients with chronic HCV genotype 2 infection, including treatment-naïve and treatment-experienced patients. Patients with compensated cirrhosis were permitted and comprised 14% of the total 266 patients enrolled in the study. The SVR12 rate among sofosbuvir-velpatasvir recipients was 99% and was superior to the SVR12 rate of 94% among those who received sofosbuvir plus ribavirin, P-value=0.02. The single patient who did not achieve SVR12 in the sofosbuvir-velpatasvir group had received only one dose of the drug and discontinued after experiencing headache and anxiety. The incidence of serious adverse events was low (1%) and not different between treatment arms. The investigators concluded the sofosbuvir-velpatasvir regimen was superior to the standard regimen of sofosbuvir plus ribavirin in patients with chronic HCV genotype 2 infection.

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ASTRAL-3

The ASTRAL-3 trial was published in tandem with the similar trial involving patients with genotype 2 infection (ASTRAL-2). In this randomized, open-label phase 3 trial, investigators compared the efficacy of the fixed-dose combination of sofosbuvir-velpatasvir for 12 weeks with sofosbuvir plus ribavirin for 24 weeks in patients with genotype 3 HCV infection. Of the 552 patients enrolled in the study, 30% had compensated cirrhosis and 26% were treatment-experienced. The overall SVR12 rate was 95% in the sofosbuvir-velpatasvir arm and 80% in the sofosbuvir plus ribavirin arm (P-value<0.001). Among those patients with cirrhosis who received sofosbuvir-velpatasvir, the SVR12 rate were 93% for treatment-naïve and 89% for treatment-experienced patients. Among the 274 patients screened for baseline NS5A resistance-associated variants, the SVR12 rate was 88% for the 43 patients who had variants compared with 97% among those who did not.The investigators concluded the 12-week regimen of sofosbuvir-velpatasvir regimen was superior to the standard 24-week regimen of sofosbuvir plus ribavirin in patients with chronic HCV genotype 3 infection. The most substantial differences occurred in treatment experienced patients with those with cirrhosis.

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ASTRAL-4

The ASTRAL-4 trial was a randomized, open-label phase 3 trial designed to examine the safety and efficacy of the fixed-dose combination of sofosbuvir-velpatasvir with or without ribavirin in patients with genotype 1, 2, 3, 4, or 6 chronic HCV infection and decompensated cirrhosis. Treatment-naïve and treatment-experienced patients with Child-Pugh-Turcotte (CTP) class B disease were randomized

to one of three arms: (1) sofosbuvir-velpatasvir for 12 weeks (n=90), (2) sofosbuvir-velpatasvir plus ribavirin for 12 weeks (n=87), or (3) sofosbuvir-velpatasvir for 24 weeks (n=90). All three regimens were highly efficacious among genotype 1 patients (88%, 96%, and 92% respectively) and genotypes 2, 4 and 6 patients (100%, 100%, and 86% respectively). Notably among patients with genotype 3, the treatment groups without ribavirin had lower SVR12 rates of 50% (each) compared with 85% in the sofosbuvir-velpatasvir plus ribavirin arm. Overall, the CTP scores improved over baseline in 47%, remained unchanged in 42%, and worsened in 11%. A total of 22 patients experienced virologic failure; most (n=18) had NS5A variants at the time of failure with the Y93H/N occurring most frequently.

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ASTRAL-5

The ASTRAL-5 study was a single-arm, open-label phase 3 trial of sofosbuvir-velpatasvir for 12 weeks in patients with HIV and HCV coinfection. The study enrolled 106 patients with genotype 1, 2, 3, 4 or 6 HCV infection; 18% had compensated cirrhosis and 29% were treatment-experienced. The mean CD4 count was 583 cells/mm^3 and all patients had HIV viral suppression. A variety of antiretroviral regimens, including tenofovir disoproxil fumarate (DF) and boosting agents (cobicistat or ritonavir), were permitted. The overall SVR12 rate was 95%; two viral relapses occurred, both in the genotype 1a subgroup. The presence of cirrhosis or treatment experience did not appear to influence treatment response. Creatinine clearance was lower among people taking boosted versus unboosted tenofovir DF, and lowest among people not taking tenofovir DF (who may have had existing kidney problems), but it remained relatively stable over time in all groups. No patient experienced HIV viral rebound on HCV treatment.

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[PubMed Abstract]

Figures

Figure 1 Sofosbuvir-Velpatasvir (*Epclusa*) Bottle

Photo: Andrew Karpenko, University of Washington

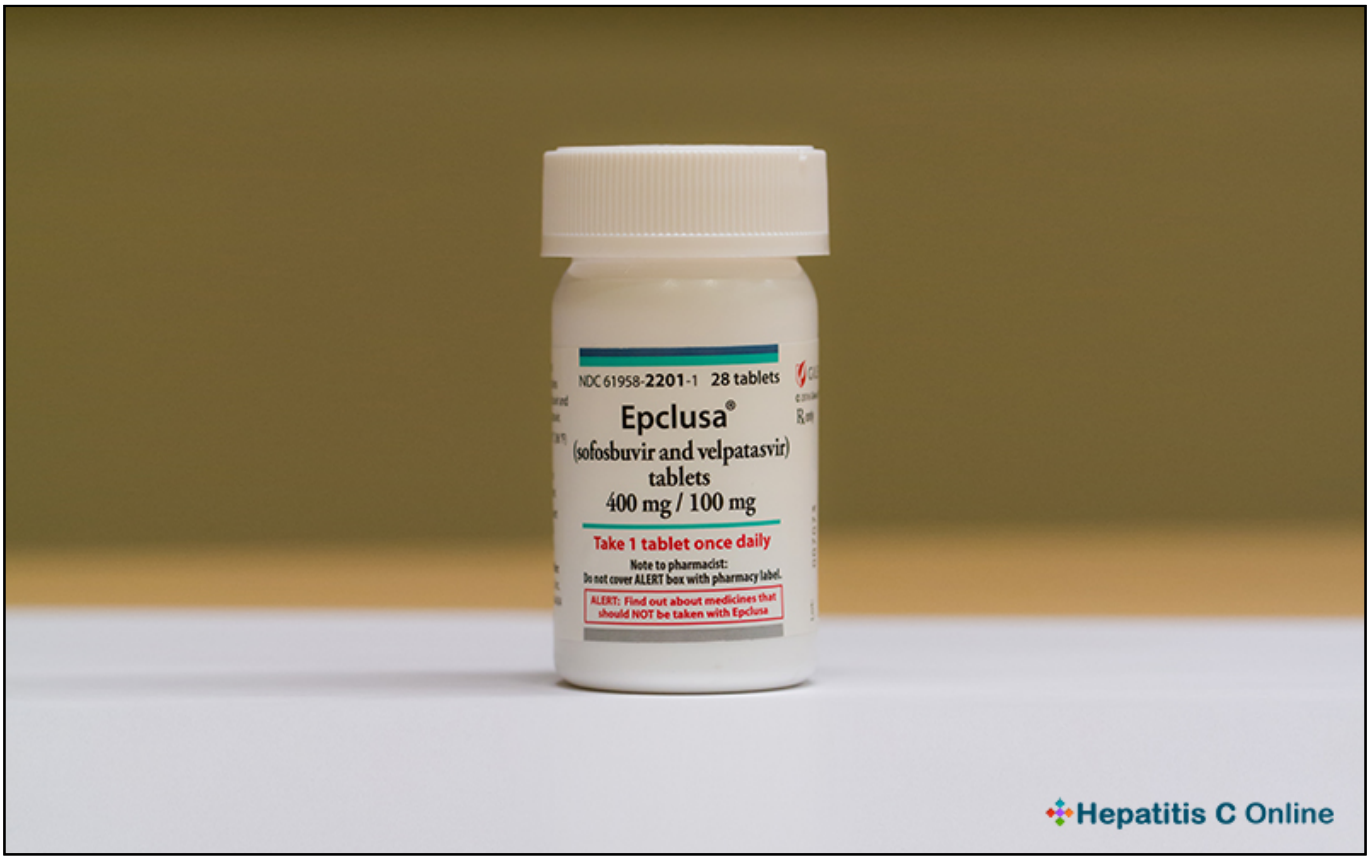

Figure 2 Sofosbuvir-Velpatasvir (*Epclusa*) Tablets

Photo: Andrew Karpenko, University of Washington