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Sofosbuvir-Velpatasvir *(Epclusa)*

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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

Sofosbuvir and velpatasvir are substrates for the drug transporter P-gp and BRCP. Thus, use of sofosbuvir-velpatasvir is not recommended with drugs that are inducers of P-gp and/or moderate to potent inducers of CYP2B6, since these combinations may result in significant lowering of plasma levels of sofosbuvir and velpatasvir. In addition, velpatasvir is an inhibitor of drug transporters OATP1B1, OATP1B3, OATP2B1, P-gp, and breast cancer resistance protein (BCRP). Note that velpatasvir solubility decreases as gastric pH increases and medications that raise gastric pH will likely decrease concentrations of velpatasvir; the coadministration of proton pump inhibitors with sofosbuvir-velpatasvir is not recommended. Detailed information on drug-drug interactions that may occur with sofosbuvir-velpatasvir and other medications is provided in the sofosbuvir-velpatasvir (*Epclusa*) Full Prescribing Information.
For complete information on sofosbuvir-velpatasvir-related drug interactions, see the Drug Interactions section in the Sofosbuvir-Velpatasvir (*Epclusa*) Prescribing Information.

Figures

Figure 1 Sofosbuvir-Velpatasvir (*Epclusa*) Bottle

Photo: Andrew Karpenko, University of Washington

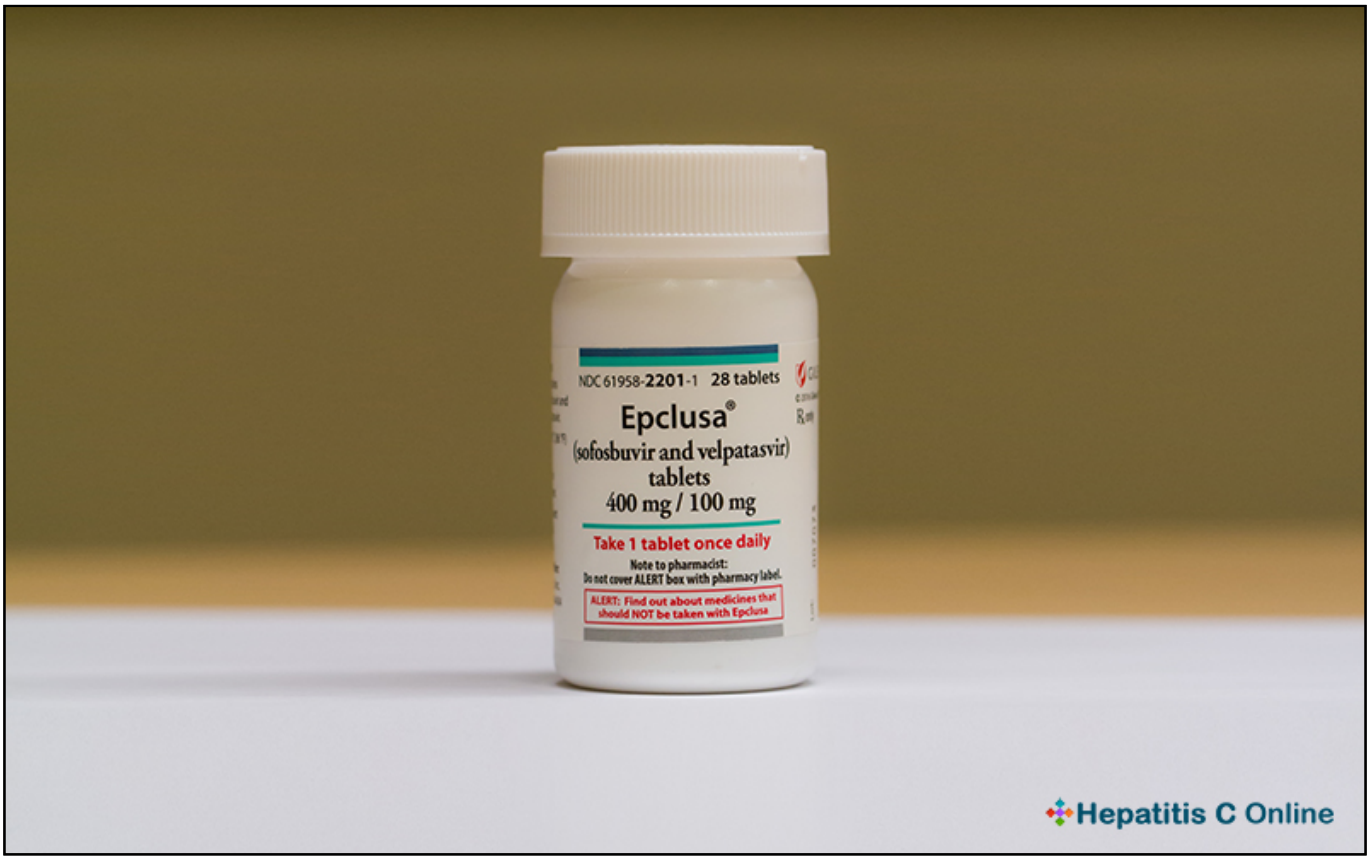

Figure 2 Sofosbuvir-Velpatasvir (*Epclusa*) Tablets

Photo: Andrew Karpenko, University of Washington