



# Sofosbuvir/Velpatasvir (Epclusa®) Drug Interactions

## A Quick Guide for Clinicians – 2023

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### Mechanism of Action and Route of Metabolism for Sofosbuvir/Velpatasvir (Epclusa®)

Medication	HCV Mechanism of Action	Route of Metabolism and Drug Interaction Potential
<ul style="list-style-type: none"> <li>• Sofosbuvir/Velpatasvir (Epclusa®)</li> </ul>	NS5b polymerase inhibitor and NS5a inhibitor	<ul style="list-style-type: none"> <li>• Sofosbuvir is a substrate for P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP). The intracellular metabolism of sofosbuvir is mediated by hydrolase and nucleotide phosphorylation pathways.</li> <li>• Velpatasvir is an inhibitor of drug transporters P-gp, BCRP, OATP1B1, OATP1B3, and OATP2B1.</li> </ul>

### Sofosbuvir/Velpatasvir (Epclusa®) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comments
<b>HIV Protease Inhibitors</b>	
<ul style="list-style-type: none"> <li>• Atazanavir (Reyataz®) + ritonavir (Norvir®)</li> <li>• Atazanavir/cobicistat (Evotaz®)</li> <li>• Darunavir (Prezista®) + ritonavir (Norvir®)</li> <li>• Darunavir/cobicistat (Prezcobix®; in Symtuza®)</li> </ul>	<ul style="list-style-type: none"> <li>• Concurrent use at standard doses appropriate.</li> <li>• If using tenofovir disoproxil fumarate in combination with sofosbuvir/velpatasvir, monitor for tenofovir-associated adverse reactions.</li> </ul>
<b>HIV Non Nucleoside Reverse Transcriptase Inhibitors</b>	
<ul style="list-style-type: none"> <li>• Efavirenz (Sustiva®; in Atripla® Symfi®, Symfi Lo®)</li> <li>• Etravirine (Intelence®)</li> <li>• Nevirapine (Viramune®)</li> </ul>	<ul style="list-style-type: none"> <li>• Co-administration of sofosbuvir/velpatasvir with efavirenz, etravirine and nevirapine is expected to decrease the concentration of sofosbuvir and velpatasvir, leading to reduced efficacy. Co-administration not recommended.</li> </ul>
<ul style="list-style-type: none"> <li>• Rilpivirine oral (Edurant®; in Complera®, Odefsey®, Juluca®)</li> <li>• Rilpivirine injection (in Cabenuva®)</li> <li>• Doravirine (Pifeltro®; in Delstrigo®)</li> </ul>	<ul style="list-style-type: none"> <li>• Concurrent use at standard doses appropriate.</li> <li>• If using tenofovir disoproxil fumarate in combination with sofosbuvir/velpatasvir, monitor for tenofovir-associated adverse reactions.</li> </ul>

## Sofosbuvir/Velpatasvir (Epclusa®) Drug Interactions with HIV Medications, continued

HIV Integrase Strand Transfer Inhibitors	
<ul style="list-style-type: none"> <li>• Bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy®)</li> <li>• Dolutegravir (Tivicay®; in Dovato®, Triumeq®, Juluca®)</li> <li>• Cabotegravir oral (Vocabria®)</li> <li>• Cabotegravir injection (Apretude®; in Cabenuva®)</li> <li>• Dolutegravir (Tivicay®; in Dovato®, Triumeq®, Juluca®)</li> <li>• Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®)</li> <li>• Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®)</li> <li>• Raltegravir (Isentress® Isentress HD®)</li> </ul>	<ul style="list-style-type: none"> <li>• Concurrent use at standard doses appropriate.</li> <li>• If using tenofovir disoproxil fumarate in combination with sofosbuvir/velpatasvir, monitor for tenofovir-associated adverse reactions.</li> </ul>
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
<ul style="list-style-type: none"> <li>• Abacavir (Ziagen®, in Epzicom®, Triumeq®, other STRs)</li> <li>• Emtricitabine (Emtriva®, in other STRs)</li> <li>• Lamivudine (Epivir®, in other STRs)</li> <li>• Tenofovir Disoproxil Fumarate (Viread®; in Cimduo®, Temixys®, Truvada®, other STRs)</li> <li>• Tenofovir Alafenamide (in Descovy®, other STRs)</li> </ul>	<ul style="list-style-type: none"> <li>• Concurrent use at standard doses appropriate.</li> <li>• If using tenofovir disoproxil fumarate in combination with sofosbuvir/velpatasvir, monitor for tenofovir-associated adverse reactions.</li> </ul>
HIV Entry Inhibitors, CCR5 Antagonists, gp120-Directed Attachment Inhibitors	
<ul style="list-style-type: none"> <li>• Fostemsavir (Rukobia®)</li> <li>• Maraviroc (Selzentry®)</li> <li>• Ibalizumab (Trogarzo®)</li> </ul>	<ul style="list-style-type: none"> <li>• Concurrent use at standard doses appropriate.</li> </ul>
HIV Capsid Inhibitor	
<ul style="list-style-type: none"> <li>• Lenacapavir (Sulenca®)</li> </ul>	<ul style="list-style-type: none"> <li>• Concurrent use at standard doses appropriate.</li> </ul>

## Sofosbuvir/Velpatasvir (Epclusa®) Drug Interactions with Common Primary Care Medications

Medication and or Class	Recommendation and Clinical Comment
• Antacids	• Separate antacids and sofosbuvir/velpatasvir administration by 4 hours.
• H2-receptor antagonists	• Administer simultaneously with or 12 hours apart from sofosbuvir/velpatasvir. Do not exceed doses comparable to famotidine 40 mg twice daily.
• Proton-pump inhibitors	• Co-administration not recommended. If medically necessary, sofosbuvir/velpatasvir should be administered with food and taken 4 hours before omeprazole 20mg. Use with other proton pump inhibitors has not been studied.
• Antiarrhythmic – Amiodarone	• Significant bradycardia expected with concurrent use. Co-administration not recommended. If concurrent use required, cardiac monitoring is recommended, see package insert for additional information.
• Antiarrhythmic – Digoxin	• Increase in digoxin levels possible. Monitor digoxin levels.
• Anticancer – topotecan	• Potential increase in topotecan levels. Coadministration not recommended.
• Anticonvulsants – carbamazepine, oxcarbazepine, phenobarbital, phenytoin	• Significant decrease in sofosbuvir/velpatasvir levels expected. Co-administration not recommended.
• Antimycobacterials – rifampin, rifabutin, rifapentine	• Significant decrease in sofosbuvir/velpatasvir levels expected. Co-administration not recommended.
• Herbal products – St. John's Wort	• Significant decrease in sofosbuvir/velpatasvir levels expected. Co-administration not recommended.
• HMG Co-A Reductase Inhibitors: Atorvastatin, Rosuvastatin	<ul style="list-style-type: none"> <li>• Increase in atorvastatin likely with sofosbuvir/velpatasvir; monitor for signs of myopathy and rhabdomyolysis.</li> <li>• Significant increase in rosuvastatin levels when used with sofosbuvir/velpatasvir leading to increased risk of myopathy, including rhabdomyolysis. Rosuvastatin may be used; Do not exceed 10mg daily.</li> </ul>

Disclaimer: The information contained in this table has been developed from various resources, including FDA product information, abstracts and posters presented at national and international meetings, and from Recommendations for the Testing, Managing and Treating of Hepatitis C from AASLD and IDSA located at [www.hivguidelines.org](http://www.hivguidelines.org). While the tables contained in this guide are complete based upon references reviewed, there may be other medications that may also be contraindicated or should be co-administered with caution. Please consult additional resources as needed.

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