



Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®) Drug Interactions: A Quick Guide for Clinicians – 2023

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Mechanism of Action and Route of Metabolism for Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®)

Medication	HCV Mechanism of Action	Route of Metabolism and Drug Interaction Potential
<ul style="list-style-type: none"> Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®) 	NS5b polymerase inhibitor, NS5a inhibitor, and NS3/4a protease inhibitor	<ul style="list-style-type: none"> 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. Velpatasvir is an inhibitor of drug transporters P-gp, BCRP, OATP1B1, OATP1B3, and OATP2B1. Voxilaprevir is a substrate for P-gp and BCRP, and a substrate for OATP1B1 and OATP1B3

Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comments
HIV Protease Inhibitors	
<ul style="list-style-type: none"> Darunavir (Prezista®) + ritonavir (Norvir®) Darunavir/cobicistat (Prezcobix®; in Symtuza®) 	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate. If using tenofovir disoproxil fumarate in combination with sofosbuvir/velpatasvir/voxilaprevir, monitor for tenofovir-associated adverse reactions. Consider monitoring for hepatotoxicity due to lack of data with combining voxilaprevir with HIV protease inhibitors.
<ul style="list-style-type: none"> Atazanavir (Reyataz®) + ritonavir (Norvir®) Atazanavir/cobicistat (Evotaz®) Lopinavir/ritonavir (Kaletra®) 	<ul style="list-style-type: none"> Co-administration of sofosbuvir/velpatasvir/voxilaprevir with atazanavir or lopinavir is expected to increase voxilaprevir levels. Co-administration not recommended.

Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®) Drug Interactions with HIV Medications, continued

Concurrent Medication	Recommendation and Clinical Comment
HIV Non-Nucleoside Reverse Transcriptase Inhibitors	
<ul style="list-style-type: none"> • Efavirenz (Sustiva®; in Atripla®, Symfi®, Symfi Lo®) • Etravirine (Intelence®) • Nevirapine (Viramune®) 	<ul style="list-style-type: none"> • Co-administration of sofosbuvir/velpatasvir/voxilaprevir with efavirenz, etravirine and nevirapine is expected to decrease the concentration of velpatasvir and voxilaprevir. Co-administration not recommended.
<ul style="list-style-type: none"> • Rilpivirine oral (Edurant®; in Complera®, Odefsey®, Juluca®) • Rilpivirine injection (in Cabenuva®) • Doravirine (Pifeltro®; in Delstrigo®) 	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate. • If using tenofovir disoproxil fumarate in combination with sofosbuvir/velpatasvir/ voxilaprevir, monitor for tenofovir-associated adverse reactions.
HIV Integrase Strand Transfer Inhibitors	
<ul style="list-style-type: none"> • Bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy®) • Cabotegravir oral (Vocabria®) • Cabotegravir injection (Apretude®; in Cabenuva®) • Dolutegravir (Tivicay®, in Dovato® Triumeq®, Juluca®) • Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®) • Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®) • Raltegravir (Isentress®, Isentress HD®) 	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate. • If using tenofovir disoproxil fumarate in combination with sofosbuvir/velpatasvir/ voxilaprevir, monitor for tenofovir-associated adverse reactions. • Consider monitoring for hepatotoxicity due to lack of data with combining voxilaprevir with elvitegravir/cobicistat.
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
<ul style="list-style-type: none"> • Abacavir (Ziagen®, in Epzicom®, Triumeq®, other STRs) • Emtricitabine (Emtriva®, in other STRs) • Lamivudine (Epivir®, in other STRs) • Tenofovir Disoproxil Fumarate (Viread®; in Cimduo®, Temixys®, Truvada®, other STRs) • Tenofovir Alafenamide (in Descovy®, other STRs) 	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate. • If using tenofovir disoproxil fumarate in combination with sofosbuvir/velpatasvir/ voxilaprevir, monitor for tenofovir-associated adverse reactions.

Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®) Drug Interactions with HIV Medications, continued

HIV Entry Inhibitors, CCR5 Antagonists, gp120-Directed Attachment Inhibitors	
• Fostemsavir (Rukobia®)	• Co-administration not recommended with fostemsavir. Use alternative HCV regimen.
• Maraviroc (Selzentry®)	• Concurrent use at standard doses appropriate.
• Ibalizumab (Trogarzo®)	• Concurrent use at standard doses appropriate.
HIV Capsid Inhibitor	
• Lenacapavir (Sunlenca)	• Concurrent use at standard doses appropriate.

Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®) Drug Interactions with Common Primary Care Medications

Medication and or Class	Recommendation and Clinical Comment
• Antacids	• Separate antacids and sofosbuvir/velpatasvir/voxilaprevir administration by 4 hours.
• H2-receptor antagonists	• Administer simultaneously with or staggered from sofosbuvir/velpatasvir/ voxilaprevir. Do not exceed doses comparable to famotidine 40 mg twice daily.
• Proton-pump inhibitors	• Concurrent use acceptable; do not exceed omeprazole 20mg daily; other proton pump inhibitors have 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 expected. Therapeutic drug monitoring for digoxin is recommended; dose adjust based upon levels.
• Anticoagulant – Dabigatran	• Increase in dabigatran levels expected. Refer to dabigatran prescribing information for guidance when used in setting of moderat renal impairment.
• Anticonvulsants – carbamazepine, oxcarbazepine, phenobarbital, phenytoin	• Significant decrease in sofosbuvir/velpatasvir/voxilaprevir levels expected. Co-administration not recommended.
• Antimycobacterials – rifampin, rifabutin, rifapentine	• Significant decrease in sofosbuvir/velpatasvir/voxilaprevir levels expected. Rifampin is contraindicated; co-administration with rifabutin, rifapentine not recommended.
• Herbal products – St. John's Wort	• Significant decrease in sofosbuvir/velpatasvir/voxilaprevir levels expected. Co-administration not recommended.
• HMG Co-A Reductase Inhibitors: Pitavastatin, Rosuvastatin	• Significant increase in pitavastatin and rosuvastatin levels likely when combined with sofosbuvir/velpatasvir/voxilaprevir; potential for increased risk of myopathy and rhabdomyolysis. Co-administration not recommended.

Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®) Drug Interactions with Common Primary Care Medications, continued

<ul style="list-style-type: none">• HMG Co-A Reductase Inhibitors: Atorvastatin, fluvastatin, lovastatin, pravastatin, simvastatin.	<ul style="list-style-type: none">• Significant increase in atorvastatin, fluvastatin, lovastatin, pravastatin and simvastatin likely with sofosbuvir/velpatasvir/voxilaprevir; monitor for signs of myopathy and rhabdomyolysis. Use lowest approved statin dose. Do not exceed pravastatin 40mg daily.
<ul style="list-style-type: none">• Immunosuppressant - Cyclosporine	<ul style="list-style-type: none">• Significant increase in voxilaprevir levels expected. Co-administration not recommended.

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. 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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