Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®) Drug Interactions: A Quick Guide for Clinicians – September 2017

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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
Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®)	NS5b polymerase inhibitor, NS5a inhibitor, and NS3/4a protease inhibitor	• 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	
Darunavir (Prezista®) + ritonavir (Norvir®) Darunavir/cobicistat (Prezcobix®) Fosamprenavir (Lexiva®) + ritonavir (Norvir ®) Nelfinavir (Viracept®) Saquinavir (Invirase®) + ritonavir (Norvir®)	• Concurrent use at standard doses appropriate.
Atazanavir (Reyataz®) + ritonavir (Norvir®) Atazanavir/cobicistat (Evotaz®) Lopinavir/ritonavir (Kaletra®) Tipranavir (Aptivus®) + ritonavir (Norvir®)	• Co-administration of Sofosbuvir/Velpatasvir/Voxilaprevir with atazanavir or lopinavir is expected to increase voxilaprevir levels. Co-administration not recommended. • Co-administration of sofosbuvir/velpatasvir/voxilaprevir with tipranavir + ritonavir has not been studied, but levels of sofsbuvir and velpatasvir are likely to be reduced. 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	
Efavirenz (Sustiva®, also contained in Atripla®)	• Co-administration of sofosbuvir/velpatasvir/voxilaprevir with efavirenz is expected to decrease the concentration of velpatasvir and voxilaprevir. Co-administration not recommended.
Etravirine (Intelence®)	• Concurrent use at standard doses appropriate.
Rilpivirine (Edurant®, also in Complera® and Odefsey®)	• Concurrent use at standard doses appropriate. • Potential increase in tenofovir levels when given as tenofovir disoproxil fumarate; monitor for renal adverse events.
HIV Integrase Strand Transfer Inhibitors	
Dolutegravir (Tivicay®, also contained in Triumeq®) Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®) Raltegravir (Isentress® Isentress HD®)	• Concurrent use at standard doses appropriate.
Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®)	• Concurrent use at standard doses appropriate. • Potential increase in tenofovir levels when given as tenofovir disoproxil fumarate; monitor for renal adverse events.
HIV Entry Inhibitors	
Maraviroc (Selzentry®)	• Concurrent use at standard doses appropriate.
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
Abacavir (Ziagen®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Tenofovir Disoproxil Fumarate (Viread®) Tenofovir Alafenamide (Descovy®) Stavudine (Zerit®) Didanosine (Videx EC®) Zidovudine (Retrovir®)	• Concurrent use at standard doses appropriate. • Potential increase in tenofovir levels when given as tenofovir disoproxil fumarate; monitor for renal adverse events.

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 – Dabigitran	• Increase in dabigatran levels expected. Refer to dabigatran prescribing information for guidance when used with P-gp inhibitors.
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. Co-administration not recommended.
Digoxin	• Increase in digoxin levels possible. Monitor digoxin levels.
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.
HMG Co-A Reductase Inhibitors: Atorvastatin, fluvastatin, lovastatin, pravastatin, simvastatin.	• 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.

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.