



Sofosbuvir/Velpatasvir (Epclusa®) Drug Interactions

A Quick Guide for Clinicians – February 2019

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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
Sofosbuvir/Velpatasvir (Epclusa®)	NS5b polymerase inhibitor and NS5a 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.

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

Concurrent Medication	Recommendation and Clinical Comments
HIV Protease Inhibitors	
Atazanavir (Reyataz®) + ritonavir (Norvir®) Atazanavir/cobicistat (Evotaz®) Darunavir (Prezista®) + ritonavir (Norvir®) Darunavir/cobicistat (Prezcobix®) Fosamprenavir (Lexiva®) + ritonavir (Norvir®) Lopinavir/ritonavir (Kaletra®) Nelfinavir (Viracept®) Saquinavir (Invirase®) + ritonavir (Norvir®) All unboosted Protease inhibitors	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate. Potential increase in tenofovir levels when given as tenofovir disoproxil fumarate; monitor for renal adverse events.
Tipranavir (Aptivus®) + ritonavir (Norvir®)	<ul style="list-style-type: none"> Co-administration of sofosbuvir/velpatasvir with tipranavir + ritonavir is expected to decrease the concentration of sofosbuvir and velpatasvir, leading to reduced efficacy. Co-administration not recommended.

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

Concurrent Medication	Recommendation and Clinical Comment
HIV Non Nucleoside Reverse Transcriptase Inhibitors	
Efavirenz (Sustiva®, also contained in Atripla®) Etravirine (Intelence®)	<ul style="list-style-type: none"> Co-administration of sofosbuvir/velpatasvir with efavirenz or etravirine is expected to decrease the concentration of sofosbuvir and velpatasvir, leading to reduced efficacy. Co-administration not recommended.
Nevirapine (Viramune®) Rilpivirine (Edurant®, also in Odefsey® which contains tenofovir alafenamide, Juluca®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate.
Rilpivirine (Edurant®, also in Complera® which contains tenofovir disoproxil fumarate) Doravirine (Pifeltro®, also contained in Delstrigo®)	<ul style="list-style-type: none"> 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	
Bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy®) Dolutegravir (Tivicay®, also contained in Triumeq®, Juluca®) Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®) Raltegravir (Isentress® Isentress HD®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate.
Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®)	<ul style="list-style-type: none"> 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	
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
Abacavir (Ziagen®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Tenofovir Disoproxil Fumarate (Viread® also contained in Cimduo® and Temixys®) Tenofovir Alafenamide (Descovy®) Stavudine (Zerit®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate. Potential increase in tenofovir levels when given as tenofovir disoproxil fumarate; monitor for renal adverse events.
Didanosine (Videx EC®) Zidovudine (Retrovir®)	<ul style="list-style-type: none"> When using ribavirin with sofosbuvir/velpatasvir, the use of didanosine or zidovudine should be avoided due to overlapping toxicity.

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

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

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.