



Simeprevir (Olysio™) and Sofosbuvir (Sovaldi™) Drug Interactions: A Quick Guide for Clinicians – April 2017

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Mechanism of Action and Route of Metabolism for Simeprevir (Olysio™) and Sofosbuvir (Sovaldi™)

Medication	HCV Mechanism of Action	Route of Metabolism and Drug Interaction Potential
Simeprevir (Olysio™)	NS3/4a protease inhibitor	<ul style="list-style-type: none"> Simeprevir is a mild inhibitor of CYP1A2 activity and intestinal CYP3A4, but does not affect hepatic CYP3A4 activity. Simeprevir also inhibits OATP1B1/3 and P-glycoprotein (P-gp) transporters.
Sofosbuvir (Sovaldi™)	NS5b polymerase 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.

Simeprevir (Olysio™) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comment
HIV Protease Inhibitors	
Atazanavir (Reyataz®) Darunavir (Prezista®) Fosamprenavir (Lexiva®) Indinavir (Crixivan®) Lopinavir/ritonavir (Kaletra®) Ritonavir (Norvir®) at any dosage Saquinavir (Invirase®) Tipranavir (Aptivus®)	<ul style="list-style-type: none"> Significant increase or decrease in simeprevir levels expected when used with any HIV protease inhibitor, when used with or without ritonavir. Co-administration not recommended.
HIV Non Nucleoside Reverse Transcriptase Inhibitors	
Efavirenz (Sustiva®) Etravirine (Intelence®) Nevirapine (Viramune®)	<ul style="list-style-type: none"> Significant decrease in simeprevir levels expected when used with efavirenz, etravirine, and nevirapine. Co-administration not recommended.
Rilpivirine (Edurant®, also contained in Complera® and Odefsey®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate.

HIV Entry Inhibitors	
Maraviroc (Selzentry®)	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
HIV Integrase Strand Transfer Inhibitors	
Dolutegravir (Tivicay®)	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®) and Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®)	<ul style="list-style-type: none"> • Significant increase in simeprevir levels expected when used with a cobicistat containing regimen. Co-administration not recommended.
Raltegravir (Isentress®)	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
Abacavir (Ziagen®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Stavudine (Zerit®) Tenofovir disoproxil fumarate (Viread®) Tenofovir alafenamide (Descovy®)	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
Didanosine (Videx EC®) Zidovudine (Retrovir®)	<ul style="list-style-type: none"> • When using ribavirin with simeprevir/sofosbuvir, the use of didanosine or zidovudine should be avoided due to overlapping toxicity.

Primary Care Medications to Avoid with Simeprevir (Olysio™)

Medication and or Class	Recommendation and Clinical Comment
Anticonvulsants - carbamazepine, oxcarbazepine, phenobarbital, phenytoin	<ul style="list-style-type: none"> • Significant decrease in simeprevir levels expected leading to reduced simeprevir efficacy. Co-administration not recommended.
Antibiotics – clarithromycin, erythromycin, telithromycin	<ul style="list-style-type: none"> • Significant increase in simeprevir or antibiotic levels due to CYP3A4 and P-glycoprotein (P-gp) inhibition. Co-administration not recommended.
Antifungals – fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole	<ul style="list-style-type: none"> • Significant increase in simeprevir levels expected due to CYP3A4 inhibition from the antifungals. Co-administration not recommended.
Antimycobacterials – rifampin, rifabutin, rifapentine	<ul style="list-style-type: none"> • Significant decrease in simeprevir levels expected leading to reduced simeprevir efficacy. Co-administration not recommended.
Corticosteroids – dexamethasone	<ul style="list-style-type: none"> • Significant decrease in simeprevir levels expected leading to reduced simeprevir efficacy. Co-administration not recommended.
Propulsive – cisapride	<ul style="list-style-type: none"> • Significant increase in cisapride levels expected leading to potential cardiac arrhythmias. Co-administration not recommended.
Herbal products – Milk Thistle, St. John’s Wort	<ul style="list-style-type: none"> • Significant increase in simeprevir levels expected when used with milk thistle. Co-administration not recommended. • Significant decrease in simeprevir levels expected when used with St. Johns Wort due to intestinal P-glycoprotein (P-gp) induction. Co-administration not recommended.

Primary Care Medications to be Used with Caution with Simeprevir (Olysio™)

Concurrent Medication	Recommendation and Clinical Comment
Digoxin	<ul style="list-style-type: none"> Increased digoxin levels expected, monitor levels
Antiarrhythmics	<ul style="list-style-type: none"> Potential increase in levels, monitor levels if possible
Calcium channel blockers	<ul style="list-style-type: none"> Potential increase in levels, monitor for hypotension
Atorvastatin	<ul style="list-style-type: none"> Increased atorvastatin levels, use lowest doses, do not exceed 40mg daily
Rosuvastatin	<ul style="list-style-type: none"> Increased rosuvastatin levels, initiate with 5mg daily, do not exceed 10 mg daily
Simvastatin, pitavastatin, pravastatin, lovastatin	<ul style="list-style-type: none"> Use lowest dose possible, titrate carefully
Oral midazolam, triazolam	<ul style="list-style-type: none"> Increased levels expected, titrate carefully, use lowest doses

Sofosbuvir (Sovaldi™) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comment
HIV Protease Inhibitors	
Atazanavir (Reyataz®) Darunavir (Prezista®) Fosamprenavir (Lexiva®) Indinavir (Crixivan®) Lopinavir/ritonavir (Kaletra®) Ritonavir (Norvir®) at any dosage Saquinavir (Invirase®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate.
Tipranavir (Aptivus®) + ritonavir (Norvir®)	<ul style="list-style-type: none"> Significant decrease in sofosbuvir levels expected leading to decreased sofosbuvir efficacy. Co-administration not recommended.
HIV Non Nucleoside Reverse Transcriptase Inhibitors	
Efavirenz (Sustiva®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate.
Etravirine (Intelence®) Nevirapine (Viramune®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate.
Rilpivirine (Edurant®, also contained in Complera® and Odefsey®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate.

HIV Integrase Strand Transfer Inhibitors	
Dolutegravir (Tivicay [®] , also contained in Triumeq [®])	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild [®]) and Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya [®])	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
Raltegravir (Isentress [®])	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
HIV Entry Inhibitors	
Maraviroc (Selzentry [®])	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
Abacavir (Ziagen [®]) Emtricitabine (Emtriva [®]) Lamivudine (Epivir [®]) Stavudine (Zerit [®]) Tenofovir disoproxil fumarate (Viread [®]) Tenofovir alafenamide (Descovy [®])	<ul style="list-style-type: none"> • Concurrent use at standard doses appropriate.
Didanosine (Videx EC [®]) Zidovudine (Retrovir [®])	<ul style="list-style-type: none"> • When using ribavirin with simeprevir/sofosbuvir, the use of didanosine or zidovudine should be avoided due to overlapping toxicity.

Non HIV Medications to Avoid with Sofosbuvir (Sovaldi[™]) Therapy

Medication and or Class	Rationale for Avoiding with Sofosbuvir
Antiarrhythmic – Amiodarone	<ul style="list-style-type: none"> • Serious symptomatic bradycardia may occur, concurrent use not recommended. See product information for additional details.
Anticonvulsants – carbamazepine, oxcarbazepine, phenobarbital, phenytoin	<ul style="list-style-type: none"> • Significant decrease in sofosbuvir levels expected leading to reduced sofosbuvir efficacy. Co-administration not recommended.
Antimycobacterials – rifampin, rifabutin, rifapentin	<ul style="list-style-type: none"> • Significant decrease in sofosbuvir levels expected leading to reduced sofosbuvir efficacy due to intestinal P-glycoprotein induction from rifampin. Co-administration not recommended.
Herbal products – St. John's Wort	<ul style="list-style-type: none"> • Significant decrease in sofosbuvir levels expected leading to reduced sofosbuvir efficacy due to intestinal P-glycoprotein induction associated with St. John's Wort. 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 information contained in this guide is 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.