



# Drug Interactions with Hepatitis C Virus Direct Acting Antivirals and HIV Medications: A Quick Guide for Clinicians – Updated February 20, 2014

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Please consult the recent changes to HCV guidelines including specific information for treating patients with HIV/HCV co-infection found at [www.hcvguidelines.org](http://www.hcvguidelines.org). The use of telaprevir and boceprevir are no longer recommended in this update, therefore and information relating to drug interactions with these HCV medications has been removed from this guide. Previous versions that included telaprevir and boceprevir can be found on our website [www.nynjaetc.org](http://www.nynjaetc.org).

## Mechanism of Action and Route of Metabolism for HCV Direct Acting Antivirals

Medication	HCV Mechanism of Action	Route of Metabolism
Sofosbuvir (Sovaldi™)	NS5b polymerase 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> </ul>
Simeprevir (Olysio™)	NS3/4A protease inhibitor	<ul style="list-style-type: none"> <li>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.</li> </ul>

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

Medication and or Class	Rationale for Avoiding with Sofosbuvir
Anticonvulsants – carbamazepine, oxcarbazepine, phenobarbital, phenytoin	<ul style="list-style-type: none"> <li>Co-administration with these medications is likely to reduce concentrations of sofosbuvir leading to reduced sofosbuvir efficacy. Co-administration not recommended.</li> </ul>
Antimycobacterials – rifampin, rifabutin, rifapentin	<ul style="list-style-type: none"> <li>Co-administration with these medications is likely to reduce concentrations of sofosbuvir leading to reduced sofosbuvir efficacy due to intestinal P-glycoprotein (P-gp) induction from rifampin.</li> </ul>
Herbal products – St. John’s Wort	<ul style="list-style-type: none"> <li>Co-administration with this herbal therapy is likely to reduce concentrations of sofosbuvir leading to reduced sofosbuvir efficacy due to intestinal P-glycoprotein (P-gp) induction associated with St. John’s Wort.</li> </ul>

## Sofosbuvir (Sovaldi™) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation
<b>HIV Protease Inhibitors</b>	
Atazanavir (Reyataz®) Darunavir (Prezista®) Fosamprenavir (Lexiva®) Indinavir (Crixivan®) Lopinavir/ritonavir (Kaletra®) Ritonavir (Norvir®) at any dosage Saquinavir (Invirase®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable. Interactions not expected based upon metabolism of sofosbuvir.</li> </ul>
Tipranavir/ritonavir (Aptivus®/Norvir®)	<ul style="list-style-type: none"> <li>Co-administration with these medications is likely to reduce concentrations of sofosbuvir and lead to reduced sofosbuvir efficacy. Co-administration not recommended.</li> </ul>
<b>HIV Non Nucleoside Reverse Transcriptase Inhibitors</b>	
Efavirenz (Sustiva®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable.</li> </ul>
Etravirine (Intelence®) Nevirapine (Viramune®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable. Interactions not expected based upon metabolism of sofosbuvir.</li> </ul>
Rilpivirine (Edurant®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable.</li> </ul>
<b>HIV Integrase Strand Transfer Inhibitors</b>	
Dolutegravir (Tivicay®) Elvitegravir (contained in Stribild®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable. Interactions not expected based upon metabolism of sofosbuvir.</li> </ul>
Raltegravir (Isentress®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable.</li> </ul>
<b>HIV Entry Inhibitors</b>	
Maraviroc (Selzentry®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable. Interactions not expected based upon metabolism of sofosbuvir.</li> </ul>
<b>HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors</b>	
Abacavir (Ziagen®) Didanosine (Videx EC®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Stavudine (Zerit®) Tenofovir (Viread®) Zidovudine (Retrovir®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable. Interactions not expected based upon metabolism of sofosbuvir.</li> </ul>

## Non HIV Medications to Avoid with Simeprevir (Olysio™ )

Medication and or Class	Rationale for Avoiding with Simeprevir
Anticonvulsants - carbamazepine, oxcarbazepine, phenobarbital, phenytoin	<ul style="list-style-type: none"> <li>Co-administration with these medications is likely to reduce concentrations of simeprevir and lead to reduced simeprevir efficacy. Co-administration not recommended.</li> </ul>
Antibiotics – clarithromycin, erythromycin, telithromycin	<ul style="list-style-type: none"> <li>Co-administration with these medications is likely to increase concentrations of either simeprevir or the antibiotic due to CYP3A4 and P-glycoprotein (P-gp) inhibition. Co-administration not recommended.</li> </ul>
Antifungals – fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole	<ul style="list-style-type: none"> <li>Co-administration with these medications is likely to increase concentrations of simeprevir due to CYP3A4 inhibition from the antifungals. Co-administration not recommended.</li> </ul>
Antimycobacterials – rifampin, rifabutin, rifapentine	<ul style="list-style-type: none"> <li>Co-administration with these medications is likely to reduce concentrations of simeprevir and lead to reduced simeprevir efficacy. Co-administration not recommended.</li> </ul>
Corticosteroids – dexamethasone	<ul style="list-style-type: none"> <li>Co-administration with dexamethasone is likely to decrease concentrations of simeprevir and lead to reduced simeprevir efficacy. Co-administration not recommended.</li> </ul>
Propulsive – cisapride	<ul style="list-style-type: none"> <li>Co-administration with cisapride may result in increased concentrations of cisapride leading to potential cardiac arrhythmias.</li> </ul>
Herbal products – Milk Thistle, St. John’s Wort	<ul style="list-style-type: none"> <li>Co-administration with milk thistle is likely to increase concentrations of simeprevir. Co-administration not recommended.</li> <li>Co-administration with St. John’s Wort is likely to reduce concentrations of simeprevir leading to reduced simeprevir efficacy, due to intestinal P-glycoprotein (P-gp) induction associated with St. John’s Wort.</li> </ul>

## Simeprevir (Olysio™) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation
<b>HIV Protease Inhibitors</b>	
Atazanavir (Reyataz®) Fosamprenavir (Lexiva®) Indinavir (Crixivan®) Lopinavir/ritonavir (Kaletra®) Ritonavir (Norvir®) at any dosage Saquinavir (Invirase®) Tipranavir (Aptivus®)	<ul style="list-style-type: none"> <li>Significant increases or decreases in simeprevir levels expected when used with any HIV protease inhibitor, when used with or without ritonavir. Co-administration not recommended</li> </ul>

## Simeprevir (Olysio™) Drug Interactions with HIV Medications, continued

Concurrent Medication	Recommendation
<b>HIV Protease Inhibitors, continued</b>	
Darunavir/ritonavir (Prezista®/Norvir®)	<ul style="list-style-type: none"> <li>Significant increase in simeprevir levels expected when used with daurnavir/ritonavir. Co-administration not recommended.</li> </ul>
<b>HIV Non Nucleoside Reverse Transcriptase Inhibitors</b>	
Efavirenz (Sustiva®) , Etravirine (Intelence®) Nevirapine (Viramune®)	<ul style="list-style-type: none"> <li>Significant reductions in simeprevir levels and reduced simeprevir efficacy due to CYP3A4 induction associated with efavirenz, etravirine, and nevirapine. Co-administration not recommended.</li> </ul>
Rilpivirine (Edurant®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable.</li> </ul>
<b>HIV Integrase Strand Transfer Inhibitors</b>	
Dolutegravir (Tivicay®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable. Interactions not expected based upon metabolism of simeprevir.</li> </ul>
Elvitegravir (contained in Stribild®)	<ul style="list-style-type: none"> <li>Significant increase in simeprevir levels expected when used with a cobicistat containing regimen. Co-administration not recommended.</li> </ul>
Raltegravir (Isentress®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable.</li> </ul>
<b>HIV Entry Inhibitors</b>	
Maraviroc (Selzentry®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable. Interactions not expected based upon metabolism of simeprevir.</li> </ul>
<b>HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors</b>	
Abacavir (Ziagen®) Didanosine (Videx EC®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Stavudine (Zerit®) Tenofovir (Viread®) Zidovudine (Retrovir®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses acceptable. Interactions not expected based upon metabolism of simeprevir.</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.