



# Elbasvir/Grazoprevir (Zepatier™) Drug Interactions

## A Quick Guide for Clinicians – February 2018

John J Faragon, PharmD, BCPS, AAHIVP

### Mechanism of Action and Route of Metabolism for Elbasvir/grazoprevir (Zepatier™)

Medication	HCV Mechanism of Action	Route of Metabolism and Drug Interaction Potential
Elbasvir/grazoprevir (Zepatier™)	NS5a inhibitor and NS3/4A protease inhibitor	<ul style="list-style-type: none"> <li>Elbasvir and grazoprevir are substrates of CYP3A4 and P-glycoprotein (P-gp). Concurrent use of medications that are moderate or severe inhibitors or inducers of CYP3A4 are likely to interact.</li> <li>Grazoprevir is a substrate of OATP1B1/3 transporters. Concurrent use of medications that inhibit OATP1B1/3 should be avoided.</li> </ul>

### Elbasvir/grazoprevir (Zepatier™) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comments
<b>HIV Protease Inhibitors</b>	
Atazanavir (Reyataz®) + ritonavir (Norvir®) Atazanavir/cobicistat (Evotaz™) Darunavir (Prezista®) + ritonavir (Norvir®) Darunavir/cobicistat (Prezcobix™) Lopinavir/ritonavir (Kaletra®) Fosamprenavir (Lexiva®) + ritonavir (Norvir®) Saquinavir (Invirase®) + ritonavir (Norvir®) Tipranavir (Aptivus®) + ritonavir (Norvir®)	<ul style="list-style-type: none"> <li>Co-administration not recommended. Use of elbasvir/grazoprevir with ritonavir boosted protease inhibitors or un-boosted protease inhibitors should be avoided due to potential for hepatotoxicity and increased grazoprevir plasma concentrations.</li> </ul>
<b>HIV Non Nucleoside Reverse Transcriptase Inhibitors</b>	
Efavirenz (Sustiva®, also contained in Atripla®) Etravirine (Intelence®) Nevirapine (Viramune®)	<ul style="list-style-type: none"> <li>Co-administration not recommended. Significant reduction in elbasvir and grazoprevir levels expected which may lead to loss of HCV response.</li> </ul>
Rilpivirine (Edurant®, also contained in Complera®, Odefsey®)	<ul style="list-style-type: none"> <li>Concurrent use at standard doses appropriate.</li> </ul>

## Elbasvir/grazoprevir (Zepatier™) Drug Interactions with HIV Medications, continued

Concurrent Medication	Recommendation and Clinical Comments
<b>HIV Integrase Strand Transfer Inhibitors</b>	
Bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy®) Dolutegravir (Tivicay®, also contained in Triumeq®) Raltegravir (Isentress®, Isentress HD®)	<ul style="list-style-type: none"> <li>• Concurrent use at standard doses appropriate.</li> </ul>
Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®) and Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®)	<ul style="list-style-type: none"> <li>• Co-administration not recommended. Use of elbasvir/grazoprevir with cobicistat containing regimens is likely to increase elbasvir and grazoprevir concentrations.</li> </ul>
<b>HIV Entry Inhibitors</b>	
Maraviroc (Selzentry®)	<ul style="list-style-type: none"> <li>• Use of maraviroc with elbasvir/grazoprevir has not been studied and should be avoided until definitive data available.</li> </ul>
<b>HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors</b>	
Abacavir (Ziagen®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Tenofovir Disoproxil Fumarate (Viread®) Tenofovir Alafenamide (in Descovy®) Stavudine (Zerit®)	<ul style="list-style-type: none"> <li>• Concurrent use at standard doses appropriate.</li> </ul>
Didanosine (Videx EC®) Zidovudine (Retrovir®)	<ul style="list-style-type: none"> <li>• When using ribavirin with elbasvir/grazoprevir, the use of didanosine or zidovudine should be avoided due to overlapping toxicity.</li> </ul>

## Elbasvir/grazoprevir (Zepatier™) Drug Interactions with Common Primary Care Medications

Medication and or Class	Recommendation and Clinical Comments
Antibiotics – nafcillin	<ul style="list-style-type: none"> <li>Decreased concentrations of elbasvir/grazoprevir levels expected. Co-administration not recommended.</li> </ul>
Anticonvulsants – carbamazepine, phenytoin	<ul style="list-style-type: none"> <li>Significant decrease in elbasvir/grazoprevir levels expected. Co-administration not recommended.</li> </ul>
Antifungals – ketoconazole	<ul style="list-style-type: none"> <li>Significant increase in elbasvir/grazoprevir levels expected, increasing risk of hepatotoxicity. Co-administration not recommended.</li> </ul>
Antimycobacterials – rifampin	<ul style="list-style-type: none"> <li>Significant decrease in elbasvir/grazoprevir levels expected. Co-administration not recommended.</li> </ul>
Endothelin Antagonists – bosentan	<ul style="list-style-type: none"> <li>Significant decrease in elbasvir/grazoprevir levels expected. Co-administration not recommended.</li> </ul>
Herbal products – St. John’s Wort	<ul style="list-style-type: none"> <li>Significant decrease in elbasvir/grazoprevir levels expected. Co-administration not recommended.</li> </ul>
HMG-CoA Reductase Inhibitors – atorvastatin, rosuvastatin, fluvastatin, lovastatin, simvastatin	<ul style="list-style-type: none"> <li>Increased statin levels expected with concurrent use of elbasvir/grazoprevir. When using together:                             <ul style="list-style-type: none"> <li>Do not exceed atorvastatin 20mg daily</li> <li>Do not exceed rosuvastatin 10mg daily</li> <li>Use lowest doses and titrate with close monitoring for fluvastatin, lovastatin, simvastatin</li> </ul> </li> </ul>
Immunosuppressants – cyclosporine	<ul style="list-style-type: none"> <li>Significant increase in grazoprevir levels which may lead to hepatotoxicity. Co-administration not recommended.</li> </ul>
Immunosuppressants – tacrolimus	<ul style="list-style-type: none"> <li>Significant increase in tacrolimus levels expected. Frequent monitoring for tacrolimus, changes in renal function, and tacrolimus associated adverse events recommended.</li> </ul>
Wakefulness- Promoting Agents – modafanil	<ul style="list-style-type: none"> <li>Significant decrease in elbasvir/grazoprevir levels expected. Co-administration not recommended.</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.**