




### Antiretroviral Treatment Options for Patients on Directly Acting Antivirals for Hepatitis C

	<b>Daclatasvir (Daklinza®, DCV)</b>	<b>Elbasvir/ Grazoprevir (Zepatier®)</b>	<b>Ledipasvir/ Sofosbuvir (Harvoni®)</b>	<b>Sofosbuvir/ Velpatasvir (Epclusa®)</b>	<b>Sofosbuvir/ Velpatasvir/ Voxilaprevir (Vosevi®)</b>	<b>Holkira Pak®/Viekira Pak® (US)</b> (paritaprevir/ ritonavir, ombitasvir 150/100/25 mg QD plus dasabuvir 250 mg BID)	<b>Glecaprevir/ Pibrentasvir (Mavyret®)</b> *dosed as glecaprevir 300 mg/pibrentasvir 120 mg = 3 tablets once daily
PIs: atazanavir	↓ daclatasvir dose to 30 mg daily with atazanavir/ritonavir or atazanavir/cobicistat. <sup>1,2</sup>	Contraindicated with atazanavir <sup>3</sup> : 10.58-fold ↑ grazoprevir AUC <sup>4</sup> and 4.76-fold ↑ elbasvir exposures. <sup>5</sup>	Potential for ↑ tenofovir concentrations when administered with concomitant booster. Monitor for toxicity. <sup>6-8</sup>	OK with atazanavir/ritonavir <sup>9</sup>	Coadministration not recommended due to ↑ voxilaprevir concentrations. <sup>10</sup>	OK with atazanavir 300 mg QD. <sup>11,12</sup>	Contraindicated due to ↑ risk of ALT elevations. <sup>13</sup>
PIs: other	No dose modifications required with darunavir/ritonavir, darunavir/cobicistat or lopinavir/ritonavir. <sup>2</sup>	Contraindicated with darunavir, lopinavir, saquinavir, tipranavir <sup>3</sup> : 7.5-12.86-fold ↑ grazoprevir AUC <sup>4</sup> and 0.66-3.7-fold ↑ elbasvir exposures. <sup>5</sup>		OK with darunavir/ritonavir, lopinavir/ritonavir. <sup>9</sup>	Darunavir/ritonavir: ↑ voxilaprevir AUC <sup>14</sup> but considered safe. <sup>10</sup>	Darunavir: take without additional ritonavir; monitor HIV viral load due to decreased darunavir Ctrough (Canadian monograph).	Darunavir/ritonavir, lopinavir/ritonavir: coadministration not recommended due to ↑ glecaprevir and pibrentasvir. <sup>13</sup>
					Lopinavir/ritonavir: Coadministration not recommended due to ↑ voxilaprevir concentrations. <sup>10</sup>	US monograph: Not recommended due to potential for decreased darunavir Ctrough. <sup>12</sup>	
					Tipranavir/ritonavir: Coadministration not recommended due to decreased DAA concentrations. <sup>10</sup>	Not recommended with lopinavir/ritonavir due to higher GI side effects and ↑ paritaprevir exposures. <sup>15</sup>	
NNRTIs	↑ daclatasvir dose to 90 mg once daily with efavirenz. <sup>1</sup>	Contraindicated with efavirenz <sup>3</sup> : (84% ↓ grazoprevir	Efavirenz OK. <sup>18</sup>	Do not use with efavirenz (50% ↓ velpatasvir AUC). <sup>19</sup>	Coadministration with efavirenz not recommended due	Contraindicated with efavirenz (increased risk of adverse	Coadministration with efavirenz not recommended due

	<b>Daclatasvir (Daklinza®, DCV)</b>  60 mg daily with sofosbuvir 400 mg daily	<b>Elbasvir/ Grazoprevir (Zepatier®)</b>  100 mg/50 mg coformulation once daily	<b>Ledipasvir/ Sofosbuvir (Harvoni®)</b>  90/400 mg coformulation once daily	<b>Sofosbuvir/ Velpatasvir (Epclusa®)</b>  400/100 mg coformulation once daily	<b>Sofosbuvir/ Velpatasvir/ Voxilaprevir (Vosevi®)</b>  400/100/100 mg coformulation once daily	<b>Holkira Pak®/Viekira Pak® (US)</b> (paritaprevir/ ritonavir, ombitasvir 150/100/25 mg QD plus dasabuvir 250 mg BID)	<b>Glecaprevir/ Pibrentasvir (Mavyret®)</b> *dosed as glecaprevir 300 mg/pibrentasvir 120 mg = 3 tablets once daily
		AUC <sup>16</sup> and 54% ↓ elbasvir AUC. <sup>17</sup>			to decreased velpatasvir and voxilaprevir. <sup>10</sup>	events including LFT elevations). <sup>12, 20</sup>	to possible decreased glecaprevir and pibrentasvir. <sup>13</sup>
	No data. Coadministration not recommended with etravirine or nevirapine due to potential for ↓ daclatasvir. <sup>21</sup>	Not recommended with etravirine <sup>3</sup> due to potential for decreased elbasvir and grazoprevir concentrations.		Avoid or use with caution until further data available.	Avoid or use with caution until further data available.	Etravirine contraindicated due to risk of decreased 3D exposures. <sup>12</sup>	Avoid or use with caution until further data available.
	Rilpivirine OK. <sup>21, 22</sup>	Rilpivirine OK. <sup>23</sup>	Rilpivirine OK. <sup>18</sup> Rilpivirine/FTC/TAF: OK. <sup>24</sup>	Rilpivirine OK. <sup>19</sup>	Rilpivirine OK. <sup>10</sup>	Not recommended with rilpivirine (116-273% ↑ rilpivirine exposures). <sup>20</sup>	Rilpivirine OK. <sup>25</sup>
InSTIs	Dolutegravir OK. <sup>21, 26</sup>	Dolutegravir OK. <sup>27</sup>	Dolutegravir OK. Monitor for tenofovir-associated toxicities if using tenofovir-based backbone. <sup>28</sup>	Dolutegravir OK. <sup>19</sup>	Dolutegravir OK. <sup>10</sup>	Dolutegravir OK. <sup>29</sup>	Dolutegravir OK. <sup>30</sup>
	Raltegravir OK. <sup>22</sup>	Raltegravir OK. <sup>17, 31</sup>	Raltegravir OK. <sup>18</sup>	Raltegravir OK. <sup>19</sup>	Raltegravir OK. <sup>10</sup>	Raltegravir OK. <sup>12, 20</sup>	Raltegravir OK. <sup>25</sup>
	↓ daclatasvir dose to 30 mg daily with cobicistat <sup>21</sup>	Not recommended with elvitegravir/co/FTC/TDF due to increased elbasvir (2.2-fold increase) and grazoprevir (5.4-fold increase)	Potential for ↑ tenofovir concentrations when administered with concomitant booster. Monitor for toxicity. <sup>7, 8</sup>	Elvitegravir/co/FTC/TDF: 40% ↑ tenofovir AUC. Monitor for toxicity. <sup>9</sup>	Elvitegravir/co/FTC/TDF: 40% ↑ tenofovir AUC. Monitor for toxicity. <sup>10</sup>	Do not coadminister elvitegravir/cobicistat since paritaprevir and ombitasvir are coformulated with ritonavir.	Elvitegravir/cobicistat OK. <sup>30</sup>

	<b>Daclatasvir (Daklinza<sup>®</sup>, DCV)</b>  60 mg daily with sofosbuvir 400 mg daily	<b>Elbasvir/ Grazoprevir (Zepatier<sup>®</sup>)</b>  100 mg/50 mg coformulation once daily	<b>Ledipasvir/ Sofosbuvir (Harvoni<sup>®</sup>)</b>  90/400 mg coformulation once daily	<b>Sofosbuvir/ Velpatasvir (Epclusa<sup>®</sup>)</b>  400/100 mg coformulation once daily	<b>Sofosbuvir/ Velpatasvir/ Voxilaprevir (Vosevi<sup>®</sup>)</b>  400/100/100 mg coformulation once daily	<b>Holkira Pak<sup>®</sup>/Viekira Pak<sup>®</sup> (US)</b> (paritaprevir/ritonavir, ombitasvir 150/100/25 mg QD plus dasabuvir 250 mg BID)	<b>Glecaprevir/ Pibrentasvir (Mavyret<sup>®</sup>)</b> *dosed as glecaprevir 300 mg/pibrentasvir 120 mg = 3 tablets once daily
		concentrations. <sup>32</sup>					
			NB: US monograph: combination not recommended. <sup>6</sup>				
		Avoid with elvitegravir/co/FTC/TAF (as above).	Elvitegravir/co/FTC/TAF: OK. <sup>28</sup>	Elvitegravir/co/FTC/TAF: OK. <sup>9</sup>	Elvitegravir/co/FTC/TAF: ↑ voxilaprevir AUC <sup>14</sup> but considered safe. <sup>10</sup>		
Maraviroc	Standard doses of both OK. <sup>21</sup>						
NRTIs	Tenofovir DF OK. <sup>1</sup>	Tenofovir DF OK. <sup>17, 31</sup>	Potential for ↑ tenofovir concentrations. Monitor for toxicity. <sup>8</sup>	Potential for 40-81% ↑ tenofovir concentrations. Monitor for toxicity. <sup>33</sup>	Potential for ↑ tenofovir concentrations. Monitor for toxicity. <sup>10</sup>	Tenofovir DF OK. <sup>11, 12</sup>	Tenofovir DF OK. <sup>13</sup>
			Tenofovir alafenamide OK. <sup>24</sup>	Tenofovir alafenamide OK. <sup>33</sup>	Tenofovir alafenamide OK. <sup>10</sup>		Tenofovir alafenamide OK. <sup>30</sup>

Key:  = avoid combination     = caution/dose adjustment     = combination OK

Co=cobicistat; FTC= emtricitabine; TAF= tenofovir alafenamide; TDF= tenofovir disoproxil fumarate

## References:

1. Bifano M, Hwang C, Oosterhuis B, et al. Assessment of HIV ARV drug interactions with the HCV NS5A replication complex inhibitor BMS-790052 demonstrates a pharmacokinetic profile which supports co-administration with tenofovir disoproxil fumarate, efavirenz, and atazanavir/ritonavir [abstract 618]. 19th Conference on Retroviruses and Opportunistic Infections, March 5-8, 2012, Seattle, WA.
2. Eley T, You X, Wang R, et al. Daclatasvir: Overview of drug–drug interactions with antiretroviral agents and other common concomitant drugs [abstract]. HIV DART, December 9-12, 2014, Miami, FL.
3. Merck Canada Inc. Zepatier (elbasvir/grazoprevir) Product Monograph. Kirkland, QD January 19, 2016.
4. Caro L, Talaty JE, Guo Z, et al. Pharmacokinetic interactions between the HCV protease inhibitor MK-5172 and ritonavir-boosted hiv protease inhibitors (atazanavir, lopinavir, darunavir) in healthy volunteers [abstract 487]. 64th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD), November 1-5, 2013, Washington, DC.
5. Yeh WY, Marshall W, Ma J, et al. Ritonavir-boosted atazanavir, lopinavir, & darunavir increase HCV NS5A inhibitor MK-8742 levels [abstract 635]. Conference on Retroviruses and Opportunistic Infections (CROI), March 3-6, 2014, Boston, MA.
6. Gilead Sciences Inc. Harvoni (ledipasvir/sofosbuvir) Product Monograph. Foster City, CA October, 2014.
7. Gilead Sciences Canada Inc. Harvoni (ledipasvir/sofosbuvir) Product Monograph. Mississauga, ON October 14, 2014.
8. German P, Garrison K, Pang P, et al. Drug-drug interactions between anti-HCV regimen ledipasvir/sofosbuvir and antiretrovirals [abstract 82]. Conference on Retroviruses and Opportunistic Infections (CROI), February 23-26, 2015, Seattle, WA.
9. Mogalian E, Stamm L, Osinusi A, et al. Drug interaction studies between sofosbuvir/velpatasvir and boosted HIV ARV regimens [abstract 100]. Conference on Retroviruses and Opportunistic Infections (CROI), February 22-25, 2016, Boston, MA.
10. Gilead Sciences I. Vosevi (sofosbuvir, velpatasvir, and voxilaprevir) Product Monograph. Foster City, CA July, 2017.
11. Menon R, Badri P, Khatri A, et al. ABT-450/ritonavir +ombitasvir + dasabuvir: drug interactions mediated by transporters. 15th International Workshop on Clinical Pharmacology of HIV & Hepatitis Therapy, May 19-21, 2014, Washington, DC.
12. Abbvie Corporation. Viekira Pak (ombitasvir, paritaprevir and ritonavir tablets; dasabuvir tablets) Prescribing Information. North Chicago, IL December, 2014.
13. Abbvie Inc. Mavyret (glecaprevir and pibrentasvir) Prescribing Information. North Chicago, IL. August 2017, 2017.

14. Garrison K, Mogalian E, Zhang H, et al. Evaluation of drug-drug interactions between sofosbuvir/velpatasvir/voxilaprevir and boosted or unboosted HIV antiretroviral regimens [Abstract O\_20]. 18th International Workshop on Clinical Pharmacology of Antiviral Therapy, June 14-16, 2017, Chicago, IL.
15. Khatri A, Dutta S, Wang H, et al. Evaluation of drug-drug interactions between hepatitis C antiviral agents ombitasvir, paritaprevir/ritonavir, and dasabuvir and HIV-1 protease inhibitors. Clin Infect Dis 2016;Jan 5 [Epub ahead of print].
16. Talaty JE, Caro L, Yeh W, et al. Pharmacokinetic interaction between the HCV protease inhibitor MK-5172 and efavirenz in normal healthy volunteers [abstract 492]. 64th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD), November, 2013, Washington, DC.
17. Yeh W, Marshall W, Mangin E, et al. Pharmacokinetic interactions between the HCV NS5A inhibitor MK-8742 and efavirenz [abstract 498]. Conference on Retroviruses and Opportunistic Infections (CROI), March 3-6, 2014, Boston, MA.
18. German P, Pang P, West S, et al. Drug interactions between direct acting anti-HCV antivirals sofosbuvir and ledipasvir and HIV antiretrovirals [abstract O\_06]. 15th International Workshop on Clinical Pharmacology of HIV and Hepatitis Therapy, May 19-21, 2014, Washington, DC.
19. Mogalian E, Stamm L, Osinusi A, et al. Drug-drug interaction studies between hepatitis C virus antivirals sofosbuvir and velpatasvir (GS-5816) and HIV antiretroviral therapies [abstract]. American Association for the Study of Liver Diseases (AASLD) Meeting, November 13-17, 2015, San Francisco, CA.
20. Khatri A, Wang T, Wang H, et al. Drug-drug interactions of the direct acting antiviral regimen of ABT-450/r, ombitasvir and dasabuvir with emtricitabine + tenofovir, raltegravir, rilpivirine and efavirenz [abstract V-483]. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), September 5-9, 2014, Washington, DC.
21. Bristol-Myers-Squibb. Daklinza (daclatasvir) Summary of Product Characteristics. European Union 2014.
22. Taburet AM, Piroth L, Paniez H, et al. Pharmacokinetics of asunaprevir, daclatasvir and raltegravir in HCV/HIV co infected patients, with or without cirrhosis, and previously null responders to pegylated interferon + ribavirin (ANRS HC30 - QUADRIH study) [abstract 1967]. American Association for the Study of Liver Diseases The Liver Meeting (AASLD), November 7-11, 2014, Boston, MA.
23. Yeh W, Feng HP, Auger P, et al. No pharmacokinetic interaction between HCV inhibitors grazoprevir/elbasvir with rilpivirine [abstract 63]. 16th International Workshop on Clinical Pharmacology of HIV & Hepatitis Therapy, May 26-28, 2015, Washington, DC.
24. Custodio J, Doyle E, Pang PS, et al. Lack of drug interactions between boosted and unboosted tenofovir alafenamide-based antiretroviral single tablet regimens (emtricitabine/rilpivirine/tenofovir alafenamide and elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) and the anti-hcv single tablet regimen ledipasvir/sofosbuvir [abstract 727]. ID Week, October 7-11, 2015, San Diego, CA.
25. Oberoi RK, Kosloski MP, Ding B, et al. Interactions between ABT-493 plus ABT-530 combination and rilpivirine or raltegravir [abstract 453]. Conference on Retroviruses and Opportunistic Infections (CROI), February 22-25, 2016, Boston, MA.

26. Song I, Jerva F, Zong J, et al. Evaluation of drug interactions between dolutegravir and daclatasvir in healthy subjects [abstract 79]. 16th International Workshop on Clinical Pharmacology of HIV & Hepatitis Therapy, May 26-28, 2015, Washington, DC.
27. Yeh W, Feng HP, Guo Z, et al. Drug-drug interaction between HCV inhibitors grazoprevir/elbasvir with dolutegravir [abstract 522]. Conference on Retroviruses and Opportunistic Infections (CROI), February 23-26, 2015, Seattle, WA.
28. Garrison K, Custodio J, Pang P, et al. Drug interactions between anti-HCV antivirals ledipasvir/sofosbuvir and integrase strand transfer inhibitor-based regimens [abstract 71]. 16th International Workshop on Clinical Pharmacology of HIV & Hepatitis Therapy, May 26-28, 2015, Washington, DC.
29. Khatri A, Trinh R, Zhao W, et al. Drug-drug interactions of ombitasvir/paritaprevir/r plus dasabuvir with dolutegravir or abacavir plus lamivudine [abstract 57]. 16th International Workshop on Clinical Pharmacology of HIV & Hepatitis Therapy, May 26-28, 2015, Washington, DC.
30. Kosloski MP, Dutta S, Viani RM, et al. Glecaprevir and pibrentasvir interactions with combination antiretroviral regimens [abstract 413]. Conference on Retroviruses and Opportunistic Infections (CROI), February 13-16, 2017, Seattle, WA.
31. Yeh W, Fraser IP, Caro L, et al. No meaningful PK interaction between HCV protease inhibitor MK-5172 and tenofovir or raltegravir [abstract 500]. 21st Conference on Retroviruses and Opportunistic Infections (CROI), Mar 3-6, 2014, Boston, MA.
32. Feng HP, Caro L, Guo Z, et al. A clinically meaningful drug-drug interaction observed between Zepatier (grazoprevir/elbasvir) and Stribild HIV fixed-dose combination in health subjects [abstract O\_22]. 17th International Workshop on Clinical Pharmacology of HIV and Hepatitis Therapy, June 8-10, 2016, Washington, DC.
33. Mogalian E, McNally J, Shen G, et al. Drug-drug interaction profile of sofosbuvir/velpatasvir fixed-dose combination [abstract FRI-168]. The International Liver Congress, April 13-17, 2016, Barcelona, Spain.