



Ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira XR™) Drug Interactions – A Quick Guide for Clinicians – April 2017

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Mechanism of Action and Route of Metabolism for Ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira XR™)

Medication	HCV Mechanism of Action	Route of Metabolism and Drug Interaction Potential
Ombitasvir	NS5a inhibitor	<ul style="list-style-type: none"> Metabolized via amide hydrolysis, and then oxidative metabolism
Paritaprevir	NS3/4a protease inhibitor	<ul style="list-style-type: none"> Metabolized via CYP3A4, and to a lesser extent CYP3A5
Ritonavir	Not active against HCV, ritonavir acts as a pharmacokinetic booster for paritaprevir	<ul style="list-style-type: none"> Metabolized via CYP3A4, and to a lesser extent CYP2D6
Dasabuvir	Non-nucleoside NS5b polymerase inhibitor	<ul style="list-style-type: none"> Metabolized via CYP2C8, and to a lesser extent CYP3A4

Ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira XR™) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comment
HIV Protease Inhibitors	
Atazanavir/ritonavir (Reyataz®/Norvir®)	<ul style="list-style-type: none"> When using atazanavir with ombitasvir/paritaprevir/ritonavir and dasabuvir, give atazanavir without supplemental ritonavir in the morning. Take atazanavir at the same time as ombitasvir/paritaprevir/ritonavir to allow for appropriate PK boosting of atazanavir.
Darunavir/ritonavir (Prezista®/Norvir®)	<ul style="list-style-type: none"> Decrease in darunavir trough levels when combined with ombitasvir/paritaprevir/ritonavir and dasabuvir. Do not co-administer.
Lopinavir/ritonavir (Kaletra®)	<ul style="list-style-type: none"> Increase in paritaprevir levels when ombitasvir/paritaprevir/ritonavir and dasabuvir was combined with lopinavir/ritonavir. Do not co-administer.
Fosamprenavir (Lexiva®) Ritonavir (Norvir®) at any dosage Saquinavir (Invirase®) Tipranavir (Aptivus®)	<ul style="list-style-type: none"> Significant interactions likely and difficult to predict. Do not co-administer.

Ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira XR™) Drug Interactions with HIV Medications, continued

Concurrent Medication	Recommendation and Clinical Comment
HIV Non Nucleoside Reverse Transcriptase Inhibitors	
Efavirenz (Sustiva®, also in Atripla®)	<ul style="list-style-type: none"> Use of ombitasvir/paritaprevir/ritonavir with efavirenz resulted in poor tolerability and increased liver enzymes. Contraindicated; Do not co-administer.
Etravirine (Intelence®) Nevirapine (Viramune®)	<ul style="list-style-type: none"> Use of ombitasvir/paritaprevir/ritonavir and dasabuvir with etravirine or nevirapine has not been studied. Interaction likely to lead to reduced ombitasvir/paritaprevir/ritonavir and dasabuvir levels. Do not co-administer.
Rilpivirine (Edurant®, also contained in Complera®, Odefsey®)	<ul style="list-style-type: none"> Increased rilpivirine levels when combined with ombitasvir/paritaprevir/ritonavir and dasabuvir leading to potential QT prolongation. Do not co-administer.
HIV Integrase Strand Transfer Inhibitors	
Raltegravir (Isentress®)	<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"> Use of cobicistat containing regimens with ombitasvir/paritaprevir/ritonavir with dasabuvir has not been studied. Do not co-administer.
Dolutegravir (Tivicay®, also in Triumeq®)	<ul style="list-style-type: none"> Concurrent use at standard doses appropriate.
HIV Entry Inhibitors	
Maraviroc (Selzentry®)	<ul style="list-style-type: none"> Use of maraviroc and ombitasvir/paritaprevir/ritonavir with dasabuvir has not been studied. Do not co-administer.
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
Abacavir (Ziagen®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Tenofovir disoproxil fumarate (Viread®) Tenofovir alafenamide (in Descovy®) Stavudine (Zerit®)	<ul style="list-style-type: none"> Concurrent use at standard doses acceptable. While only tenofovir/emtricitabine was allowed in co-infection studies of ombitasvir/paritaprevir/ritonavir with dasabuvir, these other medications are unlikely to interact.
Didanosine (Videx EC®) Zidovudine (Retrovir®)	<ul style="list-style-type: none"> When using ribavirin with ombitasvir/paritaprevir/ritonavir with dasabuvir, the use of didanosine or zidovudine should be avoided due to overlapping toxicity.

Medications Contraindicated or to be Avoided with Ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira XR™)

Medication and or Class	Rationale for Avoiding with ombitasvir/paritaprevir/ritonavir with dasabuvir
Alpha 1-antagonist (alfluzosin)	<ul style="list-style-type: none"> Significant increase in alfluzosin levels and potential for severe hypotension. Contraindicated; Do not co-administer.
Anticonvulsants (carbamazepine, oxcarbazepine, phenytoin, phenobarbital)	<ul style="list-style-type: none"> Significant decrease in ombitasvir/paritaprevir/ritonavir and dasabuvir likely due to CYP450 induction from anticonvulsant. Contraindicated; Do not co-administer
Antifungal (voriconazole)	<ul style="list-style-type: none"> Significant decrease in voriconazole levels likely when used with ombitasvir/paritaprevir/ritonavir with dasabuvir. Do not co-administer unless other options unavailable. (See next page for information on ketoconazole)
Antihyperlipidemic (gemfibrozil)	<ul style="list-style-type: none"> Significant (10-fold) increase in dasabuvir levels leading to increased risk of QT prolongation when taken with gemfibrozil. Contraindicated; Do not co-administer.
Antimycobacterial (rifampin)	<ul style="list-style-type: none"> Significant decrease in ombitasvir/paritaprevir/ritonavir and dasabuvir likely leading to HCV treatment failure. Contraindicated; Do not co-administer.
Beta adrenoceptor agonist (long acting salmeterol)	<ul style="list-style-type: none"> Potential increased risk of cardiovascular adverse events, including QT prolongation, palpitations and sinus tachycardia when combined with ombitasvir/paritaprevir/ritonavir and dasabuvir. Avoid concurrent use.
Corticosteroids (inhaled or nasal fluticasone)	<ul style="list-style-type: none"> Significant increase in fluticasone levels with nasal or inhaled use which can lead to Cushing's Syndrome. Avoid concurrent use. Select alternative corticosteroid, such as beclomethasone, especially for long term use.
Ergot derivatives (ergotamine, dihydroergotamine, ergonovine, methylergonovine)	<ul style="list-style-type: none"> Significant increase in ergot derivative levels likely leading to acute ergot toxicity characterized by vasospasm, tissue ischemia. Contraindicated; Do not co-administer.
Ethinyl estradiol containing products (Oral contraceptives)	<ul style="list-style-type: none"> Liver function test (ALT) elevations associated with concurrent use of ethinyl estradiol and ombitasvir/paritaprevir/ritonavir with dasabuvir. Contraindicated; Do not co-administer.
Herbal therapy (St. John's Wort)	<ul style="list-style-type: none"> Significant decrease in ombitasvir/paritaprevir/ritonavir and dasabuvir levels due to CYP450 induction associated with St. John's Wort. Contraindicated; do not co-administer.
HMG-CoA reductase inhibitors (lovastatin, simvastatin)	<ul style="list-style-type: none"> Significant increase in lovastatin and simvastatin levels likely when used with ombitasvir/paritaprevir/ritonavir and dasabuvir. Contraindicated; do not co-administer. (See next page for dosing of other statins)
Neuroleptic (pimozide)	<ul style="list-style-type: none"> Increase levels of pimozide likely leading to cardiac arrhythmias. Contraindicated; do not co-administer.

Medication and or Class	Rationale for Avoiding with ombitasvir/paritaprevir/ritonavir with dasabuvir
Phosphodiesterase-5 inhibitor (sildenafil when used in Pulmonary Arterial Hypertension)	<ul style="list-style-type: none"> Increased potential for sildenafil adverse events such as priapism, visual disturbances and hypotension when dosed for treatment of pulmonary hypertension. Contraindicated; Do not co-administer.
Sedative/hypnotics (oral midazolam, triazolam)	<ul style="list-style-type: none"> Significant increases in oral midazolam and triazolam when used with ombitasvir/paritaprevir/ritonavir and dasabuvir. Contraindicated; Do not co-administer.

Medications Requiring Adjustment or Monitoring with Ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira XR™)

Medication and or Class	Recommendation and Clinical Comment
Antiarrhythmics (amiodarone, bepredil, disopyramide, flecainide, lidocaine, mexilitine, propafenone, quinidine)	<ul style="list-style-type: none"> Caution with concurrent use. Therapeutic concentration monitoring recommended if available when used with ombitasvir/paritaprevir/ritonavir and dasabuvir.
Angiotensin Receptor Blockers (candesartan, olmesartan, telmisartan)	<ul style="list-style-type: none"> Consider dosage reduction when using ARBs with ombitasvir/paritaprevir/ritonavir and dasabuvir; monitor closely for hypotension.
Antifungal (ketoconazole)	<ul style="list-style-type: none"> When using ketoconazole with ombitasvir/paritaprevir/ritonavir and dasabuvir, the dose of ketoconazole should not exceed 200mg daily.
Calcium channel blocker (amlodipine, diltiazem, felodipine, nicardipine, nifedipine, nisoldipine, verapamil)	<ul style="list-style-type: none"> Consider dosage reduction for calcium channel blockers; monitor closely for hypotension and bradycardia.
Diuretic (furosemide)	<ul style="list-style-type: none"> Possible increase in furosemide levels; monitor closely based upon response.
HMG-CoA reductase inhibitors (atorvastatin, pravastatin and rosuvastatin)	<ul style="list-style-type: none"> Increase in atorvastatin, pravastatin and rosuvastatin likely requiring dosage limitations. Do not exceed atorvastatin 20mg, pravastatin 40mg, or rosuvastatin 10mg with concurrent use of ombitasvir/paritaprevir/ritonavir and dasabuvir.
Immunosuppressants (cyclosporine, tacrolimus)	<ul style="list-style-type: none"> Reduce cyclosporine dose to 1/5th of current dosage upon initiation of ombitasvir/paritaprevir/ritonavir and dasabuvir. Monitor cyclosporine levels. Upon discontinuation of ombitasvir/paritaprevir/ritonavir and dasabuvir, resumption of previous cyclosporine dose should be based upon therapeutic drug monitoring. Tacrolimus dosing needs to be reduced when used with ombitasvir/paritaprevir/ritonavir and dasabuvir. Do not administer tacrolimus on the day ombitasvir/paritaprevir/ritonavir and dasabuvir is administered, the day after ombitasvir/paritaprevir/ritonavir and dasabuvir is administered, reinstate tacrolimus at a reduced dose based upon tacrolimus levels. Typical tacrolimus dosing is 0.5mg once weekly. Measure tacrolimus levels and adjust accordingly. Upon discontinuation of ombitasvir/paritaprevir/ritonavir and dasabuvir, resumption of previous tacrolimus dose should be based upon therapeutic drug monitoring.

Medication and or Class	Recommendation and Clinical Comment
Narcotic analgesics (buprenorphine/naloxone)	<ul style="list-style-type: none"> • No dosage adjustment is required, however monitoring for sedation is appropriate.
Phosphodiesterase-5 inhibitor (when used for erectile dysfunction)	<ul style="list-style-type: none"> • If patients receiving sildenafil for erectile dysfunction, recommended dose is 25mg maximum in a 48 hour period. • In patients receiving tadalafil for erectile dysfunction, recommended dose is 10mg maximum in a 72 hour period. • In patients receiving vardenafil for erectile dysfunction, recommended dose is 2.5mg
Proton pump inhibitor (omeprazole)	<ul style="list-style-type: none"> • Monitor for decreased efficacy of omeprazole. Consider increasing omeprazole dose in patients not well controlled. Do not exceed omeprazole 40mg daily.
Sedative/hypnotic (alprazolam)	<ul style="list-style-type: none"> • Monitor for excess sedation. Decrease in alprazolam dose can be considered based upon response.

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.