

# ANTIRETROVIRAL CONTRAINDICATIONS AND DRUG INTERACTIONS (Part 1 of 5)

Generic & Class	Brand & Company	Contraindications and Drug Interactions†
<b>CCR5 Co-Receptor Antagonists</b>		
maraviroc (MVC)	<b>Selzentry</b> (Pfizer)	<ul style="list-style-type: none"> <li>• Severe renal impairment or ESRD (CrCl &lt;30mL/min) patients taking concomitant potent CYP3A inhibitors or inducers.</li> <li>• Concomitant St. John's wort: not recommended.</li> <li>• May affect, or be affected by, CYP3A inhibitors or inducers and drugs affected by p-glycoprotein (eg, potentiated by ketoconazole, lopinavir/ritonavir, ritonavir, darunavir/ritonavir, saquinavir/ritonavir, atazanavir; antagonized by rifampin, etravirine, efavirenz).</li> <li>• Caution with antihypertensives.</li> </ul>
<b>Fusion Inhibitors</b>		
enfuvirtide (ENF, T-20)	<b>Fuzeon</b> (Roche)	<ul style="list-style-type: none"> <li>• May cause false (+) ELISA test for HIV.</li> </ul>
<b>HIV-1 Integrase Strand Transfer Inhibitors</b>		
raltegravir (RAL)	<b>Isentress</b> (Merck)	<ul style="list-style-type: none"> <li>• Antagonized by rifampin, possibly other strong UGT1A1 inducers. May be potentiated by UGT1A1 inhibitors.</li> <li>• Caution with other drugs that can cause myopathy (eg, statins).</li> </ul>
<b>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)</b>		
delavirdine mesylate (DLV)	<b>Rescriptor</b> (Pfizer)	<ul style="list-style-type: none"> <li>• <b>CYP3A substrates that may cause serious events if blood levels are elevated (eg, cisapride, pimozide, alprazolam, midazolam, triazolam, ergots).</b></li> <li>• Concomitant lovastatin or simvastatin, NNRTIs: not recommended.</li> <li>• May increase levels of antiarrhythmics (eg, bepridil, quinidine), calcium channel blockers (eg, nifedipine), clarithromycin, rifabutin, indinavir, saquinavir, maraviroc (monitor ALT/AST), amprenavir, amphetamines, tetracycline, warfarin, sildenafil, atorvastatin, fluvastatin, immunosuppressants, methadone, fluticasone (long-term use); serious or life-threatening adverse reactions may occur with some of these drugs (avoid or adjust dose).</li> <li>• Delavirdine levels may be decreased by phenytoin, phenobarbital, carbamazepine, rifabutin, rifampin, chronic H<sub>2</sub> antagonists or PPIs, dexamethasone, St. John's wort: not recommended; didanosine and vice versa (separate dosing by at least 1 hour).</li> <li>• Delavirdine levels increased by fluoxetine, ketoconazole.</li> <li>• Absorption reduced by antacids (separate dosing by at least 1 hour).</li> <li>• Reduce indinavir dose (consider indinavir 600mg three times daily).</li> </ul>
efavirenz (EVF)	<b>Sustiva</b> (Bristol Myers-Squibb)	<ul style="list-style-type: none"> <li>• <b>Concomitant bepridil, cisapride, ergots, midazolam, triazolam, pimozide, St. John's wort.</b></li> <li>• Avoid concomitant other efavirenz-containing products (eg, Atripla), atazanavir (treatment-experienced), posaconazole, alcohol, psychoactive and/or other hepatotoxic drugs.</li> <li>• Caution with drugs metabolized by, or that affect activity of, CYP2C9, CYP2C19, CYP3A4.</li> <li>• Efavirenz levels decreased by carbamazepine, phenytoin, phenobarbital, rifampin, rifabutin.</li> <li>• May decrease levels of indinavir (increase indinavir to 1g every 8 hours), amprenavir, atazanavir, clarithromycin, calcium channel blockers (eg, diltiazem, felodipine, nifedipine, verapamil), itraconazole, ketoconazole, lopinavir (adjust dose: see literature), maraviroc, raltegravir, bupropion, methadone, rifabutin (increase dose: see literature), sertraline, simvastatin, atorvastatin, pravastatin, progestins (eg, norelgestromin, levonorgestrel), etonogestrel, immunosuppressants (eg, cyclosporine, sirolimus, tacrolimus).</li> <li>• Efavirenz increases nelfinavir plasma levels.</li> <li>• May affect or be affected by voriconazole (adjust dose).</li> <li>• Levels of both drugs increased with ritonavir (monitor liver function and for adverse events).</li> <li>• Levels of both drugs are decreased with telaprevir, or saquinavir (do not use as sole protease inhibitor).</li> <li>• Closely monitor warfarin, anticonvulsants (esp. phenytoin, phenobarbital, carbamazepine), rifabutin, others.</li> <li>• May cause false (+) cannabis screening test (CEDIA DAU multi-level THC assay).</li> </ul>
etravirine (ETR)	<b>Intelence</b> (Tibotec)	<ul style="list-style-type: none"> <li>• Concomitant tipranavir/ritonavir, fosamprenavir/ritonavir, atazanavir/ritonavir, PIs without ritonavir (eg, atazanavir, fosamprenavir, nelfinavir, indinavir), ritonavir (600mg twice daily), NNRTIs (eg, efavirenz, nevirapine, delavirdine): not recommended.</li> <li>• Avoid rifampin, rifapentine, St. John's wort, carbamazepine, phenytoin, phenobarbital; rifabutin with darunavir/ritonavir.</li> <li>• May affect, or be affected by, drugs that induce or inhibit, or that are substrates of, CYP3A4, CYP2C9, CYP2C19 (eg, azole antifungals, immunosuppressants); monitor.</li> <li>• Potentiated by lopinavir/ritonavir.</li> <li>• May antagonize antiarrhythmics (eg, amiodarone, bepridil, disopyramide, flecainide, lidocaine, mexiletine, propafenone, quinidine) (monitor), sildenafil.</li> <li>• May potentiate warfarin, diazepam.</li> <li>• May be antagonized by anticonvulsants, dexamethasone.</li> <li>• Clarithromycin (consider azithromycin for treating IMAC).</li> <li>• Adjust statin dose (except pravastatin, rosuvastatin).</li> <li>• Rifabutin (adjust dose with etravirine monotherapy).</li> </ul>
nevirapine (NVP)	<b>Viramune</b> (Boehringer Ingelheim) <b>Viramune XR</b> (Boehringer Ingelheim)	<ul style="list-style-type: none"> <li>• <b>Moderate-to-severe hepatic impairment.</b></li> <li>• Potentiated by fluconazole (monitor).</li> <li>• Antagonizes ketoconazole, oral contraceptives: not recommended (use nonhormonal contraception), clarithromycin (consider alternative).</li> <li>• Antagonized by St. John's wort, rifampin: not recommended.</li> <li>• May antagonize methadone (monitor for withdrawal symptoms; increase methadone dose if needed), or drugs metabolized by CYP3A4 or CYP2B6.</li> <li>• Monitor warfarin, rifabutin, other CYP450 substrates.</li> </ul>
rilpivirine	<b>Edurant</b> (Janssen)	<ul style="list-style-type: none"> <li>• <b>Concomitant carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole, dexamethasone (more than single dose), St. John's wort.</b></li> <li>• Concomitant NNRTIs: not recommended.</li> <li>• May affect, or be affected by CYP3A inhibitors or inducers (see Contraindications).</li> <li>• May antagonize azole antifungals (monitor for breakthrough fungal infections), or methadone (monitor).</li> <li>• Separate antacids (by ≥2 hours before or ≥4 hours after) and H<sub>2</sub>-receptor antagonists (by ≥12 hours before or 4 hours after).</li> <li>• Drugs that increase gastric pH may result in decreased plasma concentrations.</li> <li>• Caution with drugs with a known risk for torsades de pointes.</li> </ul>

(continued)

# ANTIRETROVIRAL CONTRAINDICATIONS AND DRUG INTERACTIONS (Part 2 of 5)

Generic & Class	Brand & Company	Contraindications and Drug Interactions†
<b>Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)</b>		
abacavir sulfate (ABC)	<b>Ziagen</b> (GlaxoSmithKline)	<ul style="list-style-type: none"> <li>• See literature regarding fatal hypersensitivity reactions (which may include fever, rash, fatigue, nausea, vomiting, diarrhea, abdominal pain, or respiratory symptoms); discontinue as soon as suspected; do not restart, regardless of HLA-B*5701 status.</li> <li>• Moderate or severe hepatic impairment.</li> <li>• May antagonize methadone.</li> <li>• May be potentiated by ethanol.</li> <li>• Triple therapy (once daily regimen) with lamivudine + tenofovir: high rate of early viral non-response (see literature).</li> </ul>
abacavir (ABC)/lamivudine (3TC)	<b>Epzicom</b> (GlaxoSmithKline)	<ul style="list-style-type: none"> <li>• See literature re: fatal hypersensitivity reactions; signs/symptoms include: fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise/fatigue, or respiratory symptoms; discontinue as soon as suspected; do not restart, regardless of HLA-B*5701 status.</li> <li>• Hepatic impairment.</li> <li>• Avoid concomitant zalcitabine or other forms of abacavir, lamivudine.</li> <li>• Do not combine with other nucleoside/nucleotide reverse transcriptase inhibitors as part of a triple-drug regimen.</li> <li>• Potentiated by ethanol, TMP/SMX, nelfinavir.</li> <li>• May antagonize methadone.</li> <li>• Monitor for treatment-associated toxicities with interferon-alpha with or without ribavirin.</li> </ul>
abacavir (ABC)/lamivudine (3TC)/zidovudine (ZDV)	<b>Trizivir</b> (GlaxoSmithKline)	<ul style="list-style-type: none"> <li>• See literature re: fatal hypersensitivity reactions; signs/symptoms include: fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise/fatigue, or respiratory symptoms; discontinue as soon as suspected; do not restart, regardless of HLA-B*5701 status.</li> <li>• Hepatic impairment.</li> <li>• Avoid zalcitabine, stavudine, doxorubicin, ribavirin, emtricitabine, tenofovir, other forms of abacavir, lamivudine, or zidovudine.</li> <li>• Abacavir may antagonize methadone.</li> <li>• TMP/SMX, nelfinavir may increase lamivudine levels.</li> <li>• Ethanol may increase abacavir levels. Atovaquone, fluconazole, methadone, nelfinavir, probenecid, ritonavir, valproic acid may affect zidovudine levels; monitor.</li> <li>• Increased hematologic toxicity with ganciclovir, other bone marrow suppressants or cytotoxic agents.</li> <li>• Triple therapy (once daily regimen) with tenofovir or with didanosine + tenofovir: high rate of early viral non-response (see literature).</li> <li>• Monitor for treatment-associated toxicities with interferon-alpha with or without ribavirin.</li> </ul>
didanosine (ddl)	<b>Videx</b> (Bristol Myers-Squibb) <b>Videx EC</b> (Bristol Myers-Squibb)	<ul style="list-style-type: none"> <li>• Concomitant allopurinol or ribavirin.</li> <li>• Avoid with hydroxyurea and stavudine.</li> <li>• Potentiated by ganciclovir, tenofovir (reduce dose of didanosine; monitor).</li> <li>• Antagonized by methadone.</li> <li>• For pediatric pwt: caution with magnesium- or aluminum-containing antacids.</li> <li>• Separate dosing of delavirdine, indinavir, nelfinavir by 1 hour; give drugs affected by gastric pH (eg, ketoconazole, itraconazole) 2 hours prior.</li> <li>• May antagonize quinolones, tetracyclines.</li> <li>• Give at least 6 hours before or 2 hours after ciprofloxacin.</li> <li>• See literature for dosing with concomitant tenofovir.</li> </ul>
emtricitabine (FTC)	<b>Emtriva</b> (Gilead Sciences)	<ul style="list-style-type: none"> <li>• Avoid concomitant drugs that contain emtricitabine or lamivudine.</li> </ul>
emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)	<b>Truvada</b> (Gilead Sciences)	<ul style="list-style-type: none"> <li>• Avoid concomitant drugs that contain emtricitabine, tenofovir, lamivudine, or adefovir dipivoxil.</li> <li>• Potentiates didanosine toxicity (&gt;60kg; reduce dose of didanosine); discontinue didanosine if toxicity develops.</li> <li>• Monitor drugs that reduce renal function or compete for renal tubular secretion (eg, adefovir dipivoxil, cidofovir, acyclovir, valacyclovir, ganciclovir, valganciclovir).</li> <li>• Avoid concomitant or recent use of nephrotoxic agents.</li> <li>• Potentiated by lopinavir/ritonavir, atazanavir; monitor for toxicity.</li> <li>• Concomitant atazanavir: must give with ritonavir.</li> <li>• Caution with triple nucleoside-only regimen (high rate of early viral non-response); monitor and consider alternative therapy.</li> <li>• See literature for dosing of concomitant didanosine or ritonavir.</li> </ul>
lamivudine (3TC)	<b>Epivir</b> (GlaxoSmithKline)	<ul style="list-style-type: none"> <li>• Concomitant zalcitabine: not recommended.</li> <li>• Avoid concomitant drugs that contain lamivudine or emtricitabine.</li> <li>• Caution with drugs eliminated by active organic cationic secretion (eg, trimethoprim). Increased lamivudine absorption with TMP/SMX (clinical significance unknown).</li> <li>• Triple therapy (once daily regimen) with abacavir + tenofovir or with didanosine + tenofovir: high rate of early viral non-response (see literature).</li> <li>• Monitor for treatment-associated toxicities with interferon-alpha with or without ribavirin.</li> </ul>
lamivudine (3TC)/zidovudine (ZDV)	<b>Combivir</b> (GlaxoSmithKline)	<ul style="list-style-type: none"> <li>• Avoid concomitant other forms of zalcitabine, stavudine, doxorubicin, ribavirin.</li> <li>• Bone marrow suppression increased by ganciclovir, interferon-alpha, cytotoxic drugs. TMP/SMX, atovaquone, fluconazole, methadone, probenecid, valproic acid, possibly others may affect lamivudine or zidovudine blood levels (clinical significance unknown); monitor.</li> <li>• Triple therapy (once daily regimen) with abacavir + tenofovir or with didanosine + tenofovir: high rate of early viral non-response (see literature).</li> <li>• Monitor for treatment-associated toxicities with interferon-alpha with or without ribavirin.</li> </ul>
stavudine (d4T)	<b>Zerit</b> (Bristol Myers-Squibb)	<ul style="list-style-type: none"> <li>• Avoid concomitant zidovudine.</li> <li>• Increased risk of toxicity with neurotoxic, hepatotoxic, or pancreatotoxic drugs (eg, didanosine and/or hydroxyurea); avoid.</li> <li>• Caution with doxorubicin, ribavirin.</li> <li>• Monitor for treatment-associated toxicities with interferon-alpha with or without ribavirin.</li> </ul>

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# ANTIRETROVIRAL CONTRAINDICATIONS AND DRUG INTERACTIONS (Part 3 of 5)

Generic & Class	Brand & Company	Contraindications and Drug Interactions†
<b>Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs) (continued)</b>		
tenofovir disoproxil fumarate (TDF)	<b>Viread</b> (Gilead Sciences)	<ul style="list-style-type: none"> <li>• Avoid concomitant drugs that contain tenofovir or adefovir dipivoxil.</li> <li>• Potentiates didanosine toxicity (&gt;60kg; reduce dose of didanosine); discontinue if toxicity develops.</li> <li>• Monitor drugs that reduce renal function or compete for renal tubular secretion (eg, cidofovir, acyclovir, valacyclovir, ganciclovir, valganciclovir).</li> <li>• Potentiated by lopinavir/ritonavir, atazanavir; monitor for toxicity.</li> <li>• Concomitant atazanavir: must give with ritonavir.</li> <li>• Caution with triple nucleoside-only regimens (high rate of early viral non-response); monitor and consider alternative therapy.</li> <li>• See literature for dosing of concomitant didanosine or ritonavir.</li> </ul>
zidovudine (ZDV)	<b>Retrovir</b> (GlaxoSmithKline)	<ul style="list-style-type: none"> <li>• Avoid stavudine, doxorubicin, ribavirin, other nucleoside analogues, other forms of zidovudine.</li> <li>• Caution with other cytotoxic or myelosuppressive drugs (eg, ganciclovir, interferon-alpha, ribavirin).</li> <li>• Fluconazole, atovaquone, lamivudine, probenecid, valproic acid, methadone increase zidovudine levels.</li> <li>• Monitor phenytoin.</li> <li>• May be antagonized by rifampin, ritonavir, nelfinavir.</li> <li>• Monitor for treatment-associated toxicities with interferon-alpha with or without ribavirin.</li> </ul>
<b>Protease Inhibitors (PIs)</b>		
atazanavir sulfate (ATV)	<b>Reyataz</b> (Bristol-Myers Squibb)	<ul style="list-style-type: none"> <li>• <b>Drugs metabolized by CYP3A or UGT1A1 that may cause serious events if blood levels are elevated (eg, alfuzosin, rifampin, irinotecan, oral midazolam, triazolam, ergots, cisapride, St. John's wort, lovastatin, simvastatin, pimozide, indinavir, sildenafil [Revatio; when used to treat PAH]).</b></li> <li>• Concomitant nevirapine: other protease inhibitors (excluding ritonavir and saquinavir), salmeterol, or fluticasone (atazanavir + ritonavir); not recommended.</li> <li>• Caution with drugs metabolized by UGT1A1 or CYP3A (eg, IV midazolam, calcium channel blockers, statins [eg, atorvastatin, rosuvastatin]; use lowest dose necessary; max rosuvastatin dose is 10mg/day), immunosuppressants, PDE5 inhibitors: reduce doses of these to treat ED; max 25mg sildenafil in 48hrs; max 2.5mg vardenafil in 24hrs or 72hrs [atazanavir + ritonavir]; max 10mg tadalafil in 72hrs; tadalafil to treat PAH [see literature]), and CYP2C8 (eg, paclitaxel, repaglinide).</li> <li>• Potentiated by CYP3A inhibitors, telaprevir.</li> <li>• Antagonized by CYP3A inducers.</li> <li>• Use cautiously and monitor diliazem, antiarrhythmics, others that affect conduction (esp. if metabolized by CYP3A).</li> <li>• Consider reducing diltiazem or clarithromycin dose by 50%; rifabutin dose by 75%.</li> <li>• Variable effects on clarithromycin; consider other drugs.</li> <li>• Plasma levels decreased by drugs that reduce gastric acidity (eg, H<sub>2</sub>-blockers, antacids).</li> <li>• Give proton pump inhibitors 12hrs before atazanavir + ritonavir; avoid in therapy-experienced.</li> <li>• Give 2hrs before or 1hr after buffered or enteric coated didanosine.</li> <li>• Antagonized by efavirenz, bosentan, tenofovir (see dose).</li> <li>• Increased risk of lactic acidosis with nucleoside analogues.</li> <li>• Potentiates saquinavir, trazodone, fluticasone, oral contraceptives, ketoconazole, itraconazole, buprenorphine (reduce dose), colchicine (esp. renal or hepatic impaired; do not use).</li> <li>• Monitor warfarin, tricyclics, rifabutin, immunosuppressants.</li> </ul>
darunavir (DRV)	<b>Prezista</b> (Tibotec)	<ul style="list-style-type: none"> <li>• <b>Concomitant rifampin, alfuzosin, ergots, cisapride, St. John's wort, lovastatin, simvastatin, pimozide, oral midazolam, triazolam, sildenafil [Revatio; only when used to treat PAH].</b></li> <li>• Voriconazole, salmeterol, boceprevir, telaprevir; not recommended.</li> <li>• Avoid protease inhibitors other than those studied (lopinavir/ritonavir, saquinavir, indinavir, atazanavir), dexamethasone, fluticasone.</li> <li>• Potentiates carbamazepine, risperidone, thioridazine, trazodone, desipramine, IV midazolam, rifabutin, digoxin, HMG-CoA reductase inhibitors (eg, pravastatin, atorvastatin, rosuvastatin); use lowest dose necessary; max atorvastatin dose is 20mg/day), sildenafil, vardenafil, tadalafil (reduce their doses).</li> <li>• Potentiates, and is potentiated by, indinavir, ketoconazole, itraconazole.</li> <li>• Increases bosentan (see literature), maraviroc, nevirapine, tenofovir, efavirenz, colchicine (dose adjustments: see literature) levels.</li> <li>• Antagonizes sertraline, paroxetine (monitor levels), ethinyl estradiol, norethindrone (use backup contraception).</li> <li>• Antagonizes and antagonized by other CYP3A4 substrates (eg, carbamazepine, phenobarbital, phenytoin).</li> <li>• Antagonized by efavirenz.</li> <li>• Monitor antiarrhythmics (eg, bepridil, systemic lidocaine, quinidine, amiodarone, flecainide, propafenone), calcium channel blockers, β-blockers, warfarin, digoxin, immunosuppressants (eg, tacrolimus, sirolimus, cyclosporine), buprenorphine, buprenorphine/naloxone, methadone (possible opiate withdrawal syndrome).</li> <li>• Reduce concomitant clarithromycin dose in renal impairment.</li> <li>• Separate dosing of didanosine.</li> </ul>
fosamprenavir calcium (FOS-APV)	<b>Lexiva</b> (GlaxoSmithKline)	<ul style="list-style-type: none"> <li>• <b>Concomitant alfuzosin, cisapride, pimozide, ergots, midazolam, triazolam, St. John's wort, rifampin, lovastatin, simvastatin, delavirdine, sildenafil [Revatio; when used for treating PAH].</b></li> <li>• <b>Concomitant flecainide, or propafenone with ritonavir-boosted fosamprenavir.</b></li> <li>• Life-threatening arrhythmias possible with amiodarone, bepridil, lidocaine (systemic), quinidine.</li> <li>• Concomitant salmeterol, nevirapine without ritonavir; not recommended.</li> <li>• Reduce rifabutin dose by at least ½ (or by 75% if with ritonavir) and monitor for neutropenia (do weekly CBCs).</li> <li>• Potentiates sildenafil, tadalafil, vardenafil; reduce doses of these.</li> <li>• May potentiate fluticasone (consider alternative therapy), trazodone (reduce trazodone dose).</li> <li>• Monitor antiarrhythmics (eg, amiodarone), anticonvulsants (eg, phenytoin), H<sub>2</sub> blockers, immunosuppressants, tricyclics, warfarin, drugs that affect or are affected by CYP3A4 (eg, azole antifungals, benzodiazepines, calcium channel blockers, NNRTIs, protease inhibitors, statins, steroids).</li> <li>• May antagonize, or be antagonized by hormonal contraceptives (use non-hormonal methods), methadone, paroxetine.</li> <li>• Concomitant bosentan, colchicine (adjust doses; see literature).</li> </ul>
indinavir sulfate (IDV)	<b>Crixivan</b> (Merck)	<ul style="list-style-type: none"> <li>• <b>Concomitant alfuzosin, amiodarone, cisapride, oral midazolam, triazolam, alprazolam, pimozide, ergots, sildenafil [Revatio; only when used to treat PAH].</b></li> <li>• Rifampin, St. John's wort, atazanavir, lovastatin, simvastatin, rosuvastatin, salmeterol, fluticasone (w. concomitant potent CYP3A4 inhibitor): not recommended; caution with other statins metabolized by CYP3A4.</li> <li>• Potentiates PDE5 inhibitors, IV midazolam, trazodone, bosentan (reduce doses; see literature); antiarrhythmics, rifabutin, calcium channel blockers, clarithromycin, immunosuppressants, others metabolized by CYP3A4.</li> <li>• Plasma levels increased by itraconazole, ketoconazole, delavirdine, CYP3A4 inhibitors.</li> <li>• Plasma levels reduced by efavirenz, rifabutin, venlafaxine, phenobarbital, phenytoin, carbamazepine, other CYP3A4 inducers.</li> <li>• Avoid concomitant colchicine if renal or hepatic impairment; otherwise: reduce dose: see literature.</li> <li>• Separate dosing of indinavir and didanosine by at least 1 hour and give both on empty stomach.</li> </ul>

(continued)

Generic & Class	Brand & Company	Contraindications and Drug Interactions†
<p>lopinavir (LPV)/ritonavir (RTV)</p>	<p><b>Kaletra</b> (AbbVie)</p>	<ul style="list-style-type: none"> <li>• <b>Loss of virologic response or resistance with alfuzosin, rifampin, St. John's wort, lovastatin, simvastatin, sildenafil (Revatio), cisapride, ergots, pimoizide, orally administered midazolam, triazolam.</b></li> <li>• <b>Drugs metabolized by CYP3A that may cause serious events if blood levels are elevated.</b></li> <li>• Voriconazole, salmeterol: not recommended.</li> <li>• Potentiates bosentan and statins metabolized by CYP3A; use atorvastatin with caution and at the lowest necessary doses; do not exceed rosvastatin 10mg daily.</li> <li>• Potentiates fentanyl, parenteral midazolam; monitor.</li> <li>• Potentiates anticancer agents (eg, vincristine, vinblastine, dasatinib, nilotinib); may need dose adjustment (see literature).</li> <li>• Potentiates colchicine; adjust dosing (see literature). Concomitant colchicine not recommended in renal or hepatic impairment.</li> <li>• Avoid oral soln with metronidazole, disulfiram.</li> <li>• Monitor other antiretrovirals, warfarin.</li> <li>• Increases levels of antiarrhythmics, dihydropyridine, calcium channel blockers, immunosuppressants (monitor); ketoconazole, itraconazole (avoid high doses); rifabutin (reduce rifabutin dose and monitor); clarithromycin (reduce clarithromycin dose in renal dysfunction), trazodone (reduce trazodone dose).</li> <li>• Give didanosine 1 hour before or 2 hours after.</li> <li>• Decreases levels of atovaquone, methadone, estrogen-containing oral contraceptives (use other or back-up contraception).</li> <li>• Lopinavir levels decreased by anticonvulsants (eg, carbamazepine, phenobarbital, phenytoin), dexamethasone, efavirenz, nevirapine.</li> <li>• Lopinavir levels may be increased by delavirdine, CYP3A inhibitors.</li> <li>• May decrease zidovudine or abacavir levels.</li> </ul>
<p>nelfinavir mesylate (NFV)</p>	<p><b>Viracept</b> (Agouron)</p>	<ul style="list-style-type: none"> <li>• <b>CYP3A substrates that may cause serious events if blood levels are elevated (eg, cisapride, pimoizide, oral midazolam, triazolam, lovastatin, simvastatin, ergots, amiodarone, quinidine, alfuzosin, rifampin, St. John's wort, sildenafil [Revatio; when used to treat PAH]).</b></li> <li>• Salmeterol: not recommended.</li> <li>• Potentiates CYP3A substrates (eg, dihydropyridine calcium channel blockers, cyclosporine, tacrolimus, sirolimus, rifabutin, rosvastatin, atorvastatin [use lowest dose necessary; max atorvastatin dose is 40mg/day]), PDE5 inhibitors (adjust dose: see literature), phenytoin (monitor).</li> <li>• Potentiates fluticasone (caution and consider alternatives w. long-term use), trazodone (use lower dose), bosentan, colchicine (adjust dose: see literature).</li> <li>• Nelfinavir levels decreased by CYP3A inducers (eg, phenytoin, carbamazepine, phenobarbital) or CYP2C19 inducers.</li> <li>• Nelfinavir levels increased by CYP3A or CYP2C19 inhibitors.</li> <li>• Antagonizes methadone, oral contraceptives (use additional or alternative contraception).</li> <li>• Indinavir, ritonavir, saquinavir increase nelfinavir levels.</li> <li>• Concomitant azithromycin: monitor for azithromycin toxicity (eg, elevated liver enzymes).</li> <li>• Administer didanosine 1hr before or 2hrs after nelfinavir.</li> <li>• Monitor INR with warfarin.</li> <li>• Others: see literature.</li> </ul>
<p>ritonavir (RTV)</p>	<p><b>Norvir</b> (AbbVie)</p>	<ul style="list-style-type: none"> <li>• <b>Concomitant alfuzosin, amiodarone, bepridil, flecainide, quinidine, propafenone, voriconazole, ergots, oral midazolam, triazolam, pimoizide, cisapride, St. John's wort, lovastatin, simvastatin, sildenafil (Revatio; only when used to treat PAH).</b></li> <li>• Rifampin, high-dose or long-term meperidine: not recommended.</li> <li>• Potentiates other protease inhibitors, PDE5 inhibitors, tramadol, propoxyphene, colchicine, clarithromycin, bosentan (reduce doses; see literature); fluticasone and salmeterol (avoid).</li> <li>• May be affected by, potentiate, or antagonize drugs that are metabolized by or induce CYP3A4, 2D6, 2C9, 3A, 1A2 or glucuronyl transferase, including: delavirdine, maraviroc, opioids, antiarrhythmics (eg, disopyramide, lidocaine, mexiletine), digoxin, anticoagulants, anticonvulsants, most antidepressants (eg, SSRIs, tricyclics, nefazodone, bupropion), antiemetics (eg, dronabinol), antihypertensives (eg, calcium channel blockers, <math>\beta</math>-blockers), antiparasitics, corticosteroids, sulfonyleureas, immunosuppressants, neuroleptics, sedative/hypnotics, CNS stimulants, statins, vinca alkaloids (eg, vincristine, vinblastine; consider withholding ritonavir); monitor these and others closely.</li> <li>• Antagonizes theophylline, oral contraceptives, methadone.</li> <li>• Separate dosing of didanosine by 2½ hours.</li> <li>• Avoid metronidazole, disulfiram; itraconazole or ketoconazole &gt;200mg/day.</li> <li>• Reduce rifabutin dose by at least ¾.</li> </ul>
<p>saquinavir mesylate (SQV)</p>	<p><b>Invirase</b> (Genentech)</p>	<ul style="list-style-type: none"> <li>• <b>Congenital long QT syndrome.</b></li> <li>• <b>Refractory hypokalemia or hypomagnesemia.</b></li> <li>• <b>Complete AV block without implanted pacemakers, or those who are at high risk.</b></li> <li>• <b>Severe hepatic impairment.</b></li> <li>• <b>Use in combination with drugs that both increase saquinavir plasma concentrations and prolong the QT interval.</b></li> <li>• <b>Concomitant alfuzosin, amiodarone, bepridil, cisapride, dofetilide, ergots, flecainide, lidocaine, oral midazolam, pimoizide, propafenone, quinidine, rifampin, sildenafil (Revatio; when used to treat PAH), lovastatin, simvastatin, trazodone, triazolam.</b></li> <li>• Limit dose of atorvastatin to 20mg daily.</li> <li>• Concomitant tipranavir/ritonavir, fluticasone, salmeterol, St. John's wort, garlic capsules: not recommended.</li> <li>• Plasma levels reduced by efavirenz, nevirapine, rifabutin, other CYP3A4 inducers (eg, carbamazepine, phenobarbital, phenytoin, dexamethasone).</li> <li>• Plasma levels increased by clarithromycin (see literature), atazanavir, indinavir, nelfinavir, lopinavir/ritonavir, ritonavir, delavirdine.</li> <li>• Antagonizes methadone, oral contraceptives.</li> <li>• Potentiates CYP3A4 substrates (eg, calcium channel blockers, atorvastatin, rosvastatin, warfarin, cyclosporine, tacrolimus, rapamycin, sildenafil, vardenafil, tadalafil), maraviroc, bosentan, colchicine, ketoconazole, itraconazole; monitor their effects; may need reduced doses.</li> <li>• Caution with digoxin, ibutilide, sotalol, tricyclics, benzodiazepines, neuroleptics (eg, clozapine, haloperidol, thioridazine), omeprazole, erythromycin, halofantrine, pentamidine, others (see literature).</li> </ul>

Generic & Class	Brand & Company	Contraindications and Drug Interactions†
<b>Protease Inhibitors (PIs) (continued)</b>		
tipranavir (TPV)	<b>Aptivus</b> (Boehringer Ingelheim)	<ul style="list-style-type: none"> <li>• Moderate to severe hepatic insufficiency (Child-Pugh B-C).</li> <li>• Concomitant potent CYP3A inducers or substrates (eg, alifuzosin, amiodarone, bepridil, flecainide, propafenone, quinidine, rifampin, ergots, cisapride, St. John's wort, lovastatin, simvastatin, pimoziide, sildenafil, oral midazolam, triazolam).</li> <li>• Concomitant salmeterol, fluticasone, fosamprenavir, lopinavir, saquinavir, atazanavir, fluconazole, ketoconazole, itraconazole ≥200mg/day: not recommended.</li> <li>• Avoid metronidazole, disulfiram.</li> <li>• May be synergistic with enfuvirtide.</li> <li>• Potentiates PDE5 inhibitors (eg, sildenafil, tadalafil, vardenafil), trazodone, desipramine; reduce dose: see literature.</li> <li>• Avoid concomitant colchicine if renal or hepatic impairment; otherwise: reduce dose: see literature.</li> <li>• Reduce rifabutin dose by 75%.</li> <li>• Antagonizes estrogens (use non-hormonal contraceptives), methadone, valproic acid, omeprazole.</li> <li>• Antagonized by carbamazepine, phenobarbital, phenytoin.</li> <li>• Potentiates atorvastatin, rosuvastatin: use lowest possible dose.</li> <li>• Monitor hypoglycemics, immunosuppressants, tricyclics, SSRIs, warfarin, drugs that affect or are affected by CYP3A4 (eg, azole antifungals, calcium channel blockers, clarithromycin, NNRTIs, PIs, statins).</li> <li>• Increased risk of bleeding with concomitant anticoagulants, antiplatelet agents, high-dose Vit.E.</li> <li>• Separate dosing of didanosine, antacids.</li> <li>• Oral soln: avoid high-dose Vit.E supplements.</li> </ul>
<b>Multiclass Fixed-Dose Combination</b>		
efavirenz (EVF)/emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)	<b>Atripla</b> (Bristol-Myers Squibb and Gilead)	<ul style="list-style-type: none"> <li>• Concomitant cisapride, ergots, midazolam, triazolam, bepridil, pimoziide, St. John's wort, voriconazole, lamivudine, atazanavir, other forms of emtricitabine, efavirenz, or tenofovir.</li> <li>• Avoid alcohol, posaconazole, other psychoactive and/or hepatotoxic drugs.</li> <li>• Potentiates didanosine toxicity (&gt;60kg; reduce dose of didanosine); discontinue didanosine if toxicity develops.</li> <li>• Potentiates, and is potentiated by ritonavir (monitor liver function and for adverse events).</li> <li>• Tenofovir levels increased by lopinavir/ritonavir; discontinue if toxicity occurs.</li> <li>• Efavirenz levels decreased by phenobarbital, carbamazepine, phenytoin, rifampin, rifabutin.</li> <li>• May decrease levels of indinavir (may be ineffective, even with increased dose), amprenavir, atazanavir, carbamazepine, phenytoin, phenobarbital, clarithromycin, calcium channel blockers (eg, diltiazem, felodipine, nifedipine, verapamil), itraconazole, ketoconazole, lopinavir (adjust dose), maraviroc, methadone, rifabutin (increase dose), sertraline, statins, progestins (eg, norelgestromin, levonorgestrel), immunosuppressants (eg, cyclosporine, sirolimus, tacrolimus).</li> <li>• Efavirenz increases nelfinavir plasma levels.</li> <li>• Antagonizes, and is antagonized by, saquinavir (do not use as sole protease inhibitor).</li> <li>• Caution with drugs metabolized by, or that affect activity of, CYP2C9, CYP2C19, CYP3A4.</li> <li>• Closely monitor warfarin, anticonvulsants (esp. phenytoin, phenobarbital, carbamazepine), rifabutin, immunosuppressants, methadone, others.</li> <li>• Monitor drugs that decrease renal function or compete for renal tubular secretion (eg, acyclovir, adefovir dipivoxil, cidofovir, ganciclovir, valacyclovir, valganciclovir).</li> <li>• May cause false (+) cannabis screening test (CEDIA DAU multilevel THC assay).</li> </ul>
emtricitabine (FTC)/rilpivirine/tenofovir disoproxil fumarate (TDF)	<b>Complera</b> (Gilead Sciences)	<ul style="list-style-type: none"> <li>• Concomitant carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole, systemic dexamethasone (more than single dose), St. John's wort.</li> <li>• Avoid concomitant drugs that contain emtricitabine, tenofovir, rilpivirine, lamivudine, or adefovir dipivoxil.</li> <li>• Emtricitabine/tenofovir: Monitor drugs that reduce renal function or compete for renal tubular secretion (eg, adefovir dipivoxil, cidofovir, acyclovir, valacyclovir, ganciclovir, valganciclovir).</li> <li>• Avoid concomitant or recent use of nephrotoxic agents.</li> <li>• Rilpivirine: Potentiated by CYP3A inhibitors.</li> <li>• Antagonized by CYP3A inducers.</li> <li>• May antagonize azole antifungals (monitor for breakthrough fungal infections), methadone (monitor).</li> <li>• Separate antacids (by at least 2 hours before or at least 4 hours after) and H<sub>2</sub>-receptor antagonists (by at least 12 hours before or 4 hours after) rilpivirine; drugs that increase gastric pH may result in decreased plasma concentrations.</li> <li>• Caution with drugs with a known risk for torsades de pointes.</li> </ul>
elvitegravir/cobicistat/emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)	<b>Stribild</b> (Gilead Sciences)	<ul style="list-style-type: none"> <li>• Concomitant alifuzosin, rifampin, ergots, cisapride, St. John's wort, lovastatin, simvastatin, pimoziide, sildenafil (when dosed for PAH), triazolam, oral midazolam.</li> <li>• Avoid with concurrent or recent use of nephrotoxic agents.</li> <li>• Do not administer with other antiretroviral agents.</li> <li>• May be potentiated by CYP3A inhibitors, antagonized by CYP3A inducers.</li> <li>• May potentiate antiarrhythmics, digoxin, clarithromycin (reduce dose by 50% if CrCl 50–60mL/min), telithromycin, carbamazepine, clonazepam, ethosuximide, SSRIs, TCAs, trazodone, ketoconazole (max 200mg/day), itraconazole (max 200mg/day), voriconazole, beta-blockers, calcium channel blockers, fluticasone (use alternative corticosteroid), atorvastatin, immunosuppressants, (monitor), neuroleptics, sedatives/hypnotics, PDE5 inhibitors (see literature for dose adjustments).</li> <li>• May antagonize CYP2C9 substrates.</li> <li>• Antagonized by carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, systemic dexamethasone.</li> <li>• Concomitant colchicine (see literature); do not coadminister to patients with renal or hepatic impairment.</li> <li>• Concomitant salmeterol: not recommended; increased risk of cardiovascular events.</li> <li>• Separate antacids by at least 2 hours.</li> <li>• Discontinue use of bosentan at least 36 hours prior to initiation of Stribild; after at least 10 days following initiation, resume bosentan.</li> <li>• Use alternative non-hormonal methods of contraception.</li> </ul>

**NOTES**

† Those listed in **bold type** are contraindications.

‡ Not an inclusive list. Please see individual monographs.