

ATAZANAVIR (ATV) (Updated February 2011)	
Trade Name	Reyataz
Classification	Protease Inhibitor
Form	100-, 150-, 200-, 300-mg capsules
Dosing Recommendations	<p>For ARV-naïve patients (able to tolerate RTV): ATV 300 mg + RTV 100 mg once daily with food <i>or</i></p> <p>For ARV-naïve patients (unable to tolerate RTV): 400 mg once daily with food</p> <p>For ARV-experienced patients: ATV 300 mg + RTV 100 mg once daily with food</p> <p>For pregnant patients: ATV should be administered with RTV. ATV can be used as an alternative to LPV/r in pregnancy. Increase to ATV 400 mg + RTV 100 mg once daily in the 2nd and 3rd trimester when ATV/r is co-administered with TDF <i>or</i> H-2 blockers</p>
Hepatic Impairment Dosing	<p>Child-Pugh Score 7-9: consider 300 mg once daily</p> <p>Child-Pugh Score >9: do not use</p> <p><i>Note:</i> Do not use ATV with RTV in patients with hepatic impairment</p>
Renal Impairment Dosing	<p>For ARV-naïve patients with ESRD: ATV 300 mg + RTV 100 mg once daily</p> <p>For ARV-experienced patients with ESRD: Avoid unboosted ATV. Higher ATV/r may be needed</p>
Food Effect	<p>Light meal increases AUC 70% and Cmax 57%</p> <p>Take with food</p>
Oral Bioavailability	Not determined (varies with food)
Serum Half-life	7 hours
Route of Metabolism	Hepatic cytochrome P450 3A4 inhibitor and substrate
Storage	Room temperature
Adverse Events	<p>GI intolerance, rash</p> <p>Hyperglycemia,^a indirect hyperbilirubinemia, nephrolithiasis</p> <p>PR interval prolongation (some patients experience asymptomatic 1st degree AV block)</p> <p>Possible increased bleeding episodes in patients with hemophilia</p> <p>Cases of lactic acidosis syndrome, sometimes fatal, and symptomatic hyperlactatemia have occurred in pregnant women using ATV in combination with nucleoside analogues. Lactic acidosis is associated with antiretroviral nucleoside analogues alone or in combination.</p> <p>Higher ATV exposures 2 months postpartum may occur; monitor for adverse events carefully</p>

FDA Pregnancy Category	B
Long-Term Animal Carcinogenicity Studies	Not completed
Animal Teratogen Studies	Negative (rats and rabbits)
Black Box Warnings	None
Drugs to Avoid	<p>As part of the ARV regimen: Efavirenz (for therapy-experienced patients) Etravirine (clinical significance unclear) Indinavir Nevirapine (may increase risk of NVP toxicity) Tenofovir (when ATV is not combined with RTV) Tipranavir/ritonavir</p> <p>Alfuzosin, alprazolam, astemizole, bepridil, cisapride, ergot derivatives, garlic supplements, irinotecan, lovastatin, midazolam,^b pimoziide, proton pump inhibitors, ranolazine, rifampin, rifapentine, high-dose sildenafil, simvastatin, pitavastatin, St. John's wort, terfenadine, triazolam</p>
Cautious Use or Dose Adjustment	
Antiretrovirals	<p>Darunavir: Dose DRV/r 600/100 mg twice daily + ATV 300 mg once daily</p> <p>Didanosine: ATV AUC ↓ 87% – Take ATV (with food) 2 hours before or 1 hour after buffered ddi</p> <p>Efavirenz: For therapy-naïve patients – Use ATV 400 mg + RTV 100 mg once daily with food and EFV 600 mg once daily on empty stomach at bedtime for initial 2 weeks, then may take EFV with or without food</p> <p>Lopinavir/ritonavir: Use ATV 300 mg once daily + LPV/r 400/100 mg twice daily</p> <p>Maraviroc: ↑ MVC AUC – ↓ MVC dose to 150 mg twice daily (not recommended with ESRD or use with close orthostatic hypotension monitoring)</p> <p>Ritonavir: ATV AUC ↑ 238% – Use ATV 300 mg + RTV 100 mg once daily</p> <p>Tenofovir: ATV C_{min} ↓ 40% – Use ATV 300 mg + RTV 100 mg + TDF 300 mg once daily</p>
Antacids	Antacids and buffered medications: May ↓ ATV concentrations – ATV should be taken 2 hours before or 1 hour after these medications
Antiarrhythmics	Amiodarone, lidocaine (systemic), quinidine: ↑ antiarrhythmics – Avoid. Consider monitoring concentrations
Anticoagulants	Warfarin: ↑ warfarin – Monitor INR closely
Anticonvulsants	Carbamazepine, phenobarbital, phenytoin: May ↓ ATV significantly. Avoid co-administration. If no alternatives, use with close monitoring of anticonvulsant levels and consider ATV therapeutic drug monitoring
Antidepressants	Amitriptyline, imipramine: ↑ tricyclics – Monitor tricyclic antidepressant concentrations. Avoid in patients with QTc prolongation

Antifungals	Voriconazole: Potential for bi-directional inhibition; when boosted with RTV, may significantly ↓ voriconazole – Monitor for toxicities and voriconazole therapeutic drug monitoring
Antigout	Colchicine: For treatment of gout flares – 0.6 mg (1 tablet) x 1 dose, then 0.3 mg (½ tablet) 1 h later. Do not repeat dose before 3 days. For prophylaxis of gout flares – adjust dose to ¼ original regimen For treatment of familial Mediterranean fever (FMF) – Max: 0.6 mg daily Do not co-administer in patients with hepatic or renal impairment
Antimalarial Agents	Atovaquone/proguanil: ATV/r decreased atovaquone AUC 46% and proguanil AUC 41%. Consider an alternative agent for malaria prophylaxis. If Atovaquone is used for PCP prophylaxis, consider an alternative agent for PCP prophylaxis
Antimycobacterials	Clarithromycin: ATV AUC ↑ 28%; CL AUC ↑ 94% and may cause QTc prolongation – Use 50% of CL dose (further reduction needed with ESRD). Consider alternative therapy (azithromycin) Rifabutin: RFB AUC ↑ 250% – ↓ RFB dose to 150 mg qod or 3x/wk ^c
Bronchodilators	Salmeterol: Co-administration not recommended. Consider formoterol
Calcium Channel Blockers	Diltiazem: AUC ↑ 125% – Start with 50% diltiazem dose (may prolong PR interval) Other: Use with caution; dose titration should be considered; ECG monitoring is recommended
Erectile Dysfunction Agents	Sildenafil: May ↑ sildenafil AUC – Use cautiously, start with reduced dose of 25 mg q48h and monitor for adverse effects Tadalafil: Substantial ↑ in tadalafil AUC and half-life – Start with a 5-mg dose; do not exceed a single 10-mg dose of tadalafil in 72 hours. If tadalafil is used for pulmonary hypertension, see “Pulmonary Hypertension Agents” Vardenafil: May ↑ vardenafil AUC – Start with 2.5-mg dose; do not exceed a single 2.5-mg dose of vardenafil in 72 hours
H₂ Receptor Antagonists	Avoid co-administration if possible. If co-administration is needed: For therapy-naïve patients: ATV 300 mg/RTV 100 mg once daily >10 hours after H2 blocker; 40 mg famotidine twice daily (Max) For therapy-experienced patients: ATV 300 mg/RTV 100 mg once daily administered >10 hours after H2 blocker; 20 mg famotidine twice daily (Max). ATV 400 mg/RTV 100 mg once daily if patient also taking TDF or H2 blocker For therapy-experienced pregnant patients in 2nd or 3rd trimester: if ATV co-administered with TDF or H2 blocker, ATV 400 mg + RTV 100 mg once daily ↓ ATV concentrations – Give ATV 2 hours before or 10 hours after H2 blocker
Immunosuppressants	Cyclosporine, sirolimus, tacrolimus: significant ↑ immunosuppressants – Monitor immunosuppressant concentrations. Significant immunosuppressant dose needed

Lipid-Lowering Agents	Atorvastatin: May ↑ ATO substantially – Use lowest possible starting dose (10 mg) of ATO with careful monitoring
Oral Contraceptives	Ethinyl estradiol (EE), norethindrone: Co-administered with ATV/RTV, OC should contain at least 35 mcg EE. Co-administered with ATV without RTV, OC should contain no more than 30 mcg EE. If other OC are used, use alternative method of nonhormonal contraceptive. May ↑ progesterone exposure substantially
Proton-pump Inhibitors	Avoid PPI with ATV. If co-administration is needed: For ARV-naïve patients: Do not exceed 20 mg omeprazole – Take 12 hours prior to ATV 300 mg/RTV 100 mg dose, but not recommended by most experts For ARV-experienced patients: Do not use proton-pump inhibitors
Pulmonary Hypertension Agents	Bosentan: In patients already taking boosted ATV for >10 days, co-administer bosentan at a reduced dose of 62.5 mg once daily or qod based on tolerability. If patient is already taking bosentan, discontinue bosentan for >36 hrs prior to initiating boosted ATV. After boosted ATV has been given for >10 days, once daily or qod bosentan can be reintroduced. Limited clinical data, use with close monitoring. Co-administration of bosentan and ATV without RTV is not recommended Tadalafil: In patients already taking boosted ATV for >1 wk, co-administer tadalafil at 20 mg once daily; increase to 40 mg once daily based on tolerability. In patients already taking tadalafil, avoid use of tadalafil during initiation of boosted ATV. Stop tadalafil >24 h prior to starting boosted ATV. At least >1 wk after initiating boosted ATV, resume tadalafil at 20 mg once daily; increase to 40 mg once daily based on tolerability. Limited clinical data, use with close monitoring
With CYP2C8 substrates (e.g., paclitaxel, repaglinide)	Unboosted ATV may ↑ CYP2C8 substrates. Monitor closely with co-administration
<p>^a Cases of worsening glycemic control in patients with preexisting diabetes, and cases of new-onset diabetes including diabetic ketoacidosis have been reported with the use of all protease inhibitors.</p> <p>^b Can be used with caution as a single dose in a monitored situation for procedural sedation.</p> <p>^c Rifabutin 3x/wk is recommended if CD4 count <100 cells/mm³.</p>	