

AMPRENAVIR (APV)^a (Updated March 2008)	
Trade Name	Agenerase
Classification	Protease Inhibitor
Form	50-capsules; 15 mg/mL oral solution ^b (capsules and solution NOT interchangeable on mg-per-mg basis)
Dosing Recommendations	Body weight \geq 50 kg: 1200 mg twice daily (capsules) or 1400 mg twice daily (oral solution) Body weight <50 kg: 20 mg/kg twice daily (capsules; max 2400 mg/day) or 1.5 mL/kg twice daily (oral solution; max 2800 mg/day)
Hepatic Impairment Dosing	Child-Pugh Score 5-8: 450 mg twice daily (capsules). Consider using FPV Child-Pugh Score 9-12: 300 mg twice daily (capsules). Consider using FPV
Food Effect	High-fat meal \downarrow AUC 21%; can be taken with or without food, but high-fat meal (>50 g) should be avoided; avoid vitamin E supplements; do not take antacids 1 hour before or after taking APV
Oral Bioavailability	Not determined in humans
Serum Half-life	7.1-10.6 hours
Route of Metabolism	P450 cytochrome 3A4 inhibitor (less than ritonavir; similar to indinavir, nelfinavir), inducer, and substrate
Storage	Room temperature
Adverse Events	GI intolerance, nausea, vomiting, diarrhea, rash, oral paresthesias Transaminase elevation, hyperglycemia, ^c fat redistribution and lipid abnormalities ^d Possible increased bleeding episodes in patients with hemophilia
FDA Pregnancy Category	C
Long-Term Animal Carcinogenicity Studies	Studies show an increase in the incidence of hepatocellular adenomas plus carcinoma in male rats and mice
Animal Teratogen Studies	Negative (but deficient ossification and thymic elongation in rats and rabbits)
Black Box Warnings	Because of the potential risk of toxicity from large amounts of the excipient propylene glycol in Agenerase Oral Solution, it is contraindicated in the following patient populations: <ul style="list-style-type: none"> • children age <4 years • pregnant women • patients with renal or hepatic failure • patients treated with disulfiram or metronidazole Oral solution should be used only when Agenerase capsules or other protease inhibitors cannot be used.
Drugs to Avoid	As part of the ARV regimen: Delavirdine Etravirine Tipranavir/ritonavir

	Alprazolam, astemizole, bepridil, cisapride, ergot derivatives, ethinyl estradiol, garlic supplements, lovastatin, midazolam, ^e norethindrone, pimozone, ranolazine, rifampin, rifapentine, simvastatin, St. John's Wort, terfenadine, triazolam
Cautious Use or Dose Adjustment	
Antiretrovirals	Didanosine: Dosing should be separated by 1 hour Efavirenz: APV AUC ↓ 36% – Use APV 600 mg + RTV 100 mg twice daily Lopinavir/ritonavir: Not recommended by some. Consider APV 750 mg twice daily plus LPV/r 600/150 mg twice daily. Consider therapeutic drug monitoring Maraviroc: ↑ MVC AUC – ↓ MVC dose to 150 mg twice daily
Antacids	Dosing should be separated by 1 hour
Anticoagulants	Warfarin: ↑ or ↓ warfarin – Monitor INR
Anticonvulsants	Carbamazepine, phenobarbital, phenytoin: May ↓ APV levels substantially – Monitor anticonvulsant levels and virologic response. Consider obtaining APV levels
Antidepressants	Amitriptyline, imipramine: ↑ tricyclics – Monitor tricyclic antidepressant concentrations
Antifungals	Itraconazole, ketoconazole: ↑ itra/keto – Consider ↓ itra/keto dose if dose is >400 mg/day Voriconazole: Potential for bi-directional inhibition; when boosted with RTV, may significantly ↓ voriconazole – Monitor for toxicities
Antimycobacterials	Rifabutin: APV AUC ↓ 15%; RFB ↑ 193% – ↓ RFB dose to 150 mg once daily or 300 mg 3x/wk. ^f If APV is boosted with RTV, use RFB 150 mg qod + APV 600 mg twice daily + RTV 100 mg twice daily
Calcium Channel Blockers	Bepridil: ↑ bepridil – Use with caution
Corticosteroids	Dexamethasone: ↓ APV – Use with caution
Erectile Dysfunction Agents	Sildenafil: Sildenafil AUC ↑ 2- to 11-fold – 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 Vardenafil: May ↑ vardenafil AUC – Start with 2.5-mg dose; do not exceed a single 2.5-mg dose of vardenafil in 72 hours
Immunosuppressants	Cyclosporine, tacrolimus, rapamycin: ↑ immunosuppressants – Monitor immunosuppressant concentrations
Lipid-Lowering Agents	Atorvastatin: May ↑ ATO substantially – Use lowest possible starting dose of ATO with careful monitoring
Synthetic Narcotics	Methadone: Methadone ↓ 13%; APV C _{min} ↓ 25% – Monitor and titrate methadone if needed. No significant change in the R-methadone (active). No withdrawal symptoms observed

- ^a Because of the availability of fosamprenavir, amprenavir capsules are no longer used or recommended. Oral solution is for short-term use in patients with an NG tube or J tube.
- ^b Oral solution contains propylene glycol, which is contraindicated in pregnant women, children <4 years old, patients with hepatic or renal failure, and patients treated with disulfiram or metronidazole.
- ^c 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.
- ^d Discontinuation of PIs may be required to reverse fat redistribution. Patients with hypertriglyceridemia or hypercholesterolemia should be evaluated for risks of cardiovascular events and pancreatitis.
- ^e Can be used with caution as a single dose in a monitored situation for procedural sedation.
- ^f Rifabutin 3x/wk is recommended if CD4 cell count <100 cells/mm³.