

FOSAMPRENAVIR (FPV)* (Updated April 2010)	
Trade Name	Lexiva
Classification	Protease Inhibitor
Form	700-mg tablets; 50-mg/mL oral solution
Dosing Recommendations	<p>For ARV-naïve patients: FPV 1400 mg + RTV 100 once daily <i>or</i> FPV 700 mg + RTV 100 mg twice daily <i>or</i> FPV 1400 mg twice daily (use only in PI-naïve patients who can not tolerate RTV)</p> <p>For PI-experienced patients: FPV 700 mg + RTV 100 mg twice daily</p>
Hepatic Impairment Dosing	<p>Child-Pugh Score 5-6: 700 mg twice daily without RTV (therapy-naïve) <i>or</i> FPV 700 mg twice daily + RTV 100 mg once daily (therapy-experienced or therapy naïve)</p> <p>Child-Pugh Score 7-9: 700 mg twice daily without RTV (therapy-naïve) <i>or</i> FPV 450 mg twice daily + RTV 100 mg once daily (therapy-experienced or therapy-naïve)</p> <p>Child-Pugh Score 10-15: Use with caution due to limited clinical data. Consider FPV 350 mg twice daily (therapy-naïve) <i>or</i> FPV 300 mg twice daily + RTV 100 mg once-daily (therapy-naïve or PI-experienced)</p> <p>No data with FPV/r in patients with severe hepatic impairment</p>
Food Effect	<p>Tablets – take with or without food Oral solution – take without food</p>
Oral Bioavailability	Not established
Serum Half-life	7.7 hours
Route of Metabolism	Hepatic cytochrome P450 3A4 inhibitor, inducer, and substrate
Storage	Room temperature
Adverse Events	<p>Myocardial infarction and hypercholesterolemia</p> <p>Increases in cholesterol^a</p> <p>GI intolerance, nausea, vomiting, diarrhea, rash, headache</p> <p>Transaminase elevation, hyperglycemia,^b fat redistribution and lipid abnormalities^c</p> <p>Possible increased bleeding episodes in patients with hemophilia</p> <p>Nephrolithiasis – rare</p>
FDA Pregnancy Category	C. FPV AUC decreased 36% in the third trimester, but trough adequate in PI-naïve patients.
Long-Term Animal Carcinogenicity Studies	<p>Not completed</p> <p>Studies for amprenavir showed an increase in the incidence of hepatocellular adenomas plus carcinoma in male rats and mice</p>

Animal Teratogen Studies	No major effects on embryo-fetal development in rats and rabbits; increased incidence of abortion in rabbits
Black Box Warnings	None
Drugs to Avoid	<p>As part of the ARV regimen: Delavirdine Etravirine (clinical significance unknown) Lopinavir/ritonavir Tipranavir/ritonavir</p> <p>Alfuzosin, alprazolam, astemizole, bepridil, cisapride, ergot derivatives, ethinyl estradiol, garlic supplements, lovastatin, midazolam,^d norethindrone, pimozone, ranolazine, rifampin, rifapentine, high-dose sildenafil, simvastatin, St. John's wort, terfenadine, triazolam</p>
Cautious Use or Dose Adjustment	
Antiretrovirals	<p>Efavirenz: FPV C_{min} ↓ 36% when FPV 1400 mg + RTV 200 mg once daily is used – Use FPV 1400 mg + RTV 300 mg once daily or FPV 700 mg + RTV 100 mg twice daily</p> <p>Maraviroc: ↑ MVC AUC – ↓ MVC dose to 150 mg twice daily</p> <p>Ritonavir: FPV AUC ↑ 100%, C_{min} ↑ 400% when combined with 200 mg RTV – ARV-experienced patients should receive RTV-boosted regimen (FPV 700 mg + RTV 100 mg twice daily)</p>
Antiarrhythmics	Amiodarone, lidocaine (systemic), quinidine: ↑ antiarrhythmics – Monitor concentrations
Anticoagulants	Warfarin: ↑ or ↓ warfarin – Monitor INR
Anticonvulsants	Carbamazepine, phenobarbital, phenytoin: May ↓ FPV levels substantially – Monitor anticonvulsant levels and virologic response. Consider obtaining FPV levels
Antidepressants	<p>Amitriptyline, imipramine: ↑ tricyclics – Monitor tricyclic antidepressant concentrations</p> <p>Paroxetine: Significant ↓ paroxetine – titrate to effect</p>
Antifungals	<p>Itraconazole, ketoconazole: FPV and itra/keto ↑ – Consider ↓ itra/keto dose if dose is >400 mg/day. If FPV is boosted with RTV, use with caution; do not exceed 200 mg/day itra/keto</p> <p>Voriconazole: Potential for bi-directional inhibition; when boosted with RTV, may significantly ↓ voriconazole – Monitor voriconazole serum concentrations and for toxicities</p>
Antigout	<p>Colchicine: For treatment of gout flares – If FPV is given without RTV, 1.2 mg (2 tablets) x 1 dose. Do not repeat dose before 3 days. For prophylaxis of gout flares – adjust dose to ½ original regimen For treatment of familial Mediterranean fever (FMF) – Max: 1.2 mg daily</p> <p>Do not co-administer in patients with hepatic or renal impairment</p>
Antimycobacterials	Rifabutin: FPV AUC ↓ 15%; RFB ↑ 193% – ↓ RFB dose to 150 mg once daily or 300 mg 3x/wk with unboosted FPV. ^d If FPV is boosted with RTV, ↓ RFB dose to 150 mg qod or 3x/wk ^e

Bronchodilators	Salmeterol: Co-administration not recommended. Consider formoterol
Calcium Channel Blockers	↑ calcium channel blockers – Use with caution
Corticosteroids	Dexamethasone: ↓ FPV – 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
Histamine H2 Blockers	FPV ↓ 30% – Use with caution; when using boosted FPV, interaction is unlikely to be significant
Immunosuppressants	Cyclosporine, tacrolimus, rapamycin: ↑ immunosuppressants – Monitor immunosuppressant concentrations
Lipid-Lowering Agents	Atorvastatin: ATO AUC ↑ 150% – Max ATO dose 20 mg/day; use with careful monitoring or consider using alternative agent
Oral Contraceptives	Ethinyl estradiol/norethindrone: Use alternative form of birth control
Proton Pump Inhibitors	No significant interaction
Pulmonary Hypertension Agents	Bosentan: In patients already taking boosted FPV 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 FPV. After boosted FPV has been given for >10 days, once daily or qod bosentan can be reintroduced. Tadalafil: In patients already taking boosted FPV 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 FPV. Stop tadalafil ≥24 h prior to starting boosted FPV. At least ≥1 wk after initiating boosted FPV, resume tadalafil at 20 mg once daily; increase to 40 mg once daily based on tolerability.
Synthetic Narcotics	Methadone: Methadone ↓ 13%; FPV C _{min} ↓ 25% – Monitor and titrate methadone if needed. No withdrawal symptoms observed
<p>* Because of the availability of fosamprenavir, amprenavir capsules are no longer available, used, or recommended. Fosamprenavir oral solution is for patients unable to tolerate pills or for short-term use in patients with an NG or J tube.</p> <p>^a Triglyceride and cholesterol testing should be performed prior to initiating FPV; monitor lipid profile.</p> <p>^b 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>^c Discontinuation of PIs may be required to reverse fat redistribution. Patients with hypertriglyceridemia or hypercholesterolemia should be evaluated for risks for cardiovascular events and pancreatitis.</p> <p>^d Can be used with caution as a single dose in a monitored situation for procedural sedation.</p> <p>^e Rifabutin 3x/wk is recommended if CD4 count <100 cells/mm³.</p>	