

SAQUINAVIR (SQV) (Updated April 2010)	
Trade Name	Invirase ^a
Classification	Protease inhibitor
Form	200-mg hard-gel capsules and 500-mg tablets
Dosing Recommendations	Must be co-administered with ritonavir (RTV) – SQV 1000 mg + RTV 100 mg twice daily <i>or</i> SQV 400 mg + RTV 400 mg twice daily
Hepatic Impairment Dosing	Use with caution in patients with hepatic impairment
Food Effect	Grapefruit juice may increase retention
Oral Bioavailability	4% erratic
Serum Half-life	1-2 hours
Route of Metabolism	P450 cytochrome 3A4 inhibitor and substrate (weak inhibitor)
Storage	Room temperature
Adverse Events	<p>GI intolerance, nausea, diarrhea, headache</p> <p>Elevated transaminase enzymes, possible increased bleeding episodes in patients with hemophilia</p> <p>Hyperglycemia,^b fat redistribution and lipid abnormalities^c</p> <p>Use of SQV/RTV in patients with a history of QT interval prolongation, preexisting conduction system disease, ischemic heart disease, cardiomyopathy, or underlying structural heart disease is not recommended.</p> <p>Use of SQV/RTV in patients currently taking Class IA (quinidine) or Class III (amiodarone) antiarrhythmic drugs or other drugs that may prolong the QT or PR interval is not recommended.</p>
FDA Pregnancy Category	B
Long-Term Animal Carcinogenicity Studies	Not completed
Animal Teratogen Studies	Negative
Black Box Warnings	May be used only if it is combined with ritonavir
Drugs to Avoid	<p>As part of the ARV regimen: Darunavir/ritonavir Etravirine (when SQV co-administered without RTV) Tipranavir/ritonavir</p> <p>Alfuzosin, alprazolam, amiodarone, astemizole, bepridil, cisapride, ergot derivatives, flecainide, garlic supplements (can be used with boosted SQV), lovastatin, midazolam,^d pimozone, propafenone, quinidine, ranolazine, rifabutin,^e rifampin, rifapentine, high-dose sildenafil, simvastatin, St. John’s wort, terfenadine, triazolam</p>

Cautious Use or Dose Adjustment	
Antiretrovirals	<p>Delavirdine: SQV ↑ 5-fold – ↓ SQV dose to 800 mg tid and monitor transaminase levels</p> <p>Efavirenz: SQV ↓ 62%; EFV ↓ 12% – Use SQV 400 mg + RTV 400 mg twice daily</p> <p>Lopinavir/ritonavir: SQV AUC and Cmin ↑ – Use SQV 800-1000 mg twice daily</p> <p>Maraviroc: ↑ MVC AUC – ↓ MVC dose to 150 mg twice daily</p> <p>Nelfinavir: SQV ↑ 3- to 5-fold; NfV ↑ 20% – ↓ SQV dose to 800 mg tid or 1200 mg twice daily</p> <p>Nevirapine: SQV ↓ 25% – SQV 400 mg + RTV 400 mg or SQV 1000 mg + RTV 100 mg twice daily</p> <p>Ritonavir: SQV ↑ 20-fold – Use SQV 1000 mg + RTV 100 mg twice daily or SQV 400 mg + RTV 400 mg twice daily</p>
Anticoagulants	Warfarin: ↑ or ↓ warfarin – Monitor INR
Anticonvulsants	Carbamazepine, phenobarbital, phenytoin: May ↓ SQV levels – Monitor anticonvulsant levels. Consider alternative anticonvulsant
Antidepressants	Amitriptyline, imipramine: May ↑ tricyclics – Monitor tricyclic antidepressant concentrations
Antifungals	<p>Ketoconazole: SQV ↑ 3-fold – If keto dose is >200 mg/day, monitor for excessive diarrhea, nausea, and abdominal discomfort, and adjust doses accordingly</p> <p>Voriconazole: Potential for bi-directional inhibition; when boosted with RTV, may significantly ↓ voriconazole – Monitor for toxicities</p>
Antigout	<p>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</p> <p>Do not co-administer in patients with hepatic or renal impairment</p>
Bronchodilators	Salmeterol: Co-administration not recommended. Consider formoterol
Cardiac Glycosides	Digoxin: Digoxin AUC ↑ 49% with RTV/SQV co-administration. Use with close monitoring
Corticosteroids	Dexamethasone: ↓ SQV – Use with caution
Erectile Dysfunction Agents	<p>Sildenafil: Sildenafil AUC ↑ 2-fold – Use cautiously, start with reduced dose of 25 mg q48h and monitor for adverse effects</p> <p>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</p> <p>Vardenafil: Vardenafil may ↑ substantially – Start with a 2.5-mg dose, and do not exceed a single 2.5-mg dose in 72 hours</p>

Immunosuppressants	Cyclosporine, tacrolimus, rapamycin: ↑ immunosuppressants – Monitor immunosuppressant concentrations
Lipid-Lowering Agents	Atorvastatin: ATO ↑ 450% when combined with SQV/RTV – Use lowest possible starting dose of ATO with careful monitoring
Oral Contraceptives	Ethinyl estradiol: ↓ EE – Use alternative or additional method of contraception
Proton Pump Inhibitors	Omeprazole: SQV ↑ 54-82% – Clinical significance unclear – Monitor for SQV toxicities
Pulmonary Hypertension Agents	<p>Bosentan: In patients already taking boosted SQV 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 SQV. After boosted SQV has been given for >10 days, once daily or qod bosentan can be reintroduced.</p> <p>Tadalafil: In patients already taking boosted SQV 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 SQV. Stop tadalafil ≥24 h prior to starting boosted SQV. At least ≥1 wk after initiating boosted SQV, resume tadalafil at 20 mg once daily; increase to 40 mg once daily based on tolerability.</p>
Synthetic Narcotics	Methadone: R-methadone (active) AUC ↓ 20% when combined with SQV 400 mg + RTV 400 mg twice daily – Monitor and titrate according to methadone response
<p>^a Fortovase (soft-gel capsule) was discontinued during the first quarter of 2006.</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 may be used with saquinavir only if it is boosted with ritonavir.</p>	