

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

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

<b>Immunosuppressants</b>	<b>Cyclosporine, tacrolimus, rapamycin:</b> ↑ immunosuppressants – Monitor immunosuppressant concentrations
<b>Lipid-Lowering Agents</b>	<b>Atorvastatin:</b> ATO ↑ 450% when combined with SQV/RTV – Use lowest possible starting dose of ATO with careful monitoring
<b>Oral Contraceptives</b>	<b>Ethinyl estradiol:</b> ↓ EE – Use alternative or additional method of contraception
<b>Proton Pump Inhibitors</b>	<b>Omeprazole:</b> SQV ↑ 54-82% – Clinical significance unclear – Monitor for SQV toxicities
<b>Pulmonary Hypertension Agents</b>	<p><b>Bosentan:</b> 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 &gt;10 days, once daily or qod bosentan can be reintroduced.</p> <p><b>Tadalafil:</b> 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>
<b>Synthetic Narcotics</b>	<b>Methadone:</b> R-methadone (active) AUC ↓ 20% when combined with SQV 400 mg + RTV 400 mg twice daily – Monitor and titrate according to methadone response
<p><sup>a</sup> Fortovase (soft-gel capsule) was discontinued during the first quarter of 2006.</p> <p><sup>b</sup> 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><sup>c</sup> 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><sup>d</sup> Can be used with caution as a single dose in a monitored situation for procedural sedation.</p> <p><sup>e</sup> Rifabutin may be used with saquinavir only if it is boosted with ritonavir.</p>	