**All Interactions with Saquinavir (Fortovase, Invirase)**

| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| AA-Ricki TEST Drug  (rickiOne, rickiTestOne) | 3222 | 122 | and the effect on MY drug is... | here's the effect on Saquinavir | lottsa clinical effects here... | no mechanism to speak of. | management is iffy.  *Alternative Agents*: **alternative agents are around somewhere** |
| Adefovir[45](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#45)  (Hepsera) | - | - | No significant change | No significant change | - | - | No dose adjustment necessary |
| Amprenavir[111](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#111)  (APV)(Agenerase) | 1200 mg BID with efavirenz 600 mg QD | 1600 mg BID (soft gel caps) | Amprenavir clearance: no significant change | Not studied | - | - | No dose adjustment necessary |
| Amprenavir[60](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#60)  (APV)(Agenerase) | 750 mg or 800 mg TID x 2 weeks (fed) | 800 mg TID x 2 weeks (fed) | Amprenavir AUC: decreased 32%; Cmax: decreased 37%; Cmin: no significant change | Saquinavir AUC: decreased 19%; Cmax: increased 21%; Cmin: decreased 48% | Decreased amprenavir effects | Induction of CYP450 3A4 by either drug | No dose adjustment necessary |
| Astemizole[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (Hismanal) | - | - | Not studied; may increase astemizole levels | - | Increased astemizole effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by saquinavir | Do not coadminister  *Alternative Agents*:  **Cetirizine Fexofenadine Loratadine** |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Atazanavir[162](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#162)  (ATV)(Reyataz) | 200 mg BID with saquinavir 1500 mg BID | 1000 mg BID with ritonavir 100 mg BID | Not studied | Saquinavir AUC: decreased 53%; Cmax: decreased 78%; Cmin: decreased 69% (when SQV/ATV BID compared to SQV/RTV BID) | Decreased saquinavir levels (when compared to SQV 100 mg with RTV 100 mg BID) | Possible induction of P450 by atazanavir | Do not coadminister |
| Atazanavir[137](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#137)  (ATV)(Reyataz) | 300 mg QD x 30 days | 1600 mg QD with ritonavir 100 mg QD x 30 days | Not studied | Saquinavir AUC: increased 61%; Cmax: increased 42%; Cmin: increased 112%;Ritonavir AUC: increased 41%; Cmax: increased 58%; Cmin: decreased 27% | Increased saquinavir effects | Inhibition of CYP450 3A4 by atazanavir and ritonavir | Dose adjustment not established |
| Atazanavir  (ATV)(Reyataz) | 400 mg QD on days 7-13 | 1200 mg (soft gel caps) QD on days 1-13 | Not studied | Saquinavir AUC: increased 449%; Cmax: increased 339%; Cmin: increased 586% | Increased saquinavir effects | Inhibition of CYP450 3A4 by atazanavir | Dose adjustment not established |
| Atazanavir[122](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#122)  (ATV)(Reyataz) | 400 mg x 7 days | 800 mg, 1200 mg, 1600 mg QD | No significant change | Saquinavir AUC: increased 440-610%; Cmin: increased 560-1660% | Increased saquinavir effects | Inhibition of CYP450 3A4 by atazanavir | Dose adjustment not established |
| Atorvastatin[215](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#215) | 40 mg QD on days 1-4 and 15-18 | 400 mg BID with ritonavir 400 mg BID on days 4-18 | Atorvastatin AUC: increased 79%; Cmax: increased 330% | Not studied | Increased atorvastatin effects (eg, myopathy, rhabdomyolysis) | Inhibition of CYP450 3A4 by saquinavir and ritonavir | Avoid combination if possible; may consider low dose atorvastatin or alternative agents; monitor for myopathy  *Alternative Agents*:  **Pravastatin** |
| Bosentan[727](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#727) | - | - | - | - | Possible increased bosentan effects | - | Start low and titrate bosentan to effect. If patient has been on protease inhibitor (other than unboosted atazanavir) for more than 10 days, start bosentan at 62.5 mg daily or every other day. If patient is currently on bosentan and requires a PI (other than unboosted atazanavir), stop bosentan for at least 36 hours prior to initiating ART. Wait 10 days and then resume bosentan starting with 62.5 mg daily or every other day. |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Carbamazepine[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (others)(Tegretol) | - | - | - | May decrease saquinavir levels | Decreased saquinavir effects | Induction of CYP450 3A4 by carbamazepine | Avoid combination if possible; consider alternative agents; monitor carbamazepine levels and adjust as indicated  *Alternative Agents*:  **Gabapentin Lamotrigine Tiagabine Topiramate** |
| Cisapride[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (Propulsid) | - | - | - | - | Increased cisapride effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by saquinavir | Do not coadminister  *Alternative Agents*:  **Metoclopramide** |
| Clarithromycin[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44),[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (Biaxin) | 500 mg BID x 7 days | 1200 mg TID x 7 days | Clarithromycin AUC: increased 45%; Cmax: increased 39%; 14-hydrooxyclarithromycin AUC: decreased 24%; Cmax: decreased 34% | Saquinavir soft gel caps AUC: increased 177%; Cmax: increased 187%; saquinavir hard gel caps AUC: increased 500% | - | Inhibition of CYP450 3A4 by clarithromycin | Dose adjustment not established |
| Colchicine[561](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#561)  (Colcrys) | - | - | - | - | Increased colchicine effects | Inhibition of P450 3A4 by saquinavir | For treatment of gout, reduce colchicine dosage to 0.6 mg x 1 then 0.3 mg one hour later. Dose not to be repeated no earlier than 3 days. For prophylaxis of gout, reduce colchicine dosage to 0.3 mg QD if on 0.6 mg BID prior to PI therapy or reduce colchicine dose to 0.3 mg QOD if on 0.6 mg QD prior to PI therapy. For treatment of familial Mediterranean fever: Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID. Do not coadminister in patients with hepatic or renal impairment. |
| Cyclosporine[308](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#308)  (Neoral, Sandimmune) | 150 mg BID | 1200 mg TID | Cyclosporine Cmin: increased 300% | - | Increased cyclosporine effects (eg, excessive bone marrow suppression, nephrotoxicity) | Inhibition of CYP450 3A4 by saquinavir; competitive binding to P-glycoprotein | Monitor and adjust cyclosporine as indicated |
| Daclatasvir[727](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#727)  (Daklinza) | - | - | - | - | - | Inhibition of CYP3A4 | Decrease daclatasvir dose to 30 mg daily |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Darunavir[161](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#161)  (DRV)(Prezista) | 400 mg BID with ritonavir 100 mg BID | 1000 mg BID | Darunavir AUC: decreased 26%; Cmax: decreased 17%; Cmin: decreased 42% | Saquinavir Cmin: decreased 18% | Decreased darunavir effects | - | Do not coadminister |
| Dasabuvir, Ombitasvir/Paritaprevir/Ritonavir[727](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#727)  (Viekira) | - | - | - | - | - | - | Do not coadminister |
| Delavirdine[88](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#88)  (DLV)(Rescriptor) | 400 mg TID | 600 mg TID | Delavirdine AUC: decreased 15% | Saquinavir AUC: increased 500% | - | Increased saquinavir effects | - |
| Delavirdine[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (DLV)(Rescriptor) | 400 mg TID x 14 days | 600 mg TID (hard gel caps) x 21 days | No significant change | Saquinavir AUC: increased 500% | Increased saquinavir effects | Inhibition of CYP450 3A4 by delavirdine | Dose adjustment not established |
| Dexamethasone[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (Decadron) | - | - | - | May decrease saquinavir levels | Decreased saquinavir effects | Possible induction of CYP450 3A4 by dexamethasone | No dose adjustment necessary |
| Digoxin[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (others)(Lanoxin) | 0.5 mg x 1 | 1000 mg BID with 100 mg ritonavir BID x 16 days | Digoxin AUC: increased 49%; Cmax: increased 27% | - | Increased digoxin levels | - | Serum concentration of digoxin should be monitored and dose of digoxin may need to be reduced. |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| DMP450[265](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#265) | 1000 mg -1500 mg x 1 dose | 400 mg x 1 dose | - | AUC: increased 1000% | - | Inhibition of CYP3A4 by DMP450 | Dose adjustment not established |
| Efavirenz[50](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#50)  (EFV)(Sustiva) | 600 mg QHS on day 10-24 | 400 mg (soft gel caps) BID with ritonavir 400 mg BID on day 1-10 | No significant change | Saquinavir Cmin: decreased 10%; ritonavir Cmin: no significant change | Not clinically significant | Induction of CYP450 3A4 by efavirenz | No dose adjustment necessary |
| Efavirenz[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75),[90](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#90)  (EFV)(Sustiva) | 600 mg x 10 days | 1200 mg (soft gel caps) Q8H x 10 days | Efavirenz AUC: decreased 12%; Cmax: decreased 13% | Saquinavir AUC: decreased 62%; Cmax: decreased 50% | Decreased saquinavir effects | Induction of CYP450 3A4 by efavirenz | Consider adding ritonavir to saquinavir containing regimen |
| Elbasvir/grazoprevir[727](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#727)  (Zepatier) | - | - | - | - | May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition | OATP1B1/3 inhibition by saquinavir/ritonavir | Do not coadminister |
| Enfuvirtide[6](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#6),[7](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#7),[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (ENF)(Fuzeon) | 90 mg SQ BID on days 1-7 | 1000 mg BID with ritonavir 100 mg BID on days 4-7 | Enfuvirtide Cmax: no significant change; Cmin: increased 26%; AUC: no significant change | No significant change | - | - | No dose adjustment necessary |
| Erythromycin[282](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#282)  (E-Base, Ilosone, E-Mycin, Eryc, Ery-Tab, others)(Eryc, E-Base) | 250 mg QID x 7 days | 1200 mg TID | - | Saquinavir AUC: increased 99%; Cmax: increased 106% when studied in HIV-infected patients | Increased saquinavir effects | Inhibition of CYP450 3A4 by erythromycin | Dose adjustment not established |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Ethinyl estradiol/norethindrone acetate[366](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#366)  (others)(Ortho-Novum) | 0.03 mg ethinyl estradiol/0.075 mg gestodene QD on days 4-22 | 600 mg saquinavir hard gel caps on days 1 and 22 | No significant change | No significant change | - | - | No dose adjustment necessary |
| Etravirine[405](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#405)  (ETR)(Intelence) | - | 1000 mg BID with 100 mg ritonavir BID | Etravirine AUC: decreased 33%; Cmax: decreased 37%; Cmin: decreased 29% | Saquinavir Cmin: decreased 20% | - | - | No dose adjustment necessary |
| Fluconazole[270](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#270)  (Diflucan)(Diflucan) | 400 mg QD on day 2, then 200 mg QD on days 3-8 | 1200 mg TID | Not reported | Saquinavir AUC: increased 50%; Cmax: increased 56% | Increased saquinavir effects | Inhibition of CYP450 3A4 by fluconazole | Dose adjustment not established |
| Fosamprenavir[138](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#138)  (FPV)(Lexiva) | 700 mg BID on days 2-22 | 1000 mg BID with ritonavir 100 mg BID on days 1-11 | Not studied | Saquinavir AUC (with ritonavir 100 mg BID): AUC: no significant change; Cmax: no significant change; Cmin: decreased 24% | - | - | No dose adjustment necessary |
| Fosamprenavir[138](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#138)  (FPV)(Lexiva) | 700 mg BID on days 2-22 | 1000 mg BID with ritonavir 200 mg BID on days 12-22 | Not studied | Saquinavir AUC (with ritonavir 200 mg BID): no significant change; Cmax: no significant change; Cmin: increased 20% | - | - | No dose adjustment necessary |
| Garlic[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75),[172](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#172)  (Allium sativum, others) | Garlic capsules (3.6 mg/caplet) BID on days 5-24 | 1200 mg (soft gel caps) TID with food x 4 days | Not studied | Saquinavir AUC: decreased 51%; Cmax: decreased 54%; Cmin: decreased 49%After a 10 day garlic washout period, pharmacokinetic values returned to only 60-70% of baseline | Decreased saquinavir effects | Possible induction of gut mucosal CYP450 3A4 by garlic; P-glycoprotein effects are also possible | Avoid garlic supplements when saquinavir is used either boosted or unboosted. |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Grapefruit juice[231](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#231) | 200 mL single strength (grapefruit juice from concentrate) | 600 mg (hard gel cap) x 1 dose | - | AUC: increased 50%Oral bioavailability: increased 100% | Increased saquinavir effects | Inhibition of gastrointestinal CYP450 3A4 by grapefruit juice | Separate grapefruit juice from saquinavir dose by at least 2 hours |
| Indinavir[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44),[43](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#43)  (IDV)(Crixivan) | 800 mg Q8H x 2 days | Saquinavir soft gel cap 800 mg or 1200 mg x 1 dose | Not studied | Saquinavir 800 mg AUC: increased 620%; Cmax: increased 551%; saquinavir 1200mg AUC: increased 364%; Cmax: increased 299% | Increased saquinavir effects | Inhibition of CYP450 3A4 by indinavir | Dose adjustment not established |
| Indinavir[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (IDV)(Crixivan) | 800 mg Q8H x 2 days | 1200 mg x 1 dose | Indinavir concentration: increased | Saquinavir AUC: increased 364%; Cmax: increased 299% | Increased saquinavir effects | Inhibition of CYP450 3A4 by indinavir | Dose adjustment not established |
| Itraconazole[276](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#276)  (Sporanox)(Sporanox) | 100 mg QD x 14 days | 800 mg or 1200 mg saquinavir soft gel caps BID with 100 mg itraconazole QD x 14 days | Not studied | No significant changes (compared to 1400 mg saquinavir soft gel caps BID with no itraconazole) | - | Inhibition of CYP450 3A4 by itraconazole | No dose adjustment necessary |
| Itraconazole[277](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#277)  (Sporanox)(Sporanox) | 200 mg BID | 400 mg BID (with ritonavir 600 mg BID) | Itraconazole half-life: increased 414% | - | Increased itraconazole effects; increased saquinavir effects | Inhibition of CYP450 3A4 by itraconazole and saquinavir and ritonavir | Consider reducing itraconazole to 100 mg BID |
| Ketoconazole[282](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#282)  (Nizoral) | 200 mg QD | 1200 mg TID | No significant change | Saquinavir AUC: increased 69%; Cmax: increased 36% when studied in HIV-infected patients | Increased saquinavir effects | Inhibition of CYP450 3A4 by ketoconazole | Dose adjustment not established |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Ketoconazole[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (Nizoral) | 200 mg QD x 6 days | 600 mg TID (hard gel caps) x 6 days | - | AUC: increased 130%; Cmax: increased 147% | Increased saquinavir effects | Inhibition of CYP450 3A4 by ketoconazole | - |
| Ketoconazole[281](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#281)  (Nizoral) | 400 mg QD x 14 days | 2000 mg x 14 days | - | Saquinavir AUC: decreased 78%; Cmax: decreased 76%; Cmin: decreased 87% (compared to saquinavir/ritonavir 2000 mg/100 mg QD) | Decreased saquinavir effects | Inadequate boosting due to ketoconazole | Do not use ketoconazole as a pharmacokinetic "booster" with saquinavir |
| Ketoconazole[282](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#282)  (Nizoral) | 400 mg QD x 7 days | 1200 mg TID | No significant change | Saquinavir AUC: increased 190%; Cmax: increased 171% | Increased saquinavir effects | Inhibition of CYP450 3A4 by ketoconazole | Dose adjustment not established |
| Lopinavir/ritonavir[78](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#78)  (LPV/r)(Kaletra) | 400 mg/100 mg BID x 10 days | 800 mg BID | - | Saquinavir AUC: no significant change; Cmin: increased | Increased saquinavir effects | Inhibition of CYP450 3A4 by lopinavir/ritonavir | Dose adjustment not established |
| Lopinavir/ritonavir[150](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#150)  (LPV/r)(Kaletra) | 400/100 mg BID | 1000 mg (soft gel caps) BID | Lopinavir AUC: no significant change; Cmax: no significant change; Cmin: no significant change; (compared to historical control) | Saquinavir AUC: no significant change; Cmax: no significant change; Cmin: increased 27% (compared to saquinavir/ritonavir control)Ritonavir AUC: decreased 54%; Cmax: decreased 37%; Cmin: decreased 60%; Clearance total: increased 107%(compared to saquinavir/ritonavir control) | - | Possibly increased clearance resulting in decreased ritonavir levels | No dose adjustment necessary |
| Lopinavir/ritonavir[108](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#108)  (LPV/r)(Kaletra) | 400/100 mg BID on days 6-20 | 1200 mg TID on days 1-5, 800 mg BID on days 6-15 | No significant change | Saquinavir AUC: increased 836%; Cmax: increased 517%; Cmin: increased 1700% | Increased saquinavir effects | Inhibition of CYP450 3A4 by lopinavir/ritonavir | Dose adjustment not established |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Lovastatin[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (Mevacor)(Mevacor) | - | - | Increased lovastatin levels | - | Increased lovastatin effects (eg, myopathy, rhabdomyolysis) | Inhibition of CYP450 3A4 by saquinavir | Do not coadminister  *Alternative Agents*:  **Atorvastatin Pravastatin** |
| Maraviroc[2](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#2)  (MVC)(Selzentry) | 100 mg BID | 1000 mg BID with ritonavir 100 mg BID | Maraviroc AUC: increased 877%; Cmax: increased 378%; Cmin: increased 1030% | - | Increased maraviroc effects | Inhibition of CYP450 3A4 by saquinavir/ritonavir | Decrease maraviroc dose to 150 mg BID |
| Maraviroc[2](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#2)  (MVC)(Selzentry) | 100 mg BID | Saquinavir 1000 mg BID with 100 mg ritonavir BID with 600 mg efavirenz QD | Maraviroc AUC: increased 400%; Cmax: increased 126%; Cmin: increased 742% | - | Increased maraviroc effects | Inhibition of CYP450 3A4 by saquinavir/ritonavir | Decrease maraviroc dose to 150 mg BID |
| Methadone[198](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#198)  (Dolophine)(Dolophine) | - | 400 mg BID combined with 400 mg BID ritonavir | S-methadone AUC: decreased 25%; R-methadone AUC: decreased 20% | Not studied | Not clinically significant | Induction of CYP450 by saquinavir/ritonavir | Monitor and adjust methadone as indicated |
| Methadone[195](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#195)  (Dolophine)(Dolophine) | 35-100 mg QD x 14 days | 1600 mg (soft gel caps) QD with ritonavir 100 mg QD x 14 days | Unbound R-methadone GMR: decreased 8%; alpha-1-acid glycoprotein GMR: increased 14% | No significant change | - | Reduction in unbound R-methadone mediated by increased alpha1-acid glycoprotein | No dose adjustment necessary |
| Methadone[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (Dolophine)(Dolophine) | 60-120 mg QD | 1000 mg BID with 100 mg ritonavir BID x 14 days | Decreased methadone levels | Saquinavir AUC: decreased 19% | - | - | Methadone dosage may need to be increased when coadministered with saquinavir/ritonavir |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Methadone[463](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#463)  (Dolophine)(Dolophine) | 60-120 mg QD | 1000mg BID with ritonavir 100 mg BID | R-methadone AUC: decreased 19%; S-methadone AUC: decreased 21% | No significant change | Decreased methadone effects (e.g. withdrawal) | - | Monitor for signs and symptoms of methadone withdrawal; some patients may need an increase in the methadone dose |
| Midazolam[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254),[258](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#258)  (Versed) | 5 mg IV x 1 dose | 600 mg TID x 8 weeks | Increased midazolam levels | - | Increased midazolam effects (eg, increased sedation, confusion, respiratory depression) | Inhibition of CYP450 3A4 by saquinavir | Parenteral midazolam can be used with caution when given as a single dose in a monitored situation for procedural sedation; chronic midazolam administration (oral or intravenous) should be avoided  *Alternative Agents*:  **Lorazepam** |
| Midazolam[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (Versed) | 7.5 mg PO x 1 | 1000 mg BID with 100 mg ritonavir BID | Midazolam AUC: increased 1144%; Cmax: increased 327% | - | Increased midazolam effects | Inhibition of CYP450 3A4 by saquinavir/ritonavir | Parenteral midazolam can be used with caution when given as a single dose in a monitored situation for procedural sedation; chronic midazolam administration (oral or intravenous) should be avoided  *Alternative Agents*:  **Lorazepam** |
| Nelfinavir[147](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#147)  (NFV)(Viracept) | 1250 mg BID on days 16-21 | 1000 mg saquinavir BID with 100 mg ritonavir BID on days 1-14 | Nelfinavir Cmax: increased 55%; M8 AUC: increased 622%; Cmax: increased 94%; Cmin: increased 179% | Saquinavir Cmax: increased 172% | - | Inhibition of CYP450 3A4 by saquinavir/ritonavir | No dose adjustment necessary |
| Nelfinavir[45](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#45),[46](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#46)  (NFV)(Viracept) | 750 mg (single dose) x 4 days | 1200 mg TID x 4 days (1200 mg single dose) | Nelfinavir AUC: increased 18% | Saquinavir AUC: increased 392% | - | Inhibition of CYP450 3A4 by both drugs | Decrease saquinavir to 800 mg TID or 1200 mg BID; no change in nelfinavir dose necessary |
| Nelfinavir[24](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#24),[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (NFV)(Viracept) | 750 mg TID x 4 days | 1200 mg (soft gel cap) x 1 dose | - | Saquinavir AUC: increased 392%; Cmax: increased 179% | Increased saquinavir effects | Inhibition of CYP450 3A4 by nelfinavir | May consider saquinavir 800 mg TID with nelfinavir 750 mg TID or saquinavir 1200 mg BID with nelfinavir 1250 mg BID |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Nelfinavir[24](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#24),[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (NFV)(Viracept) | 750 mg x 1 dose | 1200 mg (soft gel caps) TID x 4 days | Nelfinavir AUC: increased 18%; Cmax: no change | Not studied | - | - | No dose adjustment necessary |
| Nevirapine[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (NVP)(Viramune) | 200 mg BID x 21 days | 600 mg (hard gel caps) TID x 7 days | No significant change | Saquinavir AUC: decreased 24%; Cmax: decreased 28% | May decrease saquinavir effects | Induction of CYP450 by nevirapine | Dose adjustment not established |
| Nevirapine[95](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#95)  (NVP)(Viramune) | 200 mg QD x 2 weeks then 200 mg BID x 28 days | 600 mg (hard gel caps) TID | No significant change | Saquinavir AUC: decreased 24%; Cmax: decreased 28% | Decreased saquinavir effects | Induction of CYP450 3A4 by nevirapine | Dose adjustment not established |
| Omeprazole[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75),[246](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#246)  (Prilosec)(Prilosec) | 40 mg QD on days 10-15 | 1000 mg BID with 100 mg ritonavir BID on days 1-15 | - | Saquinavir AUC: increased 82%; Cmax: increased 75%; Cmin: increased 106%; Ritonavir: no significant effect | Increased saquinavir effects | Possibly due to increased saquinavir absorption | Monitor for increased saquinavir toxicity particularly GI symptoms, increased triglycerides or deep vein thrombosis  *Alternative Agents*:  **H2-antagonists** |
| Phenobarbital[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (Luminal, others)(Luminal) | - | - | - | May decrease saquinavir levels | May decrease saquinavir effects | Induction of CYP450 3A4 by phenobarbital | Avoid combination if possible; consider alternative agents; monitor phenobarbital levels and adjust as indicated  *Alternative Agents*:  **Gabapentin Lamotrigine Tiagabine Topiramate** |
| Phenytoin[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (Dilantin) | - | - | - | May decrease saquinavir levels | May decrease saquinavir effects | Induction of CYP450 3A4 by phenytoin | Avoid combination if possible; consider alternative agents. Monitor phenytoin levels and adjust as indicated. Monitor virologic response.  *Alternative Agents*:  **Gabapentin Lamotrigine Tiagabine Topiramate** |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Pimozide[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44),[176](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#176)  (Orap)(Orap) | - | - | Not studied; may increase pimozide levels | - | Increased pimozide effects (eg, hypotension, cardiac arrhythmias) | Inhibition of CYP450 3A4 by saquinavir | Do not coadminister |
| Pravastatin[215](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#215)  (Pravachol)(Pravachol) | 40 mg QD on days 1-4 and 15-18 | 400 mg BID with ritonavir 400 mg BID on days 4-18 | Pravastatin AUC: decreased 50%; Cmax: decreased 42% | Not studied | Decreased pravastatin effects | Induction of glucuronidation by ritonavir | No dose adjustment necessary |
| Ranitidine[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (Zantac)(Zantac) | 150 mg x 2 doses | 600 mg x 1 dose | - | AUC: increased 67%; Cmax: increased 74% | - | Inhibition of CYP450 3A4 by ranitidine | No dose adjustment necessary |
| Ranolazine[709](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#709)  (Ranexa) | - | - | Not studied; may increase ranolazine levels | Not studied; may increase saquinavir levels | Potential increased ranolazine adverse effects (e.g. prolonged QT, cardiac arrythmias). | - | Do not coadminister |
| Rifabutin[339](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#339)  (Mycobutin) | 150 mg Q3D or 300 mg Q7D | 400 mg with ritonavir 400 mg BID | Rifabutin weekly AUC: no significant difference between dosing regimens | - | Avoidance of increased rifabutin effects | Inhibition of CYP450 3A4 by both ritonavir and saquinavir | Reduce rifabutin dose to 150 mg daily or 300 mg 3x/week. Monitor for antimicrobial activity and/or consider therapeutic drug monitoring. |
| Rifabutin[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (Mycobutin) | 300 mg QD x 14 days | 600 mg (hard gel caps) TID x 14 days | - | AUC: decreased 43%; Cmax: decreased 30% | Decreased saquinavir effects | Induction of CYP450 3A4 by rifabutin | Reduce rifabutin dose to 150 mg daily or 300 mg 3x/week. Monitor for antimicrobial activity and/or consider therapeutic drug monitoring. |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Rifabutin[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (Mycobutin) | 300 mg x 1 | 1200 mg TID | Rifabutin AUC: increased 44%; Cmax: increased 45% | Saquinavir AUC: decreased 47%; Cmax: decreased 39% | Increased rifabutin effects | inhibition of CYP450 3A4 by saquinavir | Reduce rifabutin dose to 150 mg daily or 300 mg 3x/week. Monitor for antimicrobial activity and/or consider therapeutic drug monitoring. |
| Rifampin[282](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#282)  (Rifampicin)(Rifadin) | 600 mg QD x 14 days | 1200 mg TID | - | Saquinavir AUC: decreased 46%; Cmax: decreased 43% when studied in HIV-infected patients | Decreased saquinavir effects | Induction of CYP450 3A4 by rifampin | Do not coadminister |
| Rifampin[282](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#282)  (Rifampicin)(Rifadin) | 600 mg QD x 14 days | 1200 mg TID | - | Saquinavir AUC: decreased 70%; Cmax: decreased 65% | Decreased saquinavir effects | Induction of CYP450 3A4 by rifampin | Do not coadminister |
| Rifampin[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44),[351](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#351)  (Rifampicin)(Rifadin) | 600 mg QD x 7 days | 600 mg (hard gel caps) TID x 14 days | - | AUC: decreased 84%; Cmax: decreased 79% | Decreased saquinavir effects | Induction of CYP450 3A4 by rifampin | Avoid if possible; may consider saquinavir 400 mg BID with ritonavir 400 mg BID  *Alternative Agents*:  **Rifabutin** |
| Ritonavir[51](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#51)  (RTV)(Norvir) | 100 mg BID | Saquinavir soft gel caps 1000 mg/ritonavir 100 mg BID or saquinavir hard gel caps 1000 mg/ritonavir 100 mg BID, adminstered with food for at least 3 weeks | Not studied | Saquinavir soft gel caps AUC: increased 30% (compared to hard gel caps/ritonavir AUC); Cmin: increased 17% (when compared to hard gel caps/ritonavir regimen Cmin) | Increased saquinavir effects (AUC achieved with hard gel caps/ritonavir regimen is comparable, but not equivalent to, soft gel caps/ritonavir AUC) | Inhibition of CYP450 3A4 by ritonavir | Consider ritonavir-boosted saquinavir |
| Ritonavir[118](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#118)  (RTV)(Norvir) | 100 mg QD | 1600 mg QD x 13 days | - | Saquinavir AUC: increased 592%; Cmax: increased 566%; Cmin: increased 424% (compared to saquinavir 1200 mg TID) | Increased saquinavir effects | Inhibition of CYP450 3A4 by ritonavir | - |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Ritonavir[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44),[47](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#47),[48](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#48),[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (RTV)(Norvir) | 400 mg BID at steady state | 400 mg (hard gel caps) BID at steady state | Not studied | Saquinavir AUC: increased 1587%; Cmax: increased 1277% | Increased saquinavir effects | Inhibition of CYP450 3A4 by ritonavir | Consider ritonavir-boosted saquinavir |
| Ritonavir[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44),[47](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#47),[48](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#48),[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75),[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (RTV)(Norvir) | 400 mg BID x 14 days | 400 mg (soft gel caps) BID x 14 days | - | Saquinavir AUC: increased by 121%; Cmax: increased 64% | Increased saquinavir effects | Inhibition of CYP450 3A4 by ritonavir | Consider ritonavir-boosted saquinavir |
| Ritonavir[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#55),[57](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#57)  (RTV)(Norvir) | Multiple doses studied; 200 mg, 300 mg, 600 mg | Multiple saquinavir hard gel caps doses studied; 200 mg, 400 mg, 600 mg | Ritonavir AUC: no significant change | Saquinavir AUC: increased 5000%; Cmax: increased 2100% | Increased saquinavir effects | Inhibition of CYP450 3A4 by ritonavir | Consider ritonavir-boosted saquinavir |
| Sildenafil[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75)  (Viagra) | 100 mg x 1 | 1200 mg TID x 8 days | Sildenafil AUC: increased 210%; Cmax: increased 140% | - | Increased sildenafil effects (eg, headache, flushing, priapism) | Inhibition of CYP450 3A4 by saquinavir | For erectile dysfunction, initiate sildenafil 25 mg every 48 hours and monitor for adverse effects. Manufacturer recommends not to exceed dose of 25 mg every 48 hours. Do not coadminister if using sildenafil for pulmonary arterial hypertension. |
| Simeprevir[727](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#727)  (Olysio) | - | - | - | - | - | Inhibition of CYP3A4 potentiating simeprevir effects | Do not coadminister |
| Simvastatin[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (Zocor)(Zocor) | - | - | Increased simvastatin levels | - | Increased simvastatin effects (eg, myopathy, rhabdomyolysis) | Inhibition of CYP450 3A4 by saquinavir | Do not coadminister  *Alternative Agents*:  **Atorvastatin Pravastatin** |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Simvastatin[215](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#215)  (Zocor)(Zocor) | 40 mg QD on days 1-4 and 15-18 | 400 mg BID with ritonavir 400 mg BID on days 4-18 | Simvastatin AUC: increased 3059%; Cmax: increased 3000% | - | Increased simvastatin effects | Inhibition of CYP450 3A4 by saquinavir and ritonavir | Do not coadminister  *Alternative Agents*:  **Atorvastatin Pravastatin** |
| St. John's Wort[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (Hypericum perforatum, hypericin, hyperforin) | - | - | - | May decrease saquinavir levels | Decreased saquinavir effects | Possible induction of CYP450 3A4 by St. John's Wort | Do not coadminister |
| Tenofovir disoproxil fumarate[145](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#145)  (TDF)(Viread) | 300 mg QD | 1000 mg saquinavir BID with 100 mg ritonavir BID | Tenofovir Cmin: increased 23% | Saquinavir AUC: increased 29%; Cmax: increased 22%; Cmin: incresed 47% | - | - | No dose adjustment necessary |
| Tenofovir disoproxil fumarate[142](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#142)  (TDF)(Viread) | 300 mg QD on days 2-14 | 1000 mg BID with 100 mg ritonavir on days 1-14 | No significant change | No significant change either for saquinavir or ritonavir | - | - | No dose adjustment necessary |
| Tenofovir disoproxil fumarate[149](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#149)  (TDF)(Viread) | 300 mg QD on days 3-14 | 1000 mg (hard gel caps) with ritonavir 100 mg BID on days 1-14 | Not studied | Saquinavir AUC: no significant change; Cmax: no significant change; Cmin: no significant changeRitonavir AUC: no significant change; Cmax: no significant change; Cmin: increased 27% | - | - | No dose adjustment necessary |
| Terfenadine[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#44)  (Seldane)(Seldane) | 60 mg BID x 11 days | 1200 mg TID x 4 days | Terfenadine AUC: increased 368%; Cmax: increased 253% | - | Increased terfenadine effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by saquinavir | Do not coadminister  *Alternative Agents*:  **Cetirizine Fexofenadine Loratadine** |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Saquinavir** | **Effect on Drug Levels** | **Effect on Saquinavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Tipranavir[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#75),[154](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#154)  (TPV)(Aptivus) | 500 mg BID with 200 mg ritonavir BID x 28 doses | 600 mg BID with 100 mg ritonavir BID x 27 doses | - | Saquinavir AUC: decreased 76%; Cmax: decreased 70%; Cmin: decreased 82% | Decreased saquinavir effects | Induction of CYP450 3A4 by tipranavir/ritonavir | Do not coadminister |
| Triazolam[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#254)  (Halcion) | - | - | Not studied; may increase triazolam levels | - | Increased triazolam effects (eg, increased sedation, confusion, respiratory depression) | Inhibition of CYP450 3A4 by saquinavir | Do not coadminister; consider alternative agents  *Alternative Agents*:  **Lorazepam Oxazepam Temazepam Trazodone** |
| Warfarin[323](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#323)  (Coumadin) | - | 600 mg TID x 8 weeks | Increased warfarin levels (INR increased from 2.1 to 4.24) | - | Increased warfarin effects (eg, increased INR and risk of bleeding) | Possible inhibition of CYP450 by saquinavir | Monitor INR and adjust warfarin as indicated |
| Zalcitabine[85](http://arv.ucsf.edu/insite?page=ar-00-02&param=4&post=4#85)  (ddC)(Hivid) | - | - | No significant change | No significant change | - | - | No dose adjustment necessary |
| "-" indicates that there are no data available | | | | | | | |

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