**All Interactions with Ritonavir (Norvir)**

| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Alfuzosin[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Uroxatral) | - | - | - | - | - | - | Do not coadminister |
| Alprazolam[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Xanax) | 1 mg x 1 | 500 mg BID x 10 d | Alprazolam AUC: no significant change; Cmax: decreased 16% | - | - | - | Avoid combination; consider alternative agents  *Alternative Agents*:  **Lorazepam** |
| Alprazolam[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55),[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178),[255](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#255)  (Xanax) | 1 mg x 1 dose | 200 mg BID | Alprazolam clearance: decreased 59%; half-life: increased 122% | - | Increased alprazolam effects (eg, increased sedation, confusion, respiratory depression) | Inhibition of CYP450 3A4 by ritonavir | Avoid combination; consider alternative agents  *Alternative Agents*:  **Lorazepam** |
| Amiodarone[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55) | - | - | Not studied; may increase amiodarone levels | - | Increased amiodarone effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister |
| Amitriptyline[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Elavil) | - | - | Increased amitriptyline levels | - | Increased amitriptyline effects (eg, dry mouth, hypotension, confusion) | Inhibition of CYP450 3A4 and 2D6 by ritonavir | Monitor and adjust amitriptyline as indicated |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Amprenavir[63](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#63),[53](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#53)  (APV)(Agenerase) | - | - | Increased amprenavir levels | Not studied | Increased amprenavir effects | Inhibition of CYP450 3A4 by ritonavir | Dose adjustment not established |
| Amprenavir[112](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#112)  (APV)(Agenerase) | 1200 mg BID | 200 mg BID | Amprenavir AUC: increased 127%; Cmin: increased 395%; | Not studied | Increased amprenavir effects | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| Amprenavir[112](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#112)  (APV)(Agenerase) | 1200 mg BID | 500 mg BID | Amprenavir AUC: increased 143%; Cmin: increased 576% | Not studied | Increased amprenavir effects | Inhibition of CYP450 3A4 by ritonavir | Dose adjustment not established |
| Amprenavir[112](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#112)  (APV)(Agenerase) | 1200 mg BID with efavirenz 600 mg QD | 200 mg BID | No significant change | Not studied | - | Inhibition of CYP450 3A4 by ritonavir and induction of CYP450 3A4 by efavirenz | No dose adjustment necessary |
| Amprenavir[60](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#60)  (APV)(Agenerase) | 1200 mg QD | 200 mg BID x 2-4 weeks | Amprenavir AUC: increased 62%; Cmin: increased 319% | Not studied | Increased amprenavir effects | Inhibition of CYP450 3A4 by ritonavir | Dose adjustment not established |
| Amprenavir[116](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#116)  (APV)(Agenerase) | 1200 mg QD on days 1-7 | 100 mg on days 8-14, 200 mg QD on days 15-21 | Amprenavir AUC: increased 119%; Cmax: no significant change; Cmin: increased 840% (with 100 mg ritonavir); no significant change with 200 mg ritonavir | Not studied | Increased amprenavir effects | Inhibition of CYP450 3A4 by ritonavir | Dose adjustment not established |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Amprenavir[60](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#60)  (APV)(Agenerase) | 600 mg BID | 100 mg BID x 2-4 weeks | Amprenavir AUC: increased 64%; Cmax: decreased 30%; Cmin: increased 508% | Not studied | Increased amprenavir effects | Inhibition of CYP450 3A4 by ritonavir | - |
| Amprenavir[115](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#115)  (APV)(Agenerase) | 900 mg Q12H | 100 mg Q12H | Amprenavir AUC: increased 109%; Cmax: no significant change; Cmin: increased 585% | Ritonavir AUC: decreased 64%; Cmax: decreased 32%; Cmin: decreased 65% | Increased amprenavir effects | Inhibition of CYP450 3A4 by ritonavir and induction of CYP450 3A4 by amprenavir | Dose adjustment not established |
| Astemizole[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Hismanal) | - | - | Not studied; may increase astemizole levels | - | Increased astemizole effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister  *Alternative Agents*:  **Cetirizine Fexofenadine Loratadine** |
| Atazanavir[99](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#99),  (ATV)(Reyataz) | 300 mg QD on days 1-20 | 100 mg QD on days 11-20 | Atazanavir AUC: increased 238%; Cmax: increased 86%; Cmin: increased 1089% | Not studied | Increased atazanavir effects | Inhibition of CYP450 3A4 by ritonavir | Dose adjustment not established |
| Beclomethasone[583](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#583) | 160 mcg inhaled BID | 100 mg BID | Beclomethasone-17-monopriopionate AUC: increased 108%; Cmax: increased 67% | Not studied | - | - | Use lowest possible dose and titrate to effect |
| Bepridil[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55) | - | - | Not studied; may increase bepridil levels | - | Increased bepridil effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Boceprevir[569](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#569)  (Victrelis) | 400 mg TID x 15 days | 100 mg QD x 12 days | Boceprevir AUC: decreased 19%; Cmax: decreased 27% | - | Potentially decreased boceprevir effects; effect on ritonavir concentrations unknown | - | Clinical significance unknown especially when combined with other protease inhibitors |
| Bosentan | - | - | - | - | 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. |
| Carbamazepine[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178),[292](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#292)  (others)(Tegretol) | 350 mg BID | 200 mg QD-TID | Not studied; May increase carbamazepine levels | Decreased ritonavir levels | Increased carbamazepine effects; decreased ritonavir effects | Induction of CYP450 2C and 3A4 | Avoid combination if possible; consider alternative agents;monitor carbamazepine levels and adjust as indicated  *Alternative Agents*:  **Gabapentin Lamotrigine Tiagabine Topiramate** |
| Cetirizine[252](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#252)  (Zyrtec) | 10 mg QD | 600 mg BID | Cetirizine AUC: increased 42%; half-life: increased 52%; clearance: decreased 29%; Cmax: no significant change | Not studied | - | - | No dose adjustment necessary |
| Cisapride[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Propulsid) | - | - | Increased cisapride levels | - | Increased cisapride effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister  *Alternative Agents*:  **Metoclopramide** |
| Clarithromycin[360](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#360),[56](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#56)  (Biaxin) | 500 mg BID | 200 mg TID | Clarithromycin AUC: increased 77%; Cmax: increased 31%; Cmin: increased 182% | AUC: no significant change; Cmax: increased 15% | Increased clarithromycin effects | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Co-trimoxazole[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (TMP/SMX, Trimethoprim/Sulfamethoxazole)(Bactrim, Septra) | 160 mg/800 mg x 1 dose | 500 mg Q12H x 12 days | Sulfamethoxazole AUC: decreased 20%; trimethoprim AUC: increased 20% | - | - | Induction of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| Colchicine[529](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#529)  (Colcrys) | 0.6 mg x 1 | 100 mg BID x 5 days | Colchicine AUC: increased 296%; Cmax: increased 184% | - | Increased colchicine effects | Inhibition of P450 3A4 by ritonavir | 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. |
| Delavirdine[88](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#88)  (DLV)(Rescriptor) | 400 or 600 mg BID | 300 mg BID | No significant change | No significant change | - | - | No dose adjustment necessary |
| Delavirdine[59](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#59)  (DLV)(Rescriptor) | 600 mg BID x 10 days | 100 mg BID x 10 days | No significant change | Ritonavir AUC: increased 81%; Cmax: increased 50%; Cmin: increased 113% | Increased ritonavir effects | Inhibition of CYP450 3A4 by delavirdine | No dose adjustment necessary |
| Desipramine[260](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#260)  (Norpramin) | - | - | Desipramine clearance: decreased 59% | - | Increased desipramine effects (eg, dry mouth, dizziness, urinary retention) | Inhibition of CYP450 2D6 by ritonavir | Monitor and adjust desipramine as indicated |
| Diazepam[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Valium) | - | - | Increased diazepam levels | - | Increased diazepam effects (eg, increased sedation, confusion, respiratory depression) | Inhibition of CYP450 3A by ritonavir | Do not coadminister  *Alternative Agents*:  **Lorazepam Oxazepam Temazepam** |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Didanosine[84](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#84)  (ddI)(Videx) | 200 mg (buffered formulation) Q12H x 4 days | 600 mg Q12H x 4 days | Didanosine AUC: no significant change; Cmax: decreased 16% | No significant change | - | - | No dose adjustment necessary |
| Didanosine[54](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#54),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (ddI)(Videx) | 200 mg (tablets) BID | 600 mg BID | Didanosine AUC: decreased 15%; Cmax: decreased 15% | Not studied | Decreased didanosine effects | Formulation incompatibility | Separate didanosine and ritonavir administration by at least 2.5 hours |
| Digoxin[385](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#385),[386](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#386)  (others)(Lanoxin) | 0.4 mg x 1 dose | 200 mg BID x 15 days | Digoxin AUC (0-8 hr): increased 29%; AUC (0-72 hr): increased 22%; clearance: decreased 30%; half-life: increased 43% | Not studied | Increased digoxin effects | Possible inhibition of P-gp by ritonavir | Monitor digoxin concentrations closely |
| Disulfiram[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Antabuse) | - | - | Oral solution (contains alcohol) and capsules | - | Disulfiram reaction (eg, headache, hypotension, flushing, vomiting) | Inhibition of aldehyde dehydrogenase by disulfiram | Do not coadminister |
| Efavirenz[56](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#56)  (EFV)(Sustiva) | 600 mg QD | Day 1: 300 mg Q12H; Day 2: 400mg Q12H; Days 3-10: 500 mg Q12H | Efavirenz AUC: increased 21% | Ritonavir AUC: increased 18% | Possible increased effects of both drugs | Inhibition of CYP450 3A4 by both drugs | May dose ritonavir at 500 mg BID when given with efavirenz; no dose adjustment required for efavirenz |
| Efavirenz[90](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#90)  (EFV)(Sustiva) | 600 mg x 10 days | 500 mg Q12H x 8 days | Efavirenz AUC: increased 21%; Cmax: no significant change | Ritonavir AUC: increased 18% after AM dose; Cmax: increased 24% after AM dose; AUC: no significant change after PM dose; Cmax: no significant change after PM dose | Increased efavirenz and ritonavir effects | Inhibition of CYP450 3A4 by both drugs | No dose adjustment necessary |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Enfuvirtide[6](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#6),[7](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#7)  (ENF)(Fuzeon) | 90 mg SQ BID on days 1-7 | 200 mg BID on days 4-7 | Enfuvirtide Cmax: increased 24%; Cmin: no significant change; AUC: increased 22% | No significant change | - | - | No dose adjustment necessary |
| Ergotamine[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178),[318](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#318),[319](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#319),[320](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#320),[321](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#321),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Cafergot, Ergot derivatives)(Cafergot, others) | - | - | Not studied; may increase ergotamine levels | - | Increased ergotamine effects (eg, ergotism) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister  *Alternative Agents*:  **5-HT agonists ("triptans")** |
| Escitalopram[387](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#387)  (Lexapro) | 20 mg x 1 dose | 600 mg x 1 dose | No significant change | No significant change | - | - | No dose adjustment necessary |
| Ethinyl estradiol/norethindrone acetate[368](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#368),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (others)(Ortho-Novum) | 50 mcg x 2 doses | 500 mg Q12H | Ethinyl estradiol Cmax: decreased 32%; AUC: decreased 41% | - | Decreased oral contraceptive effectiveness | Induction CYP450 3A4 by ritonavir | Use alternative contraceptive method  *Alternative Agents*:  **Barrier devices; Condoms** |
| Etravirine[405](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#405)  (ETR)(Intelence) | - | 600 mg BID | Etravirine AUC: decreased 46%; Cmax: decreased 32% | - | - | Induction of CYP450 by ritonavir | - |
| Fentanyl[179](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#179)  (Duragesic) | 5 mcg/kg | Day 1: 200 mg TID; Day 2: 300 mg TID; Day 3: 300 mg QAM | Fentanyl clearance: decreased 67% | - | Increased fentanyl effects (eg, increased sedation, confusion, respiratory depression) | Inhibition of CYP450 3A4 by ritonavir | Monitor closely when using together; start with low dose and titrate to pain response as indicated |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Flecainide[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Tambocor)(Tambocor) | - | - | Not studied; may increase flecainide levels | - | Increased flecainide effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister |
| Fluconazole[273](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#273)  (Diflucan)(Diflucan) | 400 mg x 1 day, then 200 mg days 2-5 | 200 mg Q6H x 4 days | - | Cmax: increased 14.5%; AUC: increased 12%; Cmin: increased 14% | - | Inhibition of CYP450 3A4 by fluconazole | No dose adjustment necessary |
| Fluoxetine[262](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#262),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Prozac) | 30 mg Q12H | 600 mg x 1 dose days 1 and 10 | - | AUC: increased 19%; Cmax: no significant change | Increased ritonavir effects; possibly increased fluoxetine effects | Inhibition of CYP450 2D6 by both drugs | No dose adjustment necessary |
| Fluticasone[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Flonase, Aerobid)(Advair, Flonase, Aerobid) | - | - | Fluticasone AUC: increased 350-fold; Cmax: increased 25-fold | - | Decreased plasma cortisol concentrations (eg, Cushing's syndrome, adrenal suppression) | - | Avoid if possible |
| Fluticasone[392](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#392)  (Flonase, Aerobid)(Advair, Flonase, Aerobid) | 200 mcg once daily x 7 d | 100 mg BID x 7 d | Fluticasone Cmax: increased 2572%; AUC: increased 36697% | - | Increased fluticasone effects (eg, Cushing's syndrome, adrenal suppression) | Inhibition of CYP450 3A4 by ritonavir | Dose adjustment not established; use caution |
| Fosamprenavir[129](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#129)  (FPV)(Lexiva) | 1400 mg QD with efavirenz 600 mg QD | 300 mg QD | Amprenavir AUC: no significant change; Cmax: increased 18%; Cmin: no significant change | Not studied | - | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Indinavir[119](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#119)  (IDV)(Crixivan) | 400 mg BID x 14 days | 400 mg BID x 14 days | Indinavir AUC: increased 62%; Cmax: no significant change; Cmin: increased 929% (compared to indinavir 800 mg Q8H) | Not studied | Increased indinavir effects | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| Indinavir[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#254),[33](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#33),[34](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#34),[35](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#35),[36](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#36),[37](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#37),[38](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#38),[39](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#39),[40](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#40),[41](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#41)  (IDV)(Crixivan) | 400 mg Q12H x 15 days | 400 mg Q12H x 15 days | Indinavir Cmin: increased 400% | Not studied | - | Inhibition of CYP450 3A4 by ritonavir | May consider indinavir/ritonavir combination as follows (BID dosing): 800/100; 800/200; 400/400 |
| Indinavir[119](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#119)  (IDV)(Crixivan) | 800 mg BID x 14 days | 100 mg BID x 14 days | Indinavir AUC: increased 170%; Cmax: increased 60%; Cmin: increased 1000% (compared to indinavir 800 mg Q8H) | Not studied | Increased indinavir effects | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| Indinavir[119](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#119)  (IDV)(Crixivan) | 800 mg BID x 14 days | 200 mg BID x 14 days | Indinavir AUC: increased 254%; Cmax: increased 77%; Cmin: increased 2356% (compared to indinavir 800 mg Q8H) | Not studied | Increased indinavir effects | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| Indinavir[119](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#119)  (IDV)(Crixivan) | 800 mg BID x 14 days | 400 mg BID x 14 days | Indinavir AUC: increased 209%; Cmax: increased 49%; Cmin: increased 2344% (compared to indinavir 800 mg Q8H) | Not studied | Increased indinavir effects | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| Itraconazole[278](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#278)  (Sporanox)(Sporanox) | - | - | - | Increased ritonavir levels | Increased ritonavir effects | Inhibition of CYP450 3A4 by itraconazole | Dose adjustment not established |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Ketoconazole[278](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#278)  (Nizoral) | - | - | - | Increased ritonavir levels | Increased ritonavir effects | Inhibition of CYP450 3A4 by ketoconazole | Dose adjustment not established |
| Levothyroxine[364](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#364)  (Synthroid, Levoxyl) | 0.125 mg | 600 mg BID | - | - | Increased TSH levels (eg, Signs and symptoms of hypothyroidism) | Induction of glucuronosyl transferases by ritonavir | Monitor and adjust levothyroxine as indicated |
| Lopinavir/ritonavir[78](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#78)  (LPV/r)(Kaletra) | 400 mg/100 mg BID x 3-4 weeks | 100 mg BID x 3-4 weeks | Lopinavir AUC: increased 46%; Cmax: increased 28%; Cmin: increased 116% | - | Increased lopinavir/ritonavir effects | Inhibition of CYP450 3A4 by ritonavir | Dose adjustment not established |
| Maraviroc[2](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#2)  (MVC)(Selzentry) | 100 mg BID | 100 mg BID | Maraviroc AUC: increased 161%; Cmin: increased 355%; Cmax: increased 28% | - | Increased maraviroc effects | Inhibition of CYP450 3A4 by ritonavir | - |
| Mefloquine[375](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#375)  (Larium)(Larium) | 250 mg QD x 3 days, then once weekly for 3 weeks | 200 mg BID x 7 days | No significant change | AUC: decreased 31%; Cmax: increased 36%; Cmin: decreased 43% | - | Unknown | Dose adjustment not established |
| Meperidine[180](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#180)  (Demerol)(Demerol) | 50 mg PO x 1 dose | 500 mg BID x 10 days | Meperidine AUC: decreased 67%; normeperidine AUC: increased 47% | - | Increased normeperidine effects | Induction of CYP450 1A2 by ritonavir; inhibition of p-glycoprotein reducing first-pass metabolism of meperidine | Avoid combination  *Alternative Agents*:  **Morphine** |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Methadone[198](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#198)  (Dolophine)(Dolophine) | - | 400 mg BID combined with 400 mg BID saquinavir | S-methadone AUC: decreased 25%; R-methadone AUC: decreased 20% | - | Not clinically significant | Induction of CYP450 by ritonavir and saquinavir | Monitor and adjust methadone as indicated |
| Methadone[196](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#196),[197](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#197)  (Dolophine)(Dolophine) | 90 mg QD x 2 years | 400 mg BID x 7 days | Methadone AUC: decreased | - | Decreased methadone effects (eg, methadone withdrawal) | Possible induction of CYP450 2C9, 3A4 and 2D6 by ritonavir | Monitor and adjust methadone as indicated |
| Methadone[187](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#187)  (Dolophine)(Dolophine) | Stable methadone dose | 100 mg BID x 7 days | No significant effect | - | - | - | Monitor and adjust methadone as indicated |
| Metronidazole[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Flagyl)(Flagyl) | - | Oral solution (contains alcohol) and capsules | - | - | Disulfiram-like reaction (eg, headache, hypotension, flushing, vomiting) | Inhibition of alcohol and aldehyde dehydrogenase by metronidazole | Do not coadminister |
| Midazolam[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178)  (Versed) | - | - | Increased midazolam levels | - | Increased midazolam effects (eg, increased sedation, confusion, respiratory depression) | Inhibition of CYP450 3A4 by 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[107](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#107)  (NFV)(Viracept) | 1250 mg BID on days 1-31 | 100 mg or 200 mg BID on days 15-31 | Nelfinavir AUC: increased 17-27% (on ritonavir 100 mg BID); M8 AUC: increased 67-82% (on ritonavir 100 mg BID); nelfinavir AUC: increased 20-53% (on ritonavir 200 mg BID); M8 AUC: increased 69-87% (on ritonavir 200 mg BID) | Not studied | - | Inhibition of CYP450 3A4 by both ritonavir and nelfinavir | Dose adjustment not established |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Nelfinavir[77](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#77)  (NFV)(Viracept) | 2000 mg/ritonavir 200 mg, 2000 mg/ritonavir 400 mg, or 2500 mg/200 mg QD with food x 15 days | 200 mg or 400 mg QD with food x 15 days | Nelfinavir 2000 mg/ritonavir 200 mg AUC: increased 100%; Cmax: increased 95%; Cmin: increased 92% (all values are compared to nelfinavir 1250 mg BID) | - | - | Inhibition of CYP450 3A4 by ritonavir | Using nelfinavir 2000 mg/ritonavir 200 mg QD with food may allow for QD dosing |
| Nelfinavir[24](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#24)  (NFV)(Viracept) | 750 mg Q8H x 5 dose | 500 mg x 1 dose | - | No significant change | - | - | No dose adjustment necessary |
| Nelfinavir[24](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#24)  (NFV)(Viracept) | 750 mg x 1 dose | 500 mg Q12H x 3 doses | Nelfinavir AUC: increased 152%; Cmax: increased 44% | Not studied | Increased nelfinavir effects | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| Nevirapine[95](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#95)  (NVP)(Viramune) | 200 mg QD x 2 weeks then 200 mg BID x 28 days | 600 mg BID | No significant change | No significant change | - | - | No dose adjustment necessary |
| Olanzapine[175](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#175)  (Zyprexa)(Zyprexa) | 10 mg QD | 500 mg BID | Olanzapine AUC: decreased 53%; half-life: decreased 50%; clearance: increased 115%; Cmax: decreased 40% | Not studied | Decreased olanzapine effects | Induction of CYP450 1A2 by ritonavir | Monitor and adjust olanzapine as indicated |
| Phenytoin[225](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#225)  (Dilantin) | - | - | Increased phenytoin levels | - | Increased phenytoin effects | - | 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 Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Pimozide[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178)  (Orap)(Orap) | - | - | Not studied; may increase pimozide levels | - | Increased pimozide effects (eg, hypotension, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister |
| Posaconazole[503](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#503),[424](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#424)  (Noxafil) | 400 mg BID | 100 mg QD | - | Ritonavir AUC: increased 80%; Cmax: increased 49% | Possibly increased ritonavir effects | Inhibition of CYP450 3A4 by posaconazole; potential inhibition of UGT 1A1 by atazanavir | Dose adjustment not necessary |
| Prednisolone[396](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#396)  (others) | 20 mg x 1 dose | 200 mg BID for 4 and 14 days | Prednisolone AUC: increased 30%; clearance: decreased 23% | - | Possibly increased prednisolone effects (adrenal insufficiency, Cushing's syndrome). | - | No dose adjustment necessary. Do not coadminister unless potential benefits of prednisone outweigh the risks of systemic corticosteroid adverse effects. |
| Propafenone[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Rythmol) | - | - | Not studied; may increase propafenone levels | - | Increased propafenone effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister |
| Quinidine[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Quindex, others)(Quindex) | - | - | Not studied; may increase quinidine levels | - | Increased quinidine effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister |
| Quinine[547](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#547) | 600 mg x 1 | 200 mg Q12 h x 9 days | Quinine AUC: increased 341%; Cmax: increased 284% | Ritonavir AUC: increased 21%; Cmax: increased 15% | Increased quinine effects | Potential competitive displacement from CYP450 3A4 and inhibition of 2D6 | Avoid combination if possible; if combination must be used a potential four-fold reduction in quinine dosage may be needed |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Raltegravir[3](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#3)  (RAL)(Isentress) | 400 mg x 1 | 100 mg BID | Raltegravir AUC: decreased 16%; Cmax: decreased 24% | - | - | - | No dose adjustment necessary |
| Raltegravir[436](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#436)  (RAL)(Isentress) | 400 mg x 1 | 100 mg BID x 16 d | Raltegravir AUC: decreased 16%; Cmax: decreased 24% | - | - | Induction of UGT1A1 by ritonavir | No dose adjustment necessary |
| Rifabutin[344](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#344),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Mycobutin)(Mycobutin) | 150 mg QD x 24 days | 300 mg on day 15; 400 mg on day 16; 500 mg on days 17-24 | Rifabutin AUC: increased 400%; Cmax: increased 250% | - | Increased rifabutin effects (eg, uveitis) | Inhibition of CYP450 3A4 by ritonavir | Decrease rifabutin to 150 mg QOD or 300 mg 3 times/week |
| Rifampin[197](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#197),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Rifampicin)(Rifadin) | 300 mg or 600 mg x 10 days | 500 mg Q12H x 20 days | - | Ritonavir AUC: decreased 35%; Cmax: decreased 25% | Decreased ritonavir effects | Induction of CYP450 3A4 by rifampin | Do not coadminister  *Alternative Agents*:  **Rifabutin** |
| Saquinavir[118](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#118)  (SQV)(Fortovase, Invirase) | 1600 mg QD x 13 days | 100 mg QD | 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 | - |
| Saquinavir[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#44),[47](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#47),[48](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#48),[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#254)  (SQV)(Fortovase, Invirase) | 400 mg (hard gel caps) BID at steady state | 400 mg BID at steady state | Saquinavir AUC: increased 1587%; Cmax: increased 1277% | Not studied | Increased saquinavir effects | Inhibition of CYP450 3A4 by ritonavir | Consider ritonavir-boosted saquinavir |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Saquinavir[44](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#44),[47](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#47),[48](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#48),[75](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#75),[254](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#254)  (SQV)(Fortovase, Invirase) | 400 mg (soft gel caps) BID x 14 days | 400 mg 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 |
| Saquinavir[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55),[57](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#57)  (SQV)(Fortovase, Invirase) | Multiple saquinavir hard gel caps doses studied; 200 mg, 400 mg, 600 mg | Multiple doses studied; 200 mg, 300 mg, 600 mg | Saquinavir AUC: increased 5000%; Cmax: increased 2100% | Ritonavir AUC: no significant change | Increased saquinavir effects | Inhibition of CYP450 3A4 by ritonavir | Consider ritonavir-boosted saquinavir |
| Saquinavir[51](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#51)  (SQV)(Fortovase, Invirase) | 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 | 100 mg BID | 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) | Not studied | 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 |
| Sildenafil[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55),[301](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#301)  (Viagra) | 100 mg x 1 dose | 300 mg, 400 mg and 500 mg BID on days 2, 3 and 4-8 | Sildenafil AUC: increased 1000%; Cmax: increased 290%; Tmax: delayed 3 hours | - | Increased sildenafil effects (eg, hypotension, priapism) | Inhibition of CYP450 3A4 by ritonavir | 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[677](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#677)  (Olysio) | 200 mg QD x 7 days | 100 mg BID x 15 days | Simeprevir AUC: increased 618%; Cmax: increased 370%; Cmin: increased 1335% | - | Increased simeprevir effects | Inhibition of P450 3A4 by ritonavir | Do not coadminister |
| St. John's Wort[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Hypericum perforatum, hypericin, hyperforin) | - | - | - | Not studied; may decrease ritonavir levels | Decreased ritonavir effects | Induction of CYP450 3A4 by St. John's Wort | Do not coadminister |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Tacrolimus[305](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#305)  (Prograf)(Prograf) | 4 mg BID | - | - | - | Increased tacrolimus effects (eg, bone marrow suppression) | Inhibition of CYP450 3A4 by ritonavir | Monitor and adjust tacrolimus as indicated |
| Tadalafil[388](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#388) | 20 mg x 1 | 200 mg BID | Tadalafil AUC: increased 124% | - | Increased tadalafil effects (eg, hypotension, priapism) | Inhibition of CYP450 3A4 by ritonavir | Initiate tadalafil at 5 mg QD; adjust dose as indicated; not recommended to exceed 10 mg in 72 hour period |
| Tadalafil[388](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#388) | 20 mg x 1 | 500 mg or 600 mg BID | Tadalafil AUC: increased 32%, Cmax: decreased 30% | - | Increased tadalafil effects (eg, hypotension, priapism) | Inhibition of CYP450 3A4 by ritonavir | Initiate tadalafil at 5 mg QD; adjust dose as indicated; not recommended to exceed 10 mg in 72 hour period |
| Telaprevir[571](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#571)  (Incivek) | 750 mg Q12H x 14 days | 100 mg Q12H x 14 days | Telaprevir AUC: decreased 24%; Cmin: decreased 32%; Cmax: decreased 15% | - | - | - | Dose adjustment not established |
| Telaprevir[571](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#571)  (Incivek) | 750 mg x 1 | 100 mg x 1 | Telaprevir AUC: increased 100%; Cmax: increased 30% | - | - | - | Dose adjustment not established |
| Terfenadine[178](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#178),[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Seldane)(Seldane) | - | - | Increased terfenadine levels | - | Increased terfenadine effects (eg, cardiac arrhythmias) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister  *Alternative Agents*:  **Cetirizine Fexofenadine Loratadine** |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Theophylline[303](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#303)  (Slo-Phyllin, Theo-Dur) | 3 mg/kg Q8H | Days 1-5 none; day 6 300 mg Q12H; day 7 400 mg Q12H; days 8-15 500 mg Q12H | Theophylline AUC: decreased 43%; Cmax: decreased 32%; Cmin: decreased 57%; half-life: decreased 57% | - | Decreased theophylline effects | Possible induction of CYP450 1A2 by ritonavir | Monitor and adjust theophylline as indicated |
| Tinidazole[328](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#328)  (Tindamax) | - | Oral solution (contains alcohol) and capsules | - | - | Disulfiram-like reaction (eg, headache, hypotension, flushing, vomiting) | Inhibition of alcohol and aldehyde dehydrogenase by tinidazole | Do not coadminister |
| Trazodone[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55)  (Desyrel)(Desyrel) | - | - | Trazodone AUC: increased 2.4-fold; Cmax: increased 34% | - | Increased trazodone effects (eg, nausea, dizziness, hypotension, syncope) | Possible inhibition of trazodone metabolism | Use with caution; if benefits outweigh risk, initiate trazodone at lower dose |
| Trazodone[259](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#259)  (Desyrel)(Desyrel) | 50 mg x 1 dose | 200 mg BID for 2 days | Trazodone AUC: increased 240%; Cmax: increased 34%; half-life: increased 220% | Not studied | Increased trazodone effects (eg, nausea, hypotension, syncope) | Inhibition of CYP450 3A4 by ritonavir | Decrease trazodone dose or start low and titrate to effect |
| Triazolam[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55),[256](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#256)  (Halcion) | 0.125 mg x 1 dose | 200 mg BID x 2 days | Triazolam AUC: increased 1939%; half-life: increased 1267%; Cmax: increased 87% | - | Increased triazolam effects (eg, increased confusion, sedation, respiratory depression) | Inhibition of CYP450 3A4 by ritonavir | Do not coadminister; consider alternative agents  *Alternative Agents*:  **Lorazepam, Oxazepam, Temazepam, Trazodone** |
| Vardenafil[741](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#741) | 5 mg daily | 600 mg BID | Vardenafil AUC increased 49-fold; Cmax increased 13-fold. T1/2 increased to 26 hours. | - | Increased tadalafil effects | Inhibition of CYP3A4 | Initiate (and do not exceed) vardenafil 2.5 mg every 72 hours and monitor for adverse effects |
| **Coadministered Drug** | **Dose of Drug** | **Dose of Ritonavir** | **Effect on Drug Levels** | **Effect on Ritonavir Levels** | **Potential Clinical Effects** | **Mechanism of Interaction** | **Management** |
| Voriconazole[507](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#507),[505](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#505),[378](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#378)  (VFend) | 400 mg Q12H | 100 mg Q12H x 9 days | Voriconazole AUC: decreased 39%; Cmax: decreased 24% | No significant change | Decreased voriconazole effects | Induction of CYP450 3A4 by ritonavir | Do not coadminister with boosted protease inhibitors unless benefit outweighs risks. If coadministering, consider therapeutic drug monitoring.  *Alternative Agents*:  **Consider use of non-ritonavir containing antiretroviral regimens** |
| Voriconazole[727](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#727),[507](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#507),[505](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#505)  (VFend) | 400 mg Q12H | 400 mg Q12H x 9 days | Voriconazole AUC: decreased 83%; Cmax: decreased 68% | No significant change | Decreased voriconazole effects | Induction of CYP450 3A4 by ritonavir | Do not coadminister with boosted protease inhibitors unless benefit outweighs risks. If coadministering, consider therapeutic drug monitoring.  *Alternative Agents*:  **Consider use of non-ritonavir containing antiretroviral regimens** |
| Warfarin[324](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#324)  (Coumadin) | 12.5 mg QD | 400 mg BID | INR: decreased | - | Decreased warfarin effects (eg, decreased INR, increased risk of clotting) | Possible inhibition of CYP450 3A4, 2C9 and 1A2 by ritonavir | Monitor INR and adjust warfarin as indicated |
| Zidovudine[55](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#55),[58](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#58)  (AZT, ZDV)(Retrovir) | 200 mg Q8H | 300 mg Q6H | Zidovudine Cmax: decreased 27%; AUC: decreased 26% | No significant change | Decreased zidovudine effects | Unknown | No dose adjustment necessary |
| Zolpidem[256](http://arv.ucsf.edu/insite?page=ar-00-02&param=8&post=4#256)  (Ambien)(Ambien) | 5 mg x 1 dose | 200 mg BID x 2 days | Zolpidem AUC: increased 28%; Cmax: increased 22% | - | Increased zolpidem effects (eg, increased sedation, confusion) | Inhibition of CYP450 3A4 by ritonavir | No dose adjustment necessary |
| "-" indicates that there are no data available | | | | | | | |

|  |  |
| --- | --- |
| 2: | Selzentry [package insert]. New York, NY: Pfizer, Inc.; August 2012. |
| 3: | Isentress [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; October 2007. |
| 6: | Boyd M, Zhang X, Dorr A, et al. Lack of enzyme-inducing effecto of rifampicin on the pharmacokinetics of enfuvirtide. J Clin Pharmacol 2003; 43: 1382-91. |
| 7: | Ruxrungtham K, Boyd M, Bellibas SE, et al. Lack of interaction between enfuvirtide and ritonavir or ritonavir-based saquinavir in HIV-1 infected patients. J Clin Pharmacol 2004; 44: 793-802. |
| 24: | Viracept [package insert]. La Jolla, CA: Agouron Pharmaceuticals, Inc.; Sept 2004. |
| 33: | Norvir [package insert]. North Chicago, IL: Abbott Laboratories; 2003. |
| 34: | Van Heeswijk RPG, Veldkamp AI, Hoetelmans RMW, et al. The steady-state plasma pharmacokinetics of indinavir alone or in combination with ritonavir in twice daily dosing regimens in HIV-1 infected patients. [abstract] AIDS. 1998;12(suppl 4):S31. |
| 35: | Burger DM, Hugen PWH, Prins J, et al. Pharmacokinetics of indinavir in a bid regimen with or without low-dose ritonavir. [abstract] AIDS. 1998;12(suppl 4):S10. |
| 36: | Hsu A, Granneman GR, Cao G, et al. Pharmacokinetic interaction between ritonavir and indinavir in healthy volunteers. Antimicrob Agents Chemother. 1998;42:2784-2791. |
| 37: | van Heeswijk, Veldkamp AI, Hoetelmans RMW, et al. The steady-state plasma pharmacokinetics of indinavir alone and in combination with a low dose of ritonavir in twice daily dosing regiments in HIV-1 infected individuals. AIDS.1999;13:F95-F99. |
| 38: | Burger DM, Hugen PWH, Prins JM, et al. Pharmacokinetics of an indinavir/ritonavir 800/100 mg bid regimen [abstract #363]. 6th Conference on Retroviruses and Opportunistic Infections; 1999 Jan 31-Feb 4; Chicago, Illinois. |
| 39: | Saah A, Winchell G, Seniuk M, et al. Multiple-dose pharmacokinetics and tolerability of indinavir and ritonavir combinations in a once-daily regimen in healthy volunteers (Merck 089) [abstract #329]. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy; 1999 Sept 26-29; San Francisco, California. |
| 40: | Saah AJ, Winchell G, Seniuk M, et al. Multiple-dose pharmacokinetics and tolerability of indinavir ritonavir combinations in healthy volunteers [abstract #362]. 6th Conference of Retroviruses and Opportunistic Infections; 1999 Jan 31-Feb 4; Chicago, Illinois. |
| 41: | Burger DM, Hugen PWH, ter Hofstede, et al. Dose-finding study of a once daily indinavir/ritonavir regimen in healthy volunteers [abstract #321]. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy; 1999 Sept 26-29; San Francisco, California. |
| 44: | Fortovase [package insert]. Basel, Switzerland: F. Hoffman-La Roche Ltd.;2003. |
| 47: | Merry C, Barry MG, Mulcahy F, et al. Saquinavir pharmacokinetics alone and in combination with ritonavir in HIV-infected patients. AIDS 1997;11(4):F29-33. |
| 48: | Flexner C. Dual protease inhibitor therapy in HIV-infected patients: Pharmacologic rationale and clinical benefits. Annu Rev Pharmacol Toxicol 2000;40:649-74. |
| 51: | Kurowski M, Arslan A, Moecklinghoff C, Hill A. Comparative pharmacokinetics of twice daily (BID) Fortovase/ritonavir and Invirase/ritonavir [abstract #3.2]. 2nd International Workshop on Clinical Pharmacology of HIV Therapy; 2001 April 2-4; Noordwijk, the Netherlands. |
| 53: | Sadler BM, Piliero PJ, Preston SL, et al. Pharmacokinetic (PK) drug-interaction between amprenavir (APV) and ritonavir (RTV) in HIV-seronegative subjects after multiple, oral dosing [abstract #77]. 7th Conference on Retroviruses and Opportunistic Infections; 2000 Jan 30-Feb 2; San Francisco, California. |
| 54: | Cato A, Qian J, Hsu A, et al. Pharmacokinetic interaction between ritonavir and didanosine when administered concurrently to HIV-infected patients. J Acquir Immune Defic Syndr Hum Retrovirol 1998;18:466-72. |
| 55: | Norvir [package insert]. North Chicago, IL: Abbott Laboratories, 2008. |
| 56: | Fiske W, Benedek IH, et al. Pharmacokinetics of efavirenz (EFV) and ritonavir (RIT) after multiple oral doses in healthy volunteers [abstract #42269]. 12th International Conference on AIDS; 1998 June 28-July 3; Geneva, Switzerland. |
| 57: | Hsu A, Granneman GR, Cao G, et al. Pharmacokinetic interactions between two human immunodeficiency virus protease inhibitors, ritonavir and saquinavir. Clin Pharmacol Ther 1998;63:453-64. |
| 58: | Cato A, Qian J, Hsu A, et al. Multidose pharmacokinetics of ritonavir and zidovudine in human immunodeficiency virus-infected patients. Antimicrob Agents Chemother 1998;42:1788-93. |
| 59: | Tran JQ, Petersen C, Garrett M, et al. Delavirdine (DLV) significantly increases exposure of low dose ritonavir (RTV) in healthy volunteers [abstract #A-494]. 41st Interscience Conference on Antimicrobial Agents and Chemotherapy; 2001 December 16-19; Chicago, Illinois. |
| 60: | Agenerase [package insert]. Research Triangle Park, NC: Glaxo Wellcome Inc; 2004. |
| 63: | Decker CJ, Laitinen LM, Bridson GW, et al. Metabolism of amprenavir in liver microsomes: Role of CYP3A4 inhibition for drug interactions. J Pharm Sci 1998;87:803-7. |
| 75: | Invirase [package insert]. Roche Laboratories Inc, Nutley, NJ, 2007. |
| 77: | Aarnoutse R, Burger D, van Oosterhout J, et al. Multiple dose pharmacokinetics (PK) and tolerability of once daily (OD) nelfinavir (NFV) and ritonavir combinations in healthy volunteers [abstract #1.3]. 2nd International Workshop on Clinical Pharmacology of HIV Therapy; 2001 April 2-4; Noordwijk, the Netherlands. |
| 78: | Kaletra [package insert]. North Chicago, IL: Abbott Laboratories; Oct 2005. |
| 84: | Videx EC [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; Oct 2005. |
| 88: | Rescriptor [package insert]. La Jolla, California: Agouron Pharmaceuticals, Inc; June 2001. |
| 90: | Sustiva [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; Dec 2011. |
| 95: | Viramune [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; Nov 2005. |
| 99: | Agarwala S, Russo R, Mummaneni V, Randall D, et al. Steady state pharmacokinetic (PK) interaction study of atazanavir (ATV) with ritonavir (RTV) in healthy subjects. [abstract #H-1716]. 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy; 2002 September 27-30; San Diego, California. |
| 107: | Kurowski M, Kaeser B, Sawyer A, et al. Low-dose ritonavir moderately enhances nelfinavir exposure. Clin Pharmacol Ther 2002;72:123-32. |
| 112: | Piscitelli S, Bechtel C, Sadler B, et al. The addition of a second protease inhibitor eliminates amprenavir-efavirenz drug interactions and increases plasma amprenavir concentrations [abstract #78]. 7th Conference on Retroviruses and Opportunitic Infections; 2000 January 30-February 4; San Francisco, California. |
| 115: | Sadler BM, Piliero PJ, Preston SL, et al. Pharmacokinetics and safety of amprenavir and ritonavir following multiple-dose, co-administration to healthy volunteers. AIDS 2001;15:1009-18. |
| 116: | Kurowski M, Staszewski S, Arslan A, et al. Influence of 50 mg, 100 mg and 200 mg ritonavir on the pharmacokinetics of amprenavir after multiple doses in healthy volunteers for once daily and twice daily regimens [abstract #351]. 1st IAS Conference on HIV Pathogenesis and Treatment; 2001 July 8-11; Buenos Aires, Argentina. |
| 118: | Kilby JM, Sfakianos G, Gizzi N, et al. Safety and pharmacokinetics of once daily regimens of soft-gel capsule saquinavir plus minidose ritonavir in hijman immunodeficiency virus-negative adults. Antimicrob Agents Chemother 2000;44:2672-8. |
| 119: | Saah AJ, Winchell GA, Nessly ML, et al. Pharmacokinetic profile and tolerability of indinavir-ritonavir combinations in healthy volunteers. Antimicrob Agents Chemother 2001;45:2710-15. |
| 129: | Wire MB, Preston SL, Ballow C, et al. An assessment of plasma amprenavir pharmacokinetics following administration of two GW433908 and ritonavir QD regimens in combination with efavirenz in healthy adult subjects (APV10009) [abstract #1737]. 41st Interscience Conference on Antimicrobial Agents and Chemotherapy; 2001 September 22-25; Chicago, Illinois. |
| 175: | Penzak SR, Lawhorn WD, Hon YY, et al. Influence of ritonavir and CYP1A2 genotype on olanzapine disposition in healthy subjects [abstract #A-493]. 41st Interscience Conference on Antimicrobial Agents and Chemotherapy; 2001 December 16-19; Chicago, Illinois. |
| 178: | Dresser GK, Spence JD, Bailey DG. Pharmacokinetic-pharmacodynamic consequences and clinical relevance of cytochrome P450 3A4 inhibition. Clin Pharmacokinet 2000;38:41-57. |
| 179: | Olkkola KT, Palkama VJ, Neuvonen PJ. Ritonavir's role in reducing fentanyl clearance and prolonging its half-life. Anesthesiology, 1999;91:681-85. |
| 180: | Piscitelli SC, Kress DR, Bertz RJ, et al. The effect of ritonavir on the pharmacokinetics of meperidine and normeperidine. Pharmacotherapy 2000;20:549-53. |
| 187: | McCance EF, Rainery PM, Friedland G, Jatlow P. The protease inhibitor lopinavir-ritonavir may produce opiate withdrawal in methadone-maintained patients. Clin Infect Dis 2003;37:476-82. |
| 196: | Geletko SM, Erickson AD. Decreased methadone effect after ritonavir initiation. Pharmacotherapy 2000;20:93-4. |
| 197: | Hsu A, Granneman GR, Bertz RJ. Rionavir. Clinical pharmacokinetics and interactions with other anti-HIV agents. Clin Pharmacokinet 1998;35:275-91. |
| 198: | Gerber JG, Rosenkranz S, Segal Y, et al. Effect of ritonavir/saquinavir on stereoselective pharmacokinetics of methadone: results of AIDS clinical trials group (ACTG) 401. J Acq Immune Defic Syndr 2001;27:153-60. |
| 225: | Brooks J, Daily J, Schwamm L. Protease inhibitors and anticonvulsants. AIDS Clin Care. 1997;9:87,90. |
| 252: | Peytavin G, Gautran C, Otoul C, et al. Lack of clinically relevant pharmacokinetic (PK) interaction between cetirazine (CTZ) and ritonavir in male healthy subjects. [abstract #H-1718]. 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy; 2002 September 27-30; Chicago, Illinois. |
| 254: | CDC. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Jan 28, 2000. [AIDS Treatment Information Service: Current Treatment] Available at: http://www.hivatis.org/trtgdlns.html. |
| 255: | Greenblatt DJ, von Moltke LL, Harmatz JS, et al. Alprazolam-ritonavir interaction: implications for product labeling. Clin Pharmacol Ther 2000;67:335-41. |
| 256: | Greenblatt DJ, von Moltke LL, Harmatz JS, et al. Differential impairment of triazolam and zolpidem clearance by ritonavir. J Acquir Immune Defic Syndr 2000;24:129-36. |
| 259: | Desyrel [package insert]. Princeton: NJ, Bristol-Myers Squibb Company, 2003. |
| 260: | von Moltke LL, Greenblatt DJ, Duan SX, et al. Inhibition of desipramine hydroxylation (Cytochrome P450-2D6) in vitro by quinidine and by viral protease inhibitors: relation to drug interactions in vivo. J Pharm Sci 1998;87:1184-9. |
| 262: | Ouellet D, Hsu A, Qian J, et al. Effect of fluoxetine on pharmacokinetics of ritonavir. Antimicrob Agents Chemother 1998;42:3107-12. |
| 273: | Cato A, Cao G, Hsu A, et al. Evaluation of the effect of fluconazole on the pharmacokinetics of ritonavir. Drug Metab Dispos 1997;25:1104-6. |
| 278: | Albengres E, Le Louet H, Tillement JP. Systemic antifungal agents. Drug interactions of clinical significance. Drug Saf 1998;18:83-97. |
| 292: | Kato Y, Mizoguchi N, Ueda K, et al. Potential interaction between ritonavir and carbamazepine. Pharmacotherapy 2000;20:851-54. |
| 301: | Muirhead GJ, Wulff MB, Fielding A, et al. Pharmocokinetic interactions between sildenafil and saquinavir/ritonavir. J Clin Pharmacol 2000;50:99-107. |
| 303: | Hsu A, Granneman GR, Witt G, et al. Assessment of multiple doses of ritonavir on the pharmacokinetics of theophylline [abstract #1200]. 11th International Conference on AIDS. 1996 Jul 7-12; Vancouver, Canada. |
| 305: | Sheikh AM, Wolf DC, Lebovics E, et al. Concomitant human immunodeficiency virus protease inhibitor therapy markedly reduced tacrolimus metabolism and increases blood levels. Transplantation 1999;68:307-9. |
| 318: | Montero A, Giovannoni AG, Tvrde P, et al. Leg ischemia in a patient receiving ritonavir and ergotamine. Ann Intern Med 1999;130:329. |
| 319: | Blanche P, Rigolet A, Gombert B, et al. Ergotism related to a single dose of ergotamine tartrate in an AIDS patient treated with ritonavir. Postgrad Med J 1999;75:546-548. |
| 320: | Caballero-Granado FJ, Viciana P, Cordero E, et al. Ergotism related to concurrent administration of ergotamine tartrate and ritonavir in an AIDS patient. Antimicrob Agents Chemother 1997;41:1207. |
| 321: | Liaudet L, Buclin T, Jaccard C, et al. Severe ergotism associated with interaction between ritonavir and ergotamine. BMJ 1999;318:771. |
| 324: | Knoell KR, Young TM, Cousins ES. Potential interaction involving warfarin and ritonavir. Ann Pharmacother 1998;32:1299-302. |
| 328: | Tindamax [package insert]. Arlington Heights, IL: Presutti Laboratories, Inc; 2004. |
| 344: | Cato A, Cavanaugh J, Shi H, et al. The effect of multiple doses of ritonavir on the pharmacokinetics of rifabutin. Clin Pharmacol Ther 1998;63:414-21. |
| 360: | Ouellet D, Hsu A, Granneman GR, et al. Pharmacokinetic interaction between ritonavir and clarithromycin. Clin Pharmacol Ther 1998;64: 355-62. |
| 364: | Tseng A, Fletcher D. Interaction between ritonavir and levothyroxine [abstract #60571]. 11th International Conference on AIDS; 1998 July 7-12; Vancouver, Canada. |
| 368: | Ouellet D, Hsu A, Qian J, et al. Effect of ritonavir on the pharmacokinetics of ethinyl estradiol in healthy female volunteers. Br J Clin Pharmacol 1998;46:111-16. |
| 375: | Khaliq Y, Gallicano K, Tisdale C, et al. Pharmacokinetic interaction between mefloquine and ritonavir in healthy volunteers. Br J Clin Pharmacol 2001;51:591-600. |
| 378: | Reyataz [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; April 2010. |
| 385: | Penzak S, Shen J, Alfar R, Remaley A, Falloon J. Influence of low-dose ritonavir on the pharmacokinetics of the P-glycoprotein (P-gp) substrate digoxin. Program and abstracts of the 4th International Workshop on Clinical Pharmacology of HIV Therapy; March 27-29, 2003; Cannes, France. Abstract 2.6. |
| 386: | Penzak SR, Shen JM, Alfaro RM, et al. Ritonavir decreases the nonrenal clearance of digoxin in healthy volunteers with known MDR1 genotypes. Ther Drug Monit 2004; 26: 322-30. |
| 387: | Gutierrez MM, Rosenberg J, Abramowitz W. An evaluation of the potential for pharmacokinetic interaction between escitalopram and the cytochrome P450 3A4 inhibitor ritonavir. Clin Ther 2003;25:1200-10. |
| 388: | Cialis [package insert]. Indianapolis, IN: Eli Lilly and Company, 2010. |
| 392: | Flonase [package insert]. Research Triangle Park, NC: GlaxoSmith Kline, March 2004. |
| 396: | Penzak S, Formentini E, Alfaro R, et al. Prednisolone pharmacokinetics in the presence and absence of ritonavir after oral prednisone administration to healthy volunteers. J Acquir Immune Defic Syndr 2005; 40: 573-80. |
| 405: | Intelence [package insert]. Raritan, NJ: Tibotec Therapeutics; 2010. |
| 424: | Noxafil [package insert]. Kenilworth, NJ: Schering-Plough; February 2009. |
| 436: | Iwamoto M, Wenning LA, Petry AS, et al. Minimal effects of ritonavir and efavirenz on the pharmacokinetics of raltegravir. Antimicrob Agents Chemother 2008; 52: 4338-4343. |
| 503: | Krishna G, Moton A, Ma L, et al. Effects of oral posaconazole on the pharmacokinetics of atazanavir alone and with ritonavir or with efavirenz in healthy adult volunteers. J Acquir Immune Defic Syndr 2009; 51: 437-44. |
| 505: | Liu P, Foster G, Gandelman K, et al. Steady-state pharmacokinetics and safety proviles of voriconazole and ritonavir in healthy male subjects. Antimicrob Ag Chemother 2007; 51: 3617-26. |
| 507: | Vfend [package insert]. New York: NY, Pfizer, June 2010. |
| 529: | Colcrys [package insert]. Philadelphia, PA: URL Pharma, Inc., May 2010. |
| 547: | Soyinka JO, Onyeji CO, Omoruyi SI, et al. Pharmacokinetic interactions between ritonavir and quinine in healthy volunteers following concurrent administration. Br J Clin Pharmacol 2010; 69: 262-70. |
| 569: | Victrelis [package insert]. Whitehouse Station, NJ: Schering Corporation; May 2011. |
| 571: | Incivek [package insert]. Cambridge, MA: Vertex Pharmaceuticals Inc; May 2011. |
| 583: | Boyd S, Hadigan C, Pau A, et al. Darunavir/ritonavir does not significantly increase plasma concentrations of orally inhaled beclomethasone in healthy volunteers [paper #611]. 19th Conference on Retroviruses and Opportunistic Infections, March 5-8, 2012. Seattle, WA. |
| 677: | Olysio [package insert]. Titusville, NJ: Janssen Therapeutics; 2013. |
| 727: | Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. |
| 741: | Levitra [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; Sept 2016 |