Lopinavir/Ritonavir

Brand Name: Kaletra
Drug Class: Protease Inhibitors

Drug Description

Lopinavir/ritonavir (lopinavir/r) is a fixed combination of two HIV protease inhibitors (PIs). Ritonavir, a potent inhibitor of the hepatic cytochrome P450 (CYP) isoenzyme CYP3A, decreases metabolism and increases plasma concentrations of lopinavir. [1]

HIV/AIDS-Related Uses

Lopinavir/r in capsule and oral solution form was approved by the FDA on September 15, 2000, for use in combination with other antiretroviral agents in the treatment of HIV infection. Lopinavir/r in tablet form was approved by the FDA on October 28, 2005.[2] Lopinavir/r should not be used alone in the treatment of HIV infection. The fixed combination of lopinavir and ritonavir and two nucleoside reverse transcriptase inhibitors is one of several preferred regimens for initial antiretroviral therapy in HIV infected adults who are treatment naive.[3]

In March 2006, the capsule formulation of lopinavir/r was phased out by the manufacturer in the U.S., in favor of the new tablet formulation.[4] The tablet form of lopinavir/r offers distinct advantages over the capsule formulation, including a lower pill burden, no required dose adjustments for concomitant use of certain non-nucleoside reverse transcriptase inhibitors (NNRTIs) in treatment-naive patients, and easier storage requirements.[5]

In November 2007, the FDA approved a low strength tablet formulation for use in children.[6]

Pharmacology

The antiviral activity of lopinavir/r is due to the lopinavir component. Lopinavir inhibits HIV protease, preventing cleavage of the Gag-Pol polyprotein and reducing the probability of viral particles reaching a mature, infectious state.[7] [8]

Ritonavir inhibits CYP3A, the principal isoenzyme that metabolizes lopinavir; coadministration results in decreased metabolism and increased plasma concentrations of lopinavir. At low doses (100 mg twice daily), ritonavir acts as a pharmacoenhancer of amprenavir, indinavir, nelfinavir, and saquinavir, as well as lopinavir.[9]

The absorption of lopinavir/r in capsule or liquid form is favorably affected by the presence of food. Administration with a high-fat meal increases the area under the curve (AUC) of lopinavir by 97% and maximum plasma concentration (Cmax) by 43% for the capsules and 130% and 56%, respectively, for the oral solution relative to administration during a fasting state.[10] [11] Lopinavir/r tablets may be taken with or without food. No clinically significant changes in Cmax and AUC were observed following administration of lopinavir/r tablets under fed conditions compared to fasted conditions. Relative to fasting, administration of lopinavir/r tablets with a moderate fat meal (500 to 682 kcal, 23% to 25% calories from fat) increased lopinavir AUC by 26.9% and Cmax by 17.6%. Relative to fasting, administration of lopinavir/ritonavir tablets with a high-fat meal increased lopinavir AUC by 18.9% but Cmax was unaffected.[12]

Peak plasma concentration of lopinavir was 9.6 +/- 4.4 mcg/ml following multiple doses of 400 mg lopinavir and 100 mg ritonavir for 3 to 4 weeks in HIV infected patients.[13] Plasma concentrations of lopinavir and ritonavir after administration of two 200/50 mg tablets are similar to three capsules under fed conditions, with less pharmacokinetic variability.[14]

QTcF interval was evaluated in a randomized, placebo and active (moxifloxacin 400 mg once-daily) controlled crossover study in 39 healthy adults, with 10 measurements over 12 hours on Day 3. The maximum mean time-matched (95% upper confidence bound) differences in QTcF interval from placebo after baseline-correction were 5.3 (8.1) and 15.2 (18.0) mseconds (msec) for 400/100 mg twice-daily and supratherapeutic 800/200 mg twice-daily KALETRA, respectively. KALETRA 800/200 mg twice daily resulted in a Day 3 mean Cmax approximately 2-fold higher than the mean Cmax observed with the approved once daily and twice daily KALETRA doses at steady state.[15]

Pharmacology (cont.)

PR interval prolongation was also noted in subjects receiving KALETRA in the same study on Day 3. The maximum mean (95% upper confidence bound) difference from placebo in the PR interval after baseline-correction were 24.9 (21.5, 28.3) and 31.9 (28.5, 35.3) msec for 400/100 mg twice-daily and supratherapeutic 800/200 mg twice-daily KALETRA, respectively.[16]

Lopinavir/r is in FDA Pregnancy Category C. No studies using lopinavir/r have been done in pregnant women. In rats given a maternally toxic dosage, early reabsorption, decreased fetal viability and body weight, and increased incidence of skeletal variation and delayed skeletal ossification occurred. Lopinavir/r should be used in pregnant women only if the potential benefit justifies the potential risk to the fetus. An Antiretroviral Pregnancy Registry has been established to monitor the outcomes of pregnant women exposed to lopinavir/r and other antiretrovirals. Physicians may register patients by calling 1-800-258-4263 or online at http://www.APRegistry.com. It is not known whether lopinavir is secreted in human milk; it is, however, secreted in the milk of laboratory rats. Because of the potential for HIV transmission and serious adverse effects in nursing infants, mothers should be instructed not to breastfeed if they are taking lopinavir/r.[17]

Protein binding of lopinavir is 98% to 99%. It binds to both alpha-1-acid glycoprotein and albumin but has a higher affinity for alpha-1-acid glycoprotein. At steady state, lopinavir protein binding remains constant over the range of observed concentrations after 400/100 mg lopinavir/r twice a day and is similar between healthy volunteers and HIV infected patients.[18]

Lopinavir is extensively metabolized by the hepatic CYP 450 system, almost exclusively by the CYP3A isoenzyme. Because ritonavir is a potent CYP3A inhibitor, it inhibits the metabolism and increases plasma levels of lopinavir. At least 13 lopinavir oxidative metabolites have been identified in humans. Ritonavir has been shown to induce metabolic enzymes, resulting in the induction of its own metabolism. Predose lopinavir concentrations decline with time during multiple dosing, stabilizing after approximately 10 to 16 days.[19] Following multiple doses of lopinavir/r, the serum half-life of lopinavir was 5 to 6 hours. Time to peak lopinavir concentration was 4 hours in HIV infected patients.[20]

Following a single 400/100 mg dose of lopinavir/r, approximately 10.4 +/- 2.3% of the administered lopinavir excreted in urine and 82.6 +/- 2.5% excreted in feces was accounted for after 8 days.[21] [22] Unchanged lopinavir accounted for approximately 2.2% and 19.8% of the administered dose in urine and feces, respectively. After multiple dosing, less than 3% of the lopinavir dose was excreted unchanged in the urine.[23]

Multiple dosing of lopinavir/r 800/200 mg once daily in treatment-naive patients produced a mean Cmax of 11.8 +/- 3.7 mcg/ml at approximately 6 hours after administration. In an ongoing study comparing once-daily and twice-daily lopinavir/r regimens in treatment-naive patients, 71% of patients on once-daily lopinavir/r and 65% of patients on twice-daily lopinavir/r achieved and maintained viral load levels below 50 copies/ml through 48 weeks of treatment.[24]

HIV-1 isolates with reduced susceptibility to lopinavir have been selected in vitro. The presence of ritonavir does not appear to influence the selection of lopinavir-resistant viruses in vitro. Resistance to lopinavir/r has emerged in patients previously treated with other protease inhibitors (PIs). In studies of 227 antiretroviral treatment-naive and PI-experienced patients, isolates from 4 of 23 patients with quantifiable viral RNA after 12 to 100 weeks of treatment with lopinavir/r showed significantly reduced susceptibility to lopinavir. Three of these patients previously had been treated with one PI, and one had been treated with multiple PIs. Following viral rebound, isolates from these patients all contained additional mutations, some of which are associated with PI resistance.[25]

Varying degrees of cross resistance have been observed among HIV PIs. In studies of the in vitro activity of lopinavir against clinical isolates from patients previously treated with a single PI, isolates that displayed a greater than fourfold reduced susceptibility to nelfinavir and saquinavir displayed

Lopinavir/Ritonavir

Pharmacology (cont.)

a less than fourfold reduced susceptibility to lopinavir. Isolates with a greater than fourfold reduced susceptibility to indinavir and ritonavir displayed a mean of 5.7- and 8.3-fold reduced susceptibility to lopinavir, respectively. Isolates from patients previously treated with two or more PIs showed greater reductions in susceptibility to lopinavir.[26]

Adverse Events/Toxicity

Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy (ART), including lopinavir/r. During the initial phase of combination ART, patients whose immune systems respond may develop an inflammatory response to indolent or residual opportunistic infections (such as Mycobacterium avium infection, cytomegalovirus, Pneumocystis carinii pneumonia, or tuberculosis) which may necessitate further evaluation and treatment.[27]

Pancreatitis has been observed in patients receiving lopinavir/r, including those who developed marked triglyceride elevations; in some cases, fatalities have occurred. Although a causal relationship with lopinavir/ritonavir has not been established, marked triglyceride elevation is a risk factor in the development of pancreatitis. Patients with advanced HIV disease may be at increased risk of elevated triglycerides and pancreatitis, and patients with a history of pancreatitis may be at increased risk for recurrence during lopinavir/r therapy. Pancreatitis should be considered if clinical symptoms suggestive of pancreatitis occur, including nausea, vomiting, abdominal pain, or abnormal laboratory values such as increased serum lipase or amylase. Patients who exhibit these signs or symptoms should be evaluated and lopinavir/r or other antiretroviral therapy should be suspended.[28]

Lopinavir/ritonavir prolongs the PR interval in some patients. Cases of second or third degree atrioventricular block have been reported. Lopinavir/ritonavir should be used with caution in patients with underlying structural heart disease, preexisting conduction system abnormalities, ischemic heart disease or cardiomyopathies, as these patients may be at increased risk for developing cardiac conduction abnormalities. [29]

Postmarketing cases of QT interval prolongation and torsade de pointes have been reported although causality of lopinavir/ritonavir could not be established. Avoid use in patients with congenital long QT syndrome, those with hypokalemia, and with other drugs that prolong the QT interval.[30]

New onset diabetes mellitus, exacerbation of pre-existing diabetes mellitus, and hyperglycemia have been reported during postmarketing surveillance of HIV infected patients receiving PI therapy. Some patients required either initiation or dose adjustments of insulin or oral hypoglycemia agents for treatment of these events; in some cases, diabetic ketoacidosis has occurred. In those patients who discontinued PI therapy, hyperglycemia persisted in some cases. Because these events have been reported voluntarily during clinical practice, estimates of frequency cannot be made and a causal relationship between PI therapy and these events has not been established.[31]

Other clinically observed adverse effects include body fat redistribution and accumulation, increased bleeding in patients with hemophilia type A and B, lipid elevations, and exacerbation of existing hepatitis or other liver disease.[32]

Other adverse effects seen with the use of lopinavir/r include diabetes mellitus or hyperglycemia, pancreatitis, bradyarrhythmias, diarrhea, nausea, abdominal pain, abnormal stools, asthenia, headache, insomnia, pain, rash, vomiting, and redistribution of body fat.[33] In one study, the incidence of diarrhea was greater in patients taking lopinavir/r once daily than for those taking it twice daily.[34]

Drug and Food Interactions

Lopinavir/r tablets can be administered with or without food. The tablet formulation also does not require dose adjustments for concomitant use with certain NNRTIs and PIs in treatment-naive patients.[35] To enhance bioavailability and minimize pharmacokinetic variability, the manufacturer recommends that lopinavir/r oral solution should be taken with food to increase absorption.[36]

Drug and Food Interactions (cont.)

Lopinavir/r tablets can be taken at the same time as didanosine without food. For patients taking lopinavir/r oral solution concurrently with didanosine, it is recommended that didanosine be given on an empty stomach; therefore, didanosine should be given one hour before or two hours after lopinavir/r oral solution is administered.[37]

Because no data exist for dosage with administerd with efavirenz, nevirapine, amprenavir, or nelfinavir, it is recomminded that lopinavir/r not be administered in combination with these drugs in patients younger than 6 months old.[38]

Lopinavir/r induces glucuronidation and has the potential to reduce plasma concentrations of zidovudine or abacavir concentrations if these drugs are taken concurrently. The clinical significance of this potential drug interaction is unknown.[39]

When taken concurrently, lopinavir/r increases tenofovir concentrations; the mechanism of this interaction is unknown. Patients taking both lopinavir/r and tenofovir should be monitored for tenofovir-associated adverse events. An increased rate of adverse events has also been observed when fosamprenavir is coadministered with lopinavir/r. Appropriate doses of both drugs with respect to safety have not been established.[40]

Lopinavir/r is an inhibitor of the CYP3A in vitro. Coadministration of lopinavir/r and drugs primarily metabolized by CYP3A may result in increased plasma concentrations of the other drug, which could increase or prolong its therapeutic and adverse effects. Lopinavir/r has also been shown in vivo to induce its own metabolism and to increase the biotransformation of some drugs metabolized by cytochrome P450 enzymes and by glucuronidation.[41] Lopinavir concentrations decrease in patients concurrently taking efavirenz, nevirapine, amprenavir, or nelfinavir, due to induction of CYP3A by these drugs; increased dosage of lopinavir/r may be required.[42] Lopinavir/r should not be given with orally administered midazolam. If lopinavir/r is coadministered with parenteral midazolam, close clinical monitoring for respiratory depression and/or prolonged sedation should be exercised, and dosage adjustment should be considered.[43]

Concentrations of antiarrhythmic drugs (amiodarone, bepridil, lidocaine, and quinidine) may be increased if taken concurrently with lopinavir/r; therapeutic monitoring of antiarrhythmic concentration may be necessary. Concomitant use of lopinavir/r with lipid lowering agents will result in an increase of concentrations of these agents. Levels of atorvastatin or cerivastatin should be lowered to the lowest possible level when used in combination with lopinavir/r. Pravastatin or fluvastatin should be considered as substitutes for atorvastatin or cerivastatin. Concomitant use of lovastatin or simvastatin with lopinavir/r is not recommended, as serious reactions such as myopathy, including rhabdomyolysis, may occur. Concurrent use of carbamazepine, dexamethasone, phenobarbital or phenytoin with lopinavir/r may decrease concentrations of lopinavir and lead to decreased effectiveness of lopinavir.[44]

The impact on the PR interval of co-administration of lopinavir/r with other drugs that prolong the PR interval (including calcium channel blockers, beta-adrenergic blockers, digoxin and atazanavir) has not been evaluated. As a result, co-administration of lopinavir/r with these drugs should be undertaken with caution, particularly with those drugs metabolized by CYP3A. Clinical monitoring is recommended.[45]

Serum concentrations of clarithromycin may increase if administered concomitantly with lopinavir/r. In patients concurrently taking clarithromycin, doses of lopinavir/r should be decreased as necessary in patients with renal impairment. Concentrations of cyclosporine, sirolimus, and tacrolimus may increase if administered concomitantly with lopinavir/r. Therapeutic monitoring is recommended for patients taking any of these immunosuppressants concurrently with lopinavir/r. Concentrations of dihydropyridine calcium channel blockers (felodipine, nicardipine, and nifedipine) may also increase if taken concomitantly with lopinavir/r; clinical monitoring is recommended.[46]

Serum concentrations of atorvastatin and rosuvastatin may increase if administered

Drug and Food Interactions (cont.)

concomitantly with lopinavir/r. The lowest possible dose of atorvastatin and rosuvastatin should be prescribed with careful monitoring when prescribed with lopinavir/r. Other HMG-CoA reductatase inhibibitors such as pravastatin or fluvastatin should be considered in patients taking lopinavir/r.[47]

Azole antifungals such as itraconazole and ketoconazole are not recommended to be taken concurrently with lopinavir/r because it may increase azole concentrations. Coadministration of voriconazole with lopinavir/r has not been studied. However, administration of voriconazole with ritonavir 400 mg every 12 hours decreased the voriconazole steady-state AUC by an average of 82%. The effect of lower ritonavir doses on voriconazole is not known at this time; until data are available, voriconazole should not be administered to patients receiving lopinavir/r. When rifabutin and lopinavir/r are administered concurrently, increased concentrations of rifabutin and rifabutin metabolite occur. A rifabutin dosage reduction by at least 75% is recommended, with further dose reduction possibly necessary.[48]

Concomitant use of ritonavir and St. John's wort (Hypericum perforatum) or products containing St. John's wort is not recommended as St. John's wort may substantially decrease lopinavir/r concentrations, resulting in suboptimal lopinavir concentrations, loss of virologic response, and possible resistance to lopinavir/r. Concomitant use of warfarin with lopinavir/r may affect warfarin serum concentrations; International Ratio Monitoring is recommended.[49] Coadministration of lopinavir/r and the phosphodiesterase (PDE) inhibitors sildenafil, tadalafil, or vardenafil is expected to substantially increase PDE inhibitor concentration and risk of adverse effects, including hypotension, prolonged erection, syncope, and visual changes. These PDE inhibitors should be used with caution, at reduced doses, and with increased monitoring for adverse events.[50]

Because contraceptive steroid concentrations may be altered when lopinavir/r is coadministered with oral and topical contraceptives containing ethinyl estradiol, alternative methods of nonhormonal contraception are recommended while a patient is taking lopinavir/r.[51]

Contraindications

Lopinavir/r is contraindicated in patients with known hypersensitivity to any of its ingredients, including ritonavir. Coadministration of lopinavir/r is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life threatening events. These drugs include antihistamines (astemizole, terfenadine), ergot derivatives (dihydroergotamine, ergonovine, ergotamine, metylergonovine), the gastrointestinal motility agent cisapride, the neuroleptic pimozide, and sedatives (midazolam, triazolam). Concurrent use of any of these drugs with lopinavir/r is contraindicated due to the potential for serious and/or life threatening reactions such as cardiac arrhythmias, prolonged or increased sedation, or respiratory depression.[52] Use of rifampin with lopinavir/r is also contraindicated, as it may lead to the loss of virologic response and possible resistance to lopinavir/r, other PIs, or any other coadministered antiretrovirals.[53]

Lopinavir/r should not be administered once daily in combination with efavirenz, nevirapine, amprenavir, or nelfinavir. Lopinavir/r administered once daily has not been evaluated in combination with fosamprenavir, indinavir, or saquinavir.[54]

Lopinavir/ritonavir prolongs the PR interval in some patients. Cases of second or third degree atrioventricular block have been reported. Lopinavir/ritonavir should be used with caution in patients with underlying structural heart disease, preexisting conduction system abnormalities, ischemic heart disease or cardiomyopathies, as these patients may be at increased risk for developing cardiac conduction abnormalities.[55]

The impact on the PR interval of co-administration of lopinavir/ritonavir with other drugs that prolong the PR interval (including calcium channel blockers, beta-adrenergic blockers, digoxin and atazanavir) has not been evaluated. As a result, co-administration of lopinavir/ritonavir with these drugs should be undertaken with caution, particularly with those drugs metabolized by

Lopinavir/Ritonavir

Contraindications (cont.)

CYP3A. Clinical monitoring is recommended.[56]

Risk-benefit should be considered if patients also have diabetes mellitus, hemophilia A or B, hepatic function impairment, hepatitis B or C virus infection, or a history of pancreatitis.[57]

Clinical Trials

For information on clinical trials that involve Lopinavir/Ritonavir, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Lopinavir/Ritonavir AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[58]

Dosage Form: Film-coated tablets containing lopinavir 200 mg and ritonavir 50 mg.[59]

Oral solution containing lopinavir 80 mg/ml and ritonavir 20 mg/ml.[60]

Soft gelatin capsules containing lopinavir 133.3 mg and ritonavir 33.3 mg.[61]

Film-coated tablets containing lopinavir 100 mg and ritonavir 25 mg.[62]

The recommended dose of lopinavir/r in treatment-experienced adults is 2 tablets (400/100 mg) twice daily taken with or without food or 400/100 mg (5 ml) twice daily with food.[63] [64] The recommended doses of lopinavir/r in treatment-naive adults are 2 tablets (400/100 mg) twice daily taken with or without food, or 4 tablets (800/200 mg) once daily taken with or without food. In children age 14 days to 6 months, the recommended dose is 16/4 mg/ml twice daily.[65] In children age 6 months to 12 years who weigh 7 to 15 kg, the recommended dose is 12/3 mg/kg twice daily. For those children who weigh 15 to 40 kg, the recommended dose is 10/2.5 mg/kg (maximum dose of 400/100 mg twice daily).[66] Once-daily dosing is not recommended in children.

In treatment-naive patients, no dosing adjustment is necessary when lopinavir/r tablets are administered as part of a twice-daily regimen with efavirenz, nevirapine, amprenavir, fosamprenavir, or nelfinavir.[67] When oral solution is used twice daily in combination with efavirenz or nevirapine, the lopinavir/r dose should be increased to 533/133 mg (6.5 ml) twice daily.[68] A dose increase of 600/150 mg (3 tablets) twice daily should be considered when lopinavir/r is used in combination with efavirenz, nevirapine, fosamprenavir without ritonavir, or nelfinavir in treatment-experienced patients where decreased susceptibility to lopinavir is suspected.[69]

Storage: Store tablets at 20 C to 25 C (68 F to 77 F); excursions permitted to 15 C to 30 C (59 F to 86 F). Exposure of tablets to high humidity outside the original container for longer than 2 weeks is not recommended.[70]

Store oral solution at 2 C to 8 C (36 F to 46 F) until dispensed. Avoid exposure to excessive heat. Patients can keep refrigerated oral solution until expiration date. If kept at room temperature up to 25 C (77 F), oral solution should be used within 2 months of dispensing.[71]

Store capsules at 2 C to 8 C (36 F to 46 F) until dispensed. Avoid exposure to excessive heat. Patients can keep refrigerated oral solution until expiration date. If kept at room temperature up to 25 C (77 F), capsules should be used within 2 months of dispensing.[72]

Chemistry

CAS Name: Lopinavir: (alphaS)-Tetrahydro-N-[(alphaS)-alpha-[(2S,3S)-2-hydroxy-4-phenyl-3-[2-(2,6-xylyloxy)acetamido] butyl]phenethyl]-alpha-isopropyl-2-oxo-1(2H)-pyrimidineacetamide[73]

Ritonavir: 5-Thiazolylmethyl [(alphaS)-alpha-[(1S,3S)-1-hydroxy-3-[(2S)-2-[3-[(2-isopropyl-4-thiazolyl)methyl]-3-methylureido]-3-methylbutyramido]-4-phenylbutyl]phenethyl] carbamate[74]

Lopinavir/ritonavir: 2,4,7,12-Tetraazatridecan-13-oic acid, 10-hydroxy-2-methyl-5-(1-methylethyl)-

Lopinavir/Ritonavir

Chemistry (cont.)

1-(2-(1-methylethyl)-4-thiazolyl)-3,6-dioxo-8,11-bis(phenylmethyl)-, 5-thiazolylmethyl ester, (5S,8S,10S,11S)-, mixt. with (aS)-N-((1S,3S,4S)-4-(((2,6-dimethylphenoxy)acetyl)amino)-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl)tetrahydro-a- (1-methylethyl) -2-oxo-1(2H)- pyrimidineacetamide[75]

CAS Number: Lopinavir: 192725-17-0[76]

Ritonavir: 155213-67-5[77]

Lopinavir/ritonavir: 369372-47-4[78]

Molecular formula: C37-H48-N4-O5.C37-H48-N6-O5[79]

Lopinavir: C70.67%, H7.69%, N8.91%, O12.72%; Ritonavir: C61.64%, H6.71%, N11.66%, O11.10%, S8.90%[80]

Molecular weight: Lopinavir: 628.80; Ritonavir: 720.96[81]

Melting point: Lopinavir: 124 to 127 C[82]

Physical Description: Lopinavir: White to light tan powder.[83]

Ritonavir: White to light tan powder with bitter metallic taste.[84]

Solubility: Lopinavir: Freely soluble in methanol and ethanol; soluble in isopropanol; practically insoluble in water.[85]

Ritonavir: Freely soluble in methanol and ethanol; soluble in isopropanol; practically insoluble in water.[86]

Other Names

LPV/RTV[87]

LPV/r[88]

Aluvia[89]

Further Reading

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Manufacturer Information

Lopinavir/Ritonavir
Abbott Laboratories
One Hundred Abbott Park Rd
Abbott Park, IL 60064-3500
(800) 633-9110

Kaletra
Abbott Laboratories
One Hundred Abbott Park Rd
Abbott Park, IL 60064-3500
(800) 633-9110

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

For More Information (cont.)

• Via Live Help: http://aidsinfo.nih.gov/live_help
Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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