REPRINTED BY

PROJECT inform

Information, Inspiration and Advocacy for People Living With HIV/AIDS

AUGUST 2004

Kaletra (lopinavir+ritonavir)

reprinted from www.aidsmeds.com, united states

What is Kaletra?

- Kaletra is an anti-HIV medication. It is in a category of HIV medicines called protease inhibitors (PIs). Kaletra prevents cells infected by HIV from producing new virus. This reduces the amount of virus in your body, and can increase the number of T-cells.
- Kaletra is manufactured by Abbott Laboratories. The U.S. Food and Drug Administration (FDA) approved it for the treatment of HIV infection, in both adults and children, in 2000.
- Kaletra is actually two drugs combined into a single capsule: lopinavir and low doses of ritonavir (Norvir®), another protease inhibitor manufactured by Abbott Laboratories. This is because ritonavir increases the amount of lopinavir in the blood, thus making it more effective against HIV. A single Kaletra capsule contains 133mg of lopinavir and 33mg of ritonavir.

What is already known about Kaletra?

- The approved dose of Kaletra is three capsules, taken twice a day.
- Kaletra should be taken with a meal or light snack.
- Refrigeration of the Kaletra capsules and oral solution is recommended but is not necessary if they are used within 2 months and stored below 77° fahrenheit (25° celsius).
- The manufacturer of Kaletra has asked the U.S. Food and Drug Administration to approve a once-daily dosing schedule for the drug: six pills (containing 800mg of lopinavir and 200mg of ritonavir) once a day. Until the FDA decides whether or not to approve this dose, it is still considered to be experimental.
- Children between the ages of 6 months and 12 years can take Kaletra. The dose they require will depend on their body weight. A liquid formulation of Kaletra is available for babies and children, which is easier to give to young children than the adult capsules.
- Clinical trials have determined that Kaletra is safe and effective when combined with other drugs, most notably two nucleoside reverse transcriptase inhibitors (NRTIs). It has shown to be effective for HIV-positive patients beginning protease inhibitor therapy for the first time and for those who have tried and failed other protease inhibitors in the past.
- For HIV-positive adults beginning anti-HIV drug therapy for the first time, Kaletra is listed as the "preferred" protease inhibitor option by the United States Department of Health and Human Services in its treatment guidelines. Other protease inhibitors, including those used with Norvir, are listed as "alternative" options.
- If your viral load becomes detectable while taking a drug regimen that contains Kaletra, your doctor can order a drug-resistance test to see which drugs your virus are becoming less sensitive to.
- Many of the currently available protease inhibitors are affected by cross-resistance. This means that, if you've tried and failed a drug regimen in the past that contained a protease inhibitor, your virus might be resistant to Kaletra, although Kaletra has worked well for many

people who have failed other protease inhibitors in the past. If you take an anti-HIV drug regimen that contains Kaletra and your virus becomes resistant to the drug, your virus might also be resistant to many of the other protease inhibitors available. This is why it is very important to use drug-resistance testing to determine which drugs your virus are no longer responding to if you experience a rebound in your viral load while taking an anti-HIV drug regimen. Drug-resistance testing can also help you figure out which protease inhibitors your virus is still sensitive to.

What about drug interactions?

- Kaletra is broken down (metabolized) by the liver, like many medications used to treat HIV and AIDS. This means that Kaletra can interact with other medications. Kaletra can lower or raise the levels of other medications in the body. Similarly, other medications can lower or raise the levels of lopinavir and/or ritonavir found in Kaletra in the body. While many interactions are not a problem, some can cause your medications to be less effective or increase the risk of side effects.
- Tell your doctors and pharmacists about all medicines you take. This includes those you buy over-the-counter and herbal or natural remedies, such as St. John's Wort. Bring all your medicines when you see a doctor, or make a list of their names, how much you take, and how often you take them. Your doctor can then tell you if you need to change the dosages of any of your medications.
- The following medications should not be taken while you are being treated with Kaletra:
  Acid reflux/heartburn medications: Propulsid® (cisapride)
  Antibiotics: Priftin® (rifapentine) and Rifadin® (rifampin)
  Antifungals: Vfend® (voriconazole)
  Antimigraine medications: Ergostat®, Cafergot®, Ercaf®, Wigraine® (ergotamine) or D.H.E. 45® (dihydroergotamine)
  Antihistamines: Hismanal® (astemizole) or Seldane® (terfenadine)
  Calcium channel blockers: Vascor® (bepridil)
  Heart arrhythmia medications: Tambocor™ (flecainide) and Rythmol® (propafenone)
  Cholesterol-lowering drugs (statins): Zocor® (simvastatin) and Mevacor® (lovastatin)
  Antipsychotics: Orap® (pimozide)
  Sedatives: Versed® (midazolam) and Halcion® (triazolam)
- Anticonvulsants, such as Tegretol® (carbamazepine), Luminal® (phenobarbital), and Dilantin® (phenytoin), may interact with Kaletra and should be used with caution.
- Anti-HIV protease inhibitors can interact with Kaletra. In fact, the interactions between Kaletra and other protease inhibitors can be very tricky, given that three protease inhibitors are being used, which can result in confusing three-way drug interactions. For example, when Kaletra is combined with Agenerase® (amprenavir) or Lexiva® (fosamprenavir), the levels of lopinavir (from the Kaletra) and the Agenerase/Lexiva in the bloodstream tend to be lower than levels seen when these drugs are paired one-on-one with Kaletra (but higher than levels seen when the drugs are used alone). Because of this interaction, Kaletra and Agenerase or Lexiva should not be taken together. Kaletra can increase Crixivan® (indinavir) levels (the Crixivan dose should be reduced to 600mg twice daily, combined with the usual dose of Kaletra). Kaletra can increase Fortovase® (saquinavir soft gel capsules) and Invirase® (saquinavir hard gel capsules) levels (The Fortovase or Invirase dose should be 1,000mg twice a day, plus the usual dose of Kaletra). When Kaletra is combined with Viracept® (nelfinavir), blood levels of lopinavir in Kaletra decrease and blood levels of Viracept increase (no dosing recommendation has been made). And little is known about Kaletra in combination with Reyataz™ (atazanavir).
- Anti-HIV non-nucleoside reverse transcriptase inhibitors (NNRTIs) can also interact with Kaletra. Viramune® (nevirapine) and Sustiva® (efavirenz), two non-nucleoside reverse transcriptase inhibitors (NNRTIs), can decrease the amount of lopinavir in Kaletra in the bloodstream. If Kaletra is combined with either Viramune or Sustiva, the dose of Kaletra needs to be increased to four capsules, twice a day (compared to the standard three capsules, twice a day dose). A third NNRTI, Rescriptor® (delavirdine), can increase the amount of Kaletra in the bloodstream. However, neither the dose of Rescriptor or Kaletra need to be changed.
- Viread® (tenofovir), a nucleotide reverse transcriptase inhibitor, can decrease Kaletra levels in the bloodstream. Kaletra increases Viread levels in the bloodstream. If Kaletra and Viread are used

together, it is important to watch out for potential side effects of Viread (e.g., kidney problems).

- Another painkiller, methadone, commonly used to treat drug addiction, can interact with Kaletra. Methadone levels in the bloodstream can decrease when combined with Kaletra. Because of this, it might be necessary to increase the dose of methadone.
- Norpramin® (desipramine) is used to treat depression. Levels of this drug can increase in the bloodstream if it is combined with Kaletra. In turn, it might be necessary to reduce the usual dosage of this drug.
- Antabuse® (disulfiram) is a medication taken by people with an alcohol-dependency problem. This medication can make people very sick if they consume even small amounts of alcohol. Because liquid Kaletra contains small amounts of alcohol, it should not be combined with Antabuse®. Kaletra capsules can be combined Antabuse.
- Flagyl® (metronidazole) is used to treat some types of parasitic infections. People should not drink alcohol—or take medications that contain alcohol—while taking this drug. The combination of alcohol and Flagyl can cause someone to become very ill. In turn, HIV-positive people taking liquid Kaletra should not take Flagyl. Kaletra capsules can be taken with Flagyl.
- Kaletra can interact with some medications used to treat TB, MAC, and other bacterial infections. Rifadin® (rifampin) can decrease Kaletra levels and Kaletra can increase Rifadin levels (these drugs should not be used together). Kaletra can increase Mycobutin® (rifabutin) (the Mycobutin dose will need be reduced to 150mg every other day or three-times-weekly). Kaletra also raises Biaxin® (clarithromycin) levels in the bloodstream (the Biaxin dose may need to be decreased).
- Kaletra can interact with some medications used to treat thrush (candidiasis) and other fungal infections. Kaletra can increase Nizoral® (ketoconazole) levels in the bloodstream. In turn, you should be taking no more than 200mg Nizoral daily while on Kaletra.
- Kaletra decreases the amount of oral contraceptives (taken by women to help avoid pregnancy) in the bloodstream. This means that there may be a higher risk of becoming pregnant if Kaletra and oral contraceptives are taken at the same time. To reduce the risk of pregnancy, barrier protection (e.g., condom) should be used.
- Cholesterol-lowering drugs, also known as "statins," can interact with Kaletra. There are two statins that should not be used with Kaletra: Zocor® (simvastatin) and Mevacor® (lovastatin). Levels of these two drugs can become significantly increased in the bloodstream if they are combined with Kaletra, which increases the risk of side effects. The two statins that are considered to be the safest in combination with Kaletra are Pravachol® (pravastatin) and Lescol® (fluvastatin). It is also possible to take Kaletra with Lipitor® (atorvastatin), although Kaletra can increase the levels of this drug in the bloodstream. If Lipitor is prescribed, it's best to begin treatment with the lowest possible dose of the drug and then increase the dose if necessary. Little is known about the newest statin, Crestor® (rosuvastatin), although it is not expected to have any serious drug interactions with Kaletra or the other protease inhibitors.
- Some patients with asthma or emphysema (chronic obstructive pulmonary disorder) take a drug called theophylline. Kaletra can decrease the amount of theophylline in the bloodstream. If these two drugs are taken at the same time, a doctor can order a blood test to check the level of theophylline in the bloodstream. If the theophylline level is too low, the dose can be increased.
- Viagra® (sildenafil), Levitra® (vardenafil) and Cialis® (tadalafil) levels in the bloodstream may increase when combined with Kaletra. In turn, it is best to use a lower dose of these drugs in order to reduce the risk of side effects.
- Herbal products can also interact with Kaletra. St. John's wort should not be used with Kaletra, since it can greatly reduce the amount of the Kaletra in the bloodstream. HIV-positive people should also be cautious about using garlic supplements or milk thistle with Kaletra—test tube studies suggest that both herbal products can interact with the same liver enzyme system (cytochrome P450 3A4) responsible for metabolizing Kaletra. This may alter the amount of Kaletra in the bloodstream. These and other herbal products should be used with caution, until further studies are conducted.
- Other drug interactions are possible. Be sure to tell your doctor about all the medications you are taking (or plan to take), including those you buy over-the-counter at your pharmacy or health-food store, while taking Kaletra.

For more treatment information, call Project Inform's toll-free National HIV/AIDS Treatment Information Hotline at 1-800-822-7422.

What are the possible side effects of Kaletra?

- The most common side effects seen in people taking Kaletra are abnormal stools (bowel movements), feeling weak/tired, headache, diarrhea, nausea, and vomiting. Children may sometimes get a skin rash.
- Blood tests in people taking Kaletra may show possible liver problems. People with liver diseases such as hepatitis B or C who take Kaletra may have worsening liver disease. Liver problems including death have occurred in patients taking Kaletra, but it is unclear if Kaletra caused these liver problems because some patients had other illnesses or were taking other medicines.
- Some people taking Kaletra can develop serious problems with their pancreas (pancreatitis), which may cause death. This is especially true in people who have had pancreatitis in the past. Tell your doctor if you have nausea, vomiting, or abdominal pain, since these may be signs of pancreatitis.
- Some people may have large increases in their lipid levels (triglycerides and cholesterol). The long-term chance of getting complications such as heart attacks or stroke due to increases in blood lipids caused by protease inhibitors is not known at this time.
- Diabetes and high blood sugar may occur in people who take Kaletra or other protease inhibitors.
- Anti-HIV drug regimens containing protease inhibitors, including Kaletra, can cause abnormal body-shape changes (lipodystrophy; including increased fat around the abdomen, breasts, and back of the neck, as well as decreased fat in the face, arms, and legs). These side effects of anti-HIV drug therapy are reviewed in our lesson on lipodystrophy.

Who should not take Kaletra?

- Before taking Kaletra, tell your doctor if you have diabetes, liver problems, or hemophilia. You may not be able to take Kaletra, or you may require a dosage adjustment or special monitoring during treatment, if you have any of these conditions.
- Kaletra is classified by the FDA as a pregnancy category C drug. All the FDA-approved anti-HIV drugs are classified as either category B or C. Pregnancy category B means that animal studies have failed to demonstrate a risk to the fetus, but there are no adequate and well-controlled studies in pregnant women. Pregnancy category C means that animal studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. HIV-positive women who become pregnant should discuss the benefits and possible side effects of anti-HIV treatment to help protect their babies from HIV.
- It is not known whether Kaletra passes into breast milk and what effect it may have on a nursing baby. To prevent transmission of the virus to uninfected babies, it is recommended that HIV-positive mothers not breast-feed.
- Kaletra has not been studied in children younger than 6 months of age.
- Side effects other than those listed here may also occur. Talk to your doctor about any side effect that seems unusual or that is especially bothersome.

Where can I learn more about clinical trials of Kaletra?

- If you would like to find out if you are eligible for any clinical trials that include Kaletra, there is an interactive web site run by amfAR, the American Foundation for AIDS Research.
- Another useful service for finding clinical trials is *AIDSinfo.nih.gov*, a site run by the U.S. National Institutes of Health. They have "health information specialists" you can talk to at their toll-free number at 1-800-HIV-0440 (1-800-448-0440).

a note about this publication

This publication is reprinted here from another source (*www.aidsmeds.com*). We do not always have the resources at Project Inform to produce our own treatment information on every treatment topic. In these cases, we try to provide reliable information from other sources but cannot confirm that every fact in these publications is accurate. References to other materials have been pulled. This information is designed to support, not replace, the relationship that exists between you and your doctor or medical provider.

TEXT LAST UPDATED: AUGUST 2004