



LOPINAVIR + ritonavir (Kaletra)

WHAT IS LOPINAVIR?

Lopinavir is a drug used as part of antiretroviral therapy (ART). It is manufactured by Abbott Laboratories. Lopinavir is a protease inhibitor. The amount of Lopinavir in the blood stream stays much higher if it is taken with a small amount of ritonavir, another protease inhibitor. See Fact Sheet 442 for more information on ritonavir. Kaletra is a combination of lopinavir and ritonavir in the same tablet. In developing countries, Kaletra is sold as Aluvia. Generic versions have been tentatively approved under PEPFAR (see fact sheet 475.)

Protease inhibitors prevent the protease enzyme from working. HIV protease acts like a chemical scissors. It cuts the raw material for HIV into specific pieces needed to build a new virus. Protease inhibitors "gum up" these scissors.

WHO SHOULD TAKE IT?

Kaletra was approved in 2000 as an antiretroviral drug (ARV) for people with HIV infection. It has been studied in adults and children. In 2008 it was approved for use in children at least 14 days old.

There are no absolute rules about when to start ART. You and your doctor should consider your CD4 cell count, your viral load, any symptoms you are having, and your attitude about taking ART. Fact Sheet 404 has more information about guidelines for the use of ART.

If you take Kaletra with other ARVs, you can reduce your viral load to extremely low levels, and increase your CD4 cell counts. This should mean staying healthier longer.

WHAT ABOUT DRUG RESISTANCE?

Many new copies of HIV are mutations. They are slightly different from the original virus. Some mutations can keep multiplying even when you are taking an ARV. When this happens, the drug will stop working. This is called "developing resistance" to the drug. See Fact Sheet 126 for more information on resistance. Sometimes, if your virus develops resistance to one drug, it will also have resistance to other ARVs. This is called "cross-resistance".

Kaletra provides blood levels that are high enough to control HIV that has already developed some resistance to other protease inhibitors.

Resistance can develop quickly. It is very important to take ARVs according to instructions, on schedule, and not to skip or reduce doses.

HOW IS IT TAKEN?

A film-coated tablet of Kaletra was approved in October 2005. The tablet replaces the original gelatin capsule version. Each tablet contains 200 milligrams (mg) of lopinavir and 50 mg of ritonavir. The normal dose is two tablets twice a day or four tablets once a day for patients whose HIV does not have significant resistance to Kaletra.

In November 2007, the FDA approved a half-strength formulation for children. It contains 100 mg of lopinavir and 25 mg of ritonavir. This version does not require refrigeration.

It is also available in liquid form. The normal adult dose is 5 milliliters (ml) twice a day. Kaletra tablets can be taken with or without food. Kaletra liquid should be taken with food.

Different doses are used in some combinations. Be sure you know how much Kaletra your doctor has prescribed for you, and when and how to take each dose.

Kaletra is approved for use by children. Their dosage is based on their body weight. Tablets should not be crushed, broken or chewed. This can result in low drug levels.

Kaletra tablets should be kept at room temperature. They are not sensitive to heat. Kaletra liquid can be refrigerated or stored at room temperature for up to 2 months.

The older capsule version of Kaletra will be phased out by Abbott. Where the capsules are used, they should be stored at or below 25 degrees Celsius (77 degrees Fahrenheit). At higher temperatures, they can become soft and sticky and form clumps. The capsules may stick together and be difficult to separate. They may lose potency.

WHAT ARE THE SIDE EFFECTS?

The most common side effects of Kaletra are diarrhea, fatigue, headache, and nausea. None of these side effects seem to be very serious. Kaletra can increase the amount of fat (cholesterol and triglycerides) in your blood. High levels of blood fats can increase your risk of problems with your heart or pancreas. Kaletra was recently found to cause changes in heart rhythm. Be

sure your health care provider knows if you have any problems with your heart.

HOW DOES IT REACT WITH OTHER DRUGS?

Kaletra is broken down by the liver and can interact with other drugs that also use the liver. **Combining these drugs can change the amount of each drug in your bloodstream and cause an under- or overdose. New interactions are constantly being identified. Make sure that your doctor knows about ALL drugs and supplements you are taking.**

Drugs to watch out for include other ARVs, drugs to treat tuberculosis (see fact sheet 518), erectile dysfunction (such as Viagra), heart rhythm (antiarrhythmics), and migraine headaches. Interactions are also possible with several antihistamines, sedatives, drugs to lower cholesterol and anti-fungal drugs, or drugs that alter heart rhythm.

If you are taking liquid Kaletra and **ddl**, you should take ddl one hour before or two hours after Kaletra. These restrictions do not apply to the new Kaletra tablets.

Take Kaletra one hour apart from antacids.

Kaletra lowers blood levels of **methadone**. If you are taking methadone you may need to increase the dose. Watch for signs of excessive sedation with **buprenorphine**.

Nelfinavir lowers blood levels of Kaletra. Your Kaletra dose may need to be increased if you are taking nelfinavir, especially if your virus is partially resistant to protease inhibitors.

Some **birth control pills** may not work if you are taking Kaletra. Talk to your doctor about how to prevent an unwanted pregnancy.

The herb **St. John's Wort** (See Fact Sheet 729) lowers the blood levels of some protease inhibitors.

Kaletra lowers blood levels of **lamotrigine**, a drug used to treat epilepsy and neuropathy. A higher dose of lamotrigine may be required.

Kaletra raises blood levels of **midazolam (Versed)**, a sedative. They should not be taken together without careful monitoring.

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