

Kaletra

Summary

Kaletra is the brand name of treatment that contains two anti-HIV drugs called protease inhibitors—lopinavir and ritonavir. The most common side effects associated with the use of Kaletra are diarrhea, feeling weak or tired, nausea and vomiting. Kaletra is available in tablets, capsules and as a liquid.

What is Kaletra?

Kaletra is the brand name of two anti-HIV drugs—lopinavir and ritonavir (Norvir)—that are sold together in one tablet, capsule or liquid. These drugs are called protease inhibitors.

How does Kaletra work?

When HIV infects a cell, it takes control of that cell. HIV then forces the cell to make many more copies of the virus. To make these copies, the cell uses proteins called enzymes. When the activity of these enzymes is reduced the production of HIV slows.

Kaletra contains two drugs, lopinavir and ritonavir, both of which belong to a group of drugs called protease inhibitors. These drugs affect an enzyme called protease, which is used by HIV-infected cells to make new viruses. Since lopinavir reduces or inhibits the activity of this protease enzyme (hence the name “protease inhibitor”), this drug causes HIV-infected cells to produce fewer viruses.

The purpose of the small amount of ritonavir inside Kaletra is to boost levels of lopinavir in the blood. Ritonavir also helps keep lopinavir levels high for many hours. This is why Kaletra can be taken once or twice daily.

How do people with HIV use Kaletra?

Kaletra is used in combination with several other anti-HIV drugs from different classes, such as nucleoside analogues (“nukes”) and non-nucleoside reverse transcriptase inhibitors (“non-nukes”).

Combinations such as this are called antiretroviral therapy, or ART. In order for Kaletra to be effective it must be taken with at least two other anti-HIV drugs. For more information on ART, see CATIE’s *Your Guide to HIV Treatment*.

FACT SHEET

**Published
2019**

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Neither Kaletra nor any other anti-HIV medication is a cure for HIV. It is therefore important that you see your doctor regularly so that he/she monitors your health.

Evidence shows that HIV-positive people who are on ART, engaged in care, and have an ongoing undetectable viral load are substantially less likely to transmit HIV to others, be it through sex, when sharing equipment to use drugs or during pregnancy and birth. In fact, the evidence for sexual transmission shows that people on ART who maintain an undetectable viral load do not pass HIV to their sexual partners. For further information see the CATIE fact sheet *HIV treatment and an undetectable viral load to prevent HIV transmission*. However, it is still a good idea to use condoms because they can reduce your risk for getting and passing on other sexually transmitted infections.

Warning

Pancreatitis

A painfully swollen pancreas gland—pancreatitis—is a rare complication that has occurred in users of Kaletra. In some of these cases, pancreatitis has been fatal. Symptoms of pancreatitis can include the following:

- nausea
- vomiting
- abdominal pain
- blood tests revealing high levels of the enzymes amylase and lipase

If you have these symptoms, contact your doctor right away.

Side effects

1. General side effects

General side effects that have been reported by some Kaletra users include the following:

- diarrhea, loose stools
- unexpected tiredness

- headache
- nausea
- vomiting

2. Liver enzymes

Because ritonavir is metabolized (processed and broken down) by the liver, blood tests may show increased levels of liver enzymes.

3. Bleeding

Women may experience heavier menstrual periods when using protease inhibitors. Hemophiliacs who use protease inhibitors may experience increased bleeding. If you are a hemophiliac who uses Kaletra and has this problem, let your doctor know about it.

4. Blood sugar

In some people with HIV who use protease inhibitors, levels of sugar (glucose) in the blood become higher than normal. Prolonged bouts of higher-than-normal blood sugar levels may lead to diabetes. At least one study has found that some HIV-positive women, particularly those who are overweight, may be at increased risk for diabetes when they use protease inhibitors. Regular monitoring of your blood to assess sugar levels and other measurements will help you and your doctor be aware of changes that might suggest problems with your blood sugar. Although the risk of developing diabetes is generally low, symptoms that may be related to diabetes (increased thirst, increased urination, unexplained weight loss, fatigue and dry, itchy skin) should be discussed with your doctor.

5. Cholesterol

Kaletra can cause increased levels of cholesterol and triglycerides in your blood.

6. Pregnancy

The effects of Kaletra on the fetus are not known. The manufacturer notes that this drug should

only be used by pregnant women if “the potential benefit justifies the potential risk to the fetus.” If you are pregnant or wish to become pregnant, and are taking Kaletra, talk to your doctor.

Drug interactions

Like many drugs, lopinavir and ritonavir are broken down and processed (metabolized) by a group of enzymes in the liver and intestines called P450. Taking Kaletra with another drug that is metabolized by the same enzymes can affect levels of each drug in the blood. As a result, levels of some drugs may increase, causing you to experience side effects or making pre-existing side effects worse. Another possibility is that levels of some drugs may decrease, resulting in little or no benefit from those drugs. If lopinavir or ritonavir levels become too low, HIV can develop resistance to lopinavir and your future treatment options may be reduced.

It is therefore important to *always* consult your doctor and pharmacist about taking any other medication—prescription or non-prescription—including herbs and supplements, to ensure that they do not interfere with your lopinavir or ritonavir levels and vice versa. If you must take a drug that has the potential to interact with your existing medications, your doctor can do the following:

- adjust your dose of either your anti-HIV drugs or other medications
- prescribe different anti-HIV drugs for you

Drug interaction warning

Below are lists of actual and potential drug interactions. These lists are not exhaustive. The manufacturer recommends that the following drugs should **not** be taken with by Kaletra users:

- heart drugs—flecainide (Tambocor), propafenone (Rythmol)
- antihistamines—astemizole (Hismanal), terfenadine (Seldane)
- ergot drugs—ergonovine, ergotamine (Ergomar)

- antibiotics—metronidazole (Flagyl), rifampin. Flagyl should not be taken with Kaletra oral solution, which contains alcohol and can lead to dangerous side effects. However, Flagyl can be taken with Kaletra oral tablets and capsules.
- gastrointestinal motility agents—cisapride (Prepulsid)
- herbs—St. John’s wort
- anti-psychotics—pimozide (Orap)
- sedatives/sleeping pills—midazolam (Versed), triazolam (Halcion)
- lipid-lowering agents—lovastatin (Mevacor), simvastatin (Zocor). The manufacturer suggests that other lipid-lowering agents such as pravastatin (Pravachol) and fluvastatin (Lescol). Atorvastatin (Lipitor) and rosuvastatin (Crestor) may be used at low doses.
- drugs to treat erectile dysfunction—sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra). Taking ritonavir with any of these drugs can lead to dangerous side effects and even death. Talk to your doctor if you have erectile dysfunction about how you might use these drugs safely.

In addition to the drugs listed above, here are some more drugs that interact or have the potential to interact with Kaletra. This list is not exhaustive.

The following drugs can *reduce* levels of lopinavir in the blood:

- non-nucleoside reverse transcriptase inhibitors—efavirenz (Sustiva), nevirapine (Viramune)
- anti-seizure drugs—carbamazepine (Tegretol), phenobarbital, phenytoin (Dilantin)
- corticosteroids—dexamethasone (Decadron)

Kaletra can *increase* levels of the following drugs:

- antibiotics—clarithromycin (Biaxin), rifabutin (Mycobutin)
- antifungals—ketoconazole (Nizoral), itraconazole (Sporanox)

- antiviral agents—all protease inhibitors, maraviroc (Celsentri), tenofovir (Viread)
- calcium channel blockers—nifedipine (Adalat), felodipine (Plendil, Renedil), nicardipine (Cardene)
- erectile dysfunction—sildenafil (Viagra) and likely other, related drugs such as vardenafil (Levitra) and tadalafil (Cialis)
- immunosuppressive agents—cyclosporine (Neoral), tacrolimus (Advagraf, Prograf), sirolimus (Rapamycin)
- corticosteroids—inhaled/nasal budesonide (Pulmicort, Rhinocort), fluticasone (Flovent, Flonase), triamcinolone (Nasocort), and mometasone (Asmanex, Nasonex); prednisone, prednisolone. Taking Kaletra with any of these drugs can lead to Cushing’s syndrome (moon face, buffalo hump, rapid weight gain, increased facial hair growth). Talk to your doctor about other options, such as beclomethasone (QVAR, Beclonase), or reducing the doses of these drugs.
- heart drugs—amiodarone
- analgesics—fentanyl (extended-release, transdermal, or transmucosal preparations)
- blood thinners—rivaroxaban (Xarelto)

Kaletra can *decrease* levels of the following drugs:

- narcotics—methadone; your dose of methadone may need to be adjusted if you are taking Kaletra
- anti-parasite—atovaquone (Mepron)
- oral contraceptives—ethinyl estradiol, norethindrone
- antidepressants—bupropion (Wellbutrin)
- antifungals—voriconazole (Vfend)

Resistance and cross-resistance

Over time, as new copies of HIV are made in the body, the virus can change its structure. These changes are called mutations and can cause HIV to resist the effect of ART. Combining Kaletra

with at least two other anti-HIV drugs delays the development of drug resistance.

To reduce the risk of developing drug resistance, all anti-HIV drugs should be taken every day exactly as prescribed and directed. It is important that you take your Kaletra every day because resistant virus can develop if levels of lopinavir or ritonavir in the blood fall too low. This may happen if doses are delayed, skipped or not taken as prescribed. If you find you are having problems taking your medication on a regular basis, as directed, speak to your doctor and nurse about this. They can find ways to help you.

Should HIV in your body become resistant to Kaletra, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

Feel free to talk with your doctor about your current and future treatment options.

Formulations

Kaletra is available in three formulations:

- capsules
- liquid
- tablets

The newest formulation is Kaletra tablets and this comes with several advantages over the older capsule formulation, which are as follows:

- a lower pill burden
- tablets do not require refrigeration
- tablets may be taken with or without food
- tablets may be associated with fewer side effects

Your doctor, nurse or pharmacist can tell you about the availability of Kaletra tablets in your region.

Dosage

Try to take your doses as scheduled. If you miss a dose, take the next dose as soon as possible and resume your normal medication schedule. If you

have trouble taking your medicines as prescribed speak to your doctor and pharmacist for advice.

1. New to treatment

For people with HIV who have never before taken anti-HIV medicines, also called treatment-naïve people with HIV, Kaletra may be taken once or twice daily. Your doctor will help you decide which schedule is best for you. For this group, the doses are as follows:

- Tablets: the recommended adult dose is 2 tablets twice daily or 4 tablets once daily, in both cases with or without food.
- Capsules: the recommended adult dose is 3 capsules twice daily or 6 capsules once daily, in both cases with food.
- Liquid: the recommended adult dose is 5 ml twice daily or 10 ml once daily, in both cases with food.

2. Treatment-experienced

Treatment-experienced people with HIV tend to have HIV that is resistant to some therapies. To maintain high levels of anti-HIV medicines in the blood and reduce the risk of developing drug-resistant HIV, dosing is often more frequent for treatment-experienced people with HIV. For this group, the manufacturer recommends the following dose and schedule:

- Tablets: the recommended adult dose is 2 tablets twice daily with or without food.
- Capsules: the recommended adult dose is 3 capsules twice daily with food.
- Liquid: the recommended adult dose is 5 mL taken twice daily with food.

If you miss a dose of Kaletra, the manufacturer recommends that you take a dose as soon as possible and then return to your normal schedule. You should not take a double dose to make up for the missed dose. If you keep forgetting to take Kaletra, talk to your doctor about this problem.

Doctors prescribing Kaletra to adults who are also taking nevirapine or efavirenz should consider

increasing the dose of Kaletra since these drugs can reduce levels of lopinavir in the blood.

In children between the ages of six months and 12 years, the dose of Kaletra is adjusted depending on the weight of the child.

Availability

Kaletra is available in tablet, capsule and liquid form. Your doctor can tell you more about the availability of Kaletra in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

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Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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Production of this document has been made possible through a financial contribution from the Public Health Agency of Canada. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada.

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