

# Saquinavir hgc (Invirase)

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## What is Invirase?

- Invirase is an anti-HIV medication. It is in a category of HIV medications called protease inhibitors (PIs). Invirase prevents T-cells that have been infected with HIV from producing new HIV.
- Invirase is manufactured by Hoffmann-La Roche. The U.S. Food and Drug Administration (FDA) approved it for the treatment of HIV infection in 1995.
- Invirase is an older version of saquinavir, the generic name for this protease inhibitor. The newer version of saquinavir, Fortovase® (saquinavir soft gel cap), was approved in 1997.
- Invirase should be taken with low doses of Norvir® (ritonavir), another protease inhibitor that boosts Invirase levels in the body (Invirase suffers from absorption problems, meaning that only a small amount of the drug is absorbed into the bloodstream from the gut). Invirase (1,000 mg twice daily) combined with Norvir (100 mg twice daily) was approved by the FDA in December 2003 for this purpose. As an alternative, people can take Fortovase either with or without low-dose Norvir. Invirase, combined with Norvir, is just as effective as Fortovase combined with Norvir.

## What is known about Invirase?

- The recommended dose of Invirase with Norvir® (ritonavir) is five 200mg Invirase capsules, plus one 100mg Norvir capsule, every 12 hours (twice a day).
- The manufacturer of Invirase is currently developing a 500mg tablet version of the drug that will be taken with a low dose of Norvir. This will reduce the number of pills that need to be taken on a daily basis (two 500mg tablets of Invirase plus one 100mg capsule of Norvir, taken together twice a day). The 500mg tablet version of Invirase is expected to be approved in early 2004. The manufacturer is also looking at the possibility of only having to take Invirase once a day. This would involve taking eight 200mg Invirase capsules plus two 100mg Norvir capsules, every 24 hours. However, until this once-daily dose has been studied and approved by the U.S. Food and Drug Administration, it should be considered highly experimental.
- Invirase should be taken with food, preferably a full nutritious meal (e.g., breakfast and dinner). Taking Invirase with food increases the amount of drug in the bloodstream, which makes Invirase more effective against the virus.

- Invirase is not yet recommended for HIV-positive children.
- Clinical trials have determined that Invirase, combined with Norvir, is safe and effective when combined with other drugs, most notably two nucleoside reverse transcriptase inhibitors (NRTIs).
- For HIV-positive adults beginning anti-HIV drug therapy for the first time, Invirase combined with Norvir is listed as an “alternative” protease inhibitor option by the United States Department of Health and Human Services in its treatment guidelines. Invirase, without Norvir, is not recommended. The protease inhibitor Kaletra® (lopinavir/ritonavir) is listed as the “preferred” option.
- If your viral load becomes detectable while taking a drug regimen that contains Invirase, 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 Invirase. Similarly, if you take an anti-HIV drug regimen that contains Invirase 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?

- Invirase is broken down (metabolized) by the liver, like many medications used to treat HIV and AIDS. This means that Invirase can interact with other medications. Invirase can lower or raise the levels of other medications in the body. Similarly, other medications can lower or raise the levels of Invirase 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 Invirase:
  - Acid reflux/heartburn medications:** Propulsid® (cisapride)
  - Antibiotics:** Priftin® (rifapentine), Rifadin® (rifampin), and Mycobutin® (rifabutin)
  - Antimigraine medications:** Ergostat®, Cafergot®, Ercaf®, Wigraine® (ergotamine) or D.H.E. 45® (dihydroergotamine)
  - Antihistamines:** Hismanal® (astemizole) or Seldane® (terfenadine)
  - 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 decrease the amount of Invirase in the bloodstream. It might be necessary to increase your dose of Invirase if you are taking any of these drugs.
- Anti-HIV protease inhibitors can interact with invirase. Crixivan® (indinavir), Norvir® (ritonavir), Kaletra® (lopinavir/ritonavir), Viracept® (nelfinavir), Reyataz™ (atazanavir), and Agenerase® and Lexiva® (amprenavir/fosamprenavir)—six protease inhibitors—can increase Invirase levels in the bloodstream. Viracept can also increase Invirase levels in the bloodstream. If Invirase is combined with Norvir, the dose should be five 200mg Invirase capsules plus one 100mg Norvir capsule twice a day. If Invirase is combined with Viracept, the dose should be six 200 mg Invirase capsules plus the usual Viracept dose. If Invirase is combined with Kaletra, the dose should be five 200mg Invirase capsules plus the usual Kaletra dose. No dosing has

- been recommended for Invirase plus either Crixivan, Reyataz, Agenerase, or Lexiva.
- Anti-HIV non-nucleoside reverse transcriptase inhibitors (NNRTIs) can also interact with Invirase. Sustiva® (efavirenz) and Viramune® (nevirapine) can decrease the amount of Invirase in the bloodstream. If either of these NNRTIs are combined with Invirase, low-dose Norvir should also be used. A third NNRTI, Rescriptor® (delavirdine), significantly increases the amount of Invirase in the bloodstream. If Rescriptor is used, the Invirase dose should be reduced to four 200mg capsules three times daily.
  - Invirase can interact with some medications used to treat TB, MAC, and other bacterial infections. Rifadin® (rifampin) decreases Invirase levels in the bloodstream; these two drugs should not be used together. Mycobutin® (rifabutin) also decreases Invirase levels in the bloodstream (a dosing change is only necessary if Norvir is also being used in the combination). Invirase can increase Biaxin® (clarithromycin) levels and Biaxin can increase Invirase levels in the bloodstream (neither dose needs to be changed).
  - Invirase can interact with some medications used to treat thrush (candidiasis) and other fungal infections. Nizoral® (ketoconazole) can increase Invirase levels and Invirase can increase Nizoral levels in the bloodstream. A Nizoral dose change may only be necessary if you have excessive diarrhea, nausea, and abdominal discomfort
  - If Invirase is combined with Norvir, it can decrease the amount of methadone in the bloodstream, a drug commonly used to treat heroin addiction. It may be necessary to monitor blood levels of methadone and increase the dose, if needed.
  - It is not known what effect Invirase has on oral contraceptives/birth-control pills. To reduce the risk of pregnancy, barrier protection (e.g., condoms) should be used.
  - Cholesterol-lowering drugs, also known as “statins,” can interact with Invirase. There are two statins that should not be used with Invirase: Zocor® (simvastatin) and Mevacor® (lovastatin). Levels of these two drugs can become significantly increased in the bloodstream if they are combined with Invirase, which increases the risk of side effects. The two statins that are considered to be the safest in combination with Invirase are Pravachol® (pravastatin) and Lescol® (fluvastatin). It is also possible to take Invirase with Lipitor® (atorvastatin), although Invirase can increase Lipitor levels 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 Invirase or the other protease inhibitors.
  - Viagra® (sildenafil), Levitra® (vardenafil) and Cialis® (tadalafil) levels in the bloodstream likely increase when combined with Invirase. 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 Invirase. St. John’s wort should not be used with Invirase, since it can greatly reduce the amount of Invirase in the bloodstream. HIV-positive people should also be cautious about using garlic supplements or milk thistle with Invirase—test tube studies suggest that both herbal products can interact with the same liver enzyme system (cytochrome P450 3A4) responsible for metabolizing Invirase. This may alter the amount of Invirase in the bloodstream. These and other herbal products should be used with caution, until further studies are conducted.
  - A number of other negative drug interactions are possible if Invirase is combined with Norvir.



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

### What about side effects?

- Short-term side effects include appetite loss, headaches, feeling crummy (malaise), diarrhea, nausea, and vomiting. Very often, these side effects improve within a few months/weeks of starting Invirase.
- Anti-HIV drug regimens containing protease inhibitors, including Invirase, can cause increased fat levels (cholesterol and triglycerides) in the blood, 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), and diabetes.

### Who should not take Invirase?

- Before taking this medication, tell your doctor if you have kidney disease or liver disease. You may not be able to take Invirase, or you may require a dosage adjustment or special monitoring during treatment if you have any of these conditions.
- Invirase is classified by the FDA as a pregnancy category B 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 Invirase passes into breast milk and what effects it may have on a nursing baby. However, to prevent HIV transmission of the virus to uninfected babies, it is recommended that HIV-positive mothers not breast-feed.

### Where can I learn more about clinical trials that are using Invirase?

- If you would like to find out if you are eligible for any clinical trials that include Invirase, 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

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