

Patients should be informed that redistribution or accumulation of body fat may occur in patients receiving protease inhibitors and that the cause and long-term health effects of these conditions are not known at this time.

17.4 Dosing Instructions

Patients should be advised that **INVIRASE must be used in combination with ritonavir, which significantly inhibits saquinavir's metabolism to provide increased plasma saquinavir levels.**

Patients should be advised that INVIRASE administered with ritonavir should be taken within 2 hours after a full meal [see *Clinical Pharmacology (12.3)*]. When INVIRASE is taken without food, concentrations of saquinavir in the blood are substantially reduced and may result in no antiviral activity. Patients should be advised of the importance of taking their medication every day, as prescribed, to achieve maximum benefit. Patients should not alter the dose or discontinue therapy without consulting their physician. If a dose is missed, patients should take the next dose as soon as possible. However, the patient should not double the next dose.

FDA-approved Medication Guide

Medication Guide

INVIRASE[®] (in-ver-ase)

(saquinavir mesylate)

Capsules and Tablets

Read this Medication Guide before you start taking INVIRASE and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or treatment. You and your healthcare provider should talk about your treatment with INVIRASE before you start taking it and at regular checkups. You should stay under a healthcare provider's care when taking INVIRASE.

Also read the Medication Guide for ritonavir (Norvir).

What is the most important information I should know about INVIRASE?

- **INVIRASE must be taken along with NORVIR[®] (ritonavir).**

INVIRASE may cause serious side effects including:

- **Interactions with other medicines.** It is important to know the medicines that should not be taken with INVIRASE. Read the section "What should I tell my healthcare provider before taking INVIRASE?"
- **Changes in your heart rhythm and the electrical activity of your heart.** These changes may be seen on an EKG (electrocardiogram) and can lead to serious heart problems. Your risk for these problems may be higher if you:
 - already have a history of abnormal heart rhythm, including Congenital Long QT Syndrome, or other types of heart disease.
 - take other medicines that can affect your heart rhythm while you take INVIRASE.

Tell your healthcare provider right away if you have any of these symptoms while taking INVIRASE:

- dizziness
- lightheadedness
- fainting
- sensation of abnormal heartbeats

See the section below "What are the possible side effects of INVIRASE?" for more information about serious side effects.

What is INVIRASE?

INVIRASE is a prescription anti-HIV medicine used in people 16 years and older. INVIRASE belongs to a class of anti-HIV medicines called protease inhibitors. INVIRASE is used with ritonavir and other anti-HIV medicines to treat people with human immunodeficiency virus (HIV-1) infection. HIV-1 is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

It is not known if INVIRASE is safe and effective in children younger than 16 years old.

Who should not take INVIRASE?

Do not take INVIRASE if:

- you are taking certain medicines. For more information about medicines you should not take with INVIRASE, please see **“What should I tell my healthcare provider before taking INVIRASE?” and talk with your healthcare provider about all other medicines you take.**
- your healthcare provider has told you that you have a condition called Congenital Long QT Syndrome.
- your healthcare provider has told you that you have complete AV (atrioventricular) block and you do not have a pacemaker or you are at risk for complete AV block.
- your healthcare provider has told you that you have low potassium or low magnesium in your blood.
- you have severe liver problems.
- you have had a severe allergic reaction to INVIRASE or any of the ingredients in INVIRASE.

What should I tell my healthcare provider before taking INVIRASE?

INVIRASE may not be right for you. Before you take INVIRASE, tell your healthcare provider if you:

- have any heart problems, including a condition called Congenital Long QT Syndrome.
- have diabetes.
- have liver problems, including Hepatitis B or Hepatitis C.
- have hemophilia. People who take INVIRASE may have increased bleeding.
- are pregnant or plan to become pregnant. It is not known if INVIRASE will harm your unborn baby. **Antiretroviral Pregnancy Registry.** If you take INVIRASE during pregnancy, talk with your healthcare provider about how you can take part in an antiretroviral pregnancy registry. The purpose of the pregnancy registry is to collect information about the health of you and your baby.
- are breastfeeding or plan to breastfeed. It is not known if INVIRASE passes into your breast milk. You should not breastfeed if you are taking INVIRASE. If you are a woman who has or will have a baby while taking INVIRASE, talk with your healthcare provider about the best way to feed your baby. The Centers for Disease Control and Prevention (CDC) recommends that HIV-infected mothers not breastfeed to avoid the risk of passing HIV infection to your baby.

Tell your healthcare provider about all the medicines you take, including prescriptions and non-prescriptions medicines, vitamins and herbal supplements. INVIRASE and other medicines may affect each other causing side effects. Do not start taking a new medicine without talking with your healthcare provider or pharmacist. Your healthcare provider can tell you if it is safe to take INVIRASE with other medicines.

Taking INVIRASE with certain other medicines can cause serious problems or life threatening reactions.

Medicines you should not take with INVIRASE and NORVIR include:

- alfuzosin (UROXATRAL[®])
- amiodarone (CORDARONE[®], PACERONE[®])

- dofetilide (TIKOSYN[®])
- flecainide (TAMBOCOR[®])
- lidocaine
- propafenone (RHYTHMOL[®])
- quinidine
- trazodone (OLEPTRO[®])
- rifampin (RIFADIN[®], RIFAMATE[®], RIFATER[®], RIMACTANE[®])
- Ergot containing medicines, including:
 - dihydroergotamine mesylate (D.H.E 45, EMBOLEX, MIGRANAL)
 - ergonovine, ergonovine and methylergonovine (Ergostrate, Methergine), ergotamine and methylergonovine
 - ergotamine tartrate (CAFERGOT, MIGERGOT, ERGOMAR, ERGOSTATE, MEDIHALER ERGOTAMINE, WIGRAINE, WIGRETTES)
- lovastatin (ADVICOR[®], ALTOPREV[®], MEVACOR[®])
- simvastatin (SIMCOR[®], VYTORIN[®], ZOCOR[®])
- pimozide (ORAP[®])
- sildenafil (REVATIO[®])
- triazolam (HALCION[®])
- midazolam hydrochloride oral syrup

The following medicines may increase blood levels and side effects of INVIRASE when taken with INVIRASE and NORVIR:

- delavirdine (RESCRIPTOR[®])
- atazanavir (REYATAZ[®])
- omeprazole (PRILOSEC[®])
- clarithromycin (BIAXIN[®])
- indinavir (CRIXIVAN[®])

INVIRASE and NORVIR may not work as well when taken together with the following medicines, herbal products, or dietary supplements:

- efavirenz (SUSTIVA[®])
- nevirapine (VIRAMUNE[®])
- tipranavir and ritonavir (APTIVUS[®], NORVIR[®] used for HIV infection)
- Anticonvulsants such as carbamazepine (CARBATROL[®], TEGRETOL[®]), phenobarbital, and phenytoin (DILANTIN[®])
- dexamethasone
- Garlic capsules, an herbal product sold as a dietary supplement
- the herbal supplement St. John's wort (*Hypericum perforatum*) or products containing St. John's wort

Your healthcare provider may need to monitor your therapy more closely if you take INVIRASE and NORVIR with the following medicines:

- medicines for erectile problems, such as tadalafil (CIALIS[®]), vardenafil (LEVITRA[®]), or sildenafil citrate (VIAGRA[®])
- a blood thinner medicine such as warfarin (COUMADIN[®], JANTOVEN[®])
- Antidepressants such as trazodone (DESYREL[®]), (amitriptyline (ELAVIL[®]), or imipramine (TORFRANIL[®])
- Benzodiazepines used as sedatives or sleeping pills such as alprazolam (XANAX[®]), clorazepate (TRANXENE[®]), diazepam (VALIUM[®]), and flurazepam (DALMANE[®])
- atorvastatin (LIPITOR[®]) and rosuvastatin (CRESTOR[®]) used for lowering cholesterol
- Calcium channel blockers used for treatment of high blood pressure or heart disease, such as diltiazem (CARDIZEM[®], CARTIA XT[®], DILACOR XR[®], DILTZAC[®], TAZTIA XT[®], TIAZAC[®]), felodipine (PLENDIL[®]), nifedipine (PROCARDIA[®]), nicardipine (CARDENE[®]), nimodipine (NIMOTOP[®]), verapamil-containing medications (such as CALAN[®], VERELAN[®]), amlodipine-containing medications (such as CADUET[®], NORVASC[®]), nisoldipine (SULAR[®]), and isradipine (DYNACIRC[®])
- ketoconazole (NIZORAL[®]) and itraconazole (SPORANOX[®]) used to treat fungal infections
- Medicines to prevent organ transplant rejection: cyclosporine SANDIMMUNE[®]), cyclosporine (NEORAL[®]), sirolimus (RAPAMUNE[®]), or tacrolimus (PROGRAF[®])
- fluticasone propionate (FLONASE[®], FLOVENT[®], ADVAIR[®]), given by nose or inhaled to treat allergic symptoms or asthma
- digoxin (LANOXIN[®]) used to treat of heart rhythm problems or other heart conditions
- bosentan (TRACLEER[®]) and tadalafil (ADCIRCA[®]) used to treat pulmonary arterial hypertension
- medicines for gout, such as colchicine (COLCRYS[®])
- Oral contraceptives containing ethinyl estradiol used for preventing pregnancy
- Methadone
- rifabutin (MYCOBUTIN[®])

If you are not sure if you take a medicine above, ask your healthcare provider or pharmacist.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take INVIRASE?

- Take INVIRASE exactly as your healthcare provider tells you.
- INVIRASE comes as a 500 mg tablet or a 200 mg capsule.
- Do not change your dose of INVIRASE or stop treatment without first talking with your healthcare provider.
- INVIRASE must be used along with ritonavir (Norvir).
- Take INVIRASE with meals or up to 2 hours after a meal.
- Do not miss a dose of INVIRASE. It is very important to take your medicine every day. If you skip doses or take less than the prescribed dose the medicine will not work as well, and the virus may become harder to treat.
- If you miss a dose of INVIRASE, you should take the next dose as soon as possible. Do not double your dose.
- If you take more than your prescribed dose of INVIRASE, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of INVIRASE?

INVIRASE can cause serious side effects.

- See “**What is the most important information I should know about INVIRASE?**”

Diabetes and high blood sugar. Some people who take protease inhibitors get new or more serious diabetes, or high blood sugar. Tell your healthcare provider if you notice an increase in thirst or urinate more often than normal while taking INVIRASE.

- **Liver problems.** People with liver problems such as Hepatitis B or C, cirrhosis or have a history of alcoholism may have worsening liver problems.

Tell your healthcare provider right away if you have any of these signs and symptoms of liver problems:

- loss of appetite
- yellowing of your skin or whites of your eyes (jaundice)
- dark-colored urine
- pale colored stools
- itchy skin
- stomach area (abdominal) pain
- **Increased bleeding in people with hemophilia.** Some people with hemophilia have increased bleeding with protease inhibitors including INVIRASE.
- **Increase in certain fat (cholesterol and triglycerides) levels in your blood.** Your healthcare provider will check your blood for high levels of cholesterol and triglycerides before you start INVIRASE and during treatment with INVIRASE.
- **Changes in body fat.** Changes in body fat have been seen in some people who take anti-HIV medications. These changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breasts, and around the trunk. Loss of fat from the legs, arms and face may also happen. The cause and long-term health effects of these conditions are not known at this time.
- **Immune System Changes (Immune Reconstitution Syndrome).** Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider if you start having new or worse symptoms of infection after you start taking INVIRASE.

The most common side effects of INVIRASE include:

- nausea
- vomiting
- diarrhea
- stomach area (abdominal) pain
- tiredness
- pneumonia

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of INVIRASE. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

You may also report side effects to Genentech at 1-800-835-2555.

How should I store INVIRASE?

- Store INVIRASE at room temperature between 59°F to 86°F (15°C to 30°C).

- Keep INVIRASE in a tightly closed container.

Keep INVIRASE and all medicine out of the reach of children.

General information about INVIRASE.

INVIRASE does not cure HIV, and it does not prevent you from getting other illness from advanced HIV infections. INVIRASE does not stop you from passing HIV infections to others. Do not share needles, or personal items that can have blood or body fluids on them, like toothbrushes and razor blades. Always practice safer sex by using condoms to lower the chance of sexual contact with semen, vaginal secretions, or blood.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use INVIRASE for a condition for which it was not prescribed. Do not give INVIRASE to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about INVIRASE. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about INVIRASE that is written for health professionals.

For more information, go to <http://www.gene.com/gene/products/information/invirase> or call 1-877-436-3683 (1-877-Genentech).

What are the ingredients in INVIRASE?

Active ingredient: saquinavir mesylate

Inactive ingredients:

200 mg Capsule: lactose, microcrystalline cellulose, povidone K30, sodium starch glycolate, talc, and magnesium stearate.

Capsule shell: gelatin and water with the following dye systems: red iron oxide, yellow iron oxide, black iron oxide, FD&C Blue #2, and titanium dioxide.

500 mg Tablet: lactose, microcrystalline cellulose, povidone K30, croscarmellose sodium, and magnesium stearate.

Film coat: hypromellose, titanium dioxide, talc, iron oxide yellow, iron oxide red, and triacetin.

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