

17.5 FDA-Approved Patient Labeling

PREZISTA® (darunavir) Tablets

Patient Information about

PREZISTA (pre-ZIS-ta)

for HIV (Human Immunodeficiency Virus) Infection

Generic name: darunavir (da-ROO-nuh-veer)

ALERT: Find out about medicines that should NOT be taken with PREZISTA. Please also read the section “Who should not take PREZISTA?”.

Please read this information before you start taking PREZISTA. Also, read the leaflet each time you renew your prescription, just in case anything has changed. Remember, this leaflet does not take the place of careful discussions with your doctor. You and your doctor should discuss your treatment with PREZISTA prior to the first time you take your medicine and at regular checkups. You should remain under a doctor’s care when using PREZISTA and should not change or stop treatment without first talking with a doctor.

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT PREZISTA?

PREZISTA, together with NORVIR® (ritonavir), has rarely been observed to cause liver problems which may be life-threatening. It was not always clear if PREZISTA caused these liver problems because some patients had other illnesses or were taking other medicines. Your healthcare professional should do blood tests prior to initiating combination treatment including PREZISTA. If you have chronic hepatitis B or C infection, your healthcare professional should check your blood tests more often because you have an increased chance of developing liver problems. Please also read the section “What are the possible side effects of PREZISTA?”.

Rarely, PREZISTA has been reported to cause a severe or life-threatening rash. Contact your healthcare provider if you develop a rash. Your healthcare provider will advise you whether your symptoms can be managed on therapy or whether PREZISTA should be stopped.

WHAT IS PREZISTA?

PREZISTA is an oral tablet used for the treatment of HIV (Human Immunodeficiency Virus) infection in adults. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome). PREZISTA is a type of anti-HIV medicine called a protease (PRO-tee-ase) inhibitor.

HOW DOES PREZISTA WORK?

PREZISTA blocks HIV protease, an enzyme which is needed for HIV to multiply. When used with other anti-HIV medicines, PREZISTA can help to reduce the amount of HIV in your blood (called “viral load”) and increase your CD4 (T) cell count. HIV infection destroys CD4 (T) cells, which are important to the immune system. The immune system helps fight infection. Reducing the amount of HIV and increasing the CD4 (T) cell count may improve your immune system and, thus, reduce the risk of death or infections that can happen when your immune system is weak (opportunistic infections).

PREZISTA is always taken with and at the same time as 100 mg of ritonavir (NORVIR®), in combination with other anti-HIV medicines. PREZISTA should also be taken with food.

DOES PREZISTA CURE HIV OR AIDS?

PREZISTA does **not** cure HIV infection or AIDS. At present, there is no cure for HIV infection. People taking PREZISTA may still develop infections or other conditions associated with HIV infection. Because of this, it is very important for you to remain under the care of a doctor. Although PREZISTA is not a cure for HIV or AIDS, PREZISTA can help reduce your risks of getting illnesses associated with HIV infection (AIDS and opportunistic infection) and eventually dying from these conditions.

DOES PREZISTA REDUCE THE RISK OF PASSING HIV TO OTHERS?

PREZISTA does **not** reduce the risk of passing HIV to others through sexual contact, sharing needles, or being exposed to your blood. For your health and the health of others, it is important to always practice safer sex by using a latex or polyurethane condom or other barrier method to lower the chance of sexual contact with any body fluids such as semen, vaginal secretions, or blood. Never re-use or share needles.

Ask your doctor if you have any questions on how to prevent passing HIV to other people.

WHAT SHOULD I TELL MY DOCTOR BEFORE I TAKE PREZISTA?

Tell your doctor about all of your medical conditions, including if you:

- are allergic to sulfa medicines.
- have diabetes. In general, anti-HIV medicines, such as PREZISTA, might increase sugar levels in the blood.
- have liver problems, including hepatitis B and/or C.
- have hemophilia. Anti-HIV medicines, such as PREZISTA, might increase the risk of bleeding.
- are pregnant or planning to become pregnant. The effects of PREZISTA on pregnant women or their unborn babies are not known. You and your doctor will need to decide if taking PREZISTA is right for you. If you take PREZISTA while you are pregnant, talk to your doctor about how you can be included in the Antiretroviral Pregnancy Registry.
- are breastfeeding. Do not breastfeed if you are taking PREZISTA. You should not breastfeed if you have HIV because of the chance of passing HIV to your baby. Talk with your doctor about the best way to feed your baby.

WHO SHOULD NOT TAKE PREZISTA?***

Together with your doctor, you need to decide whether taking PREZISTA is right for you.

Do not take PREZISTA if you:

- are allergic to darunavir or any of the other ingredients in PREZISTA
- are allergic to ritonavir (NORVIR®)
- take any of the following types of medicines because you could experience serious side effects:

<u>Type of Drug</u>	<u>Examples of Generic Names (Brand Names)</u>
Ergot Derivatives (to treat migraine and headaches)	dihydroergotamine (D.H.E. 45®, Migranal®) ergonovine ergotamine (Cafergot®, Ergomar®) methylergonovine
Gastrointestinal Motility Agent (to treat some digestive conditions)	cisapride

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PREZISTA[®] (darunavir) Tablets

Neuroleptic (to treat psychiatric conditions)	pimozide (Orap [®])
Sedative/hypnotics (to treat trouble with sleeping and/or anxiety)	oral midazolam triazolam (Halcion [®])
Herbal Product	St. John's wort (<i>Hypericum perforatum</i>)
HMG-CoA Reductase Inhibitors (also known as statins) (to lower cholesterol levels)	lovastatin (Mevacor [®] , Altoprev [®] , Advicor [®]) simvastatin (Zocor [®] , Simcor [®] , Vytorin [®])
Antimycobacterial (to treat tuberculosis or <i>Mycobacterium avium</i> complex)	rifampin (Rifadin [®] , Rifater [®] , Rifamate [®] , Rimactane [®])

CAN PREZISTA BE TAKEN WITH OTHER MEDICATIONS? **

Tell your doctor about all the medicines you take including prescription and nonprescription medicines, vitamins, and herbal supplements. PREZISTA and many other medicines can interact. Sometimes serious side effects will happen if PREZISTA is taken with certain other medicines (see "Who should not take PREZISTA?").

Tell your doctor if you are taking estrogen-based contraceptives (birth control). PREZISTA might reduce the effectiveness of estrogen-based contraceptives. You must take additional precautions for birth control such as a condom.

Tell your doctor if you take other anti-HIV medicines. PREZISTA can be combined with some other anti-HIV medicines while other combinations are not recommended.

Tell your doctor if you are taking any of the following medicines:

<u>Type of Drug</u>	<u>Examples of Generic Names (Brand Names)</u>
Antiarrhythmics (to treat abnormal heart rhythms)	bepiridil lidocaine (Lidoderm [®]) quinidine amiodarone (Cordarone [®]) digoxin (Lanoxin [®]) flecainide (Tambocor [®]) propafenone (Rythmol [®])
Anticoagulants (to treat and prevent blood clots)	warfarin (Coumadin [®])
Anticonvulsants (to treat epilepsy and prevent seizures)	carbamazepine (Tegretol [®] , Carbatrol [®]) phenobarbital phenytoin (Dilantin [®] , Phenytek [®])
Antidepressants (to treat depression)	trazodone (Desyrel [®]) desipramine (Norpramin [®])
Anti-infectives (to treat bacterial infections)	clarithromycin (Biaxin [®])

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PREZISTA[®] (darunavir) Tablets

Type of Drug

Antifungals
(to treat fungal infections)

Antimycobacterials
(to treat tuberculosis or *Mycobacterium avium* complex)

β -Blockers
(to treat high blood pressure, heart attack, or heart failure or to lower pressure in the eye)

Benzodiazepines
(to treat anxiety and/or trouble with sleeping)

Calcium Channel Blockers
(to treat heart disease)

Corticosteroids
(to treat inflammation or asthma)

HMG-CoA Reductase Inhibitors (also known as statins)
(to lower cholesterol levels)

Immunosuppressants
(to prevent organ transplant rejection)

Narcotic Analgesics
(to treat narcotic withdrawal and dependence)

Neuroleptics
(to treat schizophrenia or bipolar disorder)

PDE-5 Inhibitors
(to treat erectile dysfunction)

Selective Serotonin Reuptake Inhibitors (SSRIs)
(to treat depression, anxiety, or panic disorder)

Examples of Generic Names (Brand Names)

ketoconazole (Nizoral[®])
itraconazole (Sporanox[®])
voriconazole (Vfend[®])

rifabutin (Mycobutin[®])

metoprolol (Lopressor[®], Toprol-XL[®])
timolol (Betimol[®], Combigan[®], Istalol[®], Cosopt[®], Timoptic[®])

midazolam administered by injection

felodipine (Plendil[®])
nifedipine (Adalat[®])
nicardipine (Cardene[®])

dexamethasone
fluticasone propionate (Advair Diskus[®], Cutivate[®], Flonase[®], Flovent Diskus[®])

atorvastatin (Lipitor[®])
pravastatin (Pravachol[®])
rosuvastatin (Crestor[®])

cyclosporine (Sandimmune[®], Neoral[®])
tacrolimus (Prograf[®])
sirolimus (Rapamune[®])

methadone

risperidone (Risperdal[®], Risperdal[®] Consta[®], Risperdal[®] M-TAB[®])
thioridazine

sildenafil (Viagra[®])
vardenafil (Levitra[®])
tadalafil (Cialis[®])

paroxetine (Paxil[®])
sertraline (Zoloft[®])

Tell your doctor if you are taking any medicines that you obtained without a prescription.

This is **not** a complete list of medicines that you should tell your doctor that you are taking. Know and keep track of all the medicines you take and have a list of them with you. Show this list to all of your doctors and pharmacists any time you get a new medicine. Both your doctor and your pharmacist can tell you if you can take these other medicines with PREZISTA. Do not start any new medicines while you are taking PREZISTA without first talking with your doctor or pharmacist. You can ask your doctor or pharmacist for a list of medicines that can interact with PREZISTA.

HOW SHOULD I TAKE PREZISTA?

Take PREZISTA tablets every day exactly as prescribed by your doctor. You must take ritonavir (NORVIR®) at the same time as PREZISTA.

- For adults who have never taken anti-HIV medicines, the usual dose is 800 mg (two 400 mg tablets) of PREZISTA, together with 100 mg (one 100 mg capsule) of ritonavir (NORVIR®), once daily *every day*.
- For adults who have taken anti-HIV medicines in the past, the usual dose is 600 mg (one 600 mg tablet or two 300 mg tablets) of PREZISTA, together with 100 mg (one 100 mg capsule) of ritonavir (NORVIR®), twice daily *every day*.

PREZISTA and ritonavir (NORVIR®) should be taken together at the same time every day. If you have questions about when to take PREZISTA and ritonavir (NORVIR®), your doctor can help you decide which schedule works for you.

Take PREZISTA and ritonavir (NORVIR®) **with food**. The type of food is not important. Swallow the whole tablets with a drink such as water or milk. Do not chew the tablets.

Continue taking PREZISTA and ritonavir (NORVIR®) unless your doctor tells you to stop. Take the exact amount of PREZISTA and ritonavir (NORVIR®) that your doctor tells you to take, right from the very start. To help make sure you will benefit from PREZISTA and ritonavir (NORVIR®), you must not skip doses or interrupt therapy. If you don't take PREZISTA and ritonavir (NORVIR®) as prescribed, the beneficial effects of PREZISTA and ritonavir (NORVIR®) may be reduced or even lost.

Patients taking 800 mg of PREZISTA once daily

If you miss a dose of PREZISTA (two 400 mg tablets) or ritonavir (NORVIR®) by more than 12 hours, wait and then take the next dose of PREZISTA (two 400 mg tablets) and ritonavir (NORVIR®) at the regularly scheduled time. If you miss a dose of PREZISTA (two 400 mg tablets) or ritonavir (NORVIR®) by less than 12 hours, take your missed dose of PREZISTA (two 400 mg tablets) and ritonavir (NORVIR®) immediately. Then take your next dose of PREZISTA (two 400 mg tablets) and ritonavir (NORVIR®) at the regularly scheduled time.

Patients taking 600 mg of PREZISTA twice daily

If you miss a dose of PREZISTA (one 600 mg tablet or two 300 mg tablets) or ritonavir (NORVIR®) by more than 6 hours, wait and then take the next dose of PREZISTA (one 600 mg tablet or two 300 mg tablets) and ritonavir (NORVIR®) at the regularly scheduled time. If you miss a dose of PREZISTA (one 600 mg tablet or two 300 mg tablets) or ritonavir (NORVIR®) by less than 6 hours, take your missed dose of PREZISTA (one 600 mg tablet or two 300 mg tablets) and ritonavir (NORVIR®) immediately. Then take your next dose of PREZISTA (one 600 mg tablet or two 300 mg tablets) and ritonavir (NORVIR®) at the regularly scheduled time.

You should always take PREZISTA and ritonavir (NORVIR®) together with food.

If a dose of PREZISTA or ritonavir (NORVIR®) is skipped, do not double the next dose. Do not take more or less than your prescribed dose of PREZISTA or ritonavir (NORVIR®) at any one time.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF PREZISTA?

Like all prescription drugs, PREZISTA can cause side effects. The following is **not** a complete list of side effects reported with PREZISTA when taken either alone or with other anti-HIV medicines. Do not rely on this leaflet alone for information about side effects. Your doctor can discuss with you a more complete list of side effects.

PREZISTA, together with NORVIR® (ritonavir), has rarely been observed to cause liver problems which may be life-threatening. It was not always clear if PREZISTA caused these liver problems because some patients had other illnesses or were taking other medicines. Your healthcare professional should do blood tests prior to initiating combination treatment including PREZISTA. If you have chronic hepatitis B or C infection, your healthcare professional should check your blood tests more often because you have an increased chance of developing liver problems.

Talk to your healthcare professional about the signs and symptoms of liver problems. These may include yellowing of your skin or whites of your eyes, dark (tea colored) urine, pale colored stools (bowel movements), nausea, vomiting, loss of appetite, or pain, aching or sensitivity on your right side below your ribs.

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Rash has been reported in 10.3% of subjects receiving PREZISTA. In some patients, PREZISTA has been reported to cause a severe or life-threatening rash. Contact your healthcare provider if you develop a rash. Your healthcare provider will advise you whether your symptoms can be managed on therapy or whether PREZISTA should be stopped.

Other relevant severe side effects reported at an uncommon or rare frequency were inflammation of the liver or pancreas, increased blood fat levels, diabetes, and changes in body fat.

Some side effects are typical for anti-HIV medicines in the same family as PREZISTA. These are:

- high blood sugar (hyperglycemia) and diabetes. This can happen in patients taking PREZISTA or other protease inhibitor medicines. Some patients have diabetes before starting treatment with PREZISTA which gets worse. Some patients get diabetes during treatment with PREZISTA. Some patients will need changes in their diabetes medicine. Some patients may need new diabetes medicine.
- increased bleeding in patients with hemophilia.
- changes in body fat. These changes can happen in patients taking anti-HIV medicines, including PREZISTA. The changes may include an increased amount of fat in the upper back and neck, breast, and around the back, chest, and stomach area. Loss of fat from the legs, arms, and face may also happen. The exact cause and long-term health effects of these conditions are not known.
- immune reconstitution syndrome. In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection, signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment, including PREZISTA, is started. It is believed that these symptoms are due to an improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms.

The most common side effects include diarrhea, nausea, headache, and abdominal pain.

Tell your doctor promptly about these or any other unusual symptoms. If the condition persists or worsens, seek medical attention.

WHAT DO PREZISTA TABLETS LOOK LIKE?

PREZISTA 300 mg tablets are orange, oval-shaped, film-coated tablets mentioning “300” on one side and “TMC114” on the other side.

PREZISTA 400 mg tablets are light orange, oval-shaped, film-coated tablets mentioning “400” on one side and “TMC” on the other side.

PREZISTA 600 mg tablets are orange, oval-shaped, film-coated tablets mentioning “600” on one side and “TMC” on the other side.

HOW SHOULD I STORE PREZISTA TABLETS?

Store PREZISTA tablets at room temperature (77°F (25°C)). Short-term exposure to higher or lower temperatures [from 59°F (15°C) to 86°F (30°C)] is acceptable. Ask your doctor or pharmacist if you have any questions about storing your tablets.

This medication is prescribed for your particular condition. Do not use it for any other condition or give it to anybody else. Keep PREZISTA and all of your medicines out of the reach of children. If you suspect that more than the prescribed dose of this medicine has been taken, contact your local poison control center or emergency room immediately.

This leaflet provides a summary of information about PREZISTA. If you have any questions or concerns about either PREZISTA or HIV, talk to your doctor.

For additional information, you may also call Tibotec Therapeutics at 1-877-REACH-TT or 1-877-732-2488.

PREZISTA[®] (darunavir) Tablets



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