

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PrPREZISTA®
darunavir tablets
darunavir oral suspension

Read this carefully before you start taking PREZISTA® and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about PREZISTA®.

What is PREZISTA® used for?

PREZISTA® is used:

- for the treatment of HIV (Human Immunodeficiency Virus) infection
- in adults
- in children 3 years of age and older who have taken anti-HIV medicines in the past
- always with a low dose (100 mg) of ritonavir (NORVIR®) and
- in combination with other anti-HIV medicines.

How does PREZISTA® work?

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. 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.

PREZISTA® does not cure HIV infection or AIDS. At present, there is no cure for HIV infection.

What are the ingredients in PREZISTA®?

Medicinal ingredients: darunavir (as darunavir ethanolate)

Non-medicinal ingredients (alphabetical):

Tablets: colloidal silicon dioxide, crospovidone, magnesium stearate, and microcrystalline cellulose. Hypromellose (800 mg tablet only).

The tablet film coatings contain:

- OPADRY® II White (polyethylene glycol, polyvinyl alcohol - partially hydrolyzed, talc, titanium dioxide) for the 75 and 150 mg tablets
- OPADRY® II Orange (polyethylene glycol, polyvinyl alcohol - partially hydrolyzed, sunset yellow FCF aluminum lake, talc, titanium dioxide) for the 600 mg tablets
- OPADRY® II Dark Red (iron oxide red, polyethylene glycol, polyvinyl alcohol - partially hydrolyzed, talc, titanium dioxide) for the 800 mg tablets

Oral Suspension: citric acid monohydrate, flavour (strawberry cream), hydroxypropyl cellulose,

masking flavour, microcrystalline cellulose and carmellose sodium, sodium methyl parahydroxybenzoate, sucralose.

PREZISTA® comes in the following dosage forms:

Tablets: 75 mg, 150 mg, 600 mg and 800 mg

Oral Suspension: 100 mg/mL

Do not use PREZISTA® if:

- you are allergic to darunavir or any of the other ingredients in PREZISTA® or components of the container
- you are allergic to ritonavir (NORVIR®)
- you have severe liver disease
- you 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> | <u>Type of Drug</u> | <u>Examples of Generic Names (Brand Names)</u> |
|---|--|--|---|
| Alpha1-Adrenoreceptor Antagonists (to treat enlarged prostate) | alfuzosin | Ergot Derivatives (to treat migraine and headaches) | dihydroergotamine (Migranal®) ergonovine ergotamine (Cafergot®) methylergonovine |
| Anti-coagulant (to prevent the clotting of red blood cells) | apixaban (Eliquis®) rivaroxaban (Xarelto®) | Gastrointestinal Motility Agents (to treat some digestive conditions) | cisapride ¹ |
| Antiarrhythmics (to treat abnormal heart rhythms) | bepidil ¹ dronedarone (Multaq®) lidocaine (when taken by injection) quinidine amiodarone (Cordarone®) | Herbal products (to improve mood) | St. John's Wort |
| Anti-gout (to treat gout and familial Mediterranean fever) if you have kidney or liver problems | colchicine | HMG-CoA Reductase Inhibitors also known as statins (to lower cholesterol) Other Lipid Modifying Agents cholesterol lowering drug | lovastatin (Mevacor®) simvastatin (Zocor®) lomitapide |
| Antihistamines (to treat allergy symptoms) | astemizole ¹ terfenadine ¹ | Neuroleptics (to treat psychiatric conditions) | lurasidone (Latuda®) pimozide (Orap®) |
| Antimycobacterials (to treat tuberculosis) | rifampin (Rifadin®, Rifater®) | PDE-5 Inhibitor (to treat pulmonary arterial hypertension) | sildenafil (Revatio®) |
| Antivirals (to treat hepatitis C infection) | elbasvir/grazoprevir (Zepatier®) | Sedatives/Hypnotics (to treat trouble with sleeping and/or anxiety) | midazolam (when taken by mouth) triazolam (Halcion®) |

¹Bepidil, astemizole, terfenadine and cisapride are not marketed in Canada.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take PREZISTA®. Talk about any health conditions or problems you may have, including if you:

- have diabetes. Anti-HIV medicines, such as PREZISTA®, might increase your blood sugar levels.
- have liver problems, including hepatitis B and/or C.
- have hemophilia. Anti-HIV medicines, such as PREZISTA®, might increase your risk of bleeding.
- are allergic to sulpha medications.
- have had pancreatitis in the past.
- have advanced HIV infection.
- are 65 years of age or older.

Other warnings you should know about:

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. Never use or share dirty needles.

People taking PREZISTA® may still develop infections or other illnesses associated with HIV infection. Because of this, it is very important for you to remain under the care of a doctor.

Pregnancy: Tell your doctor immediately if you are pregnant or planning to get pregnant. It is not known if PREZISTA® can harm your unborn baby. You must not take PREZISTA during pregnancy, unless your doctor believes the benefit is greater than the risk to your unborn baby. If you take PREZISTA® while you are pregnant, talk to your doctor about how you can be included in the Antiretroviral Pregnancy Registry.

Breast-feeding: Do not breast-feed if you are taking PREZISTA® because of the possibility of your baby becoming infected with HIV through your breast milk and because of the unknown effects of the medicine on your baby. Talk with your doctor about the best way to feed your baby.

PREZISTA® should not be used in children under 3 years of age. Talk to your doctor if your child has never taken an HIV medicine before.

PREZISTA® must always be used with low-dose ritonavir (NORVIR®). Your doctor will tell you how to take PREZISTA® and which medicines you can take with PREZISTA®. Tell your doctor if you take other anti-HIV medicines (e.g., rilpivirine). PREZISTA® can be combined with some other anti-HIV medicines while other combinations are not recommended.

PREZISTA® can interact with many other medicines. Sometimes serious side effects will happen if you take PREZISTA® with some other medicines (see **Do not use PREZISTA® if:**).

PREZISTA® should not be used with phenobarbital, phenytoin, rifapentine, rifampin or St. John's wort because PREZISTA® may not work as well if you take these medicines with it.

PREZISTA® should not be used with vardenafil, because you may be at increased risk of side effects of vardenafil such as low blood pressure, visual changes and penile erection lasting more than 4 hours.

Tell your doctor if you are taking estrogen-based contraceptives. PREZISTA® might reduce the effectiveness of estrogen-based contraceptives (birth control). Therefore, additional or alternative (non-hormonal) methods of contraception, such as a condom, are recommended.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with PREZISTA®:

| <u>Type of Drug</u> | <u>Examples of Generic Names (Brand Names)</u> | <u>Type of Drug</u> | <u>Examples of Generic Names (Brand Names)</u> |
|---|--|--|---|
| Antiarrhythmics (for the heart) | Digoxin disopyramide flecainide mexiletine propafenone | Endothelin receptor Antagonists (to treat pulmonary arterial hypertension) | bosentan (Tracleer®) |
| Anticancer Agents | dasatinib (Sprycel®) nilotinib (Tasigna®) vinblastine vincristine everolimus (Afinitor®) | HIV- CCR5 Antagonist (to treat HIV infection) | Maraviroc (Celsentri®) |
| Anticoagulants (to prevent the clotting of red blood cells) | apixaban (Eliquis®) dabigatran (Pradaxa®) rivaroxaban (Xarelto®) warfarin (Coumadin®) edoxaban (Lixiana®) | HIV- Integrase strand transfer Inhibitors (to treat HIV infection) | dolutegravir (Tivicay®) elvitegravir (Stribild®) |
| Anticonvulsants (to treat epilepsy and prevent seizures) | carbamazepine (Tegretol®) clonazepam phenobarbital phenytoin (Dilantin®) | HIV- Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) (to treat HIV infection) | delavirdine (Rescriptor®) |
| Antigout (to treat gout and familial Mediterranean fever) | colchicine | HIV- Protease Inhibitors (to treat HIV infection) | lopinavir/ritonavir (Kaletra®) saquinavir (Invirase®) indinavir (Crixivan®) |
| Anti-bacterials (to treat bacterial infections) | clarithromycin (Biaxin®) | HMG-CoA Reductase Inhibitors (to lower cholesterol levels) | atorvastatin (Lipitor®) pravastatin (Pravachol®) rosuvastatin (Crestor®) |
| Antidepressants (to treat depression, anxiety, or panic disorder) | amitriptyline desipramine imipramine nortriptyline paroxetine (Paxil®) sertraline (Zoloft®) trazodone (Oleptro®) | Immunosuppressants (to prevent organ transplant rejection) | cyclosporine (Sandimmune®, Neoral®) tacrolimus (Prograf®) sirolimus (Rapamune®) everolimus (Afinitor®) |
| Antifungals (to treat fungal infections) | ketoconazole (Nizoral®) itraconazole (Sporanox®) voriconazole (Vfend®) posaconazole (Posanol®) clotrimazole fluconazole | Inhaled beta agonist (to treat asthma) | salmeterol (Advair®) |
| Antimalarials (to treat malarial infections) | artemether/lumefantrine (Riamet® and Coartem®) Artemether/lumefantrine are not approved for use in Canada. | Narcotic Analgesics (to treat opioid dependence) | methadone meperidine buprenorphine/naloxone (Suboxone®) fentanyl oxycodone (Oxycontin®) tramadol |
| Contraceptives (to prevent pregnancy) | Norethindrone and drospirenone-containing | | |

| Type of Drug | Examples of Generic Names (Brand Names) | Type of Drug | Examples of Generic Names (Brand Names) |
|--|---|---|---|
| | estrogen-based contraceptives | | |
| Antimycobacterials (to treat bacterial infections) | rifabutin (Mycobutin®) rifampin (Rifadin®, Rifater®) rifapentine | Neuroleptics (to treat psychotic disorders) | risperidone (Risperdal®, Risperdal Consta®) thioridazine quetiapine (Seroquel®) perphenazine |
| Antivirals (to treat Hepatitis C infection) | glecaprevir/pibrentasvir (Maviret™) | PDE-5 Inhibitors (to treat erectile dysfunction) | sildenafil (Viagra®) vardenafil (Levitra®) tadalafil (Cialis®) |
| Beta-Blockers (to treat heart disease) | carvedilol metoprolol (Betaloc®, Lopresor®) timolol | Sedatives/Hypnotics (to treat trouble with sleeping and/or anxiety) | bupirone (Bustab®) clorazepate diazepam (Diazemuls®, Valium®) estazolam flurazepam (Dalmane®, Som-Pam®) zoldipem midazolam (taken by injection) |
| Calcium Channel Blockers (to treat heart disease) | amlodipine (Caduet®, Twynsta®) diltiazem (Cardizem®, Tiazac®) felodipine nifedipine (Adalat®) nicardipine verapamil (Isoptin®, Verelan®) | Platelet Aggregation Inhibitors (to prevent the clotting of platelets) | ticagrelor (Brilinta®) |
| Corticosteroids (to treat inflammation or asthma) | Betamethasone Budesonide (Pulmicort®, Rhinocort®, Symbicort®) dexamethasone fluticasone (Advair Diskus®, Cutivate®, Flonase®, Flovent Diskus®) mometasone prednisone (Winpred®) triamcinolone | | |

If you have also been prescribed enteric-coated didanosine as well as PREZISTA® and ritonavir, take didanosine 2 hours before or after the PREZISTA®/ritonavir combination.

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. Do not start any new medicines while you are taking PREZISTA® without first talking with your doctor or pharmacist.

How to take PREZISTA®:

- Your doctor will tell you how much PREZISTA® to take and when to take it.
- Always take PREZISTA® exactly as your doctor has told you for the medicine to work properly.
- Do not stop taking it, skip doses or interrupt the use of PREZISTA® unless your doctor tells you to.

- You must check with your doctor if you are not sure how to take it.
- You must take ritonavir (NORVIR®) at the same time as PREZISTA®.
- Always take PREZISTA® with food.
- Swallow PREZISTA® tablets whole with water.
- If you have trouble swallowing PREZISTA® tablets your doctor might prescribe PREZISTA® oral suspension to you.
- Your doctor will decide whether you should take PREZISTA® tablets or PREZISTA® oral suspension.
- Shake the PREZISTA® oral suspension well before use.
- Only use the oral dosing pipette (syringe) provided with PREZISTA® to accurately measure your dose. This should not be used for any other medicine.

Removing the child-resistant cap of the PREZISTA® oral suspension:



- Push the plastic screw cap down while turning it counter clockwise.
- Remove the unscrewed cap.

Usual dose:

Adults:

For adults who have never taken anti-HIV medicines the usual dose is 800 mg (one 800 mg tablet or 8 mL oral suspension) of PREZISTA®, together with 100 mg of ritonavir (NORVIR®), once every day.

For adults who have taken anti-HIV medicines in the past, the usual dose is either 800 mg (one 800 mg tablet or 8 mL oral suspension) of PREZISTA® together with 100 mg of ritonavir (NORVIR®), once every day **OR** 600 mg (one 600 mg tablet or 6 mL oral suspension) of PREZISTA® together with 100 mg ritonavir (NORVIR®), twice every day. Your doctor will tell you which dose is right for you.

Children:

- Your child's doctor will tell you how much PREZISTA® your child should take.
- The dose that they are given will be based on their weight.
- PREZISTA® is used in children who are 3 years or age and older and who weigh at least 22 lbs (10 kg).
- It is used in children who have taken anti-HIV medicines in the past.
- Your child's doctor will also tell you how much ritonavir (NORVIR®) your child should take along with PREZISTA®.
- If your child does not tolerate ritonavir (NORVIR®), talk to your doctor for advice.

Overdose:

If you think you have taken too much PREZISTA®, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

Patients taking 800 mg of PREZISTA® once a day:

If you miss a dose **by less than 12 hours**, take it as soon as you remember. Then, take your next dose of PREZISTA® and ritonavir (NORVIR®) at the regularly scheduled time.

If you miss a dose **by more than 12 hours**, wait until your next scheduled dose of PREZISTA® and ritonavir (NORVIR®) and take it then.

Never take a double dose to make up for a missed dose.

Patients taking 600 mg of PREZISTA® twice a day:

If you miss a dose **by less than 6 hours**, take it as soon as you remember. Then, take your next dose of PREZISTA® and ritonavir (NORVIR®) at the regularly scheduled time.

If you miss a dose **by more than 6 hours**, wait until your next scheduled dose of PREZISTA® and ritonavir (NORVIR®) and take it then.

Never take a double dose to make up for a missed dose.

What are possible side effects from using PREZISTA®?

These are not all the possible side effects you may feel when taking PREZISTA®. If you experience any side effects not listed here, contact your healthcare professional.

Rash has been reported in 10.3% of patients receiving PREZISTA®. Occasionally a rash can be severe or potentially life threatening. In patients taking PREZISTA® and raltegravir, rashes (generally mild or moderate) may occur more frequently than in patients taking either drug separately. **If you develop a severe rash (e.g. blisters, peeling skin) which may be accompanied with symptoms such as fever, fatigue, muscle aches and pain, and liver problems, stop use of PREZISTA® and contact your doctor right away.**

Liver problems that may occasionally be severe have been reported. Your doctor should do blood tests before you take PREZISTA® and while you are taking it. If you have chronic hepatitis B or C infection, your doctor should check your blood tests more often because you have an increased chance of developing liver problems.

Common side effects may include:

- diarrhea
- nausea and vomiting
- headache
- abdominal pain

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

- high blood sugar (hyperglycemia) and diabetes or worsening of diabetes. You may need to start or change your diabetes medicine.
- increased bleeding in patients with hemophilia.
- changes in body fat which 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.

- increases in triglycerides and cholesterol (forms of fat that are found in your blood). Your doctor may order blood testing for you.
- development of pancreatitis (inflammation of the pancreas) with symptoms such as abdominal pain, nausea and vomiting.
- changes in your immune system (Immune Reconstitution Inflammatory Syndrome). Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time, or you could develop an autoimmune disease in which your immune system reacts against your own body (e.g. Grave's disease (which affects the thyroid gland), Guillain-Barre syndrome (which affects the nervous system) or polymyositis (which affects the muscles). This may develop at any time, sometimes months after the start of HIV therapy. Sometimes symptoms can be severe, so if you develop high temperature (fever), joint or muscle pain, redness, rash, swelling, or fatigue or any new symptoms contact your doctor right away.

| Serious side effects and what to do about them | | | |
|---|--------------------------------------|--------------|---|
| Symptom / effect | Talk to your healthcare professional | | Stop taking drug and get immediate medical help |
| | Only if severe | In all cases | |
| UNCOMMON <u>Severe and potentially life-threatening rash</u> (blisters, peeling skin) which may be accompanied by fever, fatigue, swelling of the face or lymph nodes, muscle aches and pain, and liver problems. | | | ✓ |
| <u>Liver problems</u> : yellowing of the skin or whites of the eyes, dark (tea coloured) urine, pale coloured stools (bowel movements), nausea, vomiting, loss of appetite, or pain, aching, or sensitivity on right side below ribs. | | ✓ | |
| <u>Diabetes</u> or worsening of diabetes or high blood sugar: excessive thirst, excessive urination, excessive eating, unexplained weight loss, poor wound healing, infections. | | ✓ | |
| <u>Inflammation of the pancreas</u> : abdominal pain, nausea and vomiting. | | ✓ | |

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Keep out of sight and reach of children.

Store PREZISTA® oral suspension at room temperature between 15-30°C. Do not refrigerate or freeze. Avoid exposure to excessive heat. Store in the original container.

Store PREZISTA® tablets at room temperature between 15-30°C.

If you want more information about PREZISTA®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>); www.janssen.com/canada or by calling 1-800-567-3331 or 1-800-387-8781.

This information is also available on the Health Canada Drug and Health Product Register at: <https://hpr-rps.hres.ca>.

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