

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrPREZCOBIX®

Darunavir (as darunavir ethanolate) /cobicistat

Film-coated Tablets

Read this carefully before you start taking **PREZCOBIX®** 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 **PREZCOBIX®**.

What is PREZCOBIX® used for?

- PREZCOBIX® is used for the treatment of HIV (Human Immunodeficiency Virus) infection in adults. PREZCOBIX is used in combination with other antiretroviral medications. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).
- Ask your doctor if you have any questions on how to prevent passing HIV to other people.

How does PREZCOBIX® work?

PREZCOBIX® contains two prescription medicines, darunavir and cobicistat. Darunavir is a type of anti-HIV medicine called a protease (PRO-tee-ase) inhibitor. It blocks HIV protease, an enzyme needed for HIV to multiply. Darunavir needs to be combined with another medicine, cobicistat. Cobicistat increases the amount of darunavir in your blood to control your HIV infection.

When used with other anti-HIV medicines, PREZCOBIX® 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 (your body’s natural defences).

PREZCOBIX® is always taken in combination with other anti-HIV medicines. PREZCOBIX® should also be taken with food.

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

What are the ingredients in PREZCOBIX®?

Medicinal ingredients: darunavir ethanolate and cobicistat

Non-medicinal ingredients: The other ingredients are crospovidone, hypromellose, magnesium stearate, and silicified microcrystalline cellulose. The tablet film coating contains OPADRY® II Pink (polyethylene glycol, polyvinyl alcohol - partially hydrolyzed, talc, titanium dioxide, iron oxide red, iron oxide black).

PREZCOBIX® comes in the following dosage forms:

Film-coated tablets containing 800 mg darunavir (as darunavir ethanolate) and 150 mg cobicistat.

Do not use PREZCOBIX® if:

- you are allergic to PREZCOBIX or any of its ingredients, including non-medical ingredients or components of the container (see “**What are the ingredients in PREZCOBIX?**”)
- you have severe liver disease
- you take any of the following types of medicines because you could experience serious side effects:

Type of Drug	Examples of Generic Names (Brand Names)
Alpha1-Adrenoreceptor Antagonists (to treat enlarged prostate)	alfuzosin
Anticoagulant	apixaban (ELIQUIS) rivaroxaban (XARELTO)
Anti-convulsants (to prevent seizures)	carbamazepine (TEGRETOL) phenobarbital phenytoin (DILANTIN)
Antiarrhythmics/ Antianginals (to treat abnormal heart rhythms)	amiodarone (CORDARONE) dronedarone (MULTAQ) ivabradine (LANCORA) lidocaine (when given by injection)
Anti-gout (to treat gout and familial Mediterranean fever)	colchicine
Antimycobacterials (to treat tuberculosis)	rifampin (RIFADIN, RIFATER)
Antivirals (to treat hepatitis C infection)	elbasvir/grazoprevir (ZEPATIER)
Ergot Derivatives (to treat migraine and headaches)	dihydroergotamine (MIGRANAL) ergonovine ergotamine (CAFERGOT)
Herbal products (to improve mood)	St. John’s Wort
HMG-CoA Reductase Inhibitors also known as statins (to lower cholesterol)	lovastatin (MEVACOR) simvastatin (ZOCOR)
Other Lipid Modifying Agents cholesterol lowering drug	lomitapide
Inhaled Beta-Agonists (to treat asthma and/or chronic obstructive pulmonary disease)	salmeterol (ADVAIR)
Neuroleptics (to treat psychiatric conditions)	lurasidone (LATUDA) pimozide (ORAP)

Type of Drug	Examples of Generic Names (Brand Names)
PDE-5 Inhibitor (to treat pulmonary arterial hypertension)	sildenafil (REVATIO)
Platelet Aggregation Inhibitor (to prevent blood clots)	ticagrelor (BRILINTA)
Sedatives/Hypnotics (to treat trouble with sleeping and/or anxiety)	triazolam (HALCION)
Opioid Antagonist (to treat opioid-induced constipation)	naloxegol (MOVANTIK)

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

- have diabetes. In general, anti-HIV medicines, such as PREZCOBIX®, might increase sugar levels in the blood.
- have mild to moderate liver problems, including hepatitis B and/or C infection. It is also possible to develop hepatitis from taking PREZCOBIX.
- have hemophilia. Anti-HIV medicines, such as PREZCOBIX®, might increase the risk of bleeding.
- have Pancreatitis (inflamed pancreas).
- have increased cholesterol or triglycerides (a type of fat in your blood) levels. Your healthcare professional will do a blood test to check your lipid (fat) levels before starting treatment with PREZCOBIX. Your healthcare professional will also check your lipid levels periodically during your treatment with PREZCOBIX.
- have Renal impairment (kidney problems). Your healthcare professional will determine your creatinine levels (kidney function tests).
- are pregnant or planning to become pregnant. It is not known if PREZCOBIX® can harm your unborn baby. You should not take PREZCOBIX® during pregnancy. If you take PREZCOBIX® while you are pregnant, talk to your doctor about how you can be included in the Antiretroviral Pregnancy Registry.
- are breast-feeding. Do not breast-feed if you are taking PREZCOBIX®. You should not breast-feed 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.
- are allergic to sulfonamide medications.
- are less than 18 years of age.

Other warnings you should know about:

PREZCOBIX® is not a cure for HIV-1 infection or AIDS. If you are taking PREZCOBIX or any other antiretroviral medication, you may continue to develop infections and other complications of HIV-1 infection.

- PREZCOBIX® 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 use or share dirty needles.

- Redistribution or accumulation of body fat has been seen in people taking antiretroviral medications such as PREZCOBIX. This can include central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting (loss of muscle), facial wasting (loss of fat in face), breast enlargement, and “cushingoid appearance”.
- During the initial phase of treatment with PREZCOBIX, you may develop infections. You may also develop autoimmune disorders (such as Graves’ disease, autoimmune hepatitis, polymyositis and Guillain-Barré syndrome) during treatment with PREZCOBIX.
- You may develop a skin reaction during treatment with PREZCOBIX. Signs and symptoms can include severe rash or rash accompanied with fever, general malaise (discomfort), fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis (pink eye), hepatitis and/or eosinophilia (increased white blood cells). If you experience any of these signs or symptoms, stop taking PREZCOBIX immediately and tell your healthcare professional.

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 PREZCOBIX®:

- PREZCOBIX® should not be combined 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. PREZCOBIX® might reduce the effectiveness of estrogen-based contraceptives (birth control). Therefore, additional or alternative methods of (non-hormonal) contraception, such as a condom, are recommended.
- Tell your doctor if you take other anti-HIV medicines (e.g. rilpivirine, tenofovir disoproxil fumarate). PREZCOBIX® can be combined with some other anti-HIV medicines while other combinations are not recommended.
- Tell your doctor about all the medicines you take including prescription and nonprescription medicines, vitamins, and herbal supplements, including St. John’s wort (*Hypericum perforatum*). PREZCOBIX® and many other medicines can interact. Sometimes serious side effects will happen if PREZCOBIX® is taken with certain other medicines (see **“When it should not be used”**)

If you are taking PREZCOBIX® you should not take:

- medications that may affect your kidneys and have not been discussed with your doctor
- other medicines that contain protease inhibitors: e.g., atazanavir (Reyataz), indinavir (Crixivan), saquinavir (Invirase), lopinavir (Kaletra), or darunavir (Prezista®)
- other medicines that contain cobicistat (Stribild)
- ritonavir (Kaletra, Norvir).
- 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/Antianginals (for the heart)	digoxin disopyramide flecainide

<u>Type of Drug</u>	<u>Examples of Generic Names (Brand Names)</u>
	mexiletine propafenone
Anticancer Agents (to treat cancer)	dasatinib (SPRYCEL) nilotinib (TASIGNA) vinblastine vincristine everolimus (AFINITOR) irinotecan
Anticoagulants (to prevent the clotting of red blood cells)	dabigatran (PRADAXA) edoxaban (LIXIANA) warfarin (COUMADIN)
Anticonvulsants (to treat epilepsy and prevent seizures)	clonazepam (CLONAPAM) ethosuximide (ZARONTIN) oxcarbazepine (TRILEPTAL)
Antidepressants (to treat depression, anxiety, or panic disorder)	amitriptyline desipramine imipramine nortriptyline paroxetine (PAXIL) sertraline (ZOLOFT) trazodone (OLEPTRO)
Anti-infectives (to treat bacterial infections)	clarithromycin (BIAXIN) erythromycin (ERYC)
Antifungals (to treat fungal infections)	fluconazole (DIFLUCAN) ketoconazole (NIZORAL) itraconazole (SPORANOX®) isavuconazole posaconazole (POSANOL) voriconazole (VFEND)
Anti-gout (to treat gout and familial Mediterranean fever)	colchicine
Antimycobacterials (to treat bacterial infections)	rifabutin (MYCOBUTIN) rifampin (RIFADIN, RIFATER)
Antiplatelets (to prevent the clotting of red blood cells)	clopidogrel (PLAVIX)

Type of Drug	Examples of Generic Names (Brand Names)
Antivirals (to treat hepatitis C infection)	glecaprevir/pibrentasvir (MAVIRET)
Beta-Blockers (to treat heart disease)	carvedilol metoprolol (BETALOC, LOPRESOR) timolol
Calcium Channel Blockers (to treat heart disease)	amlodipine (CADUET, TWYNSTA) diltiazem (CARDIZEM, TIAZAC) felodipine nifedipine (ADALAT) verapamil (ISOPTIN, VERELAN)
Corticosteroids (to treat inflammation or asthma)	betamethasone budesonide (PULMICORT, RHINOCORT, SYMBICORT) dexamethasone fluticasone propionate (ADVAIR DISKUS, CUTIVATE, FLONASE, FLOVENT DISKUS) mometasone prednisone (WINPRED) triamcinolone
Endothelin Receptor Antagonists (to treat pulmonary arterial hypertension)	bosentan (TRACLEER®)
Estrogen-Based Contraceptives	ethinyl estradiol norethindrone norgestimate drospirenone
Eugeroics	modafinil
HIV- CCR5 Antagonist (to treat HIV infection)	maraviroc (CELSENTRI)
HIV- Integrase strand transfer Inhibitors (to treat HIV infection)	elvitegravir (STRIBILD)
HIV- Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) (to treat HIV infection)	delavirdine (RESCRIPTOR) efavirenz (SUSTIVA) etravirine (INTELENCE®) nevirapine (VIRAMUNE)
HMG-CoA Reductase Inhibitors (to lower cholesterol levels)	atorvastatin (LIPITOR) pravastatin (PRAVACHOL)

Type of Drug	Examples of Generic Names (Brand Names)
	rosuvastatin (CRESTOR)
Immunosuppressants (to prevent organ transplant rejection)	cyclosporine (SANDIMMUNE, NEORAL) tacrolimus (PROGRAF) sirolimus (RAPAMUNE) everolimus (AFINITOR)
Narcotic Analgesics (to treat opioid dependence)	buprenorphine/naloxone (SUBOXONE) fentanyl (ABSTRAL, DURAGESIC®) methadone meperidine oxycodone tramadol (DURELA, RALIVIA, TRAMACET®, TRIDURAL, ULTRAM®, ZYTRAM XL)
Neuroleptics (to treat psychotic disorders)	perphenazine risperidone (RISPERDAL®, RISPERDAL CONSTA®) quetiapine (SEROQUEL)
PDE-5 Inhibitors (to treat erectile dysfunction)	sildenafil (VIAGRA) vardenafil (LEVITRA) tadalafil (CIALIS)
Sedatives/Hypnotics (to treat trouble with sleeping and/or anxiety)	bupirone clorazepate diazepam (DIAZEMULS, VALIUM) midazolam (taken by injection) flurazepam (DALMANE, SOM-PAM) zolpidem
Antiemetics (to manage symptoms of upper gastrointestinal motility disorders)	domperidone
Urinary antispasmodics (to treat overactive bladder)	fesoterodine solifenacin

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 PREZCOBIX®. Do not start any new medicines while you are taking PREZCOBIX® without first talking with your doctor or pharmacist. You can ask your doctor or pharmacist for a list of medicines that can interact with PREZCOBIX®.

How to take PREZCOBIX®:

- Always use PREZCOBIX® exactly as your doctor has told you. You must check with your doctor if you are not sure.
- PREZCOBIX® tablets must be swallowed whole without breaking or crushing. Swallow with water if needed.
- If you have questions about when to take PREZCOBIX® your doctor can help you decide which schedule works for you.
- **You should always take PREZCOBIX® with food.** The type of food is not important.
- Continue taking PREZCOBIX® unless your doctor tells you to stop. Take the exact amount of PREZCOBIX® that your doctor tells you to take, right from the very start. To help make sure you will benefit from PREZCOBIX®, you must not skip doses or interrupt therapy. If you don't take PREZCOBIX® as prescribed, the beneficial effects of PREZCOBIX® may be reduced or even lost.
- If you have also been prescribed enteric-coated didanosine as well as PREZCOBIX®, take didanosine at least 1 hour before or 2 hours after PREZCOBIX®

Usual dose:

Usual adult dose:

Take PREZCOBIX® tablets every day exactly as prescribed by your doctor.

The dose of PREZCOBIX® is 1 tablet once a day (1 tablet containing 800 mg darunavir and 150 mg cobicistat).

Overdose:

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

Missed Dose:

If you miss a dose of PREZCOBIX® by more than 12 hours, wait and then take the next dose of PREZCOBIX® at the regularly scheduled time. If you miss a dose by less than 12 hours, take your missed dose of PREZCOBIX® immediately. Then take your next dose of PREZCOBIX® at the regularly scheduled time.

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

Do not stop using PREZCOBIX® without talking to your doctor first.

What are possible side effects from using PREZCOBIX®?

These are not all the possible side effects you may have when taking PREZCOBIX®. If you experience any side effects not listed here, tell your healthcare professional.

Like all prescription drugs, PREZCOBIX® can cause side effects. The following is **not** a complete list of side effects reported with PREZCOBIX® 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.

Liver problems that may occasionally be severe have been reported. Your doctor should do blood tests prior to initiating PREZCOBIX®. 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. Talk to your doctor about the signs and symptoms of liver problems. These may include yellowing of your skin or whites of your eyes, dark (tea coloured) urine, pale coloured stools (bowel movements), nausea, vomiting, loss of appetite, or pain, aching, or sensitivity on your right side below your ribs.

Rash has been reported in 15.7% of patients receiving PREZCOBIX®. In patients taking PREZCOBIX® and raltegravir, rashes (generally mild or moderate) may occur more frequently than in patients taking either drug separately. Contact your doctor immediately if you develop a rash. Your doctor will advise you whether your symptoms can be managed on therapy or whether PREZCOBIX® should be stopped.

In some patients, severe or life-threatening rash has been reported. **If you develop a severe rash (e.g., blisters, peeling skin) which may be accompanied with symptoms such as fever, fatigue, swelling of the face or lymph glands, muscle aches and pain, and liver problems, immediately discontinue PREZCOBIX® and contact your doctor.**

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.

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

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

- high blood sugar (hyperglycemia) and diabetes. This can happen in patients taking PREZCOBIX® or other protease inhibitor medicines. Some patients have diabetes before starting treatment with PREZCOBIX®, which gets worse. Some patients get diabetes during treatment with PREZCOBIX®. Some patients will need changes in their diabetes medicine. Some patients may need new diabetes medicine.
- increased bleeding in patients with hemophilia (a disorder in which the blood cannot clot properly). This may happen in patients taking PREZCOBIX® as it has been reported with other protease inhibitor medicines.
- changes in body fat. These changes can happen in patients taking anti-HIV medicines. 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.
- 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. If you suffer these symptoms while taking PREZCOBIX®, contact your doctor.
- changes in your immune system (Immune Reconstitution Inflammatory Syndrome) can happen when you start taking HIV medicines. 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. These can include Grave's disease (which affects the thyroid gland), autoimmune hepatitis, Guillain-Barre syndrome (which affects the nervous system) or polymyositis (which affects the muscles). It may develop at any time, sometimes months later after the start of HIV therapy. Sometimes symptoms can be severe. If you develop any of the following symptoms, tell your doctor right away:
 - high temperature (fever)
 - joint or muscle pain
 - redness, rash, swelling
 - abdominal pain
 - yellowing of the skin and eyes
 - fatigue
 - any new symptoms

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

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM			
Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Uncommon			
Severe and sometimes life-threatening rash: blisters and peeling skin which may be accompanied by fever, fatigue, swelling of the face or lymph glands, muscle aches and pain, and liver problems.			✓
Liver problems, disease or failure: 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.		✓	

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Diabetes (high blood sugar): excessive thirst, excessive urination, excessive eating, unexplained weight loss, poor wound healing, infections.		✓	
Pancreatitis (Inflammation of the pancreas): 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, tell 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 reach and sight of children.

Store PREZCOBIX[®] tablets in the original container, at room temperature between 15-30°C. 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 PREZCOBIX[®] 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 centre or emergency room immediately.

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

If you want more information about PREZCOBIX[®]:

- 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://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.janssen.com/canada, or by contacting the manufacturer at: 1-800-567-3331 or 1-800-387-8781.

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