

PART III: CONSUMER INFORMATION

PrPREZCOBIX™
darunavir/cobicistat Tablets

This leaflet is Part III of a three-part "Product Monograph" published when PREZCOBIX™ was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PREZCOBIX™. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

PREZCOBIX™ is an oral tablet used for the treatment of HIV (Human Immunodeficiency Virus) infection in adults when co-administered with other antiretroviral medications. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

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.

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

What it does:

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, that 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.

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.

When it should not be used:

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

Do not take PREZCOBIX™ if you:

- are allergic to darunavir, cobicistat or any of the other ingredients in PREZCOBIX™ (see **What the nonmedicinal ingredients are**)
- have severe liver disease
- take any of the following types of medicines because you could experience serious side effects:

Type of Drug

Examples of Generic Names (Brand Names)

Alpha-Adrenoreceptor Antagonists
(to treat enlarged prostate)

alfuzosin

Antiarrhythmics
(to treat abnormal heart rhythms)

amiodarone (Cordarone®)
bepidil¹
dronedarone (Multaq®)
lidocaine (when given by injection)
quinidine

Anti-gout
(to treat gout and familial Mediterranean fever)

colchicine

Antihistamines
(to treat allergy symptoms)

astemizole¹
terfenadine¹

Antimycobacterials
(to treat tuberculosis)

rifampin (Rifadin®,
Rifater®)

Ergot Derivatives
(to treat migraine and headaches)

dihydroergotamine (Migranal®)
ergonovine
ergotamine (Cafergot®)
methylergonovine

Gastrointestinal Motility Agents
(to treat some digestive conditions)

cisapride¹

Herbal products
(to improve mood)

St. John's Wort

HMG-CoA

lovastatin (Mevacor®)

Type of Drug	Examples of Generic Names (Brand Names)
Reductase Inhibitors also known as statins (to lower cholesterol)	simvastatin (Zocor [®])
Inhaled Beta-Agonists (to treat asthma and/or chronic obstructive pulmonary disease)	salmeterol (Advair [®])
Neuroleptics (to treat psychiatric conditions)	pimozide (Orap [®])
PDE-5 Inhibitor (to treat pulmonary arterial hypertension)	sildenafil (Revatio [®])
Sedatives/Hypnotics (to treat trouble with sleeping and/or anxiety)	oral midazolam triazolam (Halcion [®])

¹Bepridil, astemizole, terfenadine and cisapride are no longer marketed in Canada.

What the medicinal ingredient is:

darunavir and cobicistat

What the nonmedicinal ingredients are:

The other ingredients are cospovidone, 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).

What dosage forms it comes in:

PREZCOBIX[™] is available as film-coated tablets containing 800 mg darunavir and 150 mg cobicistat.

WARNINGS AND PRECAUTIONS

BEFORE you use PREZCOBIX[™] talk to your doctor or pharmacist if you:

- have diabetes. In general, anti-HIV medicines, such as PREZCOBIX[™], might increase sugar levels in the blood.
- have liver problems, including hepatitis B and/or C.
- have hemophilia. Anti-HIV medicines, such as PREZCOBIX[™], might increase the risk of bleeding.
- are pregnant or planning to become pregnant. It is not known if PREZCOBIX[™] can harm your unborn baby. You and your doctor will need to decide if taking PREZCOBIX[™] is right for you. 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 sulpha medications.
- are less than 18 years of age.

INTERACTIONS WITH THIS MEDICATION

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**”).

PREZCOBIX[™] should not be combined with phenobarbital, phenytoin, rifampin or St. John’s wort because the combination may significantly lower the amount of PREZCOBIX[™] in your blood and reduce the effects of 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, 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.

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 (for the heart)	digoxin disopyramide flecainide mexiletine propafenone
Anticancer Agents (to treat cancer)	dasatinib (Sprycel [®]) nilotinib (Tasigna [®]) vinblastine vincristine
Anticoagulants (to prevent the clotting of red blood cells)	apixaban (Eliquis [®]) dabigatran etexilate (Pradaxa [®]) rivaroxaban (Xarelto [®]) warfarin (Coumadin [®])
Anticonvulsants (to treat epilepsy and prevent seizures)	carbamazepine (Tegretol [®]) clonazepam (Clonapam [®]) ethosuximide (Zarontin [®]) oxcarbazepine (Trileptal [®]) phenobarbital phenytoin (Dilantin [®])
Anti-infectives (to treat bacterial infections)	clarithromycin (Biaxin [®]) erythromycin (Eryc [®])
Antifungals (to treat fungal infections)	fluconazole (Diflucan [®]) ketoconazole (Nizoral [®]) itraconazole (Sporanox [®]) posaconazole (Posanol [®]) voriconazole (Vfend [®])
Anti-gout (to treat gout and familial Mediterranean fever)	colchicine
Antimalarials (to treat malarial infections)	artemether/lumefantrine (Riamet [®] and Coartem [®]) Artemether/lumefantrine are not approved for use in Canada.
Antimycobacterials (to treat bacterial infections)	rifabutin (Mycobutin [®]) rifampin (Rifadin [®] , Rifater [®])
Beta-Blockers	carvedilol

<u>Type of Drug</u>	<u>Examples of Generic Names (Brand Names)</u>
(to treat heart disease)	metoprolol (Betaloc [®] , Lopresor [®]) timolol
Calcium Channel Blockers (to treat heart disease)	amlodipine (Caduet [®] , Twynsta [®]) diltiazem (Cardizem [®] , Tiazac [®]) felodipine nifedipine (Adalat [®]) nicardipine verapamil (Isoptin [®] , Verelan [®])
Corticosteroids (to treat inflammation or asthma)	budesonide (Pulmicort [®] , Rhinocort [®] , Symbicort [®]) dexamethasone fluticasone propionate (Advair Diskus [®] , Cutivate [®] , Flonase [®] , Flovent Diskus [®]) prednisone (Winpred [®])
Endothelin receptor Antagonists (to treat pulmonary arterial hypertension)	bosentan (Tracleer [®])
Estrogen-Based Contraceptives	ethinyl estradiol norethindrone norgestimate
Eugeroics	modafinil
HMG-CoA Reductase Inhibitors (to lower cholesterol levels)	atorvastatin (Lipitor [®]) pravastatin (Pravachol [®]) 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 [®] MAT) methadone oxycodone tramadol (Durela [®] , Ralivia [®] , Tramacet [®] , Tridural [®] , Ultram [®] , Zytram [®] XL)

<u>Type of Drug</u>	<u>Examples of Generic Names (Brand Names)</u>
Neuroleptics (to treat psychotic disorders)	perphenazine risperidone (Risperdal [®]), Risperdal Consta [®])
NS3-4A Protease Inhibitors: (to treat Hepatitis C Virus [HCV])	boceprevir (Victrelis [™]) telaprevir (Incivek [™])
PDE-5 Inhibitors (to treat erectile dysfunction)	sildenafil (Viagra [®]) vardenafil (Levitra [®]) tadalafil (Cialis [®])
Sedatives/Hypnotics (to treat trouble with sleeping and/or anxiety)	bupirone (Bustab [®]) clorazepate diazepam (Diazemuls [®] , Valium [®]) midazolam (taken by injection) flurazepam (Dalmane [®] , Som-Pam [®])
Selective Serotonin Reuptake Inhibitors (SSRIs) (to treat depression, anxiety, or panic disorder)	desipramine paroxetine (Paxil [®]) sertraline (Zoloft [®]) trazodone (Oleptro [®])

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[™].

PROPER USE OF THIS MEDICATION

Always use PREZCOBIX[™] exactly as your doctor has told you. You must check with your doctor if you are not sure.

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).

PREZCOBIX[™] tablets must be swallowed whole without breaking or crushing.

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 2 hours before or after PREZCOBIX[™].

Overdose:

In case of drug overdose, contact a health care practitioner, 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 of 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.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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 16% 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, 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. 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.
- 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 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. You could develop an autoimmune disease in which your immune system reacts against your own body (e.g., Graves' disease, which affects your thyroid gland, Guillain-Barré syndrome, which affects the nervous system, or polymyositis, which affects the muscles) and it may develop at any time, sometimes months after the start of HIV therapy.

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

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Uncommon	<u>Severe and sometimes life-threatening rash</u> (blisters, peeling skin) which may be accompanied by fever, fatigue, swelling of the face or lymph glands, muscle aches and pain, and liver problems.			✓
	<u>Liver problems</u> with symptoms such as 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> with symptoms such as excessive thirst, excessive urination, excessive eating, unexplained weight loss, poor wound healing, infections.		✓	
	<u>Inflammation of the pancreas</u> with symptoms such as abdominal pain, nausea and vomiting.		✓	

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.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on www.healthcanada.gc.ca/medeffect.

NOTE: *Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.*

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.janssen.ca>

or by contacting the sponsor, Janssen Inc., at: 1-800-567-3331 or 1-800-387-8781

This leaflet was prepared by Janssen Inc. Toronto, Ontario M3C 1L9

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HOW TO STORE IT

Keep out of the reach and sight of children.

Store PREZCOBIX™ tablets at room temperature between 15-30°C. Ask your doctor or pharmacist if you have any questions about storing your tablets.