

Prezcobix

Summary

Prezcobix contains two medicines—darunavir and cobicistat. Darunavir belongs to the class of drugs called protease inhibitors; it blocks the production of HIV from infected cells. Cobicistat is a booster; it raises and maintains levels of darunavir in the blood. Prezcobix is used as part of combination HIV treatment (ART) in adults and taken at a dose of one pill once daily with food. The type of food does not matter. Overall, Prezcobix was well-tolerated in clinical trials. General side effects were uncommon and included diarrhea and nausea; these were usually of mild to moderate intensity, and temporary.

What is Prezcobix

Prezcobix contains two medicines—darunavir and cobicistat. Darunavir belongs to the class of drugs called protease inhibitors. Cobicistat belongs to the class of drugs called boosters; it raises and maintains levels of darunavir so that Prezcobix need only be taken once daily. Darunavir was approved in Canada in 2006 and cobicistat was approved in 2012. What is noteworthy about Prezcobix is that it combines darunavir and cobicistat in one pill.

How does Prezcobix work?

Darunavir in Prezcobix works by interfering with enzymes needed by HIV called protease. Cobicistat does not have any activity against HIV. Using darunavir alone is not enough to suppress HIV. Therefore, Prezcobix is meant to be used with other anti-HIV drugs as part of combination therapy against HIV. Using Prezcobix together with other anti-HIV drugs greatly reduces HIV's ability to infect cells and make copies of itself.

How do people with HIV use Prezcobix?

Prezcobix is meant to be used together with other anti-HIV drugs. Prezcobix is taken once daily with food; the type of food does not matter.

For more information about HIV treatment, see CATIE's *Your Guide to HIV Treatment*.

FACT SHEET

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For many people with HIV, the use of ART (HIV treatment or antiretroviral therapy) has increased their CD4+ cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to greatly reduce the risk of developing a life-threatening infection or an AIDS-related cancer. Neither Prezcobix nor any other treatment regimen (ART) is a cure for HIV. It is therefore important that you see your doctor for checkups and lab tests on a regular basis.

Evidence shows that HIV-positive people who are on ART, engaged in care, and have an ongoing undetectable viral load are substantially less likely to transmit HIV to others, be it through sex, when sharing equipment to use drugs or during pregnancy and birth. In fact, the evidence for sexual transmission shows that people on ART who maintain an undetectable viral load do not pass HIV to their sexual partners. For further information see the CATIE fact sheet *HIV treatment and an undetectable viral load to prevent HIV transmission*. However, it is still a good idea to use condoms because they can reduce your risk for getting and passing on other sexually transmitted infections.

Warnings

Special populations

1. Pregnant people

A clinical trial has found that levels of darunavir, even when used with the booster cobicistat, are substantially lower in the blood of pregnant HIV-positive women compared with levels in these women after they gave birth. Therefore, the manufacturer of Prezcobix, Janssen, recommends "Prezcobix should not be initiated in pregnant women. An alternative regimen is recommended for women who become pregnant during treatment with Prezcobix." If you are taking Prezcobix and are pregnant or want to have a baby, speak to your doctor right away.

2. Older people

Prezcobix has not been studied in large numbers of people aged 65 and older.

3. Hemophiliacs

HIV-positive people who are hemophiliacs and who use protease inhibitors (including darunavir in Prezcobix) may experience more frequent bleeding under the skin and/or in the joints. It is not certain why this may occur. However, Janssen recommends "the frequency of bleeding episodes should be closely monitored in patients on Prezcobix."

Other warnings

Cholesterol and blood sugar

Levels of cholesterol and sugar in your blood may increase when you take Prezcobix or other anti-HIV drugs. Janssen suggests regular monitoring of cholesterol and sugar (glucose) levels in the blood.

Lactic acidosis

In rare cases, levels of lactic acid may accumulate in the blood of some people who use nucleoside analogues (nukes), which are a common part of treatment regimens. This is called lactic acidosis. Excess lactic acid levels can cause the liver to become enlarged. Excess lactic acid can be detected with a blood test.

If left unmanaged, lactic acidosis can sometimes become a life-threatening condition in some people with HIV. Twenty-five years ago, lactic acidosis was more common, often linked to use of nukes that commonly caused side effects. However, today, the nukes used as part of treatment regimens are much safer and lactic acidosis is very rare. Another factor that likely adds to the rarity of lactic acidosis today is that people with HIV tend to initiate treatment relatively early, before their overall health becomes weak.

Early symptoms of excess lactic acid in the blood can include the following:

- tiredness or lack of energy
- nausea
- stomach pain
- unintentional weight loss

If these are persistent, contact your doctor.

If left untreated, lactic acid levels can become very high and cause life-threatening complications, including the following:

- rapid heartbeat when you are at rest
- rapid breathing when you are at rest
- yellowing of the skin (jaundice) and whites of the eyes
- muscle weakness

If you have these symptoms, contact your doctor or go to the Emergency Department of a hospital.

Here are some typical risk factors for lactic acidosis among HIV-positive people:

- being female
- pregnancy
- obesity
- pre-existing liver injury
- low CD4+ cell count (less than 200 cells/mm³)

Liver health

Prezcobix has not been tested in people with underlying liver injury.

In rare cases, the liver may become injured in some people who take darunavir (in Prezcobix). According to the manufacturer of Prezcobix, liver injury among darunavir users has “generally occurred” in patients with one or more of the following:

- advanced HIV infection
- infection/coinfection with hepatitis B virus or hepatitis C virus
- taking multiple additional medicines (for different conditions)
- immune reconstitution inflammatory syndrome

In cases of new or worsening liver dysfunction (including clinically significant elevation of liver enzymes and/or symptoms such as fatigue, anorexia, nausea, jaundice, dark urine, liver tenderness and swollen liver), you should contact your doctor right away.

Pancreatic health

The pancreas gland in the abdomen produces insulin to help regulate blood sugar. In rare cases, inflammation of the pancreas gland (pancreatitis) has occurred in people who were using darunavir. It is not clear if darunavir caused this problem.

General risk factors for inflammation of the pancreas gland include the following:

- smoking tobacco
- excess intake of alcohol
- elevated levels of a fatty substance in the blood called triglycerides
- having disorders such as inflammatory bowel disease, lupus (SLE) and other diseases whereby the immune system attacks the body

Symptoms of an acute inflamed pancreas gland can include pain that:

- begins slowly or suddenly in your upper abdomen
- sometimes spreads to your back
- can be mild or severe
- may last for several days

Other symptoms may include the following:

- fever
- nausea and vomiting
- fast heartbeat
- swollen or tender abdomen

According to the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, “People with acute pancreatitis usually look and feel seriously ill and need to see a doctor right away.”

Kidney health

Kidney injury or dysfunction has occurred in some people who use cobicistat (in Prezcobix) alongside tenofovir DF (tenofovir disoproxil fumarate).

Therefore, Janssen recommends that doctors first screen patients for kidney injury prior to prescribing Prezcobix and a regimen containing tenofovir DF.

The company recommends that Prezcobix and tenofovir DF not be used in patients who have an estimated glomerular filtration rate of less than 70 mL/minute.

Janssen advises that patients taking Prezcobix “should not take medications that may affect your kidneys and have not been discussed with your doctor.”

The following drugs and substances have the potential to weaken the health of the kidneys (this list is not comprehensive—speak to your pharmacist to find out more about the safety of drugs for your kidneys):

- antibiotics – gentamycin, amikacin, vacomycin, rifampin
- anti-cancer drugs – Cisplatin (cis-platinum), carboplatin, bevacizumab (Avastin), gemcitabine
- anti-fungal drugs – amphotericin B, pentamidine
- anti-viral drugs – foscarnet (Foscavir), cidofovir (Vistide), acyclovir, valacyclovir (Valtrex)
- non-steroidal anti-inflammatory drugs (NSAIDs) – Aspirin (acetylsalicylic acid), celecoxib (Celebrex), diclofenac (Voltaren), ibuprofen (Advil, Motrin); indomethacin, naproxen, ketorolac (Acular)
- street drugs – cocaine, heroin

Your doctor, nurse or pharmacist may recommend the temporary use of one of the above listed medicines because they are necessary. However, repeated or long-term use of some of these medicines, such as NSAIDs, may increase your risk for kidney injury.

Skin and hypersensitivity reactions

In one analysis, Janssen has reported that out of 3,063 people who used darunavir (in Prezcobix), 0.4% developed “severe skin reactions [...] accompanied by fever and/or elevations of liver enzymes.” Furthermore, Janssen noted that life-threatening skin reactions (called “Stevens-Johnson Syndrome”) were rare, occurring in less than 0.1% of people who used darunavir.

Signs or symptoms of severe skin reactions can include severe rash or rash accompanied by one or more of the following symptoms:

- fever
- generally feeling unwell and in discomfort
- muscle or joint pain/ache
- blisters
- lesions in the mouth and on the lips
- the tissue lining the eyelids and whites of eyes becomes inflamed
- liver inflammation

If these problems occur, contact your doctor right away.

Side effects

1. General

In clinical trials, Prezcobix was generally well-tolerated and effective. However, as with any treatment, there were side effects but these were mostly uncommon and included the following:

- diarrhea
- nausea
- rash
- lack of energy

In general, these side effects should be temporary. However, should these or other side effects persist or become bothersome, speak to your doctor.

2. The skin

Rash is a common side effect of darunavir-containing medicines such as Prezcobix. According to Janssen, such rashes are “mostly mild to moderate, often occurring within the first four weeks of treatment and resolves with continued dosing.” Should the rash become severe or bothersome speak to your doctor right away.

Drug interactions

Some drugs (including prescribed and over-the-counter), herbs and supplements can interfere with the absorption and/or effectiveness of Prezcobix. Such interference is called a drug interaction. Some drugs can reduce the levels of the medicines in Prezcobix in your blood. This can make Prezcobix less effective and lead to treatment failure, reducing your future treatment options. Other drugs can raise the levels of medicines in Prezcobix in your blood, resulting in enhanced side effects or new side effects. Therefore, it is important to disclose to your doctor and pharmacist all the supplements, drugs, and herbs you are taking.

This factsheet is not comprehensive and only lists some of the potential and actual drug interactions with Prezcobix. Speak to your pharmacist to find out more about drug interactions with Prezcobix.

Not to be used

Janssen recommends that people taking Prezcobix should *not* use the following drugs:

- for prostate problems – alfuzosin (Xatral)
- for treatment of abnormal heart rhythm – amiodarone, dronedarone, ivabradine, lidocaine (injected into the body), quinidine
- for reducing the risk of blood clots – apixaban, dabigatran, rivaroxaban; ticagrelor
- anti-seizure drugs – carbamazepine, phenobarbital, phenytoin
- for the treatment of gout – colchicine (in people with kidney or liver injury)
- anti-histamines – astemizole, terfenadine
- antibiotics – rifampin
- for treatment of migraine and severe headaches – dihydroergotamine, ergonovine, ergotamine, methylergonovine
- for treating hepatitis C virus infection – Zepatier (elbasvir + grazoprevir)
- for treating high cholesterol – lomitapide, lovastatin, simvastatin

- for treating asthma and other lung issues – salmeterol (Advair, Advair Diskus, Serevent Diskhaler Disk, Serevent Diskus)
- for treating psychosis – lurasidone (Latuda), pimozide
- for treating pulmonary arterial hypertension – sildenafil (Revatio)
- for treating sleeping problems – triazolam

Prezcobix does not interfere (or vice versa) with acid-reducing agents, including those containing aluminum, calcium or magnesium.

Herbs

Many herbs used for medicinal purposes can interact with HIV treatments, particularly protease inhibitors such as darunavir (in Prezcobix). Janssen recommends that people who are using Prezcobix do not also use the herb St. John's wort (or its extracts – hypericin, hyperforin). This herb has significant potential to reduce levels of darunavir and cobicistat in the blood

Acid-reducing agents

Prezcobix does not interfere (or vice versa) with acid-reducing agents, including those containing aluminum, calcium or magnesium.

Resistance and cross-resistance

Over time, as new copies of HIV are made in the body, the virus changes its structure. These changes, called mutations, can cause HIV to resist the effects of anti-HIV drugs, which means those drugs will no longer work for you.

To reduce the risk of developing drug resistance, all anti-HIV drugs should be taken every day exactly as prescribed and directed. If doses are delayed, missed or not taken as prescribed, the level of drugs in Prezcobix in the blood may fall too low. If this happens, the HIV in your body can become resistant to the medication. If you find you are having problems taking your medications as directed, speak to your doctor, nurse or pharmacist about this. They can find ways to help you.

When HIV becomes resistant to one drug in a class, it sometimes becomes resistant to other drugs in that class. This is called cross-resistance. Feel free to talk with your doctor about your current and future treatment options. To help you decide what these future options might be, at some point your doctor can have a small sample of your blood analyzed to test for resistance.

Dosage

Prezcobix is supplied as pink, oval-shaped tablets. Each tablet contains darunavir 800 mg and cobicistat 150 mg. The recommended adult dose of Prezcobix is one pill taken once daily with food; the type of food does not matter. Prezcobix must be taken with food so that it is absorbed.

If you forget to take a dose, here is advice from Janssen:

- If you notice within 12 hours of the time you usually take Prezcobix, take the tablet immediately with food. Then take the next dose at your usual time.
- If you notice after 12 hours of the time you usually take Prezcobix, do not take the missed dose. Wait to take the next dose with food at your usual time.
- Do not take a double dose (two doses together).
- Call your doctor or pharmacist if you are not sure what to do.

Availability

Prezcobix is licensed in Canada. Your doctor or pharmacist can tell you more about the availability and coverage of Prezcobix in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

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