

# Atazanavir (Reyataz)

## Summary

Atazanavir is a type of anti-HIV drug called a protease inhibitor. It is generally well tolerated. Some people who use atazanavir may develop nausea, headache, stomach pain and yellowing of the skin and whites of the eyes. In adults, atazanavir is usually taken at a dose of 300 mg once daily along with 100 mg of ritonavir (Norvir) once daily, with food.

## What is atazanavir?

Atazanavir, sold under the brand name Reyataz, is a type of anti-HIV (antiretroviral) drug called a protease inhibitor. Atazanavir is used in combination with other anti-HIV drugs to treat (but not cure) HIV.

## How does atazanavir work?

When HIV infects a cell, it takes control of that cell. HIV then forces the cell to make many more copies of the virus. To make these copies, the cell uses proteins called enzymes. When the activity of these enzymes is reduced the production of HIV slows.

Atazanavir belongs to a group or class of drugs called protease inhibitors. Atazanavir interferes with an enzyme called protease, which is used by HIV-infected cells to make new viruses. Since atazanavir inhibits, or reduces, the activity of this enzyme, this drug causes HIV-infected cells to produce fewer viruses.

## How do people with HIV use atazanavir?

Atazanavir is used in combination with other anti-HIV drugs, usually nucleoside analogues (“nukes”), and sometimes drugs from other classes such as non-nucleoside reverse transcriptase inhibitors (“non-nukes”). Such combinations are called antiretroviral therapy, or ART. For more information on ART, see CATIE’s *Your Guide to HIV Treatment*.

Neither atazanavir nor any other anti-HIV medication is a cure for HIV. It is therefore important that you see your doctor regularly so that he or she can monitor your health.

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

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**Published**  
2019

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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.

## Side effects

### 1. General

General side effects that have been reported by some atazanavir users include: nausea, headache, rash, stomach pain, difficulty falling asleep, and unexpected tiredness.

### 2. Liver enzymes

Because atazanavir is metabolized (processed and broken down) by the liver, blood tests may show increased levels of liver enzymes, particularly in people co-infected with hepatitis B or C.

### 3. Yellowing of the skin (jaundice) and whites of the eyes

In clinical trials, up to 8% of atazanavir users developed this problem. It occurs because levels of a waste product called bilirubin build up in the blood of some atazanavir users. This does not damage your skin or eyes. However, if it occurs, tell your doctor right away. Should you develop jaundice or yellowing of the eyes, your skin and eyes should return to their normal colour when you stop taking atazanavir.

### 4. Abnormal heart rhythms

In clinical trials, about 6% of atazanavir users developed abnormal heart rhythms. However, in most cases, this was only detectable with diagnostic testing (electrocardiogram). Should you develop feelings of dizziness or being light-headed, let your doctor know right away, as this may be a sign of

abnormal heart rhythms or other atazanavir-related side effects.

### 5. Rash

About 20% of participants in controlled clinical trials of atazanavir developed a rash. However, this problem usually clears after several weeks and is not usually serious.

### 6. Blood sugar

In some people with HIV who use protease inhibitors, levels of sugar (glucose) in the blood become higher than normal. Prolonged bouts of higher-than-normal blood sugar levels can lead to diabetes. At least one study has found that some HIV-positive women, particularly those who are overweight, may be at increased risk for diabetes when they use protease inhibitors. Regular monitoring of your blood to assess sugar levels and other measurements will help you and your doctor be aware of changes that might suggest problems with your blood sugar. Although the risk of developing diabetes is generally low, symptoms that may be related to diabetes (such as increased thirst, increased urination, fatigue, dry and itchy skin, and unexplained weight loss) should be discussed with your doctor.

### 7. Women and pregnancy

In experiments on female rats, atazanavir at doses double that used in people altered menstrual periods. This problem has not been reported in women who used the drug. In pregnant rabbits and rats, use of atazanavir has not resulted in birth defects. According to the manufacturer, data suggests that atazanavir does not increase the risk of birth defects in infants born to women who used this drug during pregnancy.

Women who are pregnant and use atazanavir may be more likely to develop higher-than-normal levels of bilirubin (hyperbilirubinemia) than women who are not using this drug. It is not clear what effect this might have on the human fetus.

There have been reports of pregnant women who used atazanavir developing serious side effects,

sometimes fatal, including lactic acidosis syndrome. Signs and symptoms of severe lactic acidosis can include the following:

- persistent nausea
- vomiting
- fatigue
- abdominal pain
- confusion
- fatty liver

Because of this and other risks, the manufacturer advises that atazanavir be used during pregnancy “only if the potential benefit justifies the potential risk.”

## 8. Bleeding

Women may experience heavier menstrual periods when using protease inhibitors. Hemophiliacs who use protease inhibitors may also experience increased bleeding. If you are a hemophiliac who uses atazanavir and has this problem, let your doctor know about it.

## 9. Kidney stones

In rare cases, some atazanavir users may develop kidney stones.

## Drug interactions

Always consult your doctor and pharmacist about taking any other prescription or non-prescription medication, including herbs, supplements and street drugs.

Some drugs can interact with atazanavir, increasing or decreasing its levels in your body. Increased drug levels can cause you to experience side effects or make pre-existing side effects worse. On the other hand, if drug levels become too low, HIV can develop resistance and your future treatment options may be reduced.

Drug resistance is a major issue with a class of medications called proton pump inhibitors, which are used to reduce the symptoms of heartburn

(or acid reflux). Specific examples of proton pump inhibitors are listed under Drug interactions for atazanavir (below). However, sometimes other acid-reducing agents are used to help relieve heartburn. These medications, when taken at or around the same time as atazanavir, can reduce the level of stomach acid and therefore significantly reduce the absorption of atazanavir. If you suffer from heartburn, speak to your doctor about ways you might be able to relieve this condition.

If you must take a drug that has the potential to interact with your existing medications, your doctor can do the following:

- adjust your dose of either your anti-HIV drugs or other medications
- prescribe different anti-HIV drugs for you

## Drug interactions for atazanavir

Below are lists of drugs that do interact and drugs that can potentially interact with atazanavir. These lists are not exhaustive.

The manufacturer recommends that the following drugs should **not** be taken by atazanavir users:

- anticancer drugs—irinotecan (Camptosar)
- antibiotics/anti-tuberculosis drugs—rifampin (Rifater), rifampicin
- antihistamines—astemizole (Hismanal), terfenadine (Seldane)
- anti-psychotic drugs—pimozide (Orap)
- drugs for abnormal heart rhythms—amiodarone (Codarone), bepridil (Vasacor) flecainide (Tambocor), propafenone (Rythmol), quinidine
- gastrointestinal motility agents—cisapride (Prepulsid)
- herbs—St. John’s wort and its extracts, hypericin and hyperforin
- HIV protease inhibitor—indinavir (Crixivan)
- lipid-lowering agents—lovastatin (Mevacor), simvastatin (Zocor)

- migraine drugs (ergot derivatives)—dihydroergotamine (Migranal), ergotamine (Ergomar), Ergonovine
- sedatives—midazolam (Versed), triazolam (Halcion)
- proton pump inhibitors—esomeprazole (Nexium), lansoprazole (Prevacid), omeprazole (Prilosec), pantoprazole (Pantoloc)
- drugs for prostate problems—alfuzosin

Atazanavir can *raise* the level of the following drugs in your body:

- antidepressants—amitriptyline (Elavil) desipramine (Norpramin), imipramine (Tofranil)
- antibiotics—clarithromycin (Biaxin), rifabutin (Mycobutin)
- blood thinning drugs—warfarin (Coumadin)
- drugs to treat erectile dysfunction—sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra). If you have erectile dysfunction, talk to your doctor about how you might use these drugs safely.

Taking atazanavir with any of these drugs can lead to dangerous side effects and even death:

- lipid-lowering agents—atorvastatin (Lipitor)
- oral contraceptives—ethinyl estradiol, norethindrone
- HIV protease inhibitors—saquinavir (Invirase), amprenavir (Agenerase)
- transplant drugs—cyclosporine (Neoral), tacrolimus (Prograf), sirolimus (Rapamune)
- stimulants—methamphetamine (“crystal meth”)

The following drugs can *lower* levels of atazanavir in your blood:

- antibiotics—rifabutin (Mycobutin)
- antacids and “buffered” medications
- HIV drugs—ddI (didanosine, Videx, Videx EC), efavirenz (Sustiva, Stocrin), tenofovir (Viread)

The following drugs can *raise* levels of atazanavir in your blood:

- antibiotics—clarithromycin (Biaxin)
- HIV drugs—ritonavir (Norvir), saquinavir (Invirase)

## Resistance and cross-resistance

Over time, as more HIV is made in the body, the virus can change its structure. These changes, called mutations, can cause HIV to resist the effect of ART. Combining atazanavir with at least two other anti-HIV drugs delays the development of drug resistance.

To reduce the risk of developing drug resistance, all anti-HIV drugs should be taken every day exactly as prescribed and directed. It is important that you take your atazanavir every day because HIV can become drug-resistant if levels of atazanavir in the blood fall too low. This may happen if doses are delayed, skipped or not taken as prescribed. If you find you are having problems taking your medication on a regular basis, speak to your doctor and nurse 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. Although atazanavir can be used as the sole protease inhibitor in a regimen, leading American treatment guidelines indicate that the combination of atazanavir with a low dose of ritonavir is preferred. This combination helps to raise and maintain atazanavir levels in the blood for prolonged periods. This reduces the risk of developing drug-resistant HIV and may help to preserve your future treatment options.

Feel free to talk with your doctor about your current and future treatment options. To help you decide what these future therapies might be, at some point your doctor can have a small sample of your blood analyzed using resistance testing. Should the HIV in your body become resistant to atazanavir, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

## Availability

Atazanavir is licensed in Canada for the treatment of HIV infection in adults, in combination with other anti-HIV drugs. Your doctor can tell you more about the availability and coverage of atazanavir in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

## Reference

Bristol-Myers Squibb. Reyataz (atazanavir capsules). *Product monograph*. 26 October, 2018.

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## Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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Production of this document has been made possible through a financial contribution from the Public Health Agency of Canada. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada.

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