Atazanavir (Reyataz)

Summary
Atazanavir is a type of anti-HIV drug called a protease inhibitor. The most common side effects of atazanavir include nausea, headache, stomach pain and yellowing of the skin and whites of the eyes. 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 nukes (nucleoside analogues), and sometimes drugs from other classes such as non-nukes (non-nucleoside reverse transcriptase inhibitors). Such combinations are called antiretroviral therapy, or ART. For more information on ART, see CATIE's Your Guide to HIV Treatment.

For many people living with HIV, the use of ART has increased their CD4 cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to reduce the risk of developing a life-threatening infection. Neither atazanavir nor any other anti-HIV medication is a cure for HIV. It is therefore important that you do the following:

• See your doctor regularly so that he or she can monitor your health.
• Continue to practice safer sex and take other precautions to avoid passing HIV on to other people.

Side effects

1. General

General side effects that have been reported by some atazanavir users include: nausea, headache, rash, stomach pain, difficulty falling asleep, depression and unexpected tiredness. Because atazanavir is a relatively new drug, new side effects may be reported in the future as more people use it.

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.

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 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.

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 to the fetus.”

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.

10. Lipodystrophy syndrome

HIV lipodystrophy syndrome is the name given to a range of symptoms that can develop over time when people use ART. Some features of lipodystrophy syndrome include:

• loss of fat just under the skin (subcutaneous fat) in the face, arms and legs
• bulging veins in the arms and/or legs due to the loss of fat under the skin
• increased waist and belly size
• fat pads at the back of the neck (“buffalo hump”) or at the base of the neck (“horse collar”)
• small lumps of fat in the abdomen
• increased breast size (in women)

Together with these physical changes, blood tests may detect the following:

• increased levels of fatty substances called triglycerides
• increased levels of LDL-cholesterol, or “bad” cholesterol
• decreased levels of HDL-cholesterol, or “good” cholesterol
• increased levels of sugar (glucose)
• increased levels of the hormone insulin
• decreased sensitivity to insulin (insulin resistance)

The precise causes of HIV lipodystrophy syndrome are not clear and are difficult to understand because in some people with HIV, there may be one or more aspects of the syndrome taking place. For instance, some people may experience fat wasting, others fat gain, and others may experience both fat wasting and gain. What is becoming increasingly clear is that unfavourable changes in a person's levels of glucose, cholesterol and triglycerides over a period of several years increase their risk of diabetes and cardiovascular disease. So far, however, the benefits of ART far outweigh the increased risk of cardiovascular disease or other side effects.

Maintaining a normal weight, eating a healthy diet, exercising regularly and quitting smoking are all important to help you to reduce your risk of diabetes, heart disease and other complications. Regular visits to your doctor for checkups and blood tests are a vital part of staying healthy. If necessary, your doctor can prescribe lipid-lowering therapy.

Researchers are studying lipodystrophy syndrome to try to discover ways to help people with HIV avoid or reduce this problem. To find out more about options for managing aspects of lipodystrophy syndrome, see CATIE’s A Practical Guide to HIV Drug Side Effects.

Atazanavir has been tested and used mostly in people who are new to anti-HIV drugs. Because it is a relatively new drug, the role of atazanavir, if any, in lipodystrophy syndrome is not clear. In clinical trials, when used as the sole protease inhibitor in a regimen, atazanavir did not usually cause large increases in cholesterol levels. This may not always be the case when atazanavir is used with another protease inhibitor, such as ritonavir (Norvir).
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. This list is 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 (Vascor) flecanaide (Tambocor), propafenone (Rhthmol), quinidine
- gastrointestinal motility agents—cisapride (Prepulsid)
- herbs—St. John’s wort
- 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)

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)
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- 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.

**References**


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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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