

PART III : CONSUMER INFORMATION

Pr **REYATAZ** *
(atazanavir sulfate)

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

ABOUT THIS MEDICATION

ALERT : Find out about medicines that should NOT be taken with REYATAZ.

What the medication is used for :

REYATAZ is a prescription medicine used in combination with antiviral drugs to treat patients who are infected with HIV (the human immunodeficiency virus), the virus that causes AIDS. HIV infection destroys CD4 (T) cells, which are important to the immune system. The immune system helps fight infection. After a large number of T cells are destroyed, AIDS develops. REYATAZ helps to block HIV protease, an enzyme that is needed for the HIV virus to multiply. REYATAZ may lower the amount of HIV in your blood, helps your body keep its supply of CD4 (T) cells, and reduce the risk of death and illness associated with HIV.

What it does :

REYATAZ belongs to a family of medicines called protease inhibitors that control HIV infection by blocking a protease enzyme that HIV needs to multiply. Protease inhibitors work in two ways : they lower the number of HIV viruses in your body and allow the number of your CD4 T-cells that fight infection in your body to increase.

Your doctor prescribed REYATAZ for you because you are infected by the HIV virus that causes AIDS. REYATAZ helps by reducing the amount of HIV virus in your body and, therefore, reducing the risk of developing illnesses associated with HIV disease.

REYATAZ is prescribed together with other anti-viral medicines that also fight HIV infection. Your doctor will determine which combination of these medicines with REYATAZ is best for you.

You should know that REYATAZ is not a cure for HIV infection and that you may continue to develop infections or other illnesses associated with HIV infection. You should, therefore, remain under the care of your doctor while taking REYATAZ.

Treatment with REYATAZ does not reduce the risk of transmission of HIV to others through sexual contact or blood contamination. It is important to continue safe sex practices and not to share needles.

When it should not be used :

- If you know that you are allergic to atazanavir or any of the other ingredients of REYATAZ (See “What the non-medicinal ingredients are”).
- If you have, or have had a severe liver disease.
- If you take rifampin (RIFADIN*, RIFATER*, or ROFACT*), midazolam (when taken by mouth)♦, triazolam, or ergot alkaloids (ex. dihydroergotamine, MIGRANAL NS*), irinotecan (CAMPTOSAR*), cisapride (PROPULSID*)♦, lovastatin (MEVACOR*), simvastatin (ZOCOR*), pimozide (ORAP*), indinavir (CRIXIVAN*), bepridil♦, quinidine (BIQUIN*) and vardenafil (LEVITRA*) when used for erectile dysfunction.
- If you take medicinal products containing St. John’s wort (*Hypericum perforatum*) as this may result in loss of efficacy and development of resistance to REYATAZ.
- If you are taking REYATAZ and ritonavir (KALETRA*, NORVIR*) together, do not take voriconazole (VFEND*.)
- If you take VIRAMUNE* (nevirapine, used for HIV infection).
- If you take XATRAL* (alfuzosin, used to treat benign enlargement of the prostate).
- If you take REVATIO* (sildenafil), used to treat pulmonary arterial hypertension).

♦ oral formulation of midazolam, cisapride and bepridil are not marketed in Canada

What the medicinal ingredient is :

Each capsule contains amounts of atazanavir sulfate corresponding to 150, 200 and 300 mg of atazanavir free base.

What the important non-medicinal ingredients are :

The non-medicinal ingredients include crospovidone, lactose monohydrate, and magnesium stearate.

What dosage forms it comes in :

Capsules for oral use.

WARNINGS AND PRECAUTIONS

BEFORE you use REYATAZ, talk to your doctor or pharmacist :

- If you suffer from liver disease because the dose of REYATAZ may need to be reduced.
- If you are intolerant to lactose because REYATAZ capsules contain small quantities of lactose. These small quantities are unlikely to induce specific symptoms of intolerance.
- If you are pregnant or planning to become pregnant, or breast feeding.
- If you have a heart problem.

Discuss the use of REYATAZ with your doctor because some conditions may require special attention before or while taking this medicine. In particular because :

- There have been changes in the way the heart beats (heart rhythm changes). Call your healthcare provider right away if you get dizzy or lightheaded. These could be symptoms of a heart problem.
- There is a possibility of increased bleeding if you have a type A or B haemophilia.
- There have been reports of increased sugar in the blood and development or worsening of diabetes mellitus when using protease inhibitors.
- Changes in body fat have been seen in some patients taking antiretroviral therapy. These changes may include increased amount of fat in the upper back and neck, breasts and around the trunk. Loss of fat from the legs, arms and face may also happen. The cause or long-term health effects of these conditions are not known at this time.
- There have been reports of kidney stones. If you develop signs or symptoms of kidney stones (pain in your side, blood in your urine, pain when you urinate) call your healthcare provider right away.

See section on SIDE EFFECTS, for more information.

Can I take REYATAZ during pregnancy and breast-feeding?

- Nursing: Breast-feeding mothers should not take

REYATAZ unless specifically directed by their doctor.

- Pregnancy: It is not known if REYATAZ can harm your unborn baby.

Pregnant women have experienced serious side effects when taking REYATAZ with other HIV medicines called nucleoside analogues. You and your healthcare provider will need to decide if REYATAZ is right for you. If you use REYATAZ while you are pregnant, talk to your healthcare provider about the Antiretroviral Pregnancy Registry.

There have been reports of a condition called lactic acidosis syndrome (excess of lactic acid in the blood) with the use of REYATAZ in combination with other medicines used to treat HIV infection. This serious side effect has occasionally been fatal. Lactic acidosis occurs more often in women, particularly if very overweight. Frequent nausea, vomiting and stomach pain might indicate the development of lactic acidosis.

Ask your doctor for advice if you get pregnant or think you are pregnant or if you want to breast-feed. It is recommended that women infected by HIV do not breast-feed in order to avoid transmission of HIV to their infant through the breast milk.

Can REYATAZ be used in children?

REYATAZ capsules can be used in children 6 years of age and older. Dosing recommendations are not available for children from 3 months to less than 6 years of age. REYATAZ should not be used in babies under the age of 3 months.

INTERACTIONS WITH THIS MEDICATION

REYATAZ may interact with other drugs, including those you take without a prescription. You must tell your doctor or pharmacist about all drugs, including prescription and non-prescription drugs, herbal products and supplements and street drugs, you are taking or planning to take before you take REYATAZ. REYATAZ should be taken in combination with other antiretroviral agents. Clinical trials have found that combination antiviral therapy is more effective than one drug alone at reducing the amount of HIV in the blood and at reducing the development of resistance.

REYATAZ should not be taken with indinavir

(CRIXIVAN^{*}) as both REYATAZ and CRIXIVAN^{*} sometimes cause increased levels of bilirubin in the blood. (Increased levels of bilirubin can cause yellowing of the skin and the white part of the eyes).

Please see section “When it should not be used”. If you are taking didanosine (VIDEX[®]) buffered tablets or antacids, take REYATAZ with a meal one hour after or more than two hours before you take these medicines. Taking them together causes lower amounts of REYATAZ in the blood making it less effective.

The following medicines may require your healthcare provider to either monitor your therapy more closely or to change the dose or dose schedule of either REYATAZ or the other medicine:

- The anticoagulant warfarin (COUMADIN^{*}).
- Corticosteroids, given by nose or inhaled, such as fluticasone propionate (FLONASE^{*} or FLOVENT^{*}). Your doctor may choose not to keep you on fluticasone, especially if you are also taking ritonavir (KALETRA^{*}, NORVIR^{*}).
- Medicines to prevent organ transplant rejection: cyclosporine (SANDIMMUNE^{*}, NEORAL^{*}), tacrolimus (PROGRAF^{*}) and sirolimus (RAPAMUNE^{*}).
- Medicines for abnormal heart rhythm: lidocaine and quinidine (also know as BIQUIN^{*}), amiodarone (CORDARONE^{*}).
- The antidepressant trazodone (DESYREL^{*}).
- Tricyclic antidepressant such as amitriptyline (ELAVIL^{*}), desipramine, imipramine (TOFRANIL^{*}).
- Rifabutin (MYCOBUTIN^{*})
- Calcium channel blockers such as diltiazem (CARDIZEM^{*} or TIAZAC^{*}), felodipine (PLENDIL^{*}), verapamil (COVERA-HS^{*} or ISOPTIN SR^{*}).
- Oral contraceptives; REYATAZ may affect the safety and effectiveness of hormonal contraceptives such as birth control pills. **Talk to your healthcare provider about choosing an effective method of contraception.** Hormonal contraceptives do not prevent the spread of HIV to others.
- Stomach acid reducing agents (eg, famotidine, also known as PEPCID AC^{*}).
- Proton-pump inhibitors used for indigestion, heart burn or ulcers (ex. omeprazole, also known as LOSEC^{*}).
- The antifungals ketoconazole (NIZORAL^{*}) and itraconazole (SPORANOX^{*}) if you are taking REYATAZ with ritonavir.
- efavirenz
- midazolam (when injected)

- Atorvastatin (LIPITOR^{*}); there is an increased chance of serious side effects if you take REYATAZ with this cholesterol-lowering medicine.
- Sildenafil (VIAGRA^{*}), or tadalafil (CIALIS^{*}), used for erectile dysfunction: Before you take sildenafil or, tadalafil with REYATAZ, talk to your doctor about possible drug interactions and side effects. Your doctor may lower your dose of sildenafil or tadalafil if you are taking REYATAZ. Vardenafil should not be co-administered with REYATAZ. If you take sildenafil or tadalafil and REYATAZ together, you may be at increased risk of side effects of sildenafil or tadalafil such as low blood pressure, visual changes, and penile erection lasting more than 4 hours. If you experience any of these side effects you should seek immediate medical assistance.
- Coadministration of REYATAZ and tadalafil (ADCIRCA^{*}) for the treatment of pulmonary hypertension is not recommended.
- REYATAZ should not be coadministered with SEREVENT DISKUS^{*} (salmeterol) and/or ADVAIR^{*} (salmeterol with fluticasone) used to treat asthma, emphysema/ chronic obstructive pulmonary disease also known as COPD.
- Bosentan (TRACLEER^{*}) when used to treat pulmonary arterial hypertension.
- Medicine to treat opioid dependence: buprenorphine (SUBOXONE^{*}).
- The antibiotic clarithromycin (BIAXIN^{*}).
- Colchicine, used to prevent or to treat gout.

Other medicines may interact with REYATAZ. Remember to tell your healthcare provider all the medicines (prescription, non-prescription) and herbal supplements you are taking or planning to take.

PROPER USE OF THIS MEDICATION

Usual dose :

For adults, who have never taken anti-HIV medicines before, the recommended dose of REYATAZ is

- 300 mg (one 300-mg capsule or two 150-mg capsules) once daily taken with ritonavir 100 mg once daily taken with food.

OR

- 400 mg (two 200-mg capsules), or as prescribed by physician, once a day with food (without ritonavir).

For adults who have taken anti-HIV medicines in the past, the usual dose is

- 300 mg (one 300-mg capsule or two 150-mg capsules) once daily taken with ritonavir 100 mg once daily taken with food.

For children from 6 to 18 years of age, the recommended dose is based on weight. Your child's physician will provide you with the correct dosing instructions. **Do not exceed the adult dose.**

It is important that you take REYATAZ with food to achieve higher, more consistent REYATAZ levels. REYATAZ capsules should not be opened, they should be swallowed whole with water.

REYATAZ must be taken every day exactly as your doctor prescribes because it gives you the best chance to slow down resistance to the medicine. Therefore do not change or stop your daily dose of REYATAZ without first asking your doctor. REYATAZ should always be taken with other antiretrovirals.

REYATAZ should be taken at about the same time each day with a meal.

If a side effect prevents you from taking REYATAZ as directed, tell your doctor right away.

Always keep REYATAZ on hand so you don't run out. When you travel or need to stay in the hospital, make sure you will have enough REYATAZ to last until you can get a new supply.

Overdose :

In case of drug overdose, contact a healthcare practitioner, hospital emergency department or regional poison control centre, even if there are no symptoms.

Missed Dose :

It is important to take the daily dose prescribed by your doctor to ensure that you get maximum benefit. If you forget to take a dose, take the dose you missed as soon as possible with some food, and then return to your normal schedule. However, if a dose is skipped, do not double the next dose. Continue as normal with your next dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, REYATAZ can have side effects.

When treating HIV infection, it is not always easy to

tell what side effects are caused by REYATAZ, by the other medicines you take, or by the HIV infection itself. For this reason, it is important that you inform your doctor of any change in your health.

Some of the most common side effects of REYATAZ taken with other anti-HIV medicines include nausea, headache, rash, abdominal pain, and yellowing of the skin or whites of the eyes.

REYATAZ can cause the following side effects :

- **Yellowing of the skin or eyes.** These effects may be due to increases in bilirubin levels in the blood. Call your healthcare provider if your skin or the white part of your eyes turn yellow. Although these effects may not be damaging to your liver, skin, or eyes, it is important to tell your healthcare provider promptly if they occur.
- **If you have liver disease** including hepatitis B or C, your liver disease may get worse when you take anti-HIV medicines like REYATAZ.
- **Rash.** Rash (redness and itching) sometimes occurs in patients taking REYATAZ, most often in the first few weeks after the medicine is started. Tell your healthcare provider if rash occurs. If severe rash occurs, seek immediate medical attention.
- **Diabetes and high blood sugar (hyperglycemia)** sometimes happen in patients taking protease inhibitor medicines like REYATAZ. Some patients had diabetes before taking protease inhibitors while others did not. Some patients may need changes in their diabetes medicine.
- **A change in the way your heart beats (heart rhythm change).** Call your healthcare provider right away if you get dizzy or lightheaded. These could be symptoms of a heart problem.
- **Gallbladder disorders** (which may include gallstones and gallbladder inflammation) have been reported in patients taking REYATAZ.

Other side effects may occur with REYATAZ. Ask your doctor or pharmacist for more information about side effects. Inform your doctor promptly about these or any other symptoms. If the condition persists or worsens, seek medical attention.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

This summary does not include everything there is to know about REYATAZ. If you have questions or concerns, or want more information about

REYATAZ, your physician and pharmacist have the complete prescribing information upon which this leaflet was based. You may want to read it and discuss it with your doctor or other healthcare professional. Remember, no written summary can replace careful discussion with your doctor.

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

Symptom/effect		Talk with your doctor or pharmacist		Stop taking drug & call Your doctor or pharmacist
		Only if severe	In all cases	
Common	Rash (redness & itching)	✓	-	-
	Yellowing of the skin or eyes	-	✓	-
Uncommon	Frequent nausea, vomiting & stomach pain (occurs more often in women, particularly if very overweight)	-	✓	-
Postmarketing cases of unknown frequency	Diabetes and high blood sugar	-	✓	-
Postmarketing cases of unknown frequency	Heart rhythms changes	-	✓	-
Postmarketing cases of unknown frequency	Gall bladder disorders	✓	-	-
Postmarketing cases of unknown frequency	Kidney stones (pain in your side, blood in your urine, pain when you urinate)	-	-	✓

This is not a complete list of side effects. If you have any unexpected effects while taking REYATAZ, contact your doctor or pharmacist.

HOW TO STORE IT

Keep out of the reach of children.
Do not store above 25°C. Protect from moisture.

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 0701C
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at 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 obtained by contacting the sponsor, Bristol-Myers Squibb Canada, at :

1-866-463-6267.

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