

The content of this leaflet was updated according to the guidelines of the Ministry of Health in May 2018

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

REYATAZ 150 mg capsules

REYATAZ 200 mg capsules

REYATAZ 300 mg capsules

The active ingredient and its quantity:

Each capsule of REYATAZ 150 mg contains: atazanavir (as sulfate) 150 mg

Each capsule of REYATAZ 200 mg contains: atazanavir (as sulfate) 200 mg

Each capsule of REYATAZ 300 mg contains: atazanavir (as sulfate) 300 mg

The capsule contains lactose.

For the list of inactive ingredients, please see section 6.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

REYATAZ is intended for adults and children above 6 years of age. This medicine is not intended for infants under 3 months of age.

REYATAZ is an HIV-1 (Human Immunodeficiency Virus-type 1) prescription medicine given in combination with other antiretroviral medicines intended to treat HIV-1 infections.

HIV-1 is the virus that causes AIDS (Acquired Immunodeficiency Syndrome).

When used with other antiretroviral medicines to treat HIV-1 infection, REYATAZ may help reduce the amount of HIV-1 in the blood (also called viral load) and to increase the number of CD4+ (T) cells in your blood that help fight off other infections.

Reducing the amount of HIV-1 and increasing the CD4+ (T) cells in your blood may help to improve your immune system and may reduce your risk of death or of infections that can occur when your immune system is weak (opportunistic infections).

REYATAZ does not cure HIV-1 infection and does not cure AIDS. Be sure to take the HIV-1 medicines to control HIV-1 infection and decrease other HIV-related illnesses.

1.WHAT IS THE MEDICINE INTENDED FOR?

REYATAZ is intended for treatment of HIV-1 (Human Immunodeficiency Virus-type 1) and is given in combination with other antiretroviral medicines intended to treat HIV-1 (antiretroviral agents) in adults and children over 6 years of age.

REYATAZ is not intended for infants under 3 months of age.

Therapeutic group: protease inhibitors.

2.BEFORE USING THE MEDICINE:

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient (atazanavir sulfate) or to any of the other ingredients of the medicine (see section 6).
- you are taking any of the following medicines. Taking REYATAZ with the following medicines may affect its activity. REYATAZ may cause serious life-threatening side effects or death when used with the following medicines: Alfuzosin; cisapride; elbasvir/grazoprevir; ergot medicines including: ergotamine, ergotamine tartrate, dihydroergotamine, dihydroergotamine mesylate, methylergonovine, ergonovine; glecaprevir/pibrentasvir; indinavir; irinotecan; lurasidone (if REYATAZ is given with ritonavir); lovastatin; midazolam (when taken by mouth for sedation); nevirapine; pimozide; rifampin; sildenafil for the treatment of pulmonary arterial hypertension; simvastatin; *Hypericum perforatum* (St. John's wort); triazolam. Serious problems may occur if you or your child take any of the medicines listed above with REYATAZ.
- you are breastfeeding.

Special warnings regarding use of the medicine:

Do not use the medicine for any purpose other than for which it was prescribed.

If you are sensitive to any food or medicine, inform the doctor before taking the medicine.

This preparation contains lactose. If you have been diagnosed with an intolerance to certain sugars - consult the doctor before taking the medicine.

Before treatment with REYATAZ, tell the doctor if:

- you are sensitive to any food or medicine.
- you have heart problems.
- you have impaired liver function, including hepatitis B or C virus infection.
- you are undergoing dialysis treatment.
- you have diabetes.
- you have hemophilia.

- you have other medical problems.
- you are using hormonal forms of birth control, such as injections, an intrauterine device or vaginal ring, a dermal contraceptive patch and birth control pills that may not work during treatment with REYATAZ. Consult the doctor about forms of birth control that may be used during treatment with REYATAZ.
- you are pregnant or are planning a pregnancy; see "Pregnancy and breastfeeding" section.
- After your baby is born, tell the doctor if his skin or the white part of his eyes turns yellow.

Tests and follow up:

Your doctor will do blood tests to check your liver function before you start REYATAZ and during treatment.

Your doctor will do blood and urine tests to check your kidney function before you start REYATAZ and during treatment.

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist, in order to prevent hazards or lack of efficacy resulting from drug interactions.

Keep the list of medicines you are taking in order to present it to the attending doctor and pharmacist. Consult the doctor or pharmacist regarding the list of medicines that interact with REYATAZ. **Do not take a new medicine without first consulting your attending doctor.** The attending doctor can advise you whether taking other medicines with REYATAZ is safe.

Do not use the medicine if you are taking any of the following medicines. Taking REYATAZ with the following medicines may affect its activity. REYATAZ may cause serious life-threatening side effects or death when used with the following medicines:

Alfuzosin; cisapride; elbasvir/grazoprevir; ergot medicines including: ergotamine, ergotamine tartrate, dihydroergotamine, dihydroergotamine mesylate, methylergonovine, ergonovine; glecaprevir/pibrentasvir; indinavir; irinotecan; lurasidone (if REYATAZ is used with ritonavir); lovastatin; midazolam (when taken by mouth for sedation); nevirapine; pimozide; rifampin; sildenafil for the treatment of pulmonary arterial hypertension; simvastatin; *Hypericum perforatum* (St. John's wort); triazolam.

Serious problems may occur if you or your child take any of the medicines listed above with REYATAZ.

Use of the following medicines with REYATAZ (with or without ritonavir) may require an adjustment in the dosage or dosing regimen of REYATAZ or of the medicines listed below. Consult the attending doctor if you are taking one or more of the following medicines:

- Medicines to treat HIV such as: didanosine, tenofovir disoproxil fumarate, efavirenz, saquinavir, ritonavir
- Boceprevir, sofosbuvir, velpatasvir, voxilaprevir to treat hepatitis C
- Antacids, buffered medications such as: famotidine, omeprazole
- Medicines to treat heart rate disturbances: amiodarone, bepridil, lidocaine (systemically administered), quinidine
- Warfarin - anticoagulant
- Antidepressants such as: tricyclic antidepressants, trazodone
- Anticonvulsants to treat epilepsy such as: carbamazepine, phenytoin, phenobarbital, lamotrigine
- Antifungals such as: ketoconazole, itraconazole, voriconazole
- Colchicine - to prevent or treat gout
- Rifabutin - an antibiotic to treat tuberculosis
- Quetiapine and lurasidone - antipsychotics
- Benzodiazepines: midazolam (parenterally administered)
- Calcium channel blockers such as: diltiazem, felodipine, nifedipine, nicardipine, verapamil
- Bosentan - to treat pulmonary hypertension
- Medicines to lower cholesterol - atorvastatin, rosuvastatin
- Hormonal contraceptives (oral contraceptives) - ethinyl estradiol, norgestimate or norethindrone
- Medicines that depress the immune system - ciclosporin, sirolimus, tacrolimus
- Salmeterol (inhaled)
- Fluticasone - a nasal spray or inhaled steroid
- Clarithromycin - a macrolide antibiotic
- Opioid analgesics: buprenorphine
- Medicines to treat pulmonary arterial hypertension or to treat impotence - sildenafil, tadalafil, vardenafil

Use of the medicine and food:

Take the medicine whole with food. Do not open the capsules.

Pregnancy and breastfeeding:

- Before treatment with REYATAZ, tell the doctor if you are pregnant or planning to become pregnant. Consult the attending doctor about taking REYATAZ during pregnancy or if you are planning a pregnancy.
- Hormonal forms of birth control, such as injections, an intrauterine device or vaginal ring, a dermal contraceptive patch, and birth control pills may not work during treatment with REYATAZ. Consult the doctor about forms of birth control that may be used during treatment with REYATAZ.
- After your baby is born, tell the doctor if his skin or the white part of his eyes turns yellow.

Do not breastfeed if you are taking REYATAZ, due to risk of transmitting HIV-1 to your baby. REYATAZ may pass to the baby through the breast milk. Consult the doctor regarding the best way to feed your baby.

Driving and using machinery:

If you feel dizzy, refer to your doctor immediately.

Important information about some of the medicine's ingredients:

REYATAZ contains lactose. If you have been diagnosed with an intolerance to certain sugars, consult the doctor before taking the medicine.

3.HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the treatment regimen of this product.

The dosage and treatment regimen will be determined by the doctor only.

REYATAZ must be taken in combination with other antiretroviral medicines.

Take the medicine at a set time every day, as instructed by the doctor. Take the medicine according to the dosage and time period determined by the doctor.

Do not exceed the recommended dose.

Take the medicine whole with food. Do not open the capsules.

Do not stop treatment or change the dosage unless the attending doctor tells you to. Adhere to the treatment regimen as recommended by the doctor.

It is important to be under the attending doctor's care throughout the period of treatment with REYATAZ.

Always be sure to have an adequate amount of REYATAZ with you so that the medicine does not run out. Stopping treatment with the medicine, even for a short time, may lead to increased HIV-1 levels in the blood. The virus may become resistant to REYATAZ and as a result, become more difficult to treat.

If you forget to take this medicine at the required time, take a dose as soon as you remember and take the next dose at the usual time. Do not take a double dose instead of the forgotten dose.

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or to a hospital emergency room, and bring the package of the medicine with you.

Do not take medicines in the dark! Check the label and dose each time you take the medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4.SIDE EFFECTS:

As with any medicine, use of REYATAZ may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

REYATAZ can cause serious side effects. Refer to a doctor in the following cases:

- Changes in the heart rhythm. Refer to a doctor immediately if you feel dizzy. This could indicate a heart problem.
- Skin rash. Skin rash is common in patients taking REYATAZ, but can sometimes be severe. Skin rash usually goes away within 2 weeks without any change in treatment. Rash may be accompanied by other serious symptoms and could be severe. If you develop a severe rash or a rash with any of the following symptoms, stop treatment with REYATAZ and refer to the doctor immediately!
 - General feeling of sickness or flu-like symptoms
 - Fever
 - Muscle or joint aches
 - Red or inflamed eyes (conjunctivitis)
 - Blisters
 - Mouth sores
 - Swelling of the face
 - Painful, warm or red lump under the skin
- Yellowing of the skin or the white part of the eyes is a common effect in patients taking REYATAZ and is usually not harmful, but could sometimes be a symptom of a serious problem. This effect may be due to an increase in bilirubin levels in the blood (bilirubin is made by the liver). Although this effect does not damage the liver, skin, or eyes, refer to a doctor immediately if you notice yellowing of the skin or the white part of the eyes.

- Liver problems. If you have liver problems, including hepatitis B or C, they may get worse during the course of treatment with REYATAZ. Your doctor will perform blood tests to check your liver function before taking REYATAZ and during the treatment. Tell the doctor immediately if you experience any of the following symptoms: dark (tea-colored) urine, your skin or the white part of your eyes turns yellow, light-colored stools, nausea, itching, stomach-area pain.
- Chronic kidney disease. REYATAZ may affect your kidneys function. Your doctor will do blood and urine tests to check your kidneys function before you start REYATAZ and during treatment.
- Diabetes or high sugar levels (hyperglycemia) have been reported or have worsened in some patients taking protease inhibitor medicines such as REYATAZ. Some patients had to start taking medicines to treat diabetes or have had to change the diabetes medicinal treatment.
- Kidney stones have been reported in some patients taking REYATAZ. Tell your doctor immediately if you experience symptoms of kidney stones which may include: pain in the low back or low stomach area, blood in the urine, or pain when urinating.
- Gallbladder problems have been reported in some patients taking REYATAZ. Tell your doctor immediately if you experience symptoms of gallbladder problems which may include: pain in the right or middle upper stomach area, fever, nausea and vomiting, yellowing of the skin or the white part of the eye.

- Hemophilia patients. Hemophilia patients reported increased bleeding during the course of treatment with protease inhibitors such as REYATAZ.
- Changes in body fat can happen in patients taking HIV-1 medicines. These changes can include an increased amount of fat in the upper back and neck, breast, and around the body trunk. You may experience loss of fat from the legs, arms, and face. The exact cause and long-term health effect of these conditions are not known.
- Immune reconstitution syndrome (changes in the immune system) - may develop in patients starting treatment with HIV-1 medicines. Your immune system may get stronger and begin to fight previously dormant infections in your body. Tell the doctor if you experience new symptoms after starting to take REYATAZ.

The most common side effects during treatment with REYATAZ include: Nausea, headache, stomach-area pain, vomiting, trouble sleeping, numbness, tingling or burning sensation in the hands or feet, dizziness, muscle pain, diarrhea, depression, fever.

If you experience side effect, if any of the side effects bothers you, worsens, or does not go away, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

This **is not** a full list of side effects of REYATAZ. For further information, refer to the attending doctor or pharmacist.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

<https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

5.HOW SHOULD THIS MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor!
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- The medicine can be used within 6 months after first opening the bottle, but no later than the expiry date that appears on the package.
- Do not use if the inner seal of the bottle is damaged or missing.
- Store at a temperature that does not exceed **25°C**. Keep the bottle tightly closed.
- Do not dispose of medicines via wastewater or waste bin. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help to protect the environment.

6.FURTHER INFORMATION:

In addition to the active ingredient, the medicine also contains:

Inactive ingredients:

Lactose monohydrate, crospovidone, and magnesium stearate.

The hard gelatin capsule shells contain: gelatin, FD&C Blue No. 2, titanium dioxide. The 300 mg capsule shells also contain: red iron oxide, black iron oxide, and yellow iron oxide.

The capsules are imprinted with ink.

The capsule contains lactose.

REYATAZ 150 mg - each capsule contains 82.2 mg lactose monohydrate.

REYATAZ 200 mg - each capsule contains 109.6 mg lactose monohydrate.

REYATAZ 300 mg - each capsule contains 164.4 mg lactose monohydrate.

What the medicine looks like and the contents of the package:

REYATAZ 150 mg:

A size #1 gelatin capsule with two parts, the top of the capsule is opaque blue and the body of the capsule is opaque light blue. The capsule includes "BMS 150mg" written on it in white and "3624" written in blue. The capsule contains white to light yellow granules.

The bottle pack contains 60 capsules.

REYATAZ 200 mg:

A size #0 gelatin capsule with two parts, the body and the top of the capsule are opaque blue. The capsule includes "BMS 200mg" and "3631" written on it in white. The capsule contains white to light yellow granules.

The bottle pack contains 60 capsules.

REYATAZ 300 mg:

A size #00 gelatin capsule with two parts, the top of the capsule is opaque red and the body of the capsule is opaque blue. The capsule includes "BMS 300mg" and "3622" written on it in white. The capsule contains white to light yellow granules.

The bottle pack contains 30 capsules.

License holder and address: Bristol-Myers Squibb Israel Ltd., 18 Aharon Bart St., Kiryat Aryeh, Petach Tikva 4951448, Israel.

Manufacturer and address: Bristol-Myers Squibb Company, New Brunswick, New Jersey, USA.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

REYATAZ 150 mg: 140-78-30959-00

REYATAZ 200 mg: 141-10-30960-06

REYATAZ 300 mg: 146-78-33389-00

This leaflet was checked and approved by the Ministry of Health in October 2016, and updated according to the guidelines of the Ministry of Health in May 2018.