

PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER

Atazanavir (as sulfate)/Ritonavir 300mg/100mg Tablets

atazanavir sulfate, ritonavir

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, health care provider or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets is and what it is used for
2. What you need to know before you take Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets
3. How to take Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets
4. Possible side effects
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1. WHAT ATAZANAVIR (AS SULFATE)/RITONAVIR 300 MG/100MG TABLETS IS AND WHAT IT IS USED FOR

The main active ingredient of Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets is atazanavir, which belongs to a class of antiviral medicines called protease inhibitors. Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets also contains ritonavir, which is also a protease inhibitor, and which is used together with atazanavir to increase its effectiveness. Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets is indicated for the treatment of Human Immunodeficiency Virus (HIV) infection in adults and children weighing 39 kg or more, in combination with other antiretroviral medicinal products.

Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets works by reducing the amount of HIV in your body and this in turn, strengthens your immune system. In this way Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets reduces the risk of developing illnesses linked to HIV infection and raises the CD4 (T) cell count. CD4 cells are a type of white blood cells that play an important role in maintaining a healthy immune system to help fight infection.

This medicine is not a cure for HIV infection. While taking Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets you may still develop infections or other illnesses associated with HIV infection.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ATAZANAVIR (AS SULFATE)/RITONAVIR 300 MG/100MG TABLETS

Do not take Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets:

- if you are allergic (hypersensitive) to atazanavir, ritonavir or any of the other ingredients of Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets (see section 6, What Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets contains);

- if you have severe liver disease.
- if you are currently taking any of the following medicines:
 - astemizole or terfenadine (commonly used to treat allergy symptoms – these medicines may be available without prescription);
 - amiodarone, bepridil, encainide, flecainide, propafenone, quinidine (used to correct irregular heartbeats);
 - dihydroergotamine, ergotamine (used to treat migraine headache);
 - ergonovine, methylergonovine (used to stop excessive bleeding that may occur following childbirth or an abortion);
 - clorazepate, diazepam, estazolam, flurazepam, triazolam or oral (taken by mouth) midazolam (used to help you sleep and/or relieve anxiety);
 - pimoziide, (used to treat abnormal thoughts or feelings);
 - pethidine, propoxyphene (used to relieve pain);
 - cisapride (used to relieve certain stomach problems);
 - rifampicin (used to prevent/treat certain infections);
 - halofantrine (used to treat malaria);
 - simvastatin, lovastatin (used to lower blood cholesterol);
 - alfuzosin (used to treat enlarged prostate gland);
 - fusidic acid (used to treat bacterial infections);
 - sildenafil if you suffer from a lung disease called pulmonary arterial hypertension that makes breathing difficult. Patients without this disease may use sildenafil for impotence (erectile dysfunction) under their doctor’s supervision (see the section on “Taking other medicines”);
 - vardenafil (used to treat erectile dysfunction);
 - products containing St John’s wort (*Hypericum perforatum*) as this may stop Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets from working properly. St John’s wort is often used in herbal medicines that you can buy without a prescription.

If you are currently taking any of the above medicines, ask your doctor about switching to a different medicine while you are taking Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets. Often, there are other medicines you can take instead.

Also read the list of medicines under ‘Taking other medicines’ for use with certain other medicines which require special care.

Warnings and precautions

General:

You will need to take Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets every day. This medicine helps to control your condition, but it is not a cure for HIV infection. You may continue to develop other infections and other illnesses associated with HIV disease (e.g. opportunistic infections). These may require specific and sometimes preventive treatment. You should keep in regular contact with your doctor or health care provider. Do not stop taking your medicine without first talking to your doctor or health care provider.

Treatment with Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets has not been shown to eliminate the risk of passing HIV infection on to others by sexual contact or by blood transfer. Appropriate precautions (e.g. use of condom) should be taken to prevent passing on the disease to others.

Tell your doctor:

- about any past or present medical problems, including liver disease due to cirrhosis
- if you have kidney problems (including back pain with or without blood in your urine)

- if you have allergies
- if you have diabetes
- if you have haemophilia.
- if you are taking oral contraceptives ("the Pill") to prevent pregnancy
- if you are taking omeprazole or other proton pump inhibitors; or famotidine or other H2-receptor antagonists (used to treat diseases related to the acid in the stomach)

It is important that your doctor or health care provider knows about all your symptoms even when you think they are not related to HIV infection.

Liver disease/hepatitis:

Please tell your doctor if you have a history of liver disease. Patients with chronic hepatitis B or C and treated with antiretroviral agents are at increased risk of severe and potentially fatal liver adverse events and may require blood tests for monitoring of liver function. If you have liver disease, your health care provider or doctor will decide whether you may be treated with Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets. Patients with liver disease being treated with Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets will be monitored closely for side effects. Talk to your doctor or health care provider if you are not sure.

Fat distribution:

Redistribution, accumulation or loss of body fat may occur in patients receiving combination antiretroviral therapy. Contact your doctor if you notice changes in your body shape.

Bone problems:

Some patients taking combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue).

Your risk of developing this disease may be higher:

- if your immune system is severely compromised,
- if you have been taken combination antiretroviral therapy for a long time,
- if you drink alcohol regularly,
- if you use corticosteroids (certain medicines suppressing your immune system),
- if you are overweight.

If you notice joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement, inform your doctor or health care provider.

Immune Reactivation Syndrome:

In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection, signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to an improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms. If you notice any symptoms of infection, please inform your doctor immediately.

Hyperbilirubinaemia and jaundice:

An increase in the level of bilirubin in the blood may occur in patients receiving Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets. The signs may be a mild yellowing of the skin or eyes (jaundice). If you notice any of these symptoms please inform your doctor.

Skin rash:

Serious skin rash has been reported in patients taking Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets. If you develop a rash inform your doctor immediately.

Heart rhythm changes:

If you notice a change in the way your heart beats, please inform your doctor.

Other medicines and Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets

It is important that you tell your doctor, health care provider or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. These may affect the action of Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets, or Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets may affect their action (see also above, sections 'do not take Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets'). Side effects of either medicine may become worse and/or the medicines may become less effective.

Sometimes your doctor may decide to adjust the dose of Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets or of the other drug. Examples of drugs that are or may be unsuitable to take together with Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets, or where dose adjustments may be necessary, include:

- medicines commonly used to treat allergy symptoms (e.g. astemizole, terfenadine),
- pimozide, a medicine used to treat abnormal thoughts or feelings,
- medicines used to correct irregular heartbeats (e.g. amiodarone, bepridil, encainide, flecainide, propafenone, quinidine),
- medicines used to treat migraine headache (e.g. dihydroergotamine, ergotamine),
- medicines used to stop excessive bleeding that may occur following childbirth or an abortion (e.g. ergonovine, methylergonovine),
- medicines to treat excess stomach acid, reflux esophagitis (heartburn) or ulcers (e.g. omeprazole, famotidine, antacids),
- cisapride, a medicine used to relieve certain stomach problems,
- medicines to treat malaria (e.g. lumefantrine, quinine),
- medicines to treat tuberculosis (TB; e.g. rifampicin, rifabutin),
- medicines to treat fungal infections (e.g. itraconazole, fluconazole, voriconazole), - medicines to suppress the body's immune response (e.g. after organ transplantation, such as cyclosporine),
- other medicines against HIV (e.g. didanosine, tenofovir disoproxil fumarate, , nevirapine, efavirenz),
- medicines to lower cholesterol (e.g. atorvastatin),
- corticosteroids (e.g. fluticasone; for the treatment of inflammation and other diseases, such as asthma or rheumatoid arthritis),
- medicines to treat erectile dysfunction ("impotence"; e.g. sildenafil, tadalafil),
- medicines used to treat pulmonary arterial hypertension (e.g. sildenafil, bosentan)
- medicines to prevent blood clots (e.g. warfarin),
- calcium channel blockers (medicines to treat high blood pressure, e.g. diltiazem, verapamil),
- sedative agents (medicines used to treat anxiety and to help you sleep, e.g. triazolam, midazolam [given by injection]), - hormonal contraceptives (e.g. "the Pill")
- medicines to treat bacterial infections (e.g. clarithromycin, erythromycin, sulphamethoxazole/trimethoprim, fusidic acid)

- alfuzosin, a medicine used to treat enlarged prostate gland
- products containing St John's wort (*Hypericum perforatum*)
- medicines used to relieve pain (e.g. pethidine, propoxyphene) - medicines used to treat asthma (e.g. salmeterol, theophylline).
- irinotecan, vincristine and vinblastine, medicines used to treat cancer
- trazodone, a medicine used to treat depression,
- medicines used to treat seizures (e.g. phenytoin, carbamazepine, phenobarbital, valproic acid, lamotrigine),
- bupropion, a medicine used for smoking cessation.

Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets with food and drink

Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets must be taken with food.

Pregnancy

If you become pregnant, or are planning to become pregnant, you must contact your doctor or health care provider to discuss the potential adverse effects and the benefits and risks of your antiretroviral therapy to you and your child.

Be sure to tell your doctor immediately if you are or may be pregnant.

Breastfeeding

If you are interested in breastfeeding your baby, you should discuss the risks and benefits with your doctor or healthcare provider.

Driving and using machines

No studies on the effects of Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets on the ability to drive and use machines have been performed. However, you should take into account the state of your health and the possible side effects of Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets before considering driving or using machines.

Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO TAKE ATAZANAVIR (AS SULFATE)/RITONAVIR 300 MG/100MG TABLETS

Always take Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets exactly as your doctor or health care provider has told you.

In adults and children weighing 39 kg or more, the recommended dose is one tablet of Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets once daily. Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets must be taken with food.

Atazanavir (as sulfate)/Ritonavir 300mg/100mg tablets should be swallowed whole and not chewed, broken or crushed.

Other formulations containing less atazanavir and ritonavir are available for dosing in patients weighing less than 39 kg.

Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets will always be taken in combination with other antiretroviral medication; please make sure to follow the instructions within the supplied package leaflets.

Do not stop taking Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets, because reducing or missing doses will increase the risk of the HIV becoming resistant to atazanavir, in which case treatment with this medicine and possibly others will become ineffective. You should check with your doctor, health care provider or pharmacist if you are not sure.

If you take more Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets than you should

If you have taken too many tablets or if someone accidentally swallows some, you should contact your doctor or health care provider, or the nearest hospital emergency department for further advice.

If you forget to take Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets

If you forget to take a dose of your medicine, take it as soon as you remember, and then continue as before. If your next dose is due in less than 6 hours, do not take the forgotten dose, but take the next regular dose when it is due. Do not take a double dose to make up for forgotten individual doses.

If you have any further questions on the use of this product, ask your doctor or health care provider or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets can cause side effects, although not everybody gets them. When treating HIV infection, it is not always possible to differentiate between unwanted effects caused by Atazanavir (as sulfate)/Ritonavir 300 mg/100mg Tablets, or those caused by any other medicines you may be taking at the same time, or by the HIV disease. For this reason, it is important that you inform your doctor or health care provider of any change in your health.

Common side effects (may affect up to 1 in 10 people)

- fat redistribution with increased fat in the abdomen (belly) and internal organs, breast enlargement and fatty lumps on the back of the neck ('buffalo hump') - headache
- yellow whites of eyes (ocular icterus)
- jaundice (yellow skin)
- nausea
- vomiting
- diarrhoea
- an uncomfortable feeling in the stomach or belching after eating
- abdominal pain
- elevated bilirubin levels in the blood
- rash
- weakness/fatigue

Uncommon side effects (may affect up to 1 in 100 people):

- decreased or abnormal skin sensation
- fainting
- loss of memory

- dizziness
- sleepiness
- altered sense of taste
- shortness of breath
- inflammation of the stomach (gastritis), liver (hepatitis), or pancreas (pancreatitis)
- swollen abdomen
- mouth ulcers and cold sores
- wind (flatulence)
- dry mouth
- increased frequency of urination
- kidney stones
- blood and/or excess protein in the urine
- itching of the skin (pruritus)
- hives
- hair loss
- serious skin rashes (allergic reactions including rash, and sometimes also a high temperature, increased levels of liver enzymes seen in blood tests, an increase in a type of white blood cell, and/or enlarged lymph nodes)
- joint pain
- muscle pain
- muscle wasting
- loss of appetite, or increase of appetite
- weight increase, or weight decrease
- high blood pressure
- chest pain
- feeling generally unwell (malaise)
- fever
- allergic reactions
- breast enlargement (in men)
- depression, disorientation, anxiety, insomnia, difficulty sleeping, and abnormal dream. - elevated liver enzymes in the blood

Rare side effects (may affect up to 1 in 1,000 people)

- swelling
- fast or irregular heart beat
- kidney pain
- widening of blood vessels
- severe or life threatening skin reaction including blisters (Stevens-Johnson syndrome) .
- aching muscles, muscle tenderness or weakness, not caused by exercise - enlargement of the liver and spleen

Side effects of unknown frequency (frequency cannot be estimated from the available data):

- gallbladder disorders, including gall stones and infection
- diabetes mellitus and increased blood sugar levels
- irregular heart beat
- life threatening irregular heart beat
- immune reactivation syndrome (see part 2, Warnings and Precautions)

Side effects associated with combination antiretroviral therapy may cause changes in body shape due to changes in fat distribution. These may include loss of fat from legs, arms and face, increased fat in the abdomen (belly) and internal organs, breast enlargement and fatty lumps on the back of the neck ("buffalo hump"). The cause and long-term health effects of these conditions

are not known. Combination antiretroviral therapy may also cause raised lactic acid and sugar in the blood, increased fats in the blood and resistance to insulin (insulin will not work as effectively).

In patients with haemophilia type A and B, there have been reports of increased bleeding while taking this treatment or another protease inhibitor. If this happens to you, seek immediate advice from your doctor.

Furthermore, osteonecrosis (death of bone tissue) and immune reactivation syndrome have been reported in patients taking combination antiretroviral therapy (see section 2).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, health care provider or pharmacist as soon as possible.

Reporting of side effects

If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE ATAZANAVIR (AS SULFATE)/RITONAVIR 300 MG and 100MG TABLETS

Keep out of the reach and sight of children.

Do not store above 30°C. Store in the original container.

Do not use Atazanavir (as sulfate)/Ritonavir 300mg/100mg Tablets after the expiry date which is stated on the label after {EXP}. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What ATAZANAVIR (AS SULFATE) and RITONAVIR 300 MG and 100MG TABLETS

The active substances are Atazanavir as sulfate and Ritonavir.

The other ingredients are Lactose monohydrate, Crospovidone, Microcrystalline cellulose, Colloidal silicon dioxide, Magnesium Stearate, Copovidone, Sorbitan Monolaurate, Sodium Stearyl Fumarate, Isopropyl alcohol, Methylene chloride, Opadry 03F190003 Clear { HPMC 2910/HYPROMELLOSE, MACROGOL/PEG }

What Atazanavir (as sulfate) and Ritonavir 300mg and 100mg Tablets looks like and contents of the pack

Bilayer, capsule shaped, biconvex, film coated tablet having one layer with White to pale yellow color and other white to off-white color, plain on both the sides. A thin line on the tablet side may be visible.

30 Tablets in HDPE Bottle with silica gel sachet: Tablets are packed in 120CC HDPE Bottle along with 2g silica gel desiccant sachet and close a bottle with 38mm non CR closure (White Round fine ribbed polypropylene, Non-Child Resistant Closures with Heat seal 123 liner). Seal the bottle by an Induction sealing process. It is labelled.

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