

WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

*This patient information leaflet focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.**

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

* https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[HA749 trade name][†]
Atazanavir (sulfate)/ritonavir

*The warnings and instructions in this leaflet are intended for the person taking the medicine.
If you are a parent or carer responsible for giving the medicine to someone else such as a child,
you will need to apply the instructions accordingly .*

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 questions about the medicine, ask your health care provider.
- 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 seem to be the same as yours.
- If you are concerned about any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [HA749 trade name] is and what it is used for
2. What you need to know before you take [HA749 trade name]
3. How to take [HA749 trade name]
4. Possible side effects
5. How to store [HA749 trade name]
6. Contents of the pack and other information

1. What [HA749 trade name] is and what it is used for

[HA749 trade name] is an antiretroviral medicine used with other medicines to treat adults and children weighing at least 25 kg who have human immunodeficiency virus (HIV) infection.

[HA749 trade name] contains the active substances:

- *atazanavir*, a medicine belonging to a group of medicines called protease inhibitors;
- *ritonavir*, a medicine which boosts the effects of atazanavir. It works by slowing down the breakdown of atazanavir so that atazanavir continues to work in the body for longer.

[HA749 trade name] used in combination with other HIV medicines reduces the amount of virus in your body and keeps it at a very low level. It is not a cure for HIV infection but if taken correctly the combination will improve your immune system and reduce the risk of developing illnesses linked to HIV infection.

[HA749 trade name] is also sometimes used with other HIV medicines in people who have just been exposed to the HIV virus, to reduce the risk of becoming infected. Your health care provider will decide if treatment including [HA749 trade name] is suitable for you in this case.

2. What you need to know before you take [HA749 trade name]

Do not take [HA749 trade name]:

- if you are allergic (hypersensitive) to atazanavir, ritonavir or any of the other ingredients of [HA749 trade name] (see section 6, What [HA749 trade name] contains);

[†] Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

- if you have severe liver disease.
- if you are currently taking any of the following medicines:
 - alfuzosin (used to treat enlarged prostate gland);
 - propoxyphene (used to relieve pain);
 - amiodarone, flecainide, quinidine (used to correct irregular heartbeats);
 - fusidic acid (used to treat bacterial infections);
 - apixaban, cliopidogrel, rivaroxaban (used to reduce the risk of blood clots)
 - astemizole or terfenadine (commonly used to treat allergy symptoms – these medicines may be available without prescription);
 - rifampicin, rifapentine (antibiotics used to treat tuberculosis and some other infections);
 - irinotecan, neratinib (cancer medicines);
 - clozapine, haloperidol, lurasidone, pimozide, quetiapine, thioridazine (used to treat abnormal thoughts or feelings, e.g. in schizophrenia or bipolar disorder);
 - grazoprevir, elbasvir, glecaprevir, pibrentasvir (used to treat chronic hepatitis C infection);
 - dihydroergotamine, ergotamine (used to treat migraine headache);
 - ergometrine, methylergometrine (used to stop excessive bleeding that may occur following childbirth or an abortion);
 - simvastatin, lovastatin, lomitapide (used to lower blood cholesterol);
 - sildenafil used 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 health care provider’s supervision (see the section on “Taking other medicines”);
 - lansoprazole, omeprazole, pantoprazole (medicines to reduce stomach acid – these medicines may be available without prescription)
 - midazolam (taken by mouth), triazolam (used to help you sleep and/or relieve anxiety);
 - products containing St John’s wort (*Hypericum perforatum*). St John’s wort is often used in herbal medicines that you can buy without a prescription.

Taking any of these medicines with [HA749 trade name] may increase the risk of serious side effects, or prevent [HA749 trade name] or your other medicines from working properly. If you are currently taking any of the above medicines, ask your health care provider about switching to a different medicine while you are taking [HA749 trade name]. 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

You need to take [HA749 trade name] 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. These may require specific and sometimes preventive treatment. You should keep in regular contact with your health care provider. Do not stop taking your medicine without first talking to your health care provider.

Tell your health care provider:

- 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 heart problems
- if you have diabetes
- if you have haemophilia.

It is important that your 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 health care provider 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 problems and may require blood tests for monitoring of liver function. If you have liver

disease, your health care provider will decide whether you may be treated with [HA749 trade name]. Patients with liver disease being treated with [HA749 trade name] will be monitored closely for side effects. Talk to your 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 health care provider 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 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 health care provider immediately.

Hyperbilirubinaemia and jaundice: An increase in the blood level of a waste product called bilirubin may occur in patients receiving [HA749 trade name]. The signs may be a mild yellowing of the skin or eyes (jaundice). If you notice any of these symptoms please inform your health care provider.

Skin rash: Serious skin rash has been reported in patients taking [HA749 trade name]. If you develop a rash inform your health care provider immediately.

Heart rhythm changes: If you notice a change in the way your heart beats, please inform your health care provider.

Contraception: If you are taking a contraceptive medicine, discuss this with your health care provider. [HA749 trade name] may reduce the effect of some contraceptives and you and your partner may need to use another method of contraception, such as a condom.

Other medicines and [HA749 trade name]

It is important that you tell your health care provider if you are taking or plan to take **any other medicines**, including medicines obtained without a prescription.

In particular, there are some medicines that you must not combine with [HA749 trade name] (see 'Do not take [HA749 trade name]', above). However, many other medicines may affect the action of [HA749 trade name], or [HA749 trade name] may affect their action. Side effects of either medicine may become worse and/or the medicines may become less effective. Your health care provider may decide to use alternative medicines or adjust the dose of [HA749 trade name] or of the other drug.

In most cases, [HA749 trade name] can be combined with HIV medicines belonging to another class. Your health care provider will work out a combination that is suitable for you.

[HA749 trade name] with food and drink

[HA749 trade name] must be taken with food.

Pregnancy

If you become pregnant, or are planning to become pregnant, you must contact your 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 health care provider 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 health care provider.

Driving and using machines

No studies on the effects of [HA749 trade name] 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 [HA749 trade name] before considering driving or using machines.

Important information about some of the ingredients of [HA749 trade name]

[HA749 trade name] contains lactose. If your health care provider has told that you have an intolerance to some sugars, contact your health care provider before taking [HA749 trade name].

3. How to take [HA749 trade name]

Always take [HA749 trade name] exactly as your health care provider has told you.

In adults and children older than 3 months weighing at least 25 kg, the recommended dose is one tablet of [HA749 trade name] once daily.

[HA749 trade name] must be taken with food.

[HA749 trade name] should be swallowed whole and not chewed, broken or crushed.

Other formulations containing less atazanavir and ritonavir should be used for dosing in patients weighing less than 25 kg.

[HA749 trade name] will always be taken in combination with other HIV medicines; please make sure to follow the instructions within the supplied package leaflets.

Do not stop taking [HA749 trade name], because reducing or missing doses will increase the risk of the HIV becoming resistant to [HA749 trade name], in which case treatment with this medicine and possibly others will become ineffective. You should check with your health care provider if you are not sure.

If you take more [HA749 trade name] than you should

Yellowing of your skin and/or the white part of your eyes, irregular heart-beat, numbness, tingling, or a “pins and needles” sensation may occur if you take too much [HA749 trade name]. If you have taken too many tablets or if someone accidentally swallows some, you should contact your health care provider, or the nearest hospital emergency department for further advice.

If you forget to take [HA749 trade name]

It is important not to miss a dose of [HA749 trade name].

If you forget to take a dose of your medicine, take it as soon as you remember, and then continue as before. However, if your next dose is due in less than 12 hours, do not take the forgotten dose, but skip it and just 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 health care provider.

4. Possible side effects

Like all medicines, [HA749 trade name] 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 [HA749 trade name], 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 health care provider of any change in your health.

Serious side effects: tell your health care provider immediately if you develop any of the following serious side effects:

- a severe rash or a rash with flu-like illness symptoms, blisters, fever, mouth sores, muscle or joint pain, swelling in the face, inflammation of the eye which causes redness (conjunctivitis), painful, warm, or red lumps (nodules).
- yellowing of your skin or the white part of your eyes. Those symptoms might be high levels of bilirubin in your blood which has been commonly reported.
- changes in the way your heart beats. These could be symptoms of a serious heart problem.
- dark (tea-colored) urine, itching, yellowing of your skin or the white part of your eyes, pain around the stomach, pale colored stools or nausea. These could be symptoms of a serious liver problem.
- pain in the right or middle upper stomach area, nausea, vomiting, fever or yellowing your skin or the white part of your eyes. These could be symptoms of a serious liver problem.
- pain in your low back or low stomach-area, blood in your urine or pain when you urinate. These could be symptoms of kidney stones.

Very common side effects (may affect more than 1 in 10 people)

- upper or lower stomach ache
- vomiting
- diarrhoea (may be severe)
- feeling sick (nausea)
- flushing, feeling hot
- headache
- dizziness
- pain in the throat
- cough
- a tingling sensation or numbness in the hands, feet or around the lips and mouth
- feeling weak/tired
- bad taste in the mouth
- damage to the nerves that can cause weakness and pain
- itching
- rash
- joint pain and back pain
- upset stomach or indigestion

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

- allergic reactions including skin rashes (may be red, raised, itchy), severe swelling of the skin and other tissues
- inability to sleep (insomnia)
- anxiety
- increase in cholesterol
- increase in triglycerides
- gout
- stomach bleeding
- inflammation of the liver and yellowing of skin or whites of the eyes
- increase in urination
- reduced kidney function
- seizures (fits)
- low levels of blood platelets
- thirst (dehydration)
- abnormally heavy periods
- wind (flatulence)

- mouth ulcer
- muscle aches (pain), tenderness or weakness
- fever
- weight loss
- laboratory test results: changes in blood test results (such as blood chemistry and blood count)
- confusion
- difficulty paying attention
- fainting
- blurred vision
- swelling of the hands and feet
- high blood pressure
- low blood pressure and feeling faint when getting up
- coldness in the hands and feet
- acne

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

- heart attack
- abnormal heart beat (torsades de pointes)
- diabetes
- weight gain
- loss of appetite
- appetite increased
- depression
- sleep disorder
- disorientation,
- loss of memory
- sleepiness
- abnormal dream
- shortness of breath
- inflammation of the pancreas
- inflammation of the stomach
- dry mouth
- abdominal distension
- severe swelling of the skin and other tissues most often the lips or the eyes
- unusual hair loss or thinning
- muscle shrinkage
- kidney inflammation
- blood in the urine
- excess protein in the urine
- breast enlargement in men
- generally feeling unwell
- high levels of sugar in the blood
- increased magnesium in the blood increased alkaline phosphatase (an enzyme in the blood)

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

- abnormal manner of walking
- enlargement of the liver and spleen (hepatosplenomegaly)
- kidney pain
- severe or life threatening skin reaction including blisters (Stevens Johnson syndrome, toxic epidermal necrolysis, vesiculobullous rash, eczema, vasodilatation)
- allergic reaction (anaphylaxis)

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

- gallbladder disorders, including gall stones and infection

- 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. Should this happen to you, seek immediate advice from your health care provider.

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 health care provider as soon as possible.

Reporting of side effects

If you get any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. If available, you can also report side effects directly through the national reporting system. By reporting side effects you can help improve understanding about the safety of this medicine.

5. How to store [HA749 trade name]

Keep this medicine out of the sight and reach of children.

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

Do not use this medicine after the expiry date stated on the label, after "EXP". The expiry date refers to the last day of that month.

Do not use this medicine if you notice description of the visible signs of deterioration that it is different from the description below.

Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [HA749 trade name] contains

- The active ingredients are atazanavir and ritonavir.
- The other ingredients of [HA749 trade name] are lactose monohydrate, partially pregelatinized starch, crospovidone, calcium silicate, ferric oxide yellow, magnesium stearate, copovidone, colloidal silicon dioxide, sorbitan monolaurate, dicalcium phosphate anhydrous, sodium stearyl fumarate, polyvinyl alcohol partially hydrolysed, talc, macrogol, titanium dioxide and iron oxide yellow.

What [HA749 trade name] looks like and contents of the pack

[HA749 trade name] is pale yellow to yellow coloured, capsule shaped, biconvex, film coated tablet debossed with 'D09' on one side and plain surface on the other side.

[HA749 trade name] is provided in a white opaque HDPE bottle with an oxygen-absorbing pouch and a polypropylene closure. Each closure consists of a polypropylene liner and a saf-cap.

Pack size: 30 tablets

Supplier and Manufacturer

Supplier

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For any information about this medicine, contact the local representative of the supplier.

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Detailed information on this medicine is available on the World Health Organization (WHO) website: <https://extranet.who.int/pqweb/medicines>