

Package leaflet: Information for the user

EVOTAZ 300 mg/150 mg film-coated tablets atazanavir/cobicistat

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, ask your doctor 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. See section 4.

What is in this leaflet

1. What EVOTAZ is and what it is used for
2. What you need to know before you take EVOTAZ
3. How to take EVOTAZ
4. Possible side effects
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1. What EVOTAZ is and what it is used for

EVOTAZ contains two active substances:

- **atazanavir, an antiviral (or antiretroviral) medicine.** It is one of a group called *protease inhibitors*. These medicines control human immunodeficiency virus (HIV) infection by stopping production of a protein that HIV needs for its multiplication. They work by reducing the amount of HIV in your body and this in turn, strengthens your immune system. In this way atazanavir reduces the risk of developing illnesses linked to HIV infection.
- **cobicistat, a booster (pharmacokinetic enhancer) to help improve the effects of atazanavir.** Cobicistat, does not directly treat your HIV, but boosts the levels of atazanavir in the blood. It does this by slowing down the breakdown of atazanavir which will make it stay in the body for longer.

EVOTAZ may be used by adults aged 18 years of age and older who are infected with HIV, the virus that causes acquired immunodeficiency syndrome (AIDS). It is used in combination with other anti-HIV medicines to help control your HIV infection. Your doctor will discuss with you which combination of these medicines with EVOTAZ is best for you.

2. What you need to know before you take EVOTAZ

Do not take EVOTAZ

- **if you are allergic** to atazanavir, cobicistat or any of the other ingredients of this medicine (listed in section 6)
- **if you have moderate to severe liver problems**
- **if you are taking any of these medicines:** see also *Other medicines and EVOTAZ*
 - rifampicin (an antibiotic used to treat tuberculosis)
 - carbamazepine, phenobarbital and phenytoin (antiepileptics used to prevent seizures)
 - astemizole or terfenadine (commonly used to treat allergy symptoms, these medicines may be available without prescription); cisapride (used to treat gastric reflux, sometimes called heartburn); pimozone (used to treat schizophrenia); amiodarone, dronedarone, quinidine,

lidocaine (injectable) or bepridil (used to correct heart rhythm); ergotamine, dihydroergotamine, ergonovine, ergometrine and methylergonovine (used to treat headaches); and alfuzosin (used to treat enlarged prostatic gland)

- quetiapine (used to treat schizophrenia, bipolar disorder and major depressive disorder); lurasidone (used to treat schizophrenia)
- medicines containing St. John's wort (*Hypericum perforatum*, a herbal preparation).
- triazolam and oral (taken by mouth) midazolam (used to help you sleep and/or to relieve anxiety)
- simvastatin, lovastatin, and lomitapide (used to lower blood cholesterol)
- avanafil (used to treat erectile dysfunction)
- colchicine (used to treat gout), if you have kidney and/or liver problems
- dabigatran and ticagrelor (used to prevent and reduce the blood clots)
- grazoprevir-containing products, including elbasvir/grazoprevir fixed dose combination, and glecaprevir/pibrentasvir fixed dose combination (used to treat chronic hepatitis C infection)

Do not take sildenafil with EVOTAZ when sildenafil is used for the treatment of pulmonary arterial hypertension. Sildenafil is also used for the treatment of erectile dysfunction. Tell your doctor if you are using sildenafil for the treatment of erectile dysfunction.

Tell your doctor at once if any of these apply to you.

Warnings and precautions

Some people will need special care before or while taking EVOTAZ. Talk to your doctor or pharmacist before taking EVOTAZ.

EVOTAZ is not a cure for HIV infection. You may continue to develop infections or other illnesses linked to HIV infection. You can still pass on HIV to other people when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your doctor the precautions needed to avoid infecting other people.

Make sure your doctor knows:

- if you have liver problems
- if you develop signs or symptoms of gall stones (pain in your right side). Gall stones have been reported in patients taking atazanavir, a component of EVOTAZ.
- if you have type A or B haemophilia. You may notice increased bleeding.
- if you have problems with your kidneys or require haemodialysis. Kidney stones have been reported in patients taking atazanavir, a component of EVOTAZ. If you develop signs or symptoms of kidney stones (pain in your side, blood in your urine, pain when you urinate), please inform your doctor immediately
- if you are taking oral contraceptives ("**the Pill**") to prevent pregnancy. If you are currently using an oral contraceptive or using a patch contraceptive to prevent pregnancy, you should use an additional or different type of contraception (e.g. condom)

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. In addition to the opportunistic infections, autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after you start taking medicines for the treatment of your HIV infection. Autoimmune disorders may occur many months after the start of treatment. If you notice any symptoms of infection or other symptoms such as muscle weakness, weakness beginning in hands and feet and moving up towards the trunk of the body, palpitations, tremor or hyperactivity, please inform your doctor immediately to seek necessary treatment.

Some patients taking combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The length of combination antiretroviral therapy, corticosteroid use, alcohol consumption, severe immunosuppression, higher body mass index, among others, may be some of the many risk factors for developing this disease. Signs of osteonecrosis are joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you notice any of these symptoms please inform your doctor.

Hyperbilirubinaemia (an increase in the level of bilirubin in the blood) has occurred in patients receiving EVOTAZ. The signs may be a mild yellowing of the skin or eyes. If you notice any of these symptoms please inform your doctor.

Serious skin rash, including Stevens-Johnson syndrome, may develop in patients taking EVOTAZ. If you develop a rash inform your doctor immediately.

EVOTAZ may affect how well your kidneys work.

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

Children and adolescents

Do not give this medicine to children and adolescents under 18 years of age. The use of EVOTAZ in children and adolescents has not yet been studied.

Other medicines and EVOTAZ

You must not take EVOTAZ with certain medicines. These are listed under Do not take EVOTAZ, at the start of section 2.

There are other medicines that may not be taken together or may require a change in their mode of administration when taken with EVOTAZ. Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. It is especially important to mention these:

- medicines containing ritonavir or cobicistat (booster agents)
- other medicines to treat HIV infection (e.g. indinavir, didanosine, tenofovir disoproxil, tenofovir alafenamide, efavirenz, etravirine, nevirapine and maraviroc)
- sofosbuvir/velpatasvir/voxilaprevir (used to treat hepatitis C)
- sildenafil, vardenafil and tadalafil (used by men to treat impotence [erectile dysfunction])
- if you are taking an oral contraceptive ("the Pill"). You should also use an additional or different type of contraception (eg. condom).
- any medicines used to treat diseases related to the acid in the stomach ("heartburn") (e.g. antacids, H₂-blockers like famotidine and proton pump inhibitors like omeprazole)
- disopyramide, flecainide, mexiletine, propafenone, digoxin, bosentan, amlodipine, felodipine, nicardipine, nifedipine, verapamil, diltiazem, metoprolol and timolol (medicines to lower blood pressure, to slow heart rate or to correct heart rhythm)
- atorvastatin, pravastatin, fluvastatin, pitavastatin and rosuvastatin (used to lower blood cholesterol)
- salmeterol (used to treat asthma)
- ciclosporin, tacrolimus and sirolimus (medicines to decrease the effects of body's immune system)
- certain antibiotics (rifabutin, clarithromycin)
- ketoconazole, itraconazole, voriconazole and fluconazole (antifungals)
- metformin (used to treat type 2 diabetes)
- warfarin, apixaban, edoxaban and rivaroxaban (used to reduce blood clots)
- irinotecan, dasatinib, nilotinib, vinblastine and vincristine (used to treat cancer)
- trazodone (used to treat depression)
- perphenazine, risperidone, thioridazine, midazolam (given by injection), buspirone, clorazepate, diazepam, estazolam, flurazepam and zolpidem (used to treat nervous system disorders)
- buprenorphine (used to treat opioid addiction and pain)

It is important to tell your doctor if you are taking: Corticosteroids including betamethasone, budesonide, fluticasone, mometasone, prednisone, triamcinolone. These medicines are used to treat allergies, asthma, inflammatory bowel diseases, inflammatory conditions of the eyes, joints and muscles and other inflammatory conditions. If alternatives cannot be used, its use should only take place after medical evaluation and under close monitoring by your doctor for corticosteroid side effects.

Pregnancy and breast-feeding

EVOTAZ should not be used during pregnancy, because the drug levels in your blood may be lower during pregnancy and may no longer be high enough to control HIV. Your doctor may prescribe different medicines if you become pregnant while taking EVOTAZ.

Atazanavir, a component of EVOTAZ is excreted in human milk. It is unknown if cobicistat, the other component of EVOTAZ, is excreted in human milk but it has been shown in animals that it is excreted in milk. Talk to your doctor about breast-feeding if you are taking EVOTAZ. Patients should not breast-feed while taking EVOTAZ. It is recommended that women infected with HIV do not breast-feed because the virus might be transmitted through the breast milk.

Driving and using machines

Some patients have reported dizziness when taking atazanavir or cobicistat, active substances of EVOTAZ. If you feel dizzy or lightheaded, do not drive, use any tools or use machines and contact your doctor immediately.

3. How to take EVOTAZ

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure. This way, you can be sure your medicine is fully effective and you reduce the risk of the HIV-virus developing resistance to the treatment.

The recommended adult dose of EVOTAZ is one tablet daily by mouth and with food, in combination with other anti-HIV medicines. The tablets have a poor taste, therefore swallow the tablet whole; do not crush or chew the tablets. This will help ensure you get the full dose.

If you take more EVOTAZ than you should

If you accidentally take more EVOTAZ than your doctor recommended, contact your doctor at once or contact the nearest hospital for advice.

If you forget to take EVOTAZ

If you miss a dose of EVOTAZ by 12 hours or less, take it right away with food and then take your next scheduled dose at the usual time. If you miss a dose and it is more than 12 hours from the time you should have taken EVOTAZ, do not take the missed dose. Wait and take the next dose at the usual time. Do not double the next dose. It is important that you do not miss any doses of EVOTAZ or your other anti-HIV medicines.

If you stop taking EVOTAZ

Do not stop taking EVOTAZ before talking to your doctor.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor if you notice anything unusual about your health.

The following side effects may occur when taking EVOTAZ

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

- yellowing of the skin or the white part of your eyes
- nausea

Common (may affect up to 1 in 10 people)

- increased levels of bilirubin in the blood
- vomiting, diarrhoea, stomach pain or discomfort, indigestion, bloated or distended tummy (abdomen), wind (flatulence)
- headache, dizziness
- extreme tiredness
- increased appetite, impairment of the sense of taste, dry mouth
- difficulty sleeping, abnormal dreams, sleepiness
- rash

Uncommon (may affect up to 1 in 100 people)

- life threatening irregular heart beat (torsade de pointes)
- allergic reaction (hypersensitivity)
- inflammation of the liver
- inflammation of the pancreas, inflammation of the stomach
- allergic reactions including rash, a high temperature, increased levels of liver enzymes seen in blood tests, an increase in a type of white blood cell [eosinophilia] and/or enlarged lymph nodes (see section 2)
- severe swelling of the skin and other tissues most often the lips or the eyes
- fainting, high blood pressure
- chest pain, generally feeling unwell, fever
- shortness of breath
- formation of kidney stones, kidney inflammation, blood in the urine, excess protein in the urine, increased frequency of urination, chronic kidney disease (how well your kidneys work)
- gallstones
- muscle shrinkage, joint pain, aching muscles
- breast enlargement in men
- depression, anxiety, sleep disorder
- unusual tiredness or weakness
- loss of appetite, weight loss, weight gain
- disorientation, loss of memory
- numbness, weakness, tingling or pain in the arms and legs
- mouth ulcers and cold sores
- itchy rash, unusual hair loss or thinning, itching

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

- allergic reactions including serious skin rash, a high temperature and enlarged lymph nodes (Stevens-Johnson syndrome, see section 2).
- fast or irregular heartbeat (QTc prolongation)
- enlargement of the liver and spleen
- gallbladder inflammation
- kidney pain
- swelling
- visible accumulation of fluid under the skin, skin rash, widening of blood vessels
- abnormal manner of walking

- aching muscles, muscle tenderness or weakness not caused by exercise

During HIV therapy there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and life style, and in the case of blood lipids sometimes to the HIV medicines themselves. Your doctor will test for these changes.

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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Malta

ADR Reporting

Website: www.medicinesauthority.gov.mt/adrportal

United Kingdom

Yellow Card Scheme

Website: at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store EVOTAZ

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

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist 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 EVOTAZ contains

- The active substances are atazanavir and cobicistat. Each film-coated tablet contains 300 mg of atazanavir (as sulphate), and 150 mg cobicistat.
- The other ingredients are:
 - Tablet core* - cellulose, microcrystalline (E460(i)), croscarmellose sodium (E468), sodium starch glycolate, crospovidone (E1202), stearic acid (E570), magnesium stearate (E470b), hydroxypropyl cellulose (E463), silica (E551)
 - Film-coating* - hypromellose (hydroxypropyl methyl cellulose, E464), titanium dioxide (E171), talc (E553b), triacetin (E1518), red iron oxide (E172)

What EVOTAZ looks like and contents of the pack

EVOTAZ film-coated tablets are pink, oval, biconvex, of approximate dimensions of 19 mm x 10.4 mm, debossed on one side with "3641" and plain-faced on the other side of the tablet.

EVOTAZ film-coated tablets are supplied in bottles of 30 tablets. The following pack sizes are available: outer cartons containing 1 bottle of 30 film-coated tablets and outer cartons containing 90 (3 bottles of 30) film-coated tablets.

Not all packages may be marketed in your country.

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.