

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

[HA403 trade name][†]
Efavirenz

*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 is for you only. Do not pass it on to others. It may harm them, even if their illness seems 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 [HA403 trade name] is and what it is used for
2. What you need to know before you take [HA403 trade name]
3. How to take [HA403 trade name]
4. Possible side effects
5. How to store [HA403 trade name]
6. Contents of the pack and other information

1. What [HA403 trade name] is and what it is used for

[HA403 trade name] is an antiretroviral medicine used for the treatment of human immunodeficiency virus (HIV) infection in adults and adolescents. It contains the active substance efavirenz, which belongs to a class of antiretroviral medicines called non-nucleoside reverse transcriptase inhibitors (NNRTIs).

[HA403 trade name] is used in combination with other antiretroviral medicines to reduce the amount of virus in your blood and keep it at a 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.

Response to treatment with [HA403 trade name] varies between patients. Your health care provider will be monitoring the effectiveness of the treatment.

To control your HIV infection, and to stop your illness from getting worse, you must take all your HIV medicines regularly, unless your health care provider tells you to stop taking any.

2. What you need to know before you take [HA403 trade name]

Do not use [HA403 trade name]:

- if you are allergic to efavirenz or any of the other ingredients of this medicine (listed in section 6). Contact your health care provider for advice.
- if you have severe liver disease.

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

- if you have a heart condition, such as changes in the rhythm or rate of the heart beat, a slow heart beat, or severe heart disease.
- if any member of your family (parents, grandparents, brothers or sisters) has died suddenly due to a heart problem or was born with heart problems.
- if your health care provider has told you that you have high or low levels of electrolytes such as potassium or magnesium in your blood.
- if you are currently taking any of the following medicines (see also “Other medicines and [HA403 trade name]”):
 - astemizole or terfenadine (used to treat allergy symptoms)
 - bepridil (used to treat heart disease)
 - ergot alkaloids (for example, ergotamine, dihydroergotamine, ergonovine, and methylergonovine) (used to treat migraine and cluster headaches)
 - midazolam or triazolam (used to help you sleep)
 - pimozide, imipramine, amitriptyline or clomipramine (used to treat certain mental conditions)
 - elbasvir or grazoprevir (used to treat hepatitis C)
 - St. John's wort (*Hypericum perforatum*) (a herbal remedy used for depression and anxiety)
 - certain antibiotics (macrolides, fluoroquinolones, imidazole)
 - triazole antifungal agents
 - certain antimalarial treatments

If you are taking any of these medicines, tell your health care provider immediately. Taking these medicines with [HA403 trade name] could create the potential for serious and/or life-threatening side-effects or stop [HA403 trade name] from working properly.

Warnings and precautions

Tell your health care provider if you have:

- **a history of liver disease, including active chronic hepatitis.** Patients with chronic hepatitis B or C who are treated with combination antiretroviral agents have a higher risk for severe and potentially life-threatening liver problems. Your health care provider may conduct blood tests in order to check how well your liver is working or may switch you to another medicine.
- **a history of mental illness,** including depression, or of substance or alcohol abuse. Tell your health care provider immediately if you feel depressed, have suicidal thoughts or have strange thoughts (see section 4, Possible side effects).
- **a history of convulsions (fits or seizures)** or if you are being treated with anticonvulsant therapy such as carbamazepine, phenobarbital and phenytoin. If you are taking any of these medicines, your health care provider may need to check the level of anticonvulsant medicine in your blood to ensure that it is not affected while taking [HA403 trade name]. Your health care provider may give you a different anticonvulsant or change the dose.
- **a heart disorder,** such as an abnormal electrical signal called prolongation of the QT interval.

You need to take [HA403 trade name] every day. This medicine helps to control HIV infection, but it is not a cure. You may still develop other infections and other illnesses associated with HIV disease (e.g. opportunistic infections). These will require specific and sometimes preventive treatment. You should keep in regular contact with your health care provider. Do not stop your medicine without first talking to the health care provider.

Once you start taking [HA403 trade name], look out for:

- **signs of dizziness, difficulty sleeping, drowsiness, difficulty concentrating or abnormal dreaming.** These side effects may start in the first 1 or 2 days of treatment and usually go away after the first 2 to 4 weeks.

If at any time during treatment you get problems with your balance or coordination, become confused or drowsy and unresponsive, get seizures (fits or convulsions), your speech becomes slurred or confused or you develop personality changes, you or someone close to you must let your health care provider know right away.
- **any signs of skin rash.** If you see any signs of a severe rash with blistering or fever, stop taking [HA403 trade name] and tell your health care provider at once. If you had a rash while taking another NNRTI, you may be at a higher risk of getting a rash with [HA403 trade name].
- **any signs of inflammation or infection.** 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 tell your health care provider 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 the hands and feet and moving up towards the trunk of the body, palpitations, tremor or hyperactivity, please inform your health care provider immediately to seek necessary treatment.
- **bone problems.** 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 health care provider.

Children and adolescents

[HA403 trade name] is not recommended for children younger than 3 years and weighing less than 10 kg.

Other medicines and [HA403 trade name]

[HA403 trade name] may interact with other medicines, including herbal preparations such as *Ginkgo biloba* extracts. As a result, the amount of [HA403 trade name] or other medicines in your blood may be affected. This may stop the medicines from working properly, or may make any side effects worse. In some cases, your health care provider may need to adjust your dose or check your blood levels.

Tell your health care provider if you are taking any of the following:

- **Other medicines used for HIV infection:**
 - protease inhibitors: darunavir, indinavir, lopinavir/ritonavir, ritonavir, ritonavir-boosted atazanavir, saquinavir or fosamprenavir/saquinavir. Your health care provider may consider giving you an alternative medicine or changing the dose of the protease inhibitors.
 - Dolutegravir. Your health care provider may need to increase the dolutegravir dose.
 - maraviroc
 - a combination tablet containing several HIV medicines. Some combination tablets should not be taken with [HA403 trade name].
- **Medicines used to treat infection with the hepatitis C virus:**

- boceprevir, telaprevir, elbasvir/grazoprevir, simeprevir, sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir, glecaprevir/pibrentasvir.
- **Medicines used to treat bacterial infections** including tuberculosis and AIDs-related mycobacterium avium complex:
 - clarithromycin, rifabutin, rifampicin. Your health care provider may consider changing your dose or giving you an alternative antibiotic. In addition, your health care provider may prescribe a higher dose of [HA403 trade name].
- **Medicines used to treat fungal infections (antifungals):**
 - voriconazole. [HA403 trade name] may reduce the amount of voriconazole in your blood and voriconazole may increase the amount of efavirenz in your blood. If you take these two medicines together, the dose of voriconazole must be increased and the dose of [HA403 trade name] must be reduced. You must check with your health care provider first.
 - Itraconazole, ketoconazole. [HA403 trade name] may reduce the amount of itraconazole or ketoconazole in your blood and your health care provider may need to check the level or use a different medicine.
 - posaconazole. [HA403 trade name] reduce the amount of posaconazole in your blood and your health care provider may recommend a different antifungal medicine.
- **Medicines used to treat malaria:**
 - artemether/lumefantrine: [HA403 trade name] may reduce the amount of artemether/lumefantrine in your blood.
 - atovaquone/proguanil: [HA403 trade name] may reduce the amount of atovaquone/proguanil in your blood.
 - amodiaquine: [HA403 trade name] may increase the amount of this medicine in your blood and thus the risk of side effects.
- **Medicines used to treat convulsions/seizures (anticonvulsants):**
 - carbamazepine, phenytoin, phenobarbital. [HA403 trade name] can reduce or increase the amount of anticonvulsant in your blood. Carbamazepine may make [HA403 trade name] less likely to work. Your health care provider may need to consider giving you a different anticonvulsant.
- **Medicines used to lower blood fats (also called statins):**
 - atorvastatin, pravastatin, simvastatin. [HA403 trade name] can reduce the amount of statins in your blood. Your health care provider will check your cholesterol levels and will consider changing the dose of your statin, if needed.
- **Medicines known as calcium channel blockers, used to treat high blood pressure or heart problems:**
 - diltiazem and similar medicines. When you start taking [HA403 trade name], your health care provider may need to adjust your dose of the calcium channel blocker.
- **Immunosuppressants (used to prevent organ transplant rejection):**
 - cyclosporin, sirolimus or tacrolimus: when you start or stop taking [HA403 trade name], your health care provider will closely monitor your plasma levels of the immunosuppressant and may need to adjust its dose.
- **Hormonal contraceptives, such as birth control pills, an injected contraceptive (for example, Depo-Provera), or a contraceptive implant (for example, Implanon):**
 - you must also use a reliable barrier method of contraception (see Pregnancy, breast-feeding and fertility). [HA403 trade name] may make hormonal contraceptives, including emergency

contraception, less likely to work. Pregnancies have occurred in women taking [HA403 trade name] while using a contraceptive implant, although it is not known for sure if the [HA403 trade name] therapy caused the contraceptive to fail.

- **Warfarin or acenocoumarol** (medicines used to reduce clotting of the blood):
 - your health care provider may need to adjust your dose of warfarin or acenocoumarol.
- **Antibiotics** from the following groups: macrolides, fluoroquinolones or imidazole.
- **Ginko biloba extracts** (a herbal preparation).
- **Methadone** (used to treat opiate addiction): your health care provider may recommend an alternative treatment.
- **Morphine** (to control severe pain). Your health care provider may need to adjust your morphine dose.

[HA403 trade name] with food and drink

[HA403 trade name] should be taken on an empty stomach or with a low-fat meal. Grapefruit juice should be avoided when taking [HA403 trade name].

Pregnancy

Current treatment guidelines recommend efavirenz in pregnant women and women of childbearing potential.

Breastfeeding

If a mother wants to breastfeed her baby, her health care provider should be asked for advice on the risks and benefits.

Driving and using machines

Dizziness, impaired concentration and drowsiness have been reported during treatment with efavirenz. If you experience these symptoms you should avoid potentially hazardous tasks such as driving or operating machinery.

[HA403 trade name] contains lactose

Lactose is a source of glucose and galactose. The small amount of lactose in each dose is unlikely to cause symptoms of lactose intolerance. If, however, you have one of the rare genetic disorders galactosaemia, glucose-galactose intolerance or congenital lactase deficiency you must talk to your health care provider before taking this medicine.

3. How to take [HA403 trade name]

Always take [HA403 trade name] exactly as the health care provider has told you. You should check with your health care provider if you are not sure.

The usual dose for *adults and adolescents weighing over 35 kg* is **1 tablet** (600 mg), taken once daily.

The dose of [HA403 trade name] may need to be increased or decreased if you are also taking certain other medicines.

How to take your dose

[HA403 trade name] should be taken on an empty stomach, preferably in the evening before going to bed.

[HA403 trade name] will always be taken in combination with other antiretroviral medication; please make sure that you also follow the instructions in the package leaflets supplied with the other products.

Children

Since [HA403 trade name] cannot be divided, the tablets are not suitable for patients whose body weight is less than 35 kg.

If you take more [HA403 trade name] than you should

If you have taken too many tablets or if someone accidentally takes some, consult your health care provider or local first aid hospital. Take the tablet container with you.

If you forget to take [HA403 trade name]

Take care not to miss a dose. If you do miss a dose, take the next dose as soon as possible. However, if the next regular dose is due within 12 hours, then simply take your normal next dose at its due time. Do not double the dose to make up for a missed dose.

If you stop taking [HA403 trade name]

Do not stop taking [HA403 trade name] unless you experience serious side effects or your health care provider has told you to. Taking the tablets regularly is very important because the amount of virus may start to increase if the medicine is stopped for even a short time. The infection may then become harder to treat.

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

4. Possible side effects

Like all medicines, [HA403 trade name] can cause side effects, but not everybody gets them. When treating HIV infection, it is not always possible to tell whether some of the unwanted effects are caused by [HA403 trade name] or by other medicines that you are taking at the same time, or by the HIV disease itself.

During treatment for HIV infection, you may experience an increase in weight and in levels of blood lipids and glucose. This is partly linked to an improvement in overall health and lifestyle, and in the case of blood lipids sometimes to the HIV medicines themselves. Your health care provider will test for these changes.

The most notable unwanted effects of efavirenz in combination with other antiretroviral medicines are skin rash and nervous system symptoms that include dizziness, insomnia, somnolence (drowsiness), impaired concentration and abnormal dreaming.

Consult your health care provider if you get a rash, because some rashes may be serious; however, in most cases the rash disappears without the need for any changes to the treatment with efavirenz. Rash is more common in children than in adults treated with efavirenz.

Nervous system side effects usually occur when treatment is first started and usually improve in the first few weeks. If these effects are troublesome, your health care provider may suggest that you take [HA403 trade name] at bedtime and on an empty stomach. Some patients may have more serious side effects that affect mood or the ability to think clearly. Some patients have committed suicide. These effects may occur more frequently in those who have a previous history of mental illness. Tell your health care provider if you have these problems or if you have any other troublesome side effects.

Tell your healthcare provider if you notice any of the following side effects:

Very common (affects more than 1 user in 10)

- rash

Common (affects 1 to 10 users in 100):

- abnormal dreams, difficulty concentrating, dizziness, headache, difficulty sleeping, drowsiness, problems with coordination and maintaining balance
- stomach pain, diarrhoea, feeling sick (nausea), vomiting
- itching
- tiredness
- feeling worried, feeling depressed
- increase in certain liver or pancreatic enzymes
- increase in triglycerides

Uncommon (affects 1 to 10 users in 100):

- nervousness, forgetfulness, confusion, fitting (seizures), abnormal thoughts
- blurred vision
- a feeling of spinning or tilting (vertigo)
- pain in the abdomen (stomach) caused by inflammation of the pancreas
- allergic reaction (hypersensitivity) that may cause severe skin reactions (erythema multiforme, Stevens-Johnson syndrome)
- yellow skin or eyes, itching, or pain in the abdomen (stomach) caused by inflammation of the liver
- breast enlargement in males
- angry behaviour, mood being affected, seeing or hearing things that are not really there (hallucinations), mania (mental condition with episodes of overactivity, elation or irritability), paranoia, suicidal thoughts, catatonia (condition in which the patient is rendered motionless and speechless for a period)
- whistling, ringing or other persistent noise in the ears
- tremor (shaking)
- flushing
- increase in cholesterol

Rare (affects 1 to 10 users in 10,000):

- itchy rash caused by a reaction to sunlight
- liver failure, in some cases leading to death or requiring liver transplantation. Most cases occurred in patients who already had liver disease, but there have been a few reports in patients who did not have liver disease.
- unexplained feelings of distress not associated with hallucinations, but it may be difficult to think clearly or sensibly
- suicide

The following side effect is of unknown frequency:

- encephalopathy (brain disorder which can be severe)

Reporting of side effects

If you get a side effect, talk to your health care provider. This includes side effects not listed in this leaflet. You may also be able to report such effects directly to your national reporting system if one is available. By reporting side effects, you can help to improve the available information on this medicine.

5. How to store [HA403 trade name]

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

Do not store above 30°C. Protect from moisture. Store in the original package.

Do not use this medicine after the expiry date stated on the blister, carton or bottle after “EXP”. The expiry date refers to the last day of that month.

Do not use this medicine if you notice visible signs of deterioration or 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 [HA403 trade name] contains

The active ingredient is efavirenz. Each tablet contains efavirenz 600mg.

The other ingredients of [HA403 trade name] are Croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose and sodium lauryl sulfate, hypromellose, iron oxide red, iron oxide yellow, polyethylene glycol 400 and titanium dioxide.

There is too little sodium in this medicine to have any effect, even if you are on a low-sodium diet.

What [HA403 trade name] looks like and contents of the pack

[HA403 trade name] is peach coloured, capsule shaped film-coated tablets, debossed with “M109” on one side and plain on other side.

White, opaque HDPE bottles fitted with white opaque screw cap with aluminium induction sealing liner: [HA403 trade name] is available in packs of 28 & 30 tablets.

Blue HDPE bottles fitted with blue opaque screw cap with aluminium induction sealing liner: [HA403 trade name] is available in packs of 28 & 30 tablets.

Blister pack comprises of clear transparent PVdC-coated PVC film with backing of aluminium foil coated with heat seal lacquer: [HA403 trade name] is available in packs of 2 × 5 tablets.

Supplier and Manufacturer

Supplier

Mylan Laboratories Limited
Plot No. 564/A/22,
Road No. 92, Jubilee Hills,
Hyderabad – 500096,
Telangana, India.

Email: ProductSafety@viatris.com

Manufacturer

Mylan Laboratories Limited
F-4, F-12, Malegaon M.I.D.C.,
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Maharashtra state, India.
Mylan Laboratories Limited
F-4, F-12, Malegaon M.I.D.C.,

Mylan Laboratories Limited
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Plot No. 11,12 & 13 Indore Special Economic
Zone, Phase – II, Sector – III, Pithampur –
454775, Dist- Dhar, M.P., India.

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

This leaflet was last revised in July 2023

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