

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

[HA466 trade name][†]

Efavirenz/lamivudine/tenofovir disoproxil fumarate

*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 [HA466 trade name] is and what it is used for
2. What you need to know before you take [HA466 trade name]
3. How to take [HA466 trade name]
4. Possible side effects
5. How to store [HA466 trade name]
6. Contents of the pack and other information

1. What [HA466 trade name] is and what it is used for

[HA466 trade name] is a combination of three antiviral medicines used to treat Human Immunodeficiency Virus (HIV) infection in adults and adolescents weighing at least 35 kg. Antiviral medicines used for HIV infection are known as antiretrovirals.

[HA466 trade name] contains the active substances:

- efavirenz, a non-nucleoside reverse transcriptase inhibitor
- lamivudine, a nucleoside reverse transcriptase inhibitor
- tenofovir disoproxil, a nucleotide reverse transcriptase inhibitor

These substances block an enzyme (reverse transcriptase) that is used by HIV for making copies of itself. By doing so, they prevent the reproduction of the virus.

[HA466 trade name] is not a cure for your HIV infection, but if taken correctly it will improve your immune system and reduce the risk of developing illnesses linked to HIV infection.

2. What you need to know before you take [HA466 trade name]

Do not take [HA466 trade name] if:

- you are allergic (hypersensitive) to efavirenz, lamivudine, tenofovir disoproxil or any of the other ingredients of [HA466 trade name] listed at the end of this leaflet (section 6).
- you have severe liver disease

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

- you have a heart condition, such as changes in the rhythm or rate of the heartbeat, a slow heartbeat, or severe heart disease.
- any member of your family (parents, grandparents, brothers or sisters) has died suddenly due to a heart problem or was born with heart problems.
- your health care provider has told you that you have high or low levels of electrolytes such as potassium or magnesium in your blood.
- you are currently taking any of the following medicines:
 - **astemizole** or **terfenadine** (used to treat hay fever or other allergies)
 - **bepriidil** (used to treat heart disease)
 - **cisapride** (used to treat heartburn)
 - **ergot alkaloids**, for example, ergotamine, dihydroergotamine, ergonovine, and methylergonovine (used to treat migraines and cluster headaches)
 - **midazolam** or **triazolam** (used to help you sleep)
 - **pimozide** (used to treat certain mental conditions)
 - **tenofovir alafenamide**
 - **voriconazole** (a drug used against fungal infections)
 - **dasabuvir + ombitasvir/paritaprevir/ritonavir** or **elbasvir/grazoprevir** (combinations of medicines used to treat infection with hepatitis C virus)
 - **St. John's wort** (*Hypericum perforatum*, a herbal remedy used for depression and anxiety).

If this applies to you, tell your health care provider immediately. Taking these medicines with [HA466 trade name] could cause serious or life-threatening side effects or stop these medicines from working properly.

Take special care with [HA466 trade name]:

Talk to your health care provider before taking [HA466 trade name].

You will need to take this medicine every day. It 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.

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 if you:

- **are taking other medicines** that contain efavirenz, lamivudine, tenofovir disoproxil, or emtricitabine, adefovir dipivoxil or tenofovir alafenamide. [HA466 trade name] should not be taken with any of these medicines.
- **have or have had kidney disease**, or if tests have shown problems with your kidneys. This medicine may affect your kidneys. Before starting this medicine, you may need blood tests to check how well your kidneys are working. Blood tests may also be required during treatment to check the health of your kidneys.
- **have 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*).
- **have 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 [HA466 trade name].
- **have a history of liver disease, including chronic active hepatitis.** Patients with liver disease including chronic hepatitis B or C, who are treated with combination antiretrovirals, have a higher risk of severe and potentially life-threatening liver problems. Your healthcare provider may conduct blood tests in order to check how well your liver is working or may switch you to another medicine. If you have severe liver disease, do not take [HA466 trade name].

- **have hepatitis B infection**, your health care provider will carefully consider the best treatment regimen for you. Your health care provider may conduct blood tests to check how well your liver is working. Tenofovir disoproxil and lamivudine, two of the active substances in [HA466 trade name], show some activity against hepatitis B virus. Symptoms of your hepatitis may become worse after discontinuation of [HA466 trade name]. Your healthcare provider may then conduct blood tests at regular intervals in order to check how well your liver is working (see section 3, if you stop taking [HA466 trade name]).
- **are over 65**. Insufficient numbers of patients over 65 years of age have been studied. If you are over 65 years of age and are prescribed [HA466 trade name], your healthcare provider will monitor you carefully.

Once you start taking [HA466 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.** Rashes may be caused [HA466 trade name]. If you see any signs of a severe rash with blistering or fever, stop taking this medicine and tell your health care provider at once. If you had a rash while taking another non-nucleoside reverse transcriptase inhibitor (NNRTI), you may be at higher risk of getting a rash with [HA466 trade name].
- **any signs of inflammation or infection.** In some patients with advanced HIV infection (AIDS) and a history of AIDS-associated (opportunistic) infection, signs and symptoms of inflammation from such previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to 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 at once.

In addition, autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may occur after you start taking medicines for the treatment of your HIV infection. These 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, irregular heartbeats, trembling or shaking, or hyperactivity, please inform your health care provider at once.

- **any signs of 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 duration of antiretroviral therapy, use of a corticosteroid such as dexamethasone or prednisolone, alcohol consumption, severe suppression of the immune system, and being overweight are some of the 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, tell your health care provider.

Bone problems (sometimes resulting in fractures) may also occur due to damage to the kidney cells (see section 4, *Possible side effects*).

The growth of bone could be affected when adolescents that are not fully grown use [HA466 trade name]. If you are an adolescent, your health care provider may check your growth and may take precautionary measures.

Taking other medicines and [HA466 trade name]

You must not take [HA466 trade name] with certain medicines. They include some common medicines and some herbal preparations (including St. John's wort) which can cause serious interactions (see **Do not take [HA466 trade name]**).

Tell your health care provider if you are taking, have recently taken, or might take any other medicines, including medicines obtained without a prescription.

Tell your health care provider if you are taking other medicines that may damage your kidneys. These include:

- aminoglycosides or vancomycin (medicines for bacterial infections)
- amphotericin B or pentamidine (medicines for fungal infections)
- foscarnet, ganciclovir, or cidofovir (medicines for viral infections)
- tacrolimus (for suppression of the immune system)
- interleukin-2 (used to treat cancer)
- non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pains)

[HA466 trade name] may interact with other medicines, including herbal preparations. As a result, the amounts of [HA466 trade name] or other medicines in your blood may be affected. This may stop your 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.

It is important to tell your health care provider if you are taking any of the following:

- **Medicines containing didanosine (for HIV infection):** Taking [HA466 trade name] with medicines that contain didanosine can raise the levels of didanosine in your blood. Rarely, inflammation of the pancreas and lactic acidosis (excess lactic acid in the blood), which sometimes caused death, has been reported when medicines containing tenofovir disoproxil and didanosine were taken together. Your health care provider will carefully consider whether to treat you with medicines containing tenofovir and didanosine.
- Other medicines used for HIV infection: **atazanavir, darunavir, etravirine, indinavir, lopinavir, maraviroc, nevirapine, ritonavir, saquinavir and tipranavir**
- **Boceprevir, daclatasvir, ledipasvir, simeprevir, sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir, and telaprevir**, used to treat infection with the hepatitis C virus
- **Clarithromycin, rifabutin, rifampicin**, used to treat bacterial infections, including tuberculosis and AIDS-related mycobacterium avium complex.
- **Itraconazole or posaconazole** (antifungals), used to treat fungal infections.
- **Atovaquone/proguanil, artemether/lumefantrine, amodiaquine/artesunate, quinine, halofantrine, artemisinins**, used to treat malaria.
- **Atorvastatin, pravastatin, simvastatin** (statins), used to lower blood fats
- **Carbamazepine, phenytoin, phenobarbital** (anticonvulsants), used to treat convulsions/seizures.
- **Hormonal contraceptive, such as birth control pills, an injected contraceptive, or a contraceptive implant:** [HA466 trade name] may make hormonal contraceptives less likely to work. You must, therefore, also use a reliable barrier method of contraception (e.g. condoms), if you are taking this medicine.
- **Methadone, buprenorphine**, used for severe pain or opiate addiction.
- **Sertraline**, used to treat depression.
- **Bupropion**, used to treat depression or to help you stop smoking.
- **Diltiazem, verapamil, felodipine, nifedipine, nicardipine** (calcium channel blockers), used to treat high blood pressure and conditions related to the heart.
- **Tacrolimus, cyclosporine, sirolimus** (immunosuppressants), used to prevent organ transplant rejection.
- **Warfarin or acenocoumarol**, used to reduce clotting of the blood.
- **Ginkgo biloba extracts** (herbal preparation).

Pregnancy and breast-feeding

Tell your health care provider if you are pregnant or trying to become pregnant. Your health care provider can explain the risks and benefits of your therapy to you and your child.

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

Driving and using machines

[HA466 trade name] may cause dizziness, impaired concentration, and drowsiness. If it affects you in this way do not drive, operate machinery or do anything that requires you to be alert.

Important information about some of the ingredients of [HA466 trade name]

[HA466 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.

This medicinal product also contains 1.9 mmol (43 mg) sodium per tablet. To be taken into consideration by patients on a controlled sodium diet.

3. How to take [HA466 trade name]

Always take this medicine exactly as your health care provider has told you. Check with your health care provider if you are not sure.

Always take the dose recommended by your health care provider. Do not change the dose unless your health care provider tells you to.

The recommended dose is:

One tablet taken each day by mouth. [HA466 trade name] should be taken on an empty stomach (1 hour before or 2 hours after a meal). It may help to take the tablet at bedtime, as this can make some side effects (for example, dizziness, drowsiness) less troublesome. The tablet should be taken with water and swallowed whole.

[HA466 trade name] must be taken every day.

[HA466 trade name] should not be used by patients weighing less than 35 kg.

If your health care provider decides to stop, or change the dose of, one of the components of [HA466 trade name], you may be given efavirenz, lamivudine and/or tenofovir separately or with other medicines for the treatment of HIV infection.

If you take more [HA466 trade name] than you should:

If you accidentally take too many [HA466 trade name], you may be at increased risk of experiencing possible side effects with this medicine (see section 4, *Possible side effects*). Contact your health care provider or the nearest emergency department for advice. Take the tablet container with you so that you can easily describe what you have taken.

If you forget to take [HA466 trade name]:

It is important not to miss a dose.

If you do miss a dose within 12 hours of when it is usually taken, take it as soon as you can, and then take your next dose at its regular time.

If it is almost time (less than 12 hours) for your next dose anyway, do not take the missed dose. Wait and take the next dose at the regular time. Do not take a double dose to make up for a forgotten tablet.

If you throw up within 1 hour of taking [HA466 trade name], you should take another tablet. Do not wait until your next dose is due. You do not need to take another tablet if you threw up more than an hour after taking [HA466 trade name].

If you stop taking [HA466 trade name]:

Don't stop taking this medicine without talking to your health care provider. Stopping this medicine can seriously affect your response to future treatment. If [HA466 trade name] is stopped, speak to your health care provider before you restart taking these tablets. Your health care provider may consider giving you the components of [HA466 trade name] separately if you are having problems or need your dose adjusted.

When your supply of [HA466 trade name] starts to run low, get more from your health care provider. This is very important because the amount of virus may start to increase if the medicine is stopped for even a short time. The virus may then become harder to treat.

If you have both HIV infection and hepatitis B, it is especially important not to stop your [HA466 trade name] treatment without talking to your health care provider first. Some patients have had blood tests or symptoms indicating that their hepatitis got worse after stopping treatment. Your health care provider may recommend that you resume hepatitis B treatment if you stop [HA466 trade name] treatment. You may require blood tests to check how your liver is working for 4 months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment is not recommended as this may lead to worsening of your hepatitis, which may be life-threatening.

Tell your health care provider immediately about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection.

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

4. Possible side effects

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 health care provider will test for these changes.

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Possible serious side effects:

Lactic acidosis (excess lactic acid in the blood) is a **rare**, but serious side effect that can be life-threatening. If you get any of the following symptoms, **tell your health care provider immediately**:

- deep rapid breathing
- drowsiness
- feeling sick (nausea), being sick (vomiting) and stomach pain.

Other potentially serious side effects:

If you think that you may have any of these serious side effects, talk to your health care provider.

The following side effects are **uncommon** (these may affect up to 1 in every 100 patients):

- allergic reaction (hypersensitivity) that may cause severe skin reactions (Stevens-Johnson syndrome, erythema multiforme, see section 2)
- swelling of the face, lips, tongue or throat
- angry behaviour, suicidal thoughts, strange thoughts, paranoia, unable to think clearly, mood being affected, seeing or hearing things that are not really there (hallucinations), suicide attempts, personality change (psychosis)
- pain in the abdomen (stomach), caused by inflammation of the pancreas
- forgetfulness, confusion, fitting (seizures), incoherent speech, tremor (shaking)
- yellow skin or eyes, itching, or pain in the abdomen (stomach) caused by inflammation of the liver
- damage to kidney tubules

Psychiatric side effects in addition to those listed above include delusions (false beliefs), neurosis. Some patients have committed suicide. These problems tend to occur more often in those who have a history of mental illness. Always notify your health care provider immediately if you have these symptoms.

Side effects to the liver: If you are also infected with hepatitis B virus, you may experience a worsening of hepatitis after stopping treatment (see section 3 *How to take* [HA466 trade name]).

The following side effects are **rare** (these may affect up to 1 in every 1000 patients):

- back pain caused by kidney problems, including kidney failure. Your health care provider may do blood tests to see if your kidneys are working properly.
- inflammation of the kidney, passing a lot of urine and feeling thirsty, damage to kidney tubule cells
- fatty liver
- liver failure, in some cases leading to death or liver transplant. Most cases occurred in patients who already had liver disease, but there have been a few reports in patients without any existing liver disease.
- softening of the bones (with bone pain and sometimes resulting in fractures)

The following side effect is of unknown frequency:

- encephalopathy (brain disorder which can be severe)

If you think that you may have any of these serious side effects, talk to your health care provider.

Most frequent side effects

The following side effects are **very common** (these may affect more than 1 user in every 10 patients):

- dizziness, diarrhoea, feeling sick (nausea), being sick (vomiting)
- rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions
- feeling weak

Tests may also show:

- decreases in phosphate levels in the blood

Other possible side effects

The following side effects are **common** (these may affect up to 1 user in every 10):

- stomach pain
- difficulty sleeping, abnormal dreams, difficulty concentrating, drowsiness
- feeling worried or depressed
- problems with digestion resulting in discomfort after meals, feeling bloated, wind (flatulence)
- loss of appetite
- tiredness
- itching
- hair loss
- disturbances of coordination and balance
- headache
- cough
- irritated or runny nose
- fever (high temperature)
- general feeling of being unwell

Tests may also show:

- increased fatty acids (triglycerides) or sugar levels in the blood
- liver and pancreas problems

The following side effects are **uncommon** (these may affect up to 1 user in every 100 patients):

- blurred vision
- a feeling of spinning or tilting (vertigo), whistling, ringing or other persistent noise in the ears
- flushing
- breast enlargement in males
- breakdown of muscle, muscle pain or weakness

Tests may also show:

- low white blood cell count that help defend against infections and low red blood cell count (anaemia)
- low red blood cell count (thrombocytes) that help to stop bleeding
- increased cholesterol in the blood
- decreases in potassium in the blood
- increases in creatinine in the blood
- proteins in urine

The breakdown of muscle, softening of the bones (with bone pain and sometimes resulting in fractures), muscle pain, muscle weakness and decreases in potassium or phosphate in the blood may occur due to damage to kidney tubule cells.

The following side effects are **rare** (these may affect up to 1 in every 1,000 patients)

- itchy rash to the skin caused by a reaction to sunlight

The following side effects are **very rare** (these may affect up to 1 user in every 10,000 patients)

- a failure of the bone marrow to produce new red blood cells (pure red cell aplasia)
- tingling or numbness of the arms, legs, hands or feet

If you get any side effects, talk to your health care provider. This includes any possible side effects not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

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 [HA466 trade name]

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

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

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 [HA466 trade name] contains

- The active ingredients are 600 mg efavirenz, 300 mg lamivudine, 300 mg tenofovir disoproxil fumarate (equivalent to tenofovir disoproxil 245 mg or tenofovir 136 mg).
- The other ingredients of [HA466 trade name] are croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, sodium chloride and sodium lauryl sulphate, polyethylene glycol 3350, polyvinyl alcohol (partially hydrolysed), talc and titanium dioxide.

What [HA466 trade name] looks like and contents of the pack

[HA466 trade name] are white coloured, capsule shaped, film-coated tablets debossed with “M 152” on one side and plain on other side, available in:

Round, white opaque, induction-sealed 100mL HDPE bottle fitted with 38mm white polypropylene screw cap and containing molecular sieve canister 2 gm (CAN TRISORB 2G) or molecular sieve sachet 2 gm as desiccant. Pack size: 30 tablets.

Round, blue opaque, induction-sealed 100mL HDPE bottle fitted with 38mm blue polypropylene screw cap and containing molecular sieve canister 2 gm (CAN TRISORB 2G) or molecular sieve sachet 2 gm as desiccant. Pack size: 30 tablets.

Round, white opaque, induction-sealed 250mL HDPE bottle fitted with white opaque polypropylene cap and containing molecular sieve canister 2 gm as desiccant. Pack size: 90 tablets.

Round, blue opaque, induction-sealed 250mL HDPE bottle fitted with blue opaque polypropylene cap and containing molecular sieve canister 2 gm as desiccant. Pack size: 90 tablets.

The tablets should not be divided.

Supplier and Manufacturer

Supplier

Mylan Laboratories Limited
Plot No. 564/A/22, Road No.92, Jubilee Hills
Hyderabad - 500096, Telangana, India
Email: Imtiyaz.Basade@viatris.com

Manufacturer

Mylan Laboratories Limited
F-4, F-12, Malegaon M.I.D.C,
Sinnar, Nashik – 422113,
Maharashtra state, India

Mylan Laboratories Limited
H-12 & H-13, M.I.D.C, Waluj
Aurangabad,– 431136
Maharashtra state, India

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

For any information about this medicine, contact the supplier.

This leaflet was last revised in March 2023

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