

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 (term to be revised).
The medicine may be authorised for additional or different uses by national medicines regulatory authorities.*

Information for the patient

[HA414 trade name]¹
lamivudine/tenofovir disoproxil fumarate

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 get 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 [HA414 trade name] is and what it is used for
2. What you need to know before you take [HA414 trade name]
3. How to take [HA414 trade name]
4. Possible side effects
5. How to store [HA414 trade name]
6. Contents of the pack and other information

1. What [HA414 trade name] is and what it is used for

[HA414 trade name] is used to treat HIV (human immunodeficiency virus) infection in adults, adolescents and children weighing at least 30 kg.

[HA414 trade name] is also used to reduce the risk of getting HIV-1 infection in adults and adolescents (weighing at least 35 kg) who are not HIV infected (i.e. HIV-negative) but are at high risk of getting infected with HIV. This is called pre-exposure prophylaxis (PrEP). It should be used in combination with safer sex practices (see section 2).

[HA414 trade name] contains two active substances, lamivudine and tenofovir disoproxil. Both are antiviral medicines. Lamivudine is a nucleoside reverse transcriptase inhibitor and tenofovir is a nucleotide reverse transcriptase inhibitor. Both active substances interfere with enzymes used by HIV for making copies of itself and thereby block the reproduction of the virus.

Antiviral medicines used for HIV infection are known as antiretrovirals. To prevent the virus become resistant, this medicine should always be given as part of antiretroviral combination therapy when treating HIV

This medicine is not a cure for HIV infection. While taking [HA414 trade name] you may still develop infections or other illnesses associated with HIV infection. You can also pass on HIV to others through sexual contact or blood contamination, so it is important to take precautions to avoid infecting other people.

¹Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

2. What you need to know before you take [HA414 trade name]

Do not take [HA414 trade name] if you

- are allergic (hypersensitive) to lamivudine or any of the other ingredients of [HA414 trade name] (see “What [HA414 trade name] contains”).

Do not take [HA414 trade name] for pre-exposure prophylaxis:

- if you already have HIV-1 infection or suspect that you might have been infected with HIV- 1 infection recently. You must be HIV-negative before you start taking [HA414 trade name] to reduce the risk of getting HIV-1. You must get tested to make sure that you do not already have HIV-1 infection. Do not take [HA414 trade name] to reduce the risk of getting HIV-1 unless you are confirmed to be HIV-negative.

If you have flu-like symptoms, you could have recently become infected with HIV-1 and you must talk to your health care provider.

Warnings and precautions

Preventive measures to reduce risk of getting HIV infection (pre-exposure prophylaxis)

[HA414 trade name] does not protect you fully against HIV infection and does not protect you from other sexually transmitted diseases. Among safe sex practice always using condoms in the correct way, male or female, is critical for reducing the risk of getting HIV-1 infection. You should be tested for other sexually transmitted infections. Other infections make it easier for HIV- 1 to infect you. Get information and support on safer sex practice.

You should not miss any doses of [HA414 trade name]. Missing doses may increase your risk of getting HIV-1 infection.

You must stay HIV-negative to keep taking [HA414 trade name] to reduce your risk of getting HIV-1. Knowing your and your partner’s HIV-1 status and regular testing for HIV-1 infection is important. Tell your health care provider if you had a flu-like illness at any time while taking this medicine. Symptoms of new HIV-1 infection include tiredness, fever, joint or muscle aches, headache, sore throat, vomiting, diarrhoea, rash, night sweats, or enlarged lymph nodes in the neck or groin. If you think you have been exposed to HIV, you should tell your health care provider right away. If you get HIV-1 infection, you may need more medicines than [HA414 trade name].

Kidney disease

Tell your health care provider if you have had kidney disease or if tests have shown problems with your kidneys. [HA414 trade name] may affect your kidneys. Before starting [HA414 trade name] you may need blood tests to check how well your kidneys are working. The tests can help to decide how you should take your medicine. Blood tests may also be required during treatment to check the health of your kidneys. [HA414 trade name] is not usually taken with other medicines that can damage your kidneys (see “Other medicines and [HA414 trade name]”). If this is unavoidable, you may need regular tests to check how well your kidneys are working.

Liver disease

Talk to your health care provider if you have had liver disease, including hepatitis. HIV-infected patients with liver disease, including chronic hepatitis B or C, who are treated with antiretrovirals, have a higher risk of severe and potentially fatal liver complications. If you are infected with HIV and hepatitis B virus, your health care provider will carefully consider the best treatment for you. If you have a history of liver disease or chronic hepatitis B infection your health care provider may conduct blood tests to monitor your liver function.

Other precautions

Talk to your health care provider if you are seriously **overweight** (especially if you are a woman).

Look out for infections. If you have advanced HIV infection (AIDS), you may develop symptoms of infection and inflammation or worsening of the symptoms of an existing, so called opportunistic infection once treatment with [HA414 trade name] is started. These symptoms may indicate that your body's improved immune system is fighting infection. Look out for signs of inflammation or infection soon after you start taking [HA414 trade name]. If you notice signs of inflammation or infection, tell your health care provider at once.

In addition to 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 so that the necessary treatment can be started promptly.

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, being overweight 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 tell your health care provider.

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

Protect other people

HIV infection is spread by sexual contact with someone who has the infection, or by transfer of infected blood (for example, by sharing injection needles). You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your health care provider the precautions needed to avoid infecting other people.

Other medicines and [HA414 trade name]

Tell your health care provider if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. These may affect the action of [HA414 trade name], or [HA414 trade name] may affect their action.

Do not take [HA414 trade name] if you are already taking other medicines containing tenofovir disoproxil, tenofovir alafenamide or lamivudine (used to treat HIV infection or hepatitis B infection). Do not take [HA414 trade name] together with medicines containing adefovir dipivoxil (a medicine used to treat chronic hepatitis B).

These medicines should not be used with [HA414 trade name]:

- emtricitabine (used to treat HIV infection)
- high doses of co-trimoxazole, an antibiotic
- cladribine (used to treat hairy cell leukaemia)
- medicines (usually liquids) containing sorbitol and other sugar alcohols (such as xylitol, mannitol, lactitol or maltitol), if taken regularly

It is very important to tell your health care provider if you are taking other medicines that may damage your kidneys. These include:

- aminoglycosides (such as gentamicin or tobramycin) or vancomycin (for bacterial infections)
- amphotericin B or pentamidine (for fungal infection)
- foscarnet, ganciclovir, or cidofovir (for viral infection)
- tacrolimus (for suppression of the immune system)
- interleukin-2 (e.g. aldesleukin to treat cancer)
- adefovir dipivoxil (for hepatitis B)
- non-steroidal anti-inflammatory drugs (NSAIDs, for pain relief).

Medicines containing didanosine (for HIV infection): Taking [HA414 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 can cause death, have been reported when medicines containing tenofovir disoproxil and didanosine were taken together.

Combining tenofovir with didanosine can also reduce the effects of antiretroviral therapy. Your health care provider will carefully consider whether to treat you with a combination of tenofovir and didanosine.

It is also important to tell your health care provider if you are taking ledipasvir/sofosbuvir, sofosbuvir/velpatasvir or sofosbuvir/velpatasvir/voxilaprevir to treat hepatitis C infection.

Taking [HA414 trade name] with food and drink

You can take [HA414 trade name] with food or between meals.

Pregnancy and breast-feeding

Ask your health care provider for advice before taking any medicine. Be sure to tell your health care provider immediately if you are or may be pregnant.

In babies born to mothers who have taken antiretroviral medicines comprising nucleoside and nucleotide analogues, the benefit of reduced risk of becoming infected with HIV outweighs the risk of side effects of these medicines.

If you want to breast-feed your baby, you should discuss the risks and benefits with your health care provider.

Driving and using machines

[HA414 trade name] can cause dizziness. If you feel dizzy while taking [HA414 trade name], do not drive or ride a bicycle and do not use hazardous tools or machines.

Excipients

This product contains lactose. If you have any intolerance or allergies to some sugars such as lactose, contact your healthcare provider before taking this medicine.

3. How to take [HA414 trade name]

Always take [HA414 trade name] exactly as your health care provider has told you. This is to make sure that your medicine works well, and to reduce the risk of developing resistance to the treatment. You should 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 usual dose for adults and adolescents is one tablet each day.

You can take [HA414 trade name] with food or between meals. Swallow [HA414 trade name] whole with water or another liquid.

For young children or patients not able to swallow the tablets whole, the tablets may be crushed and added to a small amount of semi-solid food or liquid, all of which should be swallowed immediately.

When used for HIV-treatment:

For children weighing less than 30 kg, appropriate dose adjustments cannot be made and other formulations should be used.

When used for reducing the risk of getting HIV-1 infection:

This medicine is not for use by adolescents weighing less than 35 kg.

If you have problems with your kidneys, your health care provider may advise you to take [HA414 trade name] less frequently.

If you take more [HA414 trade name] than you should:

If you accidentally take too many tablets of [HA414 trade name], contact your health care provider or 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 [HA414 trade name]:

It is important not to miss a dose of [HA414 trade name].

If it is less than 12 hours after it is usually taken, take it as soon as you can, and then take your next dose at its regular time.

If it is more than 12 hours since you should have taken it, forget about 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 vomit less than 1 hour after taking [HA414 trade name], take another tablet. You do not need to take another tablet if you were sick more than 1 hour after taking [HA414 trade name].

If you stop taking [HA414 trade name]:

Don't stop taking [HA414 trade name] without your health care provider's advice. Stopping [HA414 trade name] may reduce the effectiveness of the treatment. Talk to your health care provider before you stop taking [HA414 trade name] for any reason, particularly if you are experiencing any side effects, have another illness, or if you think you are no longer at risk of getting infected with HIV. Contact your health care provider before you restart taking [HA414 trade name].

If you have HIV and hepatitis B together (co-infection), it is very important not to stop taking [HA414 trade name] without talking to your health care provider first. Some patients have had blood tests or symptoms indicating that their hepatitis has got worse after stopping [HA414 trade name]. You may require blood tests for several months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment with [HA414 trade name] is not recommended as this may lead to worsening of hepatitis.

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, [HA414 trade name] can cause side effects, although not everybody gets them.

• **Lactic acidosis** (excess lactic acid in the blood) is a **rare** (affects up to 1 in 1000 patients treated) but serious side effect that can be fatal. The following may be signs of lactic acidosis:

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

If you think you may have lactic acidosis, tell your health care provider immediately

• **Any signs of inflammation or infection.** In some patients with advanced HIV infection (AIDS) and a history of opportunistic infections (infections that occur in people with a weak immune system), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is thought 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.

• **Autoimmune disorders**, when the immune system attacks healthy body tissue, may also occur after you start taking medicines to treat HIV infection. Autoimmune disorders may occur many months after the start of treatment. Look out for 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

If you notice these or any symptoms of inflammation or infection, tell your health care provider immediately

Some side effects may be serious. Tell your health care provider if you get any of the following:

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

- diarrhoea, being sick (vomiting), feeling sick (nausea)
- dizziness
- rash
- feeling weak

Tests may also show:

- decreases in phosphate in the blood

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

- pain, stomach pain
- feeling bloated, flatulence
- headache
- difficulty sleeping,
- rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions, itching, changes in skin colour including darkening of the skin in patches
- other allergic reactions, such as wheezing, swelling or feeling light-headed
- hair loss

Tests may also show:

- liver problems

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

- pain in the abdomen (tummy) caused by inflammation of the pancreas
- anaemia (low red blood cell count)
- breakdown of muscle, muscle pain or weakness which may occur due to damage to the kidney tubule cells

Tests may also show:

- decreases in potassium in the blood
- increased creatinine in your blood

- increase in liver enzymes
- pancreas problems
- decrease in the number of cells involved in blood clotting

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

- Lactic acidosis
- fatty liver
- yellow skin or eyes, itching, or pain in the abdomen (tummy) caused by inflammation of the liver
- inflammation of the kidney, passing a lot of urine and feeling thirsty, kidney failure, damage to kidney tubule cells
- softening of the bones (with bone pain and sometimes resulting in fractures)
- back pain caused by kidney problems. Damage to kidney tubule cells may be associated with 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.

Very rare side effects (may affect up to 1 in 10,000 people)

- shortness of breath
- nerve injury causing weakness and sensations of tingling, pricking, or numbness of the skin, especially in the feet and hands (peripheral neuropathy)

Tests may also show:

- damage to kidney tubule cells

The frequency of the following side effects is not known.

Bone problems. Some patients taking combination antiretroviral medicines such as [HA414 trade name] may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). Taking this type of medicine for a long time, taking corticosteroids, drinking alcohol, having a very weak immune system, and being overweight, may be some of the many risk factors for developing this disease. Signs of osteonecrosis are:

- joint stiffness
- joint aches and pains (especially of the hip, knee and shoulder)
- difficulty with movement

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your health care provider.

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 provide more information on the safety of this medicine.

5. How to store [HA414 trade name]

Keep out of the reach and sight of children.

Do not use [HA414 trade name] after the expiry date which is stated on the bottle and carton after {EXP}. The expiry date refers to the last day of that month.

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

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

6. Contents of the pack and other information

What [HA414 trade name] contains

- The active ingredients are lamivudine 300 mg and tenofovir disoproxil fumarate 300 mg (equivalent to tenofovir disoproxil 245 mg or tenofovir 136 mg).
- The other ingredients are:
- Core tablet: croscarmellose sodium, lactose monohydrate, magnesium stearate and microcrystalline cellulose.
- Film coat: hypromellose, propylene glycol and titanium dioxide.

What [HA414 trade name] looks like and contents of the pack

White to off white coloured, oval shaped, biconvex, film-coated tablets debossed "M112" on one side and plain on the other side packaged in:

60cc white round HDPE bottle fitted with 33mm white polypropylene screw cap closure with SG-75M liner and containing a molecular sieve desiccant. Pack size: 30 tablets.

250cc white round HDPE bottle fitted with 53mm white polypropylene screw cap with Selig M1 liner and containing molecular sieve desiccant and rayon. Pack size: 100 tablets.

60cc blue HDPE opaque bottle fitted with 33mm blue opaque polypropylene screw cap with SG-100 liner and containing a molecular sieve desiccant. Pack size: 30 tablets.

Supplier

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For any information about this medicinal product, please contact the supplier.

This leaflet was last revised in November 2019. Section 6 updated in May 2021.

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