

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/prequal/sites/default/files/document_files/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[HA414 trade name][†]

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 [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 and adolescents weighing at least 30 kg. It should always be used in combination with another medicine to treat HIV infection.

[HA414 trade name] is also used for reducing the risk of getting HIV infection in adults and adolescents weighing more than 30 kg who are at high risk of getting infected with HIV. This is called pre-exposure prophylaxis (PrEP). When taking [HA414 trade name] for PrEP, you should do so in combination with safer sex practices (see section 2)

[HA414 trade name] is also used for reducing the risk of getting HIV infection in adults and adolescents weighing more than 30 kg who have been exposed to HIV, for example, after having sexual contact with someone who has the infection. This is called post-exposure prophylaxis (PEP). For PEP, you should preferably also take another HIV medicine.

[HA414 trade name] is also used for chronic hepatitis B, an infection with hepatitis B virus (HBV), in adults and adolescents aged over 12 years and weighing more than 30 kg. You do not have to have HIV infection to be treated with [HA414 trade name] for chronic hepatitis B, although the medicine can be used as part of combination treatment in patients with both infections.

[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 are generally known as NRTIs and they work by interfering with the normal

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

working of enzymes (in HIV, reverse transcriptase; in hepatitis B, DNA polymerase) that are essential for the viruses to reproduce themselves.

This medicine is not a cure for HIV infection but it reduces the amount of virus in your body and keeps it at a low level so it cannot be passed on. Reducing the amount of virus helps to increase the number of white blood cells, called CD4 cells, that are important for fighting infection.

[HA414 trade name] does not work equally well in everybody. Your health care provider will check how well your treatment is working.

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 [HA414 trade name]

Do not take [HA414 trade name]

- **Do not take this medicine if you are allergic** (hypersensitive) to lamivudine, tenofovir, tenofovir disoproxil or any of the ingredients of [HA414 trade name] listed at the end of this leaflet.
- **Do not take this medicine for pre-exposure prophylaxis (PrEP) to reduce the risk of getting HIV if you have not been tested for HIV infection.** You must get tested to make sure that you do not already have HIV infection. Do not take [HA414 trade name] for PrEP unless you are confirmed to be HIV negative.

People who do have HIV must take [HA414 trade name] in combination with other medicines.

Many HIV tests can miss a recent infection. If you get a flu-like illness, it could mean you have recently been infected with HIV. These may be signs of HIV infection:

- tiredness
- fever
- joint or muscle aches
- headache
- vomiting or diarrhoea
- rash
- night sweats
- enlarged lymph nodes in the neck or groin

Tell your health care provider about any flu-like illness – either in the month before you start taking [HA414 trade name] or at any time while taking [HA414 trade name].

Warnings and precautions

While taking [HA414 trade name] for pre-exposure prophylaxis (PrEP):

- Do not miss any doses of [HA414 trade name] or stop taking it. Missing doses may increase your risk of getting HIV infection.
- Get tested for HIV regularly.
- If you think you were infected with HIV, tell your health care provider straight away. More tests may be necessary to make sure you are still HIV negative.
- **Just taking [HA414 trade name] for PrEP may not stop you getting HIV. You should also:**
 - always practise safer sex. Use condoms to reduce contact with semen, vaginal fluids or blood.
 - not share personal items that can have blood or body fluids on them, such as razor blades.
 - not share or re-use needles or other injection or drug equipment.
 - get tested for other sexually transmitted infections such as syphilis and gonorrhoea. These infections make it easier for HIV to infect you.

Ask your health care provider if you have any more questions about how to prevent getting HIV or spreading HIV to other people.

While taking [HA414 trade name] to treat HIV, for pre-exposure prophylaxis (PrEP) or treat chronic hepatitis B:

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. Symptoms of hepatitis B can flare up during treatment or for a time after stopping treatment with [HA414 trade name], and your health care provider may carry out regular tests of your liver function.

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.

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*).

Other medicines and [HA414 trade name]

Tell your health care provider if you are taking, have recently taken or are planning to take any other medicines. This includes medicines that you buy without a prescription and herbal medicines.

Some medicines can affect how [HA414 trade name] works or increase side effects. [HA414 trade name] can also affect how some other medicines work.

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

- 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

Other HIV medicines

Tell your health care provider before you start this medicine if you are already taking any medicines for HIV.

[HA414 trade name] contains a combination of medicines to treat HIV. Your health care provider will discuss your HIV treatment with you when prescribing this medicine. You may not need other medicines for HIV when you take [HA414 trade name], or doses may need to be adjusted to reduce the risk of side effects or ensure treatment works properly.

Medicines for hepatitis B or C

Some medicines for hepatitis B or C may contain similar active ingredients to [HA414 trade name]. Others may increase the risk of side effects or your treatment may not work properly. Make sure you tell your health care provider about any medicines you are taking for hepatitis B or C.

Medicines that affect your kidneys

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

- aminoglycosides, pentamidine or vancomycin (for bacterial infection)
- amphotericin B (for fungal infection)
- foscarnet, ganciclovir, or cidofovir (for viral infection)
- adefovir dipivoxil (for hepatitis B virus infection)
- tacrolimus (for suppression of the immune system)
- interleukin-2 (to treat cancer)
- non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pains) such as aspirin and ibuprofen.

If you are taking any of these, your health care provider may adjust your dose or arrange extra check-ups.

Taking [HA414 trade name] with food and drink

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

Children and adolescents

[HA414 trade name] is not for use in children and adolescents weighing less than 30 kg.

Pregnancy and breast-feeding

Pregnancy

[HA414 trade name] can be used during pregnancy. If you are pregnant or think you might be pregnant, talk to your health care provider to make sure you get the most suitable treatment for you and your baby.

Breast-feeding

Although the active substances of [HA414 trade name] pass into breast milk, [HA414 trade name] may be used during breast-feeding.

Fertility

There is limited information on the effects of [HA414 trade name] on fertility in humans, but animal studies do not show harmful effects.

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

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 medicine may contain traces of cow's milk proteins. If you are allergic to cow's milk, talk to your health care provider before taking this medicine.

Lactose is a source of glucose. If you have diabetes, you should take account of the amount of lactose in this medicine (168 mg in each tablet).

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.

When taking [HA414 trade name] for treating HIV infection

For treating HIV infection, you should take 1 tablet each day.

When taking [HA414 trade name] for pre-exposure prophylaxis (PrEP)

There are two ways to take [HA414 trade name] for pre-exposure prophylaxis: continuously once a day (daily PrEP) or for short periods during times of high risk (event-driven PrEP). Your health care provider will advise you on which is the most suitable way for you to take the medicine.

- **For daily PrEP**, you should take one tablet each day starting 7 days before possible exposure to HIV. When intending to stop daily PrEP, continue taking one tablet each day for 7 days after your last possible exposure to HIV.
- **For event-driven PrEP**, you should take two tablets 2 to 24 hours before potential exposure to HIV and then continue with one tablet once a day until two days after the last potential exposure.

Event-driven PrEP is only for men who are not taking oestrogen-based hormone treatments. If you are a transwoman or gender diverse person who was assigned male at birth and are taking oestrogen-based hormonal treatments, you should not use [HA414 trade name] for event-driven PrEP.

When taking [HA414 trade name] for post-exposure prophylaxis (PEP)

For post-exposure prophylaxis, you should take one tablet each day for 28 days. You should start as early as possible after a potential exposure to HIV and ideally within 72 hours.

When taking [HA414 trade name] for treating chronic hepatitis B

For treating chronic hepatitis B infection, you should take 1 tablet each day.

If you have hepatitis B your health care provider may offer you an HIV test to see if you have both hepatitis B and HIV. If you have both hepatitis B and HIV infection, you will also need to take another HIV medicine along with [HA414 trade name].

How to take [HA414 trade name]

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

Swallow [HA414 trade name] whole with water or another liquid. If you are not able to swallow 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.

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].

Do not stop taking [HA414 trade name]:

- Do not stop taking [HA414 trade name] without your health care provider's advice, including when you are experiencing any side effects or have another illness. You should also contact your health care provider before you restart taking [HA414 trade name].
- If you have HIV infection stopping [HA414 trade name] may reduce the effectiveness of the treatment.
- If you are taking [HA414 trade name] for daily pre-exposure prophylaxis (PrEP), stopping your daily PrEP or missing doses may increase your risk of getting HIV infection. If you think you no longer need daily PrEP, speak to your health care provider.
- If you are taking [HA414 trade name] for event-driven PrEP, do not stop until two days after your last possible exposure to HIV. Not completing event-driven PrEP could increase your risk of getting HIV infection.
- If you are taking [HA414 trade name] for post-exposure prophylaxis (PEP), do not stop taking it until you have finished the 28-day course.
- 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 lifestyle, 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.

Serious but rare side effects

• **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

• **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. Signs to look out for include;

- swelling
- pain in different parts of the body
- fever or chills

• **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

Other side effects you should tell your health care provider about:

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)

- joint 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)

- 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 (see Serious side effects, above)

- Severe pain in the belly (abdomen) caused by inflammation of the pancreas
- 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
- swelling under the skin or in the throat (angioedema)
- weakening 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)
- inability of bone marrow to make enough red blood cells (red cell aplasia)

Tests may also show:

- damage to kidney tubule cells

Side effects whose frequency 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 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 [HA414 trade name]

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

Do not use this medicine after the expiry date stated on the bottle after expiry date. 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.

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 [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 ingredient(s) of [HA414 trade name] are excipients: Core tablet: croscarmellose sodium, lactose monohydrate, magnesium stearate and microcrystalline cellulose and Film coat: hypromellose, propylene glycol 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 [HA414 trade name] looks like and contents of the pack

[HA414 trade name] is a white to off white, oval, film-coated tablets. They are biconvex (rounded on top and bottom) with a flat edge. The tablets have 'M112' debossed (stamped into) one side and plain on the other side.

[HA414 trade name] is packaged as follows:

- Round, white or blue, plastic (HDPE) bottle containing 30 tablets. It also contains a sachet of desiccant (molecular sieve drying material). The bottle has a white or blue, childproof plastic (polypropylene) screw cap. Or
- Round, white, plastic (HDPE) bottle containing 100 tablets. It also contains a sachet of desiccant (molecular sieve drying material). The bottle has a white, childproof plastic (polypropylene) screw cap.

Supplier and Manufacturer

Supplier

Mylan Laboratories Limited
Plot No. 564/A/22,
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Hyderabad – 500096
Telangana,
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Manufacturer

‡Mylan Laboratories Limited
Plot: F-4, F-12, Malegaon MIDC,
Sinnar, Nashik District – 422 113,
Maharashtra State,
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Mylan Laboratories Limited
Plot No. H-12 & H-13,
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Chhatrapati Sambhajnagar– 431136
Maharashtra,
India

Mylan Laboratories Limited
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 September 2024

*Detailed information on this medicine is available on the World Health Organization (WHO) website:
<https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products>*

‡ Formerly known as Matrix Laboratories Limited at time of prequalification