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

[HA417 trade name][†]
Emtricitabine/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 [HA417 trade name] is and what it is used for

HIV infection

[HA417 trade name] is used to treat human immunodeficiency virus (HIV) infection in adults and adolescents weighing more than 30 kg. For HIV treatment, you should always take [HA417 trade name] with another HIV medicine to stop the virus from becoming resistant to treatment.

[HA417 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 [HA417 trade name] for PrEP, you should do so in combination with safer sex practices (see section 2).

[HA417 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.

Hepatitis B

[HA417 trade name] can also be used to treat chronic hepatitis B (an infection with the hepatitis B virus, HBV) in adults and children from 12 years of age, if a medicine containing only tenofovir disoproxil (one of the active substances in this medicine) is not available.

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

[HA417 trade name] contains the active substances emtricitabine and tenofovir disoproxil. Emtricitabine is a nucleoside reverse transcriptase inhibitor, while tenofovir disoproxil is a nucleotide reverse transcriptase inhibitor. Both are generally known as NRTIs and they work by interfering with the normal working of an enzyme (reverse transcriptase) that is essential for HIV to reproduce itself.

They also interfere with the action of an enzyme produced by the hepatitis B virus called DNA polymerase, which the virus uses to make its DNA.

2. What you need to know before you take [HA417 trade name]

Do not take [HA417 trade name]

- **Do not take this medicine if you are allergic** (hypersensitive) to emtricitabine, tenofovir, tenofovir disoproxil or any of the ingredients of [HA417 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 be HIV negative before you start to take [HA417 trade name] for PrEP You must get tested to make sure that you do not already have HIV infection. Do not take [HA417 trade name] for PrEP unless you are confirmed to be HIV negative.
  People who do have HIV must take [HA417 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 [HA417 trade name] or at any time while taking [HA417 trade name].

Warnings and precautions

While taking [HA417 trade name] for HIV pre-exposure prophylaxis (PrEP):

- Do not miss any doses of [HA417 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 [HA417 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 [HA417 trade name] to treat HIV, hepatitis B or for pre-exposure prophylaxis (PrEP):

- **[HA417 trade name] may affect your kidneys**. Before and during treatment, your health care provider may order blood tests to measure your kidney function. Tell your health care provider if you have had kidney disease or if tests have shown kidney problems. If you have kidney problems, your health care provider may advise you to stop taking [HA417 trade name] for prevention or, if you have HIV or hepatitis B, to take [HA417 trade name] less frequently. [HA417 trade name] is not recommended if you have severe kidney disease or are on dialysis.
- **Bone problems** (manifesting as persistent or worsening bone pain and sometimes resulting in fractures) may also occur due to damage to the kidneys (see section 4, Possible side effects). Tell your health care provider if you have bone pain or fractures.
  Tenofovir disoproxil may also cause loss of bone mass. The most bone loss was seen in studies when patients were treated with tenofovir disoproxil in combination with a boosted protease inhibitor (a class of medicine for HIV).
  Tell your health care provider if you know you suffer from osteoporosis (a disease in which bones are fragile). Patients with osteoporosis are at a higher risk of fractures.
- **Talk to your health care provider if you have or have ever had liver disease, including hepatitis.** Patients infected with HIV who also have liver disease (including chronic hepatitis B or C) and are being treated with antiretrovirals have a higher risk of severe and potentially fatal liver complications. If you also have hepatitis B or C, your health care provider will carefully consider the best treatment regimen for you.
- **Talk to your health care provider if you have hepatitis B virus (HBV) infection status**. If you have hepatitis B virus infection, there is a serious risk of liver problems when you stop taking [HA417 trade name], whether or not you also have HIV. It is important not to stop taking [HA417 trade name] without talking to your health care provider (see section 3 'Do not stop taking [HA417 trade name]').
- **Talk to your health care provider if you are over 65.** Emtricitabine/tenofovir disoproxil has not been studied in patients over 65 years of age.

While taking [HA417 trade name] for HIV post-exposure prophylaxis (PEP):

It is important to take [HA417 trade name] for as long as your health care provider has told you to. Keeping to your health care provider's instructions is crucial for preventing HIV infection after you have been exposed to HIV.

Children

[HA417 trade name] should not be used in children and adolescents weighing less than 30 kg.

Other medicines and [HA417 trade name]

Tell your health care provider if you are taking any other medicines or have recently taken other medicines. Make sure you mention herbal medicines you might have been taking.

Do not take [HA417 trade name] if you are already taking other medicines that contain the components of [HA417 trade name] (emtricitabine and tenofovir disoproxil) or any other antiviral medicines that contain tenofovir alafenamide, lamivudine or adefovir dipivoxil.

Taking [HA417 trade name] with other medicines that can damage your kidneys: it is especially important to tell your health care provider if you are taking any of these medicines, including:

- aminoglycosides (for bacterial infection)
- amphotericin B (for fungal infection)
- foscarnet (for viral infection)

- ganciclovir (for viral infection)
- pentamidine (for infections)
- vancomycin (for bacterial infection)
- interleukin-2 (to treat cancer)
- cidofovir (for viral infection)
- non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pain).

If you are taking another type of antiviral medicine called a protease inhibitor to treat HIV, your health care provider may order blood tests to closely monitor your kidney function.

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 [HA417 trade name] with other medicines containing didanosine (for treatment of HIV infection)

Taking [HA417 trade name] with other antiviral medicines that contain didanosine can raise the levels of didanosine in your blood and may reduce CD4 cell counts. Rarely, inflammation of the pancreas and lactic acidosis (excess lactic acid in the blood), which sometimes causes death, have been reported when medicines containing tenofovir disoproxil and didanosine were taken together. Your health care provider will carefully consider whether to treat you with combinations of tenofovir disoproxil and didanosine.

Tell your health care provider if you are taking any of these medicines. Tell your health care provider if you are taking, have recently taken or might take any other medicines.

[HA417 trade name] with food and drink

You can take [HA417 trade name] with food or between meals.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your health care provider for advice before taking this medicine.
If you have taken [HA417 trade name] during your pregnancy, your health care provider may request regular blood tests and other diagnostic tests to monitor the development of your child. In children whose mothers took NRTIs during pregnancy, the benefit from the protection against HIV outweighed the risk of side effects.
If you are interested in breastfeeding your baby, you should discuss the risks and benefits with your health care provider.

Driving and using machines

[HA417 trade name] can cause dizziness. If you feel dizzy while taking [HA417 trade name], do not drive and do not use any hazardous tools or machines.

Other ingredients of [HA417 trade name]

[HA417 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 [HA417 trade name]

Always take [HA417 trade name] exactly as your health care provider has told you to. This is to make sure that your medicine is and remains fully effective. You should check with your health care provider if you are not sure. Do not change the dose unless your health care provider tells you to.

When taking [HA417 trade name] for treating HIV infection and chronic hepatitis B

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

When taking [HA417 trade name] for HIV pre-exposure prophylaxis (PrEP)

There are two ways to take [HA417 trade name] for pre-exposure prophylaxis: continuously once a day (daily PrEP) or for short periods during times of high risk (event-driven PrEP).

- **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.
- **Event-driven PrEP is only for adult males who are not taking oestrogen-based hormone treatments.** All other people, for example cisgender women or transwomen taking oestrogen-based hormonal treatments, should not use [HA417 trade name] for event-driven PrEP.
  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.

When taking [HA417 trade name] for HIV 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.

[HA417 trade name] with food and drink

You can take [HA417 trade name] with food or between meals.

Swallow [HA417 trade name] whole with water or another liquid.

If you take more [HA417 trade name] than you should

If you accidentally take too much of [HA417 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 [HA417 trade name]

It is important not to miss a dose of [HA417 trade name]. If you miss a dose of this medicine, take it as soon as you can, and then take your next dose at its regular time. However, if your next dose is due within 12 hours, do not take the missed dose. Wait and take the next dose at the usual time. Do not take a double dose to make up for a forgotten tablet.

If you vomit less than 1 hour after taking [HA417 trade name], take another tablet. You do not need to take another tablet if you vomit more than 1 hour after taking this medicine.

Do not stop taking [HA417 trade name]

- Do not stop taking [HA417 trade name] for any reason without your health care provider's advice, including when you are experiencing side effects or have another illness. You should also contact your health care provider before you start taking [HA417 trade name] again.
- If you have HIV infection, stopping [HA417 trade name] may reduce the effectiveness of the HIV treatment.
- If you are taking [HA417 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 [HA417 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 [HA417 trade name] for post-exposure prophylaxis (PEP), do not stop taking it until you have finished the 28-day course.
- If you have hepatitis B it is very important not to stop taking [HA417 trade name] without talking to your health care provider first. You may require blood tests for several months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment is not recommended as this may lead to a 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 about this medicine, ask your health care provider.

4. Possible side effects

Like all medicines, this medicine can cause side effects. Possible side effects of this medicine are listed below but they affect people differently and not everybody gets them.

Possible serious side effects:

- **Lactic acidosis** (excess lactic acid in the blood) is a rare but potentially life-threatening side effect. Lactic acidosis occurs more often in women, particularly if they are overweight, and in people with liver disease. The following may be signs of lactic acidosis:
  - deep rapid breathing
  - drowsiness
  - feeling sick (nausea), being sick (vomiting)
  - stomach pain.

  If you think you may have lactic acidosis, get medical help immediately.
- **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** (conditions in which the immune system attacks healthy body tissue) may 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
  - palpitations, tremour or hyperactivity.

  If you notice these or any symptoms of inflammation or infection, get medical help immediately.

Possible side effects:

Very common side effects

(may affect more than 1 in 10 people)

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

Tests may also show:

- decreases in phosphate in the blood

- increased creatine kinase.

Common side effects

(may affect up to 1 in 10 people)

- pain, stomach pain
- difficulty sleeping, abnormal dreams
- problems with digestion resulting in discomfort after meals, feeling bloated, flatulence
- 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
- loss of bone mass

Tests may also show:

- low white blood cell count (a reduced white blood cell count can make you more prone to infection)
- increased blood levels of triglycerides (a type of fat), sugar and bilirubin (a breakdown product of red blood cells).
- liver and pancreas problems.

Uncommon side effects

(may affect up to 1 in 100 people)

- pain in the abdomen (tummy) caused by inflammation of the pancreas
- swelling of the face, lips, tongue or throat
- 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
- changes to your urine.

Rare side effects

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

- lactic acidosis (see above *Possible serious side effects*)
- 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. **If you notice any of these side effects or if any of the side effects get serious**, talk to your health care provider.

The frequency of the following side effects is not known:

- **Bone problems**. Some patients taking a combination of antiretroviral medicines such as [HA417 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 you notice any of these symptoms tell your health care provider.

During treatment for HIV 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.

Other effects in children

Children given emtricitabine very commonly experience:

- changes in skin colour, including darkening of the skin in patches
- low red blood cell count (anaemia), which may cause tiredness or breathlessness.

If you notice any of these symptoms, 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 [HA417 trade name]

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

Blisters: Do not store above 30°C. Store in the original container.

Bottles: Do not store above 30°C. Store in the original container. Do not remove desiccant from container.

Do not use this medicine after the expiry date stated on the carton, blister 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 [HA417 trade name] contains

- The active ingredients are 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate.
- The other ingredients of [HA417 trade name] are:

  Core tablet: croscarmellose sodium, lactose monohydrate, magnesium stearate and microcrystalline cellulose.

  Film coat: FD&C Blue#2, hypromellose, lactose monohydrate, titanium dioxide and triacetin.

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

What [HA417 trade name] looks like and contents of the pack

Blue-coloured, oval-shaped, film-coated tablets with "M117" debossed on (stamped into) one side and plain on the other side.
[HA417 trade name] tablets are available in:

- Aluminium foil blisters.
  Pack size: 10 tablets per blister card and 3 blister cards per carton (total of 30 tablets).

- White, opaque plastic (HDPE) bottle with a white, opaque cap and containing a desiccant (drying material).
  Pack sizes: 28, 30 and 100 tablets.
- Blue, opaque plastic (HDPE) bottle with a blue, opaque plastic (polypropylene) screw cap and containing a desiccant (drying material).
  Pack size: 30 tablets.

Supplier

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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