

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.

Information for the patient

[HA516 trade name][†]
Tenofovir disoproxil fumarate

If you are a carer or parent looking after the person who takes this medicine, use this leaflet to give the medicine correctly and take note of the warnings and side effects.

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 [HA516 trade name] is and what it is used for
2. What you need to know before you take [HA516 trade name]
3. How to take [HA516 trade name]
4. Possible side effects
5. How to store [HA516 trade name]
6. Contents of the pack and other information

1. What [HA516 trade name] is and what it is used for

HIV infection

[HA516 trade name] is used in combination with other medicines for the treatment of HIV (human immunodeficiency virus) infection in adults and adolescents weighing 30 kg or more.

[HA516 trade name] is used to reduce the risk of getting HIV infection in adults and adolescents weighing 30 kg or more 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 other means of reducing your risk such as safer sex practices (see section 2).

[HA516 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 also take other HIV medicines.

Hepatitis B

[HA516 trade name] is used for chronic hepatitis B, an infection with hepatitis B virus (HBV), in adults and adolescents aged over 12 years.

[HA516 trade name] may also be used in pregnant women with HBV infection to prevent transmission of the virus to their babies. If you are pregnant and have HBV infection, your health care provider will advise you on preventing transmission to your child in line with official guidance.

[HA516 trade name] contains the active substance tenofovir disoproxil. Tenofovir interferes with enzymes that the HIV and HBV viruses need for making copies of themselves – in HIV tenofovir interferes with virus reverse transcriptase and in HBV it interferes with virus DNA polymerase. By blocking these enzymes, tenofovir prevents the infection from multiplying and spreading. Because of its actions, tenofovir is known as nucleotide reverse transcriptase inhibitor (often abbreviated NRTI).

Antiviral medicines used for HIV infection are known as antiretrovirals. To prevent the HIV virus from becoming resistant, tenofovir should always be given in combination with other antiretrovirals when treating HIV.

2. What you need to know before you take [HA516 trade name]

Do not take [HA516 trade name]:

- if you are allergic (hypersensitive) to tenofovir disoproxil or any of the other ingredients of [HA516 trade name] listed at the end of this leaflet.

Do not take [HA516 trade name] for HIV pre-exposure prophylaxis:

- if you already have HIV infection or suspect that you might have been infected with HIV infection recently.

You must be HIV-negative before you start regular use of [HA516 trade name] to reduce the risk of getting HIV-1. [HA516 trade name] is not suitable for use on its own if you already have HIV infection, so your health care provider will need to prescribe a treatment that includes other medicines if a test shows that you have been infected with the virus.

Many HIV tests can miss a recent infection. If you have flu-like symptoms, you could have recently become infected with HIV. These may be sign 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 [HA516 trade name] or at any time while taking [HA516 trade name].

Warnings and precautions

While taking [HA516 trade name] for HIV pre-exposure prophylaxis (PrEP):

- Do not miss any doses of [HA516 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 [HA516 trade name] for PrEP may not stop you getting HIV. You should also:**
 - use condoms when you have sex to reduce contact with semen, vaginal fluids or blood. Using condoms correctly is an important way of reducing the risk of getting HIV infection and other sexually transmitted infections.

- get tested for other sexually transmitted infections such as syphilis and gonorrhoea. Other infections make it easier for HIV to infect you.
- 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.

Ask your healthcare provider how to get information and support on safer sex practice.

While taking [HA516 trade name] for HIV post-exposure prophylaxis (PEP):

It is important to take [HA516 trade name] together with the other HIV medicines you have been prescribed 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.

Kidney disease

[HA516 trade name] may affect your kidneys. Tell your health care provider if you have had kidney disease or if tests have shown problems with your kidneys.

Before starting [HA516 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.

If you have kidney problems, your health care provider may advise you to stop taking [HA516 trade name] or, if you already have HIV, to take [HA516 trade name] less frequently. [HA516 trade name] is not recommended if you have severe kidney disease or are on dialysis.

[HA516 trade name] is not usually taken with other medicines that can damage your kidneys (see "Other medicines and [HA516 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 [HA516 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 HIV medicines, 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

Look out for infections. If you have advanced HIV infection (AIDS), your body is not able to fight off other so-called opportunistic infections. Once you start treatment with [HA516 trade name] these other infections may flare up or you may get signs of inflammation (for example in your lungs or eyes). 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 [HA516 trade name]. If you notice signs of inflammation or infection, tell your health care provider at once.

In addition to 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 treatments for HIV may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The risk depends on various factors including how long you have been on treatment, whether you are taking other medicines called corticosteroids, how much alcohol you drink, how badly your immune system is affected by HIV, and whether you are overweight.

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 [HA516 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 [HA516 trade name], or [HA516 trade name] may affect their action.

Do not take [HA516 trade name] if you are already taking other medicines containing tenofovir disoproxil or tenofovir alafenamide. Do not take [HA516 trade name] and adefovir dipivoxil at the same time.

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 (for fungal infection)
- pentamidine (for 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 [HA516 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 [HA516 trade name] with food and drink

You should take [HA516 trade name] with food.

Pregnancy and breast-feeding

Pregnancy

[HA516 trade name] can be used during pregnancy.

Breast-feeding

Although the active substances of [HA516 trade name] pass into breast milk, [HA516 trade name] may be used during breast-feeding. Ask your health care provider for advice on breast-feeding.

Fertility

There is limited information on the effects of [HA516 trade name] on fertility in humans, but animal studies do not show harmful effects.

Driving and using machines

[HA516 trade name] can cause dizziness. If you feel dizzy while taking [HA516 trade name], do not drive or ride a bicycle and do not use hazardous tools or machines.

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[HA516 trade name] can cause dizziness. If you feel dizzy while taking [HA516 trade name], do not drive or ride a bicycle and do not use hazardous tools or machines.

This medicine 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.

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

3. How to take [HA516 trade name]

Always take [HA516 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 [HA516 trade name] for treating HIV infection

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

If you have problems with your kidneys, your health care provider may advise you to take [HA516 trade name] less frequently.

When taking [HA516 trade name] for pre-exposure prophylaxis (PrEP)

There are two ways to take [HA516 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 from 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, then 1 tablet once a day during the period of potential exposure, and one tablet once a day for two days after the potential exposure. This is known as the '2+1+1' schedule. **Event-driven PrEP is only for adult males who are not taking oestrogen-based hormone treatments.**

When taking [HA516 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 [HA516 trade name] for treating hepatitis B

For treating chronic hepatitis B, 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 other HIV medicines along with [HA516 trade name].

Take [HA516 trade name] with food

Swallow [HA516 trade name] whole with water or another liquid. If you cannot swallow the tablet, break or crush the tablet (by using the tip of a spoon) and add it to a small amount of liquid or semi-solid food. Swallow all the mixture immediately.

If you take more [HA516 trade name] than you should:

If you accidentally take too many tablets of [HA516 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 [HA516 trade name]:

It is important not to miss a dose of [HA516 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 [HA516 trade name], take another tablet. You do not need to take another tablet if you were sick more than 1 hour after taking [HA516 trade name].

Do not stop taking [HA516 trade name]:

- Do not stop taking [HA516 trade name] without your health care provider's advice. Stopping [HA516 trade name] may reduce the effectiveness of the treatment. Talk to your health care provider before you stop taking [HA516 trade name] for any reason, particularly if you are experiencing any side effects, have another illness, or think you are no longer at risk of getting infected with HIV. Contact your health care provider before you restart taking [HA516 trade name].
- If you have HIV infection, stopping [HA516 trade name] may reduce the effectiveness of the treatment.
- If you are taking [HA516 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 [HA516 trade name] for event-driven PrEP, do not stop until 2 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 [HA516 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 (either on its own or together with HIV), it is particularly important not to stop taking [HA516 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 [HA516 trade name]. You may require blood tests for several months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping tenofovir treatment is not recommended as this may lead to worsening of hepatitis.

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

Like all medicines, [HA516 trade name] can cause side effects, although not everybody gets them.

The following side effects have been observed in patients who were treated with tenofovir disoproxil.

Serious but rare side effects - tell your health care provider immediately

- **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

Other possible side effects with [HA516 trade name]

Very common side effects (affecting at least 10 in every 100 patients treated)

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

Tests may also show:

- abnormally low levels of phosphate in the blood

Common side effects (affecting up to 10 in every 100 patients treated)

- headache, stomach pain, feeling tired, feeling bloated, flatulence, loss of bone mass

Tests may also show:

- liver problems

Uncommon side effects (affecting at least 1 in every 1,000 patients treated, but less than 1 in every 100 patients treated)

- breakdown of muscle, muscle pain or weakness

Tests may also show

- decreases in potassium in the blood
- increased creatinine in the blood
- pancreas problems

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.

Rare side effects (affecting at least 1 in every 10,000 patients treated, but less than 1 in every 1,000 patients treated)

- pain in the abdomen caused by inflammation of the liver
- swelling of the face, lips, tongue and throat

Tests may also show

- damage to kidneys

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 [HA516 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 carton and 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 [HA516 trade name] contains

- The active ingredient(s) is 300 mg tenofovir disoproxil fumarate (equivalent to tenofovir disoproxil 245 mg or tenofovir 136 mg).
- The other ingredients of [HA516 trade name] are croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinised starch, lactose monohydrate, hypromellose, titanium dioxide and triacetin, FD & C Blue #2 (indigo carmine aluminium lake).

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

What [HA516 trade name] looks like and contents of the pack

Light blue, oval, film coated tablets. They are biconvex (rounded on top and bottom) with a flat edge. The tablets have “CL 77” debossed (stamped into) one side and plain on the other side.

The medicine is available in the following pack:

Round, opaque white 75 cc plastic (HDPE) bottle containing 30 tablets. It also contains a sachet of desiccant (drying material) and a piece of rayon wool to keep the tablets in place. The bottle has a white opaque plastic (polypropylene) screw cap and a sealed liner.

Pack size: 30 tablets.

Supplier and Manufacturer

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

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

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