

# **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

[HA516 trade name] <sup>1</sup>  
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 [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

[HA516 trade name] is used in combination with other medicines for the treatment for human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents weighing more than 30 kg.

[HA516 trade name] can also be 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).

[HA516 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 35 kg. You do not have to have HIV infection to be treated with [HA516 trade name] for chronic hepatitis B.

[HA516 trade name] contains the active substance tenofovir disoproxil. [HA516 trade name] is a medicine for the treatment of HIV infection or chronic hepatitis B, or for patients with both infections. Tenofovir interferes with enzymes used for making copies of these viruses – in HIV tenofovir interferes with virus reverse transcriptase and in HBV it interferes with virus DNA polymerase. This stops the viruses from multiplying.

Antiviral medicines used for HIV infection are known as antiretrovirals. Tenofovir is a type of antiretroviral known as a nucleotide reverse transcriptase inhibitor (often abbreviated NRTI). To prevent the virus from becoming resistant, tenofovir should always be given in combination with other antiretrovirals when treating HIV.

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

**This medicine is not a cure for HIV infection.** While taking [HA516 trade name] you may still develop infections or other illnesses associated with HIV infection. You can also pass on HIV or HBV to others through sexual contact or blood contamination, so it is important to take precautions to avoid infecting other people.

[HA516 trade name] is prescribed for use in combination with other antiviral medicines. Your health care provider will discuss with you which medicines are best for you.

## 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 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 [HA516 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 [HA516 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)*

[HA516 trade name] does not protect you fully against HIV infection and does not protect you from other sexually transmitted diseases. Safe sex practices including always using a condom in the correct way, are critical for reducing the risk of getting HIV 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 [HA516 trade name]. Missing doses may increase your risk of getting HIV-1 infection.

If you get HIV-1 infection, you may need more medicines than [HA516 trade name]. 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.

### *Kidney disease*

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

**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 [HA516 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 [HA516 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 [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 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 [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 can take [HA516 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**

[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.

### **[HA516 trade name] contains lactose**

If you have been told by your health care provider that you have an intolerance to some sugars, contact your health care provider before taking this medicinal product.

## **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.

The usual dose for adults and adolescents is one tablet each day.

You can take [HA516 trade name] with food or between meals. 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.

#### 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 children weighing less than 35 kg.

#### When used for treatment of chronic Hepatitis B-infection:

This medicine is not for use by children under 12 years of age.

For treatment of established HIV-infection: Your health care provider will prescribe [HA516 trade name] with at least one other antiretroviral medicine. Please refer to the patient information leaflets of the other antiretrovirals for guidance on how to take those medicines.

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

Do not stop any anti-HIV medicines prescribed by your health care provider when you start [HA516 trade name] if you have both HBV and HIV infection.

If you have HBV your health care provider may offer you an HIV test to see if you have both HBV and HIV.

**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].

**If you stop taking [HA516 trade name]:**

Don't 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 if you 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 hepatitis B or HIV and hepatitis B together (co-infection), it is very 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 for established HIV-1 infection.

**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 serious side effects - contact your health care provider**

**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

*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)

- pain in the abdomen caused by inflammation of the pancreas, breakdown of muscle, muscle pain or weakness

*Tests may also show*

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

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

- back pain caused by kidney problems, including kidney failure
- yellow skin or eyes, itching, or pain in the abdomen (tummy) caused by inflammation of the liver
- passing large amount of urine and feeling thirsty, resulting from inflammation of the kidney and kidney damage
- bone pain and bone fracture which may be caused by kidney damage
- accumulation of fat in the liver
- 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

**Adults not infected with HIV and using tenofovir to reduce the risk of getting HIV-1 infection** in clinical trials had no side effects other than those described above. The following side effects were reported: Headache, abdominal pain, weight decrease and syphilis (a sexually transmitted infection).

**Side effects with unknown frequency:**

The following side effects have been reported in HIV infected patients treated with medicines of the group of NRTIs, to which [HA516 trade name] belongs:

- increases in blood fats (hyperlipaemia) and an abnormal increase in blood sugar. Your health care provider will test for these changes.
- appearance of infection as part of ‘immune reactivation syndrome’ (see “Warnings and precautions”).

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 [HA516 trade name]

Store at a temperature not exceeding 30°C, protected from moisture. Keep this medicine out of the sight and reach of children.

Do not use [HA516 trade name] after the expiry date stated on the bottle and carton after {EXP}. The expiry date refers to the last day of that month.

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 is 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, microcrystalline cellulose and pregelatinised starch.

*Film coat:* lactose monohydrate, hypromellose, titanium dioxide and triacetin, FD & C Blue #2 (indigo carmine aluminium lake).

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

Blue-coloured, oval-shaped, biconvex, film-coated tablets, debossed with “CL77” on one side and plain on the other side, packaged in white, opaque, round HDPE bottle with polypropylene continuous thread closure with wad having induction seal liner. The bottle also contains a silica gel sachet and rayon.

Pack size: 30 tablets.

The tablets cannot be halved for part dose.

### Supplier and Manufacturer

#### Supplier

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For any information about this medicine, contact the supplier.

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