

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/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

†Formerly Strides Shasun Limited.

Information for the patient

[HA535 trade name][†]
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 [HA535 trade name] is and what it is used for
2. What you need to know before you take [HA535 trade name]
3. How to take [HA535 trade name]
4. Possible side effects
5. How to store [HA535 trade name]
6. Contents of the pack and other information

1. What [HA535 trade name] is and what it is used for

[HA535 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.

[HA535 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 [HA535 trade name] for chronic hepatitis B, although the medicine can be used as part of combination treatment in patients with both infections.

[HA535 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).

[HA535 trade name] contains the active substance tenofovir disoproxil fumarate. 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.

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

2. What you need to know before you take [HA535 trade name]

Do not take [HA535 trade name]:

- if you are allergic (hypersensitive) to tenofovir disoproxil or any of the other ingredients of [HA535 trade name] listed at the end of this leaflet.

Do not take [HA535 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 have a test to confirm that you are HIV-negative before you start regular use of [HA535 trade name] to reduce the risk of getting HIV-1. [HA535 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.

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 (PrEP)

[HA535 trade name] reduces the chance of getting HIV infection if you take it as instructed and do not miss doses, but a small risk may remain. Because of this, and because it does not protect you from other sexually transmitted diseases, you should also take other measures to keep yourself safe. These include:

- using condoms (male or female) when you have sex. Using condoms correctly is an important way of reducing the risk of getting HIV infection and other sexually transmitted infections.
- being tested for other sexually transmitted infections. Other infections make it easier for HIV to infect you.
- knowing your and your partner's HIV status, and testing regularly for HIV.

You must stay HIV-negative to keep taking [HA535 trade name] for PrEP. Symptoms of new HIV infection are like those of flu and include tiredness, fever, joint or muscle aches, headache, sore throat, vomiting, diarrhoea, rash, night sweats, or enlarged lymph nodes in the neck or groin. Tell your health care provider if you get symptoms like these while taking this medicine. Also tell your health care provider right away if you think you have been exposed to HIV. If you get HIV infection, you will need treatment that combines several medicines.

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

Kidney disease

[HA535 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 [HA535 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.

[HA535 trade name] is not usually taken with other medicines that can damage your kidneys (see "Other medicines and [HA535 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 [HA535 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 [HA535 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 [HA535 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 [HA535 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 [HA535 trade name], or [HA535 trade name] may affect their action.

Do not take [HA535 trade name] if you are already taking other medicines containing tenofovir disoproxil or tenofovir alafenamide. Do not take [HA535 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 [HA535 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 [HA535 trade name] with food and drink

You should take [HA535 trade name] with food.

Pregnancy and breast-feeding

Pregnancy

[HA535 trade name] can be used during pregnancy.

Breast-feeding

Although the active substances of [HA535 trade name] pass into breast milk, [HA535 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 [HA535 trade name] on fertility in humans, but animal studies do not show harmful effects.

Driving and using machines

[HA535 trade name] can cause dizziness. If you feel dizzy while taking [HA535 trade name], do not drive or ride a bicycle and do not use hazardous tools or machines.

Other ingredients of [HA535 trade name]

[HA535 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 in other patients'. 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.

It is important to consider the contribution of excipients from all the medicines that the patient is taking.

3. How to take [HA535 trade name]

Always take [HA535 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.

If you have problems with your kidneys, your health care provider may advise you to take [HA535 trade name] less frequently.

Swallow [HA535 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 or for reducing the risk of getting HIV-1 infection (PrEP):

This medicine is not for use by children weighing less than 30 kg.

If [HA535 trade name] is being used to lower your risk of getting HIV infection (PrEP), it can be used on its own. However, if you already have HIV infection and this medicine is for your treatment, your health care provider will prescribe it along with other HIV medicines.

It is important to take all the medicines as your health care provider has told you. Read the patient information leaflet of the other medicines for guidance on how to take them, and always check with your health care provider if you are unsure.

When used for treatment of chronic hepatitis B-infection:

This medicine is not for use by children under 12 years of age and weighing less than 35 kg.

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 [HA535 trade name].

If you take more [HA535 trade name] than you should:

If you accidentally take too many tablets of [HA535 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 [HA535 trade name]:

It is important not to miss a dose of [HA535 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 [HA535 trade name], take another tablet. You do not need to take another tablet if you were sick more than 1 hour after taking [HA535 trade name].

If you stop taking [HA535 trade name]:

Don't stop taking [HA535 trade name] without your health care provider's advice. Stopping [HA535 trade name] may reduce the effectiveness of the treatment. Talk to your health care provider before you stop taking [HA535 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 [HA535 trade name].

If you have hepatitis B (either on its own or together with HIV), it is particularly important not to stop taking [HA535 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 [HA535 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, [HA535 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 [HA535 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

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

Side effects associated with HIV treatment in general

The following side effects have been reported with unknown frequency in HIV infected patients treated with HIV medicines:

- increases in blood fats (hyperlipaemia) and 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 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 [HA535 trade name]

Do not store above 30°C. Protect from moisture.

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

Do not use this medicine after the expiry date stated on the bottle, blister and carton after <EXP>. The expiry date refers to the last day of that month.

Do not use this medicine if you notice description of the visible signs of deterioration 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 [HA535 trade name] contains

- The active ingredient is tenofovir disoproxil fumarate 300 mg (equivalent to tenofovir disoproxil 245 mg).
- The other ingredients of [HA535 trade name] are:

Core tablet: Croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose and pregelatinised starch.

Film coat: hypromellose, titanium dioxide and polyethylene glycol.

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

What [HA535 trade name] looks like and contents of the pack

White, circular, film-coated, convex tablets engraved TDF on one side and plain on the other side. The tablets should not be divided.

Al/Al cold form blisters containing 10 tablets. 3 blister cards per box. Pack size: 30 tablets.

Round, white opaque HDPE bottle, with white opaque screw cap with induction sealed liner and containing a silica gel sachet as desiccant. Pack size: 30 tablets.

Supplier and Manufacturer

Supplier

Strides Pharma Science Limited
Strides House, Opp. IIMB,
Bilekahalli
Bannerghatta Road
Bangalore – 560 076
India.
Tel: +91-80-67840738/215
Email: ashokkumar.j@strides.com

Manufacturer

Strides Pharma Science Limited
Oral solid dosage forms division
Tablet Block
36/7, Suragajakkanahalli
Indlavadi cross
Anekal Taluk
Bangalore - 562 106
India.
Tel: 91-80-67840600
Email: Pandurang.P@strides.com

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

Region: East Africa
Country: Kenya
Address: M/s. Universal Corporation Ltd,
Club Road, Past Kikuyu Post Office
P.O Box 1748-00902
Kikuyu, Kenya
Contact Person: Mr. Palu Dhanani
Email: palu.dhanani@ucl.co.ke

Region: East Africa

Country: Uganda
Address: M/s. Delmaw Enterprises Limited
Plot 9/5 & 6, Gathani House
Bombo Road
P.O Box No. 1574
Kampala – Uganda
Contact Person: Mr. Gerald
Email: delmaw.regulatory@artemislife.com

Region: East Africa

Country: Tanzania
Address: M/s. Samiro Pharmaceuticals Ltd
P.O.BOX 38062
Uhuru Street, Kariakoo,
Dar-es-Salaam, Tanzania
Contact Person: Mr. Abbas Mohammed
Email: info@samiropharma.com

Region: Central Africa

Country: DR Congo
Address: M/s. Gulf africa investments SARL
(Division: Gulf Africa Pharma)
B.P. 14009
Avenue du Marche No: PL 6356
Commune de la Gombe
Kinshasa RD- Congo
Contact Person: Mr. Leonard Netto
Email: leonard.netto@artemislife.com

Region: West Africa

Country: Nigeria
Address: M/s. Strides Lifesciences Ltd,
Chenline House
7,Obasa St. Off Oba Akran Ave
Ikeja, Lagos, Nigeria
Contact Person: Mr. Smatt Aguba
Email: SP@strides.com

Region: Southern Africa

Country: Zambia
Address: M/s. Yash Pharmaceuticals Ltd
Plot 27 Lilayi Road, Lusaka
P.O BOX: 34562 Zambia
Contact Person: Mr. Himanshu Patel
Email: h.patel@yashpharmaceuticals.com

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