

Patient leaflet in accordance with the Pharmacists' (Products) Regulations - 1986

This medicine is dispensed according to a physician's prescription only

TRUVADA[®]
Film-coated tablets

Active ingredients: Each film-coated tablet contains –
emtricitabine 200 mg
tenofovir disoproxil 245 mg
(equivalent to 300 mg of tenofovir disoproxil fumarate or 136 mg of tenofovir)

Inactive agents and allergens: See section 6 “*Additional information*”.

Read the entire leaflet carefully before using the medicine. This leaflet contains summary information about the medicine. If you have any other questions, refer to the physician or the pharmacist. This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their medical condition is similar to yours.

The medicine is intended for adults above the age of 18.

In addition to the patient leaflet, the product Truvada has a patient safety card which contains important safety data that you should be aware of before receiving Truvada treatment and following the treatment. You should follow this information. Read the patient safety card and the patient leaflet before treatment initiation. Keep the patient safety card, you may need to read it again.

1. What is Truvada intended for?

Truvada is a treatment for Human Immunodeficiency Virus (HIV) infection in adults aged 18 years and over, in combination with other anti-retroviral medicinal products.

Therapeutic Group: Antiviral reverse transcriptase inhibitors.

Truvada contains two active substances, *emtricitabine* and *tenofovir disoproxil*. Both of these active substances are *antiretroviral* medicines which are used to treat HIV infection. Emtricitabine is a *nucleoside reverse transcriptase inhibitor* and tenofovir is a *nucleotide reverse transcriptase inhibitor*. However, both are generally known as NRTIs and they work by interfering with the normal working of an enzyme (reverse transcriptase) that is essential for the virus to reproduce itself.

- **Truvada is used to treat Human Immunodeficiency Virus 1 (HIV-1) infection in adults aged 18 years and over.**
 - Truvada should always be used combined with other medicines to treat HIV infection.
 - Truvada can be administered in place of emtricitabine and tenofovir disoproxil used separately at the same doses.

People who are HIV positive can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your doctor the precautions needed to avoid infecting other people.

This medicine is not a cure for HIV infection. While taking Truvada you may still develop infections or other illnesses associated with HIV infection.

- **Truvada is also used to reduce the risk of getting HIV-1 infection in adults,** when used as a daily treatment, together with safer sex practices:

See section 2 for a list of precautions to take against HIV infection.

2. Before taking Truvada

X Do not use the medicine if:

- you are allergic to emtricitabine, tenofovir, tenofovir disoproxil, or any of the other ingredients of this medicine (listed in section 6).

→ If this applies to you, tell your doctor immediately.

! Special warnings regarding the use of Truvada

Before taking Truvada to reduce the risk of getting HIV:

Truvada can only help reduce your risk of getting HIV **before** you are infected.

- **You must be HIV negative before you start to take Truvada to reduce the risk of getting HIV.** You must get tested to make sure that you do not already have HIV infection. Do not take Truvada to reduce your risk unless you are confirmed to be HIV negative. People who do have HIV must take Truvada in combination with other drugs.
- **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 doctor about any flu-like illness** – either in the month before starting Truvada, or at any time while taking Truvada.

Warnings and precautions

While taking Truvada to reduce the risk of getting HIV:

- Take Truvada every day **to reduce your risk, not just when you think you have been at risk of HIV infection.** Do not miss any doses of Truvada, 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 doctor straight away. They may want to do more tests to make sure you are still HIV negative.
- **Just taking Truvada may not stop you getting HIV.** Therefore, you should take the following actions:
 - Always practice safer sex. Use condoms to reduce contact with semen, vaginal fluids, or blood.
 - Do not share personal items that can have blood or body fluids on them, such as toothbrushes and razor blades.
 - Do 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 doctor if you have any more questions about how to prevent getting HIV or spreading HIV to other people.

While taking Truvada to treat HIV or to reduce the risk of getting HIV:

- **Truvada may affect your kidneys.** Before and during treatment, your doctor may order blood tests to measure kidney function. Tell your doctor if you have had kidney disease, or if tests have shown kidney problems. If you have kidney problems, your doctor may advise you to stop taking Truvada or, if you already have HIV, to take Truvada less frequently. Truvada 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 kidney tubule cells (see section 4, *Side effects*). Tell your doctor if you have bone pain or fractures.

Tenofovir disoproxil may also cause loss of bone mass. The most pronounced bone loss was seen in clinical studies when patients were treated for HIV with tenofovir disoproxil in combination with a boosted protease inhibitor.

Overall, the effects of tenofovir disoproxil on long term bone health and future fracture risk in adult and paediatric patients are uncertain.

Tell your doctor if you know you suffer from osteoporosis. Patients with osteoporosis are at a higher risk of fractures.

- **Talk to your doctor if you have a history of liver disease, including hepatitis.** Patients infected with HIV who also have 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 have hepatitis B or C, your doctor will carefully consider the best treatment regimen for you.
- **Know your hepatitis B virus (HBV) infection status** before starting Truvada. If you have HBV, there is a serious risk of liver problems when you stop taking Truvada, whether or not you also have HIV. It is important not to stop taking Truvada without talking to your doctor: see section 3, *Do not stop taking Truvada*.
- **Talk to your doctor if you are over 65.** Truvada has not been studied in patients over 65 years of age.
- **Talk to your doctor if you are intolerant to lactose** (see *Truvada contains lactose* later in this section).

Children and adolescents

Truvada is not for use in children and adolescents under 18 years of age.

Other medicines and Truvada

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

If you are taking or have recently taken other medicines, including non- prescription medicines and dietary supplements, inform your doctor or pharmacist.

Taking Truvada with other medicines that can damage your kidneys: it is especially important to tell your doctor 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 pains)

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

It is also important to tell your doctor if you are taking ledipasvir/sofosbuvir, sofosbuvir/velpatasvir or sofosbuvir/velpatasvir/voxilaprevir to treat hepatitis C infection.

Taking Truvada with other medicines containing didanosine (for treatment of HIV infection):

Taking Truvada 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 doctor will carefully consider whether to treat you with combinations of tenofovir and didanosine.

→ **Tell your doctor** if you are taking any of these medicines. Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Truvada with food and drink

- Whenever possible, Truvada should be taken with food.

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 doctor or pharmacist for advice before taking any medicine.

If you have taken Truvada during your pregnancy, your doctor 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.

- **Do not breast-feed during treatment with Truvada.** This is because the active substances in this medicine pass into human breast milk.
- If you are a woman with HIV it is recommended that you do not breast-feed, to avoid passing the virus to the baby in breast milk.

Driving and using machines

Truvada can cause dizziness. If you feel dizzy while taking Truvada, **do not drive** and do not use any tools or machines.

Important information about some ingredients of the medicine

Truvada contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Truvada contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Truvada

- **Always take this medicine exactly as your doctor has told you.** Check with your doctor or pharmacist if you are not sure.

The recommended dose of Truvada to treat HIV or to reduce the risk of getting HIV is:

- **Adults:** one tablet each day. Whenever possible, Truvada should be taken with food.
- **Do not exceed the recommended dose.**

If you have difficulty swallowing, you can use the tip of a spoon to crush the tablet. Then mix the powder with about 100 mL (half a glass) of water, orange juice or grape juice, and drink immediately.

- **Always take the dose recommended by your doctor.** This is to make sure that your medicine is fully effective, and to reduce the risk of developing resistance to the treatment. Do not change the dose unless your doctor tells you to.
- **If you are being treated for HIV infection** your doctor will prescribe Truvada with other antiretroviral medicines. Please refer to the patient information leaflets of the other antiretrovirals for guidance on how to take those medicines.
- **If you are an adult taking Truvada to reduce the risk of getting HIV,** take Truvada every day, not just when you think you have been at risk of HIV infection.

Ask your doctor if you have any questions about how to prevent getting HIV or prevent spreading HIV to other people.

If you take more Truvada than you should

If you accidentally take more than the recommended dose of Truvada, contact your doctor or nearest emergency department for advice. Keep the tablet bottle with you so that you can easily describe what you have taken.

If you miss a dose

It is important not to miss a dose of Truvada.

- **If you notice within 12 hours** of the time you usually take Truvada, take the tablet preferably with food as soon as possible. Then take the next dose at your usual time.
- **If you notice 12 hours or more after** the time you usually take Truvada, forget about the missed dose. Wait and take the next dose, preferably with food, at your usual time.

If you vomit less than 1 hour after taking Truvada, take another tablet. You do not need to take another tablet if you were sick more than 1 hour after taking Truvada.

Do not stop taking Truvada

- **If you take Truvada for treatment of HIV infection**, stopping tablets may reduce the effectiveness of the anti-HIV therapy recommended by your doctor.
- **If you are taking Truvada to reduce the risk of getting HIV**, do not stop taking Truvada or miss any doses. Stopping use of Truvada, or missing doses, may increase your risk of getting HIV infection.
 - ➔ **Do not stop taking Truvada without contacting your doctor.**
- **If you have hepatitis B**, it is especially important not to stop your Truvada treatment without talking to your doctor 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 worsening of your hepatitis, which may be life-threatening.
 - ➔ **Tell your doctor immediately** about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Tell your doctor about any of the following side effects:

Possible serious side effects: tell a doctor immediately

- **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.**
- **Any 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**, 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
- **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

Tests may also show:

- low white blood cell count (a reduced white blood cell count can make you more prone to infection)
- increased triglycerides (fatty acids), bile or sugar in the blood
- 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 *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 the side effects listed above or if any of the side effects get serious, talk to your doctor or pharmacist.**

The frequency of the following side effects is not known.

- **Bone problems.** Some patients taking combination antiretroviral medicines such as Truvada 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 doctor.**

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 life style, and in the case of blood lipids sometimes to the HIV medicines themselves. Your doctor will test for these changes.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

You can report any side effects to the Ministry of Health by clicking on the link "Report side effects due to medical treatment" that is located on the Ministry of Health homepage (www.health.gov.il) which will direct you to the online form for reporting side effects or by clicking on the link: <https://sideeffects.health.gov.il>.

You can also report any side effects directly to the registration holder via email: DrugSafety.Israel@gilead.com.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Truvada

Prevent poisoning! Keep this medicine out of the sight and reach of children and/or babies. In this way you will prevent poisoning. Do not induce vomiting without a doctor's express instruction.

Do not use this medicine after the expiry date which is stated on the bottle and carton after {EXP}. The expiry date refers to the last day of that month.

Store in the original package in order to protect from moisture. Store at room temperature and not above 30°C. Keep the bottle tightly closed.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional Information

In addition to the active agents the medicine also contains:

Microcrystalline cellulose (E460), lactose monohydrate, croscarmellose sodium, pregelatinised starch and magnesium stearate (E572).

Film-coating: lactose monohydrate, hypromellose (E464), titanium dioxide (E171), glycerol triacetate (E1518), indigo carmine aluminium lake (E132).

What Truvada looks like and contents of the pack

Truvada film-coated tablets are blue, capsule-shaped tablets, debossed on one side with the word “GILEAD” and on the other side with the number “701”. Truvada comes in bottles of 30 tablets. Each bottle contains a silica gel desiccant that must be kept in the bottle to help protect your tablets. The silica gel desiccant is contained in a separate sachet or canister and should not be swallowed.

The following pack size is available: outer cartons containing 1 bottle of 30 film-coated tablets.

Registration Holder:

Gilead Sciences Israel Ltd.
4 HaHarash Street
Hod Hasharon 4524075
Israel

Manufacturer:

Gilead Sciences Ireland UC
IDA Business & Technology Park
Carrigtohill
County Cork
Ireland

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 31125

For simplicity and ease of reading, this leaflet was phrased in the masculine verb. Nevertheless, Truvada is intended for both genders.

Revised in January 2023 according to MoH guidelines.

Reference: EU label from May 2021.

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