

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS’ REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor’s prescription only

TENOVAMED INOVAMED

Film-coated tablets

Active ingredients:

Each film-coated tablet contains:

- emtricitabine 200 mg
 - tenofovir disoproxil 245 mg
- (equivalent to 300 mg tenofovir disoproxil fumarate)

For the list of inactive and allergenic ingredients in the preparation: see section 6 “Further information”. In addition, see “Important information about some of the ingredients of the medicine” in section 2 of this leaflet.

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist. This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

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

In addition to the leaflet, Tenovamed Inovamed has a patient safety information booklet. This booklet contains important safety information that you must know and adhere to before starting and during the course of treatment with Tenovamed Inovamed. Read the patient safety information booklet and the patient leaflet before starting to use the preparation. Keep the booklet for further reference, if needed.

1. WHAT IS THE MEDICINE INTENDED FOR?

Tenovamed Inovamed is a treatment for human immunodeficiency virus (HIV) infection in adults aged 18 years and over, in combination with other antiretroviral medicines.

Therapeutic group: Antiviral reverse transcriptase inhibitors.

Tenovamed Inovamed 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 medicines are generally known as nucleoside reverse transcriptase inhibitors (NRTIs) and they work by interfering with the normal activity of an enzyme (reverse transcriptase) that is essential for HIV to reproduce itself.

- Tenovamed Inovamed is used to treat human immunodeficiency virus 1 (HIV-1) infection in adults aged 18 years and over.**
- Tenovamed Inovamed should always be used combined with other medicines to treat HIV infection.
- Tenovamed Inovamed can be administered instead of separately taking emtricitabine and tenofovir disoproxil at the same dosages.

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

- Tenovamed Inovamed is also used to reduce the risk of getting HIV-1 infection in adults,** when used as a daily treatment, together with safe sex practices:
See section 2 for a list of precautions to take against HIV-1 infection.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are allergic** to emtricitabine, tenofovir, tenofovir disoproxil, or to any of the additional ingredients contained in the medicine (listed in section 6 and in section 2 “Important information about some of the ingredients of the medicine”).

If any of these apply to you, tell the doctor immediately.

Special warnings regarding use of the medicine

Before using Tenovamed Inovamed to reduce the risk of getting HIV:

Tenovamed Inovamed can help reduce the risk of getting HIV only before you are infected.

- You must not be an HIV carrier before you start to take Tenovamed Inovamed to reduce the risk of getting HIV.** You must get tested to make sure that you are not an HIV carrier. Do not take Tenovamed Inovamed to reduce the risk unless you have confirmed that you are not an HIV carrier. HIV carriers must take Tenovamed Inovamed in combination with other medicines.
- Many HIV tests may miss a recent infection.** If you are sick with a flu-like illness, it could mean you have recently been infected with HIV.

The signs that can indicate HIV infection are:

- tiredness
 - fever
 - joint or muscle aches
 - headaches
 - vomiting or diarrhea
 - 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 treatment with Tenovamed Inovamed, or at any time while taking Tenovamed Inovamed.

Warnings and precautions

While taking Tenovamed Inovamed to reduce the risk of getting HIV:

- Take Tenovamed Inovamed every day **to reduce the risk, not just when you think you have been at risk of HIV infection.** Do not miss any dose of Tenovamed Inovamed, or stop taking the medicine. Missing a dose may increase your risk of getting HIV infection.

- Get tested for HIV regularly.

- Tell your doctor straight away if you think you were infected with HIV. The doctor may do more tests to make sure you are not an HIV carrier.
- Just taking Tenovamed Inovamed does not ensure that you will not be infected by the virus.** Therefore, you should take the following actions:
 - Always practice safe sex. Use a condom 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 injection accessories or medical equipment.
 - Get tested for other sexually transmitted infections, such as syphilis and gonorrhoea. These infections make it easier for HIV to infect you.

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

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

- Tenovamed Inovamed may affect your kidneys.** Before starting and during treatment, the doctor may refer you for blood tests to measure kidney function. Tell the doctor if you have had a kidney disease, or if the tests have shown kidney problems. If you have kidney problems, the doctor may advise you to stop taking Tenovamed Inovamed, or if you are an HIV carrier, the doctor may tell you to take Tenovamed Inovamed less frequently. Tenovamed Inovamed treatment is not recommended if you have severe kidney disease or are on dialysis.
- Tell your doctor if you suffer from osteoporosis, if you have a history of bone fractures or if you have problems with your bones.**
Bone problems (manifesting as persistent or worsening bone pain that sometimes result 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 among patients 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 adults are uncertain.

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

Children and adolescents

Tenovamed Inovamed is not intended for use in children and adolescents under 18 years of age.

Drug interactions

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

If you are taking, or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Taking Tenovamed Inovamed with other medicines that may damage your kidneys: it is especially important to tell the doctor if you are taking one of the following medicines, including:

- aminoglycosides (to treat bacterial infection)
- amphotericin B (to treat fungal infection)
- foscarnet (to treat viral infection)
- ganciclovir (to treat viral infection)
- pentamidine (to treat infections)
- vancomycin (to treat bacterial infection)
- interleukin-2 (to treat cancer)
- cidofovir (to treat 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, the doctor may refer you for blood tests to closely monitor your kidney function.

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

Taking Tenovamed Inovamed with other medicines containing didanosine (for treatment of HIV infection): Taking Tenovamed Inovamed with other antiviral medicines that contain didanosine may raise the levels of didanosine in your blood and may reduce CD4 cell count. 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. The doctor will carefully consider whether to treat you with combinations of tenofovir and didanosine.

Tell the 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.

Use of the medicine and food

- Whenever possible, Tenovamed Inovamed should be taken with food.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask the doctor or pharmacist for advice before taking any medicine.

If you have taken Tenovamed Inovamed during pregnancy, the doctor may request that you have 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 breastfeed during treatment with Tenovamed Inovamed.** This is because the active substances in this medicine pass into breast milk.
- Breastfeeding is not recommended in women living with HIV because HIV infection can be passed on to the baby through breast milk.
- If you are breastfeeding or thinking about breastfeeding, **you should discuss it with your doctor as soon as possible.**

Driving and operating machinery

Tenovamed Inovamed may cause dizziness. If you feel dizzy while taking Tenovamed Inovamed, **do not drive** or operate tools or machinery.

Important information about some of the ingredients of the medicine

Tenovamed Inovamed contains lactose

This medicine contains lactose anhydrous and lactose monohydrate, which are types of sugar. If you have been told by the doctor that you have an intolerance to lactose, or if you can not digest certain sugars, consult the doctor before taking this medicine.

Tenovamed Inovamed contains sodium

This medicine contains less than 1 mmol (23 mg) sodium per tablet and is therefore considered sodium-free.

3. HOW SHOULD YOU USE THE MEDICINE?

- Always use the preparation according to the doctor’s instructions.** Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation. **The dosage and treatment regimen will be determined by the doctor only.**
- The **recommended dosage of Tenovamed Inovamed to treat HIV or to reduce the risk of getting HIV is:**
 - Adults:** one tablet each day. Whenever possible, Tenovamed Inovamed 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 dosage recommended by the 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 dosage unless the doctor tells you to.

- If you are being treated for HIV infection,** your doctor will prescribe Tenovamed Inovamed 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 Tenovamed Inovamed to reduce the risk of getting HIV,** take Tenovamed Inovamed every day, not just when you think you have been at risk of HIV infection.

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

If you take a higher dosage of Tenovamed Inovamed than you should

If you accidentally took a higher dosage of Tenovamed Inovamed than needed, refer to the doctor or proceed to the nearest emergency room for advice. Bring the package of tablets with you so that you can easily describe what you have taken.

If you forget to take the medicine

It is important not to miss a dose of Tenovamed Inovamed.

- If you notice within 12 hours** of the time you usually take Tenovamed Inovamed, take the tablet as soon as possible, preferably with food. Then take the next dose at the usual time.
- If you notice 12 hours or more** after the time you usually take Tenovamed Inovamed, do not take the missed dose. Wait and take the next dose at your usual time, preferably with food.

If you vomit less than 1 hour after taking Tenovamed Inovamed, take another tablet. If you vomit more than one hour after taking Tenovamed Inovamed, there is no need to take another tablet.

Do not stop taking Tenovamed Inovamed

- If you take Tenovamed Inovamed for treatment of HIV infection,** stopping tablets may reduce the effectiveness of the anti-HIV therapy recommended by the doctor.
- If you are taking Tenovamed Inovamed to reduce the risk of getting HIV,** do not stop taking Tenovamed Inovamed or miss any doses. Stopping use of Tenovamed Inovamed, or missing a dose, may increase the risk of getting HIV infection.

Do not stop taking Tenovamed Inovamed without contacting the doctor.

- If you have an hepatitis B infection,** it is especially important not to stop your Tenovamed Inovamed treatment without talking to the 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 the hepatitis, which may be life-threatening.

Tell the doctor immediately about new or unusual symptoms that occurred after you stopped the treatment, particularly symptoms you associate with hepatitis B infection.

Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them. If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Tenovamed Inovamed may cause side effects in some users, although not everybody gets them. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Tell the 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. Possible signs of lactic acidosis:
 - deep and rapid breathing
 - drowsiness
 - nausea, vomiting
 - stomach pains
- If you think you may have lactic acidosis, get medical help immediately.**
- Any sign 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, which enables the body to fight infections that were present with no obvious symptoms.
- Autoimmune disorders,** a condition in which the immune system attacks healthy body tissues, which may also occur after you start taking medicines to treat HIV infection. Autoimmune disorders may develop 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 – effects that occur in more than one user in ten

- diarrhea, vomiting, nausea
- dizziness, headache
- rash
- feeling weak

Tests may also show:

- decrease in phosphate level in the blood
- increase in creatine kinase level

Common side effects – effects that occur in 1-10 in 100 users

- pains, stomach pains
- difficulty sleeping, abnormal dreams
- problems with digestion resulting in discomfort after meals, feeling bloated, flatulence
- rashes (including red spots or large red blotches, sometimes with blistering and swelling of the skin), which may be allergic reactions, itching, changes in skin color including formation of dark patches in the skin
- 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 may make you more prone to infections)
- high level of triglycerides (fatty acids), bile or sugar in the blood
- liver and pancreas problems

Uncommon side effects – effects that occur in 1-10 in 1,000 users

- pain in the abdomen caused by inflammation of the pancreas
 - swelling of the face, lips, tongue or throat
 - anemia (low red blood cell count)
 - breakdown of muscles, muscle pain or weakness which may occur due to damage to the kidney tubule cells
- Tests may also show:
- decrease in potassium levels in the blood
 - increase creatinine levels in the blood
 - changes in the urine

Rare side effects – effects that occur in 1-10 in 10,000 users

- lactic acidosis (see “Possible serious side effects”)
- fatty liver
- yellowing of the skin or eyes, itching, or pain in the abdomen caused by inflammation of the liver
- inflammation of the kidneys, passing a lot of urine and feeling thirsty, kidney failure, damage to kidney tubule cells
- softening of the bones (with bone pain. Sometimes this results 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 levels in the blood.

If you notice any of the side effects listed in this leaflet or if any of the side effects worsens, tell the doctor or pharmacist.

The frequency of the following side effects is not known (effects whose frequency has not been determined):

- Bone problems.** Some patients taking combination antiretroviral medicines such as Tenovamed Inovamed 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 include:
 - 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 with medicines 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 body lipids, sometimes to the HIV medicines themselves. The doctor will perform test to identify these changes

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

By reporting side effects, you will help provide more details about the safety of this medicine.

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Store at a temperature below 30°C. Store in the original package to protect from moisture.

Bottle package: shelf life after first opening the bottle containing 30 film-coated tablets: can be used for 90 days, but no later than the expiry date of the preparation.

Keep the bottle tightly closed.

Do not discard any medicines in the household or household waste bin. Consult a pharmacist as to how to dispose of medicines that you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredients, the medicine also contains: Cellulose microcrystalline, lactose anhydrous, croscarmellose sodium, opadry II blue 32K505040, magnesium stearate, Opadry II blue 32K505040: hypromellose 2910 (E464), lactose monohydrate, titanium dioxide (E171), triacetin, FD&C blue #2 indigo carmine aluminum lake (E132).

What the medicine looks like and the contents of the package: A blue-colored, capsule shaped, film-coated biconvex tablet, debossed with “LA49” on one side and plain on the other side.

Package type: The medicine is provided in the following two types of packages:

- A carton package that contains trays/blisters with 30 or 72 film-coated tablets in total.
- A plastic bottle that contains 30 film-coated tablets and a desiccant. The bottle contains a silica gel desiccant provided as a separate canister that should not be swallowed. The desiccant must remain in the bottle to protect the tablets. The bottle is closed with a child-proof cap. Instructions for opening: To remove the cap, press down while turning toward the left (counter-clockwise). Instructions for closing: Place the cap on the open end of the bottle and turn toward the right (clockwise) until it is fully closed.

Not all package sizes may be marketed.

Licence holder and importer: Inovamed Ltd., P.O.B. 62, Even Yehuda 40500.

Manufacturer: Laurus Labs Ltd., Hyderabad, Telangana, India.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 171-61-36295

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