Package Leaflet – Information for the user

Lamivudine/Tenofovir disoproxil 300 mg/245 mg film-coated tablets

Lamivudine/Tenofovir disoproxil

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 any further questions, ask your doctor, pharmacist or nurse.
- 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 are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Lamivudine/Tenofovir disoproxil Tablets is and what it is used for

Lamivudine/Tenofovir disoproxil Tablets contains two active substances lamivudine and tenofovir disoproxil. These active substances are *antiretroviral* or antiviral medicines which are used to treat HIV infection. Lamivudine is a *nucleoside reverse transcriptase inhibitor*. Tenofovir is a *nucleotide reverse transcriptase inhibitor.* Both active substances interfere with enzymes used by HIV for making copies of itself and, by doing so, block the reproduction of the virus.

This medicine is a treatment for Human Immunodeficiency Virus (HIV) infection in adults over 18 years of age.

Antiviral medicines used for HIV infection are known as antiretrovirals. To prevent the virus become resistant, this medicine should always be given as part of antiretroviral combination therapy when treating HIV.

This medicine is not a cure for HIV infection. While taking Lamivudine/Tenofovir disoproxil Tablets you may still develop infections or other illnesses associated with HIV infection. You can also pass on HIV to others, so it is important to take precautions to avoid infecting other people.

2. What you need to know before you take Lamivudine/Tenofovir disoproxil Tablets

Do not take Lamivudine/Tenofovir disoproxil Tablets
- if you are allergic to lamivudine, tenofovir disoproxil or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to peanut or soya, as this medicine contains lecithin (soya).

Warnings and precautions

Talk to your doctor or pharmacist before taking Lamivudine/Tenofovir disoproxil Tablets,
- **Take care not to infect other people.** You 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. You must continue to take precautions to avoid this.
- **Talk to your doctor or pharmacist if you have had kidney disease or if tests have shown problems with your kidneys.** This medicine should not be given to adolescents with existing kidney problems. Before starting treatment, your doctor may order blood tests to assess your kidney function. This medicine may affect your kidneys during treatment. Your doctor may order blood tests during treatment to monitor how your kidneys work. If you are an adult, your doctor may advise you to take the tablets less often. Do not reduce the prescribed dose, unless your doctor has told you to do so.

  Lamivudine/Tenofovir disoproxil Tablet is not usually taken with other medicines that can damage your kidneys (see *Other medicines and Lamivudine/Tenofovir disoproxil Tablets*). If this is unavoidable, your doctor will monitor your kidney function once a week.
- **Bone problems.** Some adult patients with HIV 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, higher body mass index, among others, 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 doctor.

  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, *Possible 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 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 for fractures.
- **Talk to your doctor if you have a history of liver disease, including hepatitis.** 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 have hepatitis B infection, your doctor will carefully consider the best treatment for you. If you have a history of liver disease or chronic hepatitis B infection your doctor may conduct blood tests to monitor your liver function.
- **Look out for infections.** If you have advanced HIV infection (AIDS) and have an infection, you may develop symptoms of infection and inflammation or worsening of the symptoms of an existing infection once treatment with this medicine 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 this medicine. If you notice signs of inflammation or infection, **tell your doctor at once.**

  In addition to the 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 doctor immediately to seek necessary treatment.
- **Talk to your doctor or pharmacist if you are over 65.** This medicine has not been studied in patients over 65 years of age. If you are older than this and are prescribed this medicine, your doctor will monitor you carefully.
- if you are seriously **overweight** (especially if you are a woman)

Protect other people

HIV infection is spread by sexual contact with someone who has the infection, or by transfer of infected blood (for example, by sharing injection needles). You 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.

Children and adolescents

Lamivudine/Tenofovir disoproxil Tablets is not for use in children and adolescents under 18 years. Ask your doctor or pharmacist for advice before taking this medicine.

Other medicines and Lamivudine/Tenofovir disoproxil Tablets

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
- **Don't stop any anti-HIV medicines** prescribed by your doctor when you start this medicine if you have both HBV and HIV.
- **Do not take this medicine** if you are already taking other medicines containing tenofovir disoproxil, tenofovir alafenamide or lamivudine (used to treat **HIV infection** or **hepatitis B infection)**. Do not take this medicine together with medicines containing adefovir dipivoxil (a medicine used to treat chronic hepatitis B).
- **It is very important to tell your doctor if you are taking other medicines that may damage your kidneys.**

These include:
  - aminoglycosides, pentamidine or vancomycin (for bacterial infection),
  - amphotericin B (for fungal infection),
  - foscarnet, ganciclovir, or cidofovir (for viral infection),
  - interleukin-2 (to treat cancer),
  - adefovir dipivoxil (for HBV),
  - tacrolimus (for suppression of the immune system),
  - non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pains).
- **Other medicines containing didanosine (for HIV infection):** Taking this medicine 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 caused 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.
- emtricitabine (used to treat **HIV infection**)
- high doses of **co-trimoxazole**, an antibiotic.
- cladribine (used to treat hairy cell leukaemia).
- It is also important to tell your doctor if you are taking ledipasvir/sofosbuvir or sofosbuvir/velpatasvir to treat hepatitis C infection.

Lamivudine/Tenofovir disoproxil Tablets with food

Take this medicine with food (for example, a meal or a snack).

Pregnancy, breast-feeding and fertility

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 this medicine.
- **You must not take this medicine during pregnancy** unless specifically discussed with your doctor.
- This medicine and similar medicines may cause side effects in unborn babies. If you become pregnant while you are taking this medicine, your baby may be given extra check-ups (including blood tests) to make sure it is developing normally.
- **If you become pregnant,** or plan to become pregnant, ask your doctor about the potential benefits and risks of your antiretroviral therapy to you and your child.
- **If you have taken this medicine** 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 medicines like this medicine (nucleoside/nucleotide reverse transcriptase inhibitors) during pregnancy, the benefit from the protection against the virus outweighed the risk of side effects.
- **Do not breast-feed during treatment with this medicine.** This is because the active substance in this medicine passes into human breast milk.
- If you are a mother with HIV do not breast-feed, to avoid passing the virus to the baby in breast milk.

Driving and using machines

Lamivudine/Tenofovir disoproxil Tablets can cause dizziness. If you feel dizzy while taking this medicine, **do not drive or ride a bicycle** and do not use any tools or machines.

Lamivudine/Tenofovir disoproxil Tablets contains sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per tablets, i.e. essentially sodium- free.

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Date: 12/05/2021

Blister Pack

3. How to take Lamivudine/Tenofovir disoproxil Tablets

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Always take the dose recommended by your doctor or health care provider. 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.

The recommended dose is:
Adults: 1 tablet each day with food (for example, a meal or a snack).

If you are an adult and have problems with your kidneys, your doctor may advise you to take this medicine less frequently.
Use in children and adolescents
Lamivudine/Tenofovir disoproxil Tablets is not for use in children and adolescents under 18 years.

If you take more Lamivudine/Tenofovir disoproxil Tablets than you should
If you accidentally take too many this medicine, you may be at increased risk of experiencing possible side effects with this medicine (see section 4, *Possible side effects*). Contact your doctor or nearest emergency department for advice. Keep the tablet bottle or pack with you so that you can easily describe what you have taken.

If you forget to take Lamivudine/Tenofovir disoproxil Tablets

If you forget to take a dose, take it as soon as you remember. Then continue your treatment as before.

Do not take a double dose to make up for a forgotten dose.

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

4. Possible side effects

During HIV therapy 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.

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Some side effects may be serious. Tell your doctor straight away if you get any of the following:

Lamivudine
Rare (may affect up to 1 in 1,000 people)
- serious allergic reaction causing swelling of the face, tongue or throat which may cause difficulty in swallowing or breathing
- inflammation of the pancreas (pancreatitis)

Very rare (may affect up to 1 in 10,000 people)
- lactic acidosis (excess lactic acid in the blood)

Tenofovir disoproxil
Uncommon (may affect up to 1 in 100 people)
- **pain in the tummy** (abdomen) caused by inflammation of the pancreas
- damage to kidney tubule cells

Rare (may affect up to 1 in 1,000 people)
- inflammation of the kidney, **passing a lot of urine and feeling thirsty**
- **changes to** your **urine** and **back pain** caused by kidney problems, including kidney failure
- softening of the bones (with **bone pain** and sometimes resulting in fractures), which may occur due to damage to kidney tubule cells
- **fatty liver**
- **lactic acidosis** (excess lactic acid in the blood) is serious side effect that can be fatal. The following side effects may be signs of lactic acidosis:
  - deep, rapid breathing
  - drowsiness
  - feeling sick (nausea), being sick (vomiting) and stomach pain

If you think that you may have **lactic acidosis, contact your doctor immediately.**

Other side effects

Lamivudine

Common (may affect up to 1 in 10 people)
- headache
- feeling sick (nausea)
- being sick (vomiting)
- diarrhoea
- stomach pains
- tiredness, lack of energy
- fever (high temperature)
- general feeling of being unwell
- muscle pain and discomfort
- joint pain
- difficulty in sleeping (insomnia)
- cough
- irritated or runny nose
- rash
- hair loss (alopecia).

Uncommon (may affect up to 1 in 100 people)
Uncommon side effects that may show up in blood tests are:
- a decrease in the number of cells involved in blood clotting (thrombocytopenia)
- a low red blood cell count (anaemia) or low white blood cell count (neutropenia)
- an increase in the level of liver enzymes.

Rare (may affect up to 1 in 1,000 people)
- breakdown of muscle tissue
- liver disorders, such as jaundice, enlarged liver or fatty liver, inflammation (hepatitis).

A rare side effect that may show up in blood tests is:
- increase in an enzyme called amylase.

Very rare (may affect up to 1 in 10,000 people)
- tingling or numbness of the arms, legs, hands or feet.

A very rare side effect that may show up in blood tests is:
- a failure of the bone marrow to produce new red blood cells (pure red cell aplasia).

Tenofovir disoproxil
Very common (may affect more than 1 in 10 people)
- diarrhoea, being sick (vomiting), feeling sick (nausea), dizziness, rash, feeling weak

Tests may also show:
- decreases in phosphate in the blood

Common (may affect up to 1 in 10 people)
- headache, stomach pain, feeling tired, feeling bloated, flatulence

Tests may also show:
- liver problems

Uncommon (may affect up to 1 in 100 people)
- breakdown of muscle, muscle pain or weakness

Tests may also show:
- decreases in potassium in the blood
- increased creatinine in your 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 (may affect up to 1 in 1,000 people)
- pain in the tummy (abdomen) caused by inflammation of the liver
- swelling of the face, lips, tongue or throat

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 also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Lamivudine/Tenofovir disoproxil Tablets

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the bottle, label and carton after EXP. The expiry date refers to the last day of the month.
- Blister: This medicine does not require any special temperature storage conditions.
- HDPE bottles: This medicine does not require any special temperature storage conditions. Store in the original bottle in order to protect from moisture. 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. Contents of the pack and other information

What Lamivudine/Tenofovir disoproxil Tablet contains
- The active substances are lamivudine and tenofovir. Each film-coated tablet contains 300 mg lamivudine and 300 mg tenofovir disoproxil fumarate equivalent to 245 mg tenofovir disoproxil
- The other ingredients are:
  - *Tablet core:* microcrystalline cellulose (E460), croscarmellose sodium (E468), starch pregelatinized Ph.Eur (maize starch 1500), magnesium stearate (E572)
  - *Tablet film-coat:* hypromellose 6cps (E464), Opadry II 85G18490 white containing polyvinyl alcohol- part hydrolyzed (E1203), titanium dioxide (E171), talc (E553b), macrogol 4000 (E1521), lecithin (soya) (E322).

What Lamivudine/Tenofovir disoproxil Tablets look like and contents of the pack

Lamivudine/Tenofovir disoproxil Tablets are white to off white coloured, capsule shaped, biconvex, film coated tablet, with “LT” debossed on one side and plain on other side. Length is 18.1 mm ± 0.2 mm and breadth is 8.6 mm ± 0.2 mm.

Lamivudine/Tenofovir disoproxil Tablets are supplied in bottles/blister containing 30 tablets and 10 tablets.

HDPE container of 30 tablets composed of 50 cc white HDPE container with 38 mm white PP child resistant cap and 1 gm Silica gel bag and bundled pack of 3 bottles of 30 tablets.

Blister pack of 10 tablets composed of 3 ply Alu-Alu film and aluminium blister foil and box of 30 tablets and bundled pack of 3 boxes of 30 tablets.

Not all pack sizes may be marketed.

This medicinal product is authorised in the Member States of the EEA under the following names:

United Kingdom:	Lamivudine/Tenofovir disoproxil 300 mg/245 mg film-coated tablets
Germany:	Lamivudin/Tenofovir*disoproxil* Cipla 300/245 mg *Film*tabletten
Spain:	Lamivudina/Tenofovir Cipla 300/245 mg Comprimidos recubiertos con película
Romania:	Lamivudină/Tenofovir disoproxil Cipla 300 mg/245 mg comprimate filmate

Marketing Authorisation Holder
Cipla (EU) Limited
Dixcart House,Addlestone Road,
Bourne Business Park Addlestone
KT15 2LE
United Kingdom.

Manufacturer
Cipla Europe NV
De Keyserlei 58-60
Box-19, 2018 Antwerp,
Belgium

Or

Cipla (EU) Limited
Dixcart House,Addlestone Road,
Bourne Business Park Addlestone
KT15 2LE
United Kingdom.

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Cipla

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PACKAGING DEVELOPMENT

Product Name: Lamivudine and Tenofovir Disoproxil Tablets 300-245 mg (Blister Pack)	**Material No.:** 21089167	**Version:** 01	**Item:** Leaflet	**Co-ordinator:** Mangesh	**Artist:** Avadhoot	**Date:** 12/05/2021
Colours: BLUE WOOL TEST VALUE 5-8 (LIGHT FASTENING DATA) ■ Black				**INK:** Oil based Ink from DIC OR MICRO		
Design: Unfolded	**Supersedes:** 21065347			**Software:** Illustrator CC		
Fonts: ------				**Links:** NA		
Actual Size: 200 x 500 mm	**Size after folding:** ---	**Pharmacode:** 2315_STD		**Grain Direction :** Parallel to length		**Screen : # __**
Material: 54 GSM Maplitho Paper				**Varnish: ---**	**Artwork Print Size:** ☐ actual ☐ scaled	
Path: Avadhoot \ F:\Export\EUROPE\DTM\Lamivudine+Tenofovir \ 21089167 Lamivudine and Tenofovir Disoproxil Tablets 300-245 mg (Blister Pack) PIL UK						

- **Instructions / Remark: NA**
- Any deviation must be brought to the notice of packaging development co-ordinator immediately.
- For any clarification, please contact packaging development co-ordinator immediately.
  NO CHANGES IN ARTWORK SHOULD BE DONE BY THE PRINTER
- The printer should verify the e-proof against the approved artwork before submitting for approval and the e-proof should have printer details .

Checked by	Artist	Cordinator	file loaded in Server	Section Head
Pharma Code	☐	☐		
2D Code	☐	☐		
QR Code	☐	☐		
Bar Code	☐	☐		
Artwork	☐	☐		
Spell check	☐	☐		