PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

ENVUTEG Film-coated tablets

Lamivudine 300 mg, tenofovir alafenamide 25 mg and dolutegravir sodium (equivalent to dolutegravir) 50 mg

Contains sugar: Mannitol 131,40 mg and lactose monohydrate 60 mg per tablet

Read all of this leaflet carefully before you start taking ENVUTEG

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- ENVUTEG has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What ENVUTEG is and what it is used for

ENVUTEG is a combination antiretroviral medicine that is used to treat human immunodeficiency virus type 1 (HIV-1) infection in adults and children weighing at least 40 kg.

HIV-1 is the virus that causes acquired immune deficiency syndrome (AIDS).

2. What you need to know before you take ENVUTEG

Do not take ENVUTEG

- If you are hypersensitive (allergic) to dolutegravir, lamivudine or tenofovir alafenamide, or any of the ingredients in ENVUTEG (see section 6).
- If you take dofetilide. Taking ENVUTEG and dofetilide can cause side effects that may be serious or life-threatening.
- If you are taking a medicine called metformin (used for the treatment of diabetes).
- If you are taking a medicine called adefovir (used for the treatment of chronic hepatitis B).
- If you are taking a medicine called pilsicainide (used for the treatment of abnormal heartbeat – cardiac dysrhythmias).
- If you are taking a medicine called didanosine (used for the treatment of hiv infection).
- If you are pregnant or breast feeding your baby.
- If you are a woman of childbearing age.
- If you are younger than 18 years.
- If you have moderate or severe liver function.
- If you have uncontrolled kidney disease.

Warnings and precautions

Take special care with ENVUTEG:

- Too much lactic acid in your blood (lactic acidosis) is a serious but rare medical emergency that can lead to death. Tell your health care provider right away if you get these symptoms: Weakness or being more tired than usual, unusual muscle pain, being short of breath of fast breathing, stomach pain with nausea and vomiting, cold or blue hands and feet, feel dizzy or lightheaded, or a fast or abnormal heartbeat.
- If you have an abnormal distribution of fat in the body including central obesity; buffalo hump (a build-up of fat between the shoulder blades); muscle and facial wasting and breast enlargement in HIV patients.
- Immune reconstitution inflammatory syndrome (IRIS): the worsening of a recognised or unrecognised pre-existing infection of improved immunologic function.

- If you suffer from osteonecrosis, when blood flow to part of a bone is reduced.
- If you suffer from mitochondrial dysfunction (when the mitochondria, which is present in cells and function is to produce energy, fail to produce enough energy for the body to function properly).
- If you have hepatitis B infection, your doctor will carefully consider the best treatment regimen for you. If you have hepatitis B infection, liver problems may become worse after you stop taking ENVUTEG. It is important not to stop taking ENVUTEG without talking to your doctor.

Lactic acid build-up in the body (causes nausea, vomiting, rapid deep breathing, and generalised weakness) and enlarged liver and fatty liver, have been reported with the use of some medicines for HIV alone or in combination with other antiretrovirals.

Tenofovir alafenamide, one component of ENVUTEG tablets, is used for the treatment of chronic hepatitis B virus (HBV) infection. Severe acute worsening of hepatitis B has been reported in patients who are also infected with HIV- and HBV and have discontinued products containing tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of ENVUTEG tablets.

Tell your doctor before taking ENVUTEG:

- If you have had liver problems, including hepatitis B or C infection.
- If you have kidney problems, including end-stage renal disease (ESRD) that requires dialysis.

Other medicines and ENVUTEG

Always tell your health care professional if you are taking any other medicine. (This includes all complementary or traditional medicines.)

You should not take ENVUTEG with medicines containing:

- Tenofovir alafenamide.
- Tenofovir disoproxil.
- Lamivudine.
- Adefovir dipivoxil.

- Dolutegravir.

Other types of medicine:

Talk to your doctor if you are taking:

- Antibiotics, used to treat bacterial infections including tuberculosis, containing: rifabutin, rifampicin and rifapentine.
- Antiviral medicines used to treat HIV: emtricitabine and tipranavir.
- Anticonvulsants, used to treat epilepsy such as: carbamazepine, oxcarbazepine, phenobarbitone and phenytoin
- Herbal remedies used to treat depression and anxiety containing St. John's wort (*Hypericum perforatum*).

You should avoid taking medicines that contain sorbitol during treatment with ENVUTEG.

Some medicines interact with ENVUTEG.

ENVUTEG may affect the way other medicines work, and other medicines may affect how ENVUTEG works. Keep a list of your medicines and show it to your health care provider and pharmacist when you get a new medicine.

You can ask your health care provider or pharmacist for a list of medicines that interact with ENVUTEG.

Do not start taking a new medicine without telling your health care provider. Your health care provider can tell you if it is safe to take ENVUTEG with other medicines.

ENVUTEG with food and drink

You can take ENVUTEG with or without food.

Pregnancy, breastfeeding, and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before you start taking ENVUTEG.

Do not take ENVUTEG tablets if you are pregnant or breastfeeding (see Do not take ENVUTEG tablets).

ENVUTEG could seriously harm your unborn child if you fall pregnant while on treatment or if you start taking ENVUTEG in the first few weeks of your pregnancy.

You should ensure that you always use effective contraception while you are taking ENVUTEG. Your health care professional can advise you on which contraceptives to take. Never stop taking ENVUTEG without first consulting your health care professional as your HIV condition may become worse.

If you are thinking about having a baby, do not stop using ENVUTEG and contraception before you have talked to your health care professional. If you think you are pregnant go to your health care professional to get a pregnancy test and to be advised on your future HIV treatment and on a pregnancy management plan.

Driving and using machines

ENVUTEG may cause dizziness and tiredness. You should not drive or operate machinery until you are sure ENVUTEG does not affect your ability to drive or use machines.

Important information about some of the ingredients of ENVUTEG tablets

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

3. How to take ENVUTEG

Do not share medicines prescribed for you with any other person.

Always take ENVUTEG exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

ENVUTEG therapy should be initiated by a health care professional experienced in the management of HIV infections.

Take ENVUTEG at the same time every day.

Take ENVUTEG each day with or without food.

If you take antacids, laxatives, or other medicines that contain aluminium, magnesium, or buffered medicines, ENVUTEG should be taken at least 2 hours before or 6 hours after you take these medicines.

If you need to take iron or calcium supplements by mouth during treatment with ENVUTEG.

If you take ENVUTEG with food, you may take these supplements at the same time that you take ENVUTEG.

If you do not take ENVUTEG with food, take ENVUTEG at least 2 hours before or 6 hours after you take these supplements.

For adults and children weighing at least 40 kg, the usual dose of ENVUTEG is one tablet each day. An extra dose of dolutegravir only may be necessary for certain populations. Your health care provider will inform you if you need to take the extra dolutegravir dose.

Stay under the care of a health care provider during treatment with ENVUTEG.

Do not run out of ENVUTEG. The virus in your blood may increase and the virus may become harder to treat. When your supply starts to run low, get more from your health care provider or pharmacy.

Your health care professional will tell you how long your treatment with ENVUTEG will last.

If you have an impression that the effect of ENVUTEG is too strong or too weak tell your health care professional or pharmacist.

If you take more ENVUTEG than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre for help.

If you forget to take ENVUTEG

If you forget to take a dose of ENVUTEG, take it as soon as you remember and then continue as before. Do not take a double dose to make up for missed individual doses.

Effects when treatment with ENVUTEG is stopped

Do not stop treatment early because this may worsen your condition and make your body resistant to ENVUTEG.

4. Possible side effects

ENVUTEG can have side effects.

Not all side effects reported for ENVUTEG are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking ENVUTEG, please consult your health care provider for advice.

If any of the following happens, stop taking ENVUTEG and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing.

These are all very serious side effects. If you have them, you may have had a serious reaction to ENVUTEG. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- **Risk of inflammation of the pancreas (pancreatitis).** Children may be at risk for developing pancreatitis during treatment with ENVUTEG if they:
  - have taken nucleoside analogue medicines in the past.
  - have a history of pancreatitis.
  - have other risk factors for pancreatitis.

Call your health care provider right away if your child develops signs and symptoms of pancreatitis including severe upper stomach area pain, with or without nausea and vomiting. Your health care provider may tell you to stop giving ENVUTEG to your child if their symptoms and blood test results show that your child may have pancreatitis.

- **New or worse kidney problems, including kidney failure**. Your health care provider may do blood and urine tests to check your kidneys before and during treatment with ENVUTEG. Tell your health care provider if you get signs and symptoms of kidney problems, including bone pain that does not go away or worsening bone pain, pain in your arms, hands, legs or feet, broken (fractured) bones, muscle pain or weakness.
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time.
- **Too much lactic acid in your blood (lactic acidosis).** Lactic acidosis is a serious medical emergency that can lead to death.

Tell your health care provider right away if you get any of the following symptoms that could be signs of lactic acidosis:

- Feel very weak or tired.
- Unusual (not normal) muscle pain.
- Trouble breathing.
- Stomach pain with nausea and vomiting.
- Feel cold, especially in your arms and legs.
- Feel dizzy or light-headed.
- Have a fast or irregular heartbeat.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- Trouble sleeping.
- Nausea.
- Diarrhoea.
- Tiredness.
- Headache.
- Dizziness.
- Abnormal dreams.
- Depression.

Less frequent side effects:

- Abdominal pain.
- Abdominal discomfort.
- Winds.
- Stomach pain.
- Vomiting.
- Inflammation of the liver.
- Inflammation of the muscle tissue.
- Suicidal thoughts and behaviour.

- Kidney problems.
- Itching.
- Increase in liver enzymes in the blood.

Frequency unknown:

- Increased weight.
- Painful joints and muscles.
- Liver failure.
- Anxiety.
- Accumulation of body fat.
- Increase in blood sugar.
- Weakness.
- Decrease in red blood cells in the blood.
- Rhabdomyolysis (breakdown of muscle fibres).
- Hair loss.
- Facial swelling, itching, and rash.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse.

You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of ENVUTEG.

5. How to store ENVUTEG

Store all medicines out of reach of children.

Store at or below 30 °C.

Keep the container tightly closed.

Store in the original container until required for use. Do not store in bathrooms.

Do not use after the expiry date stated on the carton/label.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What ENVUTEG contains

Each ENVUTEG film-coated tablet contains the following active ingredients: lamivudine 300 mg, tenofovir alafenamide 25 mg and dolutegravir sodium (equivalent to dolutegravir) 50 mg.

Contains sugar: mannitol 131,40 mg and lactose monohydrate 60 mg per tablet.

The other ingredients are: croscarmellose sodium, lactose monohydrate, magnesium stearate, mannitol, microcrystalline cellulose, povidone, sodium starch glycolate, Opadry II white.

What ENVUTEG looks like and contents of the pack

White to off white, film-coated, capsule shaped, biconvex, bevelled edge tablet debossed with M on one side of the tablet and LD on the other side.

The product is presented in the following marketable packs:

30’s bottle pack (with 4 g molecular sieve):

Pack type	Configuration	Primary packaging components
HDPE bottle pack (with desiccant)	30’s count with 4 g desiccant	**Container:** Bottle HDPE 75 ml 38 mm blue round (HWT) TP. **Closure:** Closure 38 mm blue screw with SG100 SP. **Desiccant:** 2 g molecular sieve canister – SC. **Desiccant:** 2 g molecular sieve sachet GDT2 reel clariant.

30’s and 28’s bottle pack (with 2 g molecular sieve):

Pack Type	Configuration	Primary packaging components
HDPE bottle pack (with desiccant)	30's count with 2 g desiccant	**Container:** Bottle HDPE 60 cc (60 ml) 38 mm blue round (12 g) TP **Closure:** Closure 38 mm blue screw with SG100 SP. **Desiccant:** 2 g molecular sieve canister
HDPE Bottle Pack (with desiccant)	28's count with 2 g desiccant	**Container:** Bottle HDPE 60 cc (60 ml) 38 mm blue round (12 g) TP **Closure:** Closure 38 mm blue screw with SG100 SP. **Desiccant:** 2 g molecular sieve canister

Holder of Certificate of Registration

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