SCHEDULING STATUS **S4**

ENVUTEG Film coated tablet

Lamivudine 300 mg, Tenofovir Alafenamide 25 mg and Dolutegravir sodium equivalent to Dolutegravir 50 mg

Contains sugar: mannitol and lactose monohydrate

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
2. What you need to know before you take **ENVUTEG**
3. How to take **ENVUTEG**
4. Possible side effects
5. How to store **ENVUTEG**
6. Contents of the pack and other information

1. What ENVUTEG is and what it is used for

ENVUTEG is a prescription medicine that is used to treat Human Immunodeficiency Virus type 1 (HIV-1) infection in adults.

HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS).

ENVUTEG contains 3 prescription medicines, dolutegravir, lamivudine and tenofovir alafenamide.

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.
- Co-administration with metformin, adefovir, pisicainide or didanosie
- if you are pregnant or breast feeding your baby.
- Woman of childbearing age
- Patients younger than 18 years
- Moderate or severe liver function
- 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 emergancy that can lead to death. Tell your healthcare 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 nasea

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
- 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 fattty liver, have been reported with the use of some medicines for HIV alone or in combination with other antiretrovirals.

Tenofovir alafenamide, once component of ENVUTEG tablets, is approved for the treatment of chronic hepatitis B virus (HBV) infection. Severe acute worsening of hepatitis B has been repored in patients who are also infected with HIV- and HBV and have discontinued products containing tenofovir

disoproxil fumarate (TDF), and may occure 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** work. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

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

Do not start taking a new medicine without telling your healthcare provider. Your healthcare 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 [**PRODUCT NAME]** in the first few weeks of your pregnancy

You should ensure that you always use effective contraception while you are taking **ENVUTEG.** Your healthcare professional can advise you on which contraceptives to take. Never stop taking **ENVUTEG** without first consulting your healthcare 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 healthcare professional. If you think you are pregnant go to your healthcare 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 medicinal product.

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 healthcare 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 aluminum, 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 healthcare provider will inform you if you need to take the extra

dolutegravir dose.

Stay under the care of a healthcare 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 healthcare provider or pharmacy.

Your healthcare 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 healthcare 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 control 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 healthcare 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 healthcare 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 healthcare provider may do blood and urine tests to check your kidneys before and during treatment with **ENVUTEG**. Tell your healthcare 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 healthcare 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 “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8. 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 ºC.

Keep the container tightly closed.

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

Store all medicines out of reach of children

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 dolutegavir 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, beveled 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

Holder of Certificate of Registration

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Access to the corresponding Professional Information

To follow

1.3.2 Patient Information Leaflet