PATIENT INFORMATION LEAFLET

SCHEDULING STATUS **S4**

PROPRIETARY NAME AND DOSAGE FORM

DOLTRITAF film-coated tablets

Emtricitabine/tenofovir alafenamide/dolutegravir 200/25/50 mg

Contains sugar: lactose monohydrate 120 mg per tablet and mannitol 145,400 mg per tablet.

Read all of this leaflet carefully before you start taking DOLTRITAF

- 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.
- DOLTRITAF 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 DOLTRITAF is and what it is used for

DOLTRITAF is used to treat Human Immunodeficiency Virus (HIV-1) infection in adults and children who weigh 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 DOLTRITAF

Do not take DOLTRITAF:

- If you are hypersensitive (allergic) to emtricitabine, tenofovir alafenamide or dolutegravir, or any of the other ingredients of DOLTRITAF (listed in section 6).
- If you take medicine containing dofetilide or pilsicainide, as taking them with DOLTRITAF can cause serious or life-threatening side effects.
- If you are taking medicine containing metformin.
- If you have moderate or severe hepatic impairment.
- If you have severe renal disease
- If your doctor has told you that your HIV-1 has the K65R mutation.
- If you are pregnant or breastfeeding.

Warnings and precautions

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 DOLTRITAF tablets, is approved 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-1 and HBV and have discontinued products containing tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of DOLTRITAF tablets.

Take special care with DOLTRITAF:

- If you have or have had liver problems, including hepatitis B or C virus infection.
- If you have kidney problems.
- If you are taking other medicines as taking them with DOLTRITAF can cause side effects (See **Using other medicines with DOLTRITAF** below).

Children and adolescents

Do not give DOLTRITAF to children who weigh less than 40 kg.

Other medicines and DOLTRITAF

Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines).

Medicines containing dofetilide should not be taken with DOLTRITAF as blood levels are raised and increased side effects can result.

Metformin blood levels are increased by DOLTRITAF. You should not take DOLTRITAF if you are also taking metformin.

Blood levels of DOLTRITAF are decreased by the following medicines and should not be used:

- rifabutin, rifampin, rifapentine (medicines used to treat tuberculosis)
- St John's wort

Blood levels of DOLTRITAF are decreased by the following medicines and your dosage will need to be adjusted or a different medicine may need to be prescribed:
Carbamazepine, oxcarbazepine, phenytoin, phenobarbitone

Some antacids or laxatives containing magnesium or aluminium, sucralfate and oral calcium or iron supplements may be used if DOLTRITAF is taken 2 hours before or 6 hours after these medicines.

DOLTRITAF with food and drink

DOLTRITAF may be taken with or without food.

Pregnancy, and breastfeeding and fertility

Women of childbearing potential:

Women of childbearing potential should be counselled about the potential risk of birth defects of the brain and spine with dolutegravir, including consideration of using effective contraceptive measures.
Perform pregnancy testing before start of DOLTRITAF in women of childbearing potential to exclude unintentional use of DOLTRITAF during the first trimester of pregnancy.
If a woman plans pregnancy, the benefits and the risks of
starting or continuing treatment with dolutegravir versus using
another antiretroviral medicine should be discussed with her.

Pregnancy:

DOLTRITAF is contraindicated in pregnancy and you must not take it if you are pregnant or are trying to become pregnant.
Use of dolutegravir during pregnancy was associated with a small increase in the birth defects of the brain and spine.
If a pregnancy is confirmed in the first trimester while on dolutegravir, the benefits and risks of continuing dolutegravir versus switching to another antiretroviral medicine should be discussed with the patient. Dolutegravir may be used during the second and third trimester of pregnancy when the expected benefit outweighs the potential risk to the foetus.

A urine pregnancy test should be carried out within 24 hours before commencing treatment with DOLTRITAF. Once treatment has started, pregnancy testing should be repeated every 4 weeks. Pregnancy testing and counselling should be performed if a woman misses her period or if there is any abnormality in menstrual bleeding.

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 taking this medicine.

Breast-feeding:
Do not breast-feed your baby if you are taking DOLTRITAF.
HIV infected women should not breast-feed their infants in order to avoid transmission of HIV or follow appropriate guidelines.
Dolutegravir is excreted in human breast milk, and there is significant exposure to the neonate/infants due to slow removal. There is insufficient information on the effects of dolutegravir in neonates/infants.

Fertility:

There are no data on the effects of dolutegravir on human male or female fertility.

Driving and using machines

DOLTRITAF may cause dizziness which can affect your ability to drive a car or operate machines.

DOLTRITAF contains lactose

DOLTRITAF contains lactose. Patients with the rare hereditary conditions of lactose or galactose intolerance, e.g. galactosaemia should not take DOLTRITAF.
DOLTRITAF also contains mannitol and may have a laxative effect.

3. HOW TO TAKE DOLTRITAF

Do not share medicines prescribed for you with any other person.
Always take DOLTRITAF exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose is one tablet taken once daily with or without food.

Your doctor will tell you how long your treatment with **DOLTRITAF** will last.
Do not run out of DOLTRITAF tablets. The virus in your blood may increase and the virus may become harder to treat.
If you have the impression that the effect of DOLTRITAF is too strong or too weak, tell your doctor or pharmacist.

If you take more DOLTRITAF 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.

If you forget to take DOLTRITAF

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

Do not miss a dose of DOLTRITAF.

If you miss a dose of DOLTRITAF take it as soon as you remember.

4. POSSIBLE SIDE EFFECTS

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

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

- Fever
- Generally ill feeling
- Tiredness
- Muscle or joint aches
- Blisters or sores in the mouth
- Blisters or peeling of the skin
- Redness or swelling of the eyes
- Swelling of the mouth, face, lips or tongue
- Difficulty in swallowing or breathing

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

Worsening of hepatitis B virus infection: DOLTRITAF tablets are not for use to treat chronic hepatitis B virus (HBV) infection. If you have hepatitis B virus (HBV) infection and take DOLTRITAF tablets, your HBV may get worse (flare-up) if you stop taking DOLTRITAF tablets. A "flare-up" is when your HBV infection suddenly returns in a worse way than before.

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

- Your skin or the white part of your eyes turns yellow (jaundice)
- Dark or "tea-coloured" urine
- Light coloured stools
- Nausea or vomiting
- Loss of appetite
- Pain, aching or tenderness on the right side of your stomach area.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following signs or symptoms of too much lactic acid in your blood**:**

- Weakness or being more tired than usual, unusual muscle pain
- Short of breath or fast breathing
- Stomach pain with nausea and vomiting
- Cold or blue hands and feet
- Feeling dizzy or lightheaded
- Fast or abnormal heartbeat

Too much lactic acid is a serious medical emergency that can lead to death.

<u>Frequent side effects</u>:

- Neutropenia (low levels of white blood cells). Symptoms are infections of the skin and other areas of the body, swollen gums, and sore mouth.

- Allergic reactions
- Inability to sleep, abnormal dreams
- Suicide
- Headache, dizziness
- Difficulty breathing
- Nausea, diarrhoea, vomiting, gas, stomach pain, indigestion
- Rash, itch, hives, skin discolouration
- Kidney problems
- Fatigue (mental or physical weakness), pain, lack of energy

Less frequent side effects:

- Changes in your immune system can happen as your immune system may get stronger and begin to fight infections in your body. Tell your healthcare provider if you start having new symptoms after you start taking DOLTRITAF
- Stomach pain or discomfort
- Liver problems

The following side effects are reported but the frequency is not known:

- Anaemia (low red blood cells)
- Inflammation of the pancreas
- Myopathy (muscle weakness)
- Osteomalacia (bone pain and muscle weakness)
- Rhabdomyolysis (breakdown of muscle tissue)

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. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reactions & Quality Problem Reporting Form", found online under SAHPRA's publications: https://sahpra.org.za/wp-content/uploads/2020/01/6.04_ARF1_v5.1_27Jan2020.pdf By reporting side effects, you can help provide more information on the safety of DOLTRITAF.

5. How to store DOLTRITAF

Store all medicines out of reach of children.

Store at or below 30 °C in original container.

6. Contents of the pack and other information

What DOLTRITAF contains

The active substances are emtricitabine 200 mg, tenofovir alafenamide fumarate equivalent to tenofovir alafenamide 25 mg and dolutegravir sodium equivalent to dolutegravir 50 mg per tablet.

Contains sugar: lactose monohydrate 120 mg per tablet and mannitol 145,400 mg per tablet.

The other ingredients are:

Croscarmellose sodium, lactose monohydrate, magnesium stearate, mannitol, microcrystalline cellulose, povidone, sodium starch glycolate.

Film coat: macrogol, polyvinyl alcohol, talc, titanium dioxide.

What DOLTRITAF looks like and contents of the pack

A white to off white, film coated, oval shaped, biconvex beveled edge tablet debossed with M on one side of the tablet and TD1 on the other side; and with the following dimensions (length: 18,00 mm; width: 9,00 mm).

Blue, opaque, HDPE bottle with blue opaque PP screw closure with aluminium induction sealing liner and desiccant canister/sachet.

Pack sizes of 30’s, 90’s & 180’s (Not all packs may be marketed).

Holder of Certificate of Registration

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