PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

DOVILAMIR

Film-coated tablets

Dolutegravir 50 mg**,** Lamivudine 300 mg and Tenofovir disoproxil fumarate 300 mg

Contains sugar (lactose monohydrate 150,4 mg and mannitol 131,38 mg per film-coated tablet)

Read all of this leaflet carefully before you start taking DOVILAMIR

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- DOVILAMIR 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 DOVILAMIR is and what it is used for
2. What you need to know before you take DOVILAMIR
3. How to take DOVILAMIR
4. Possible side effects
5. How to store DOVILAMIR

6. Contents of the pack and other information

WARNING

TOO MUCH ACID IN THE BODY DUE TO LACTIC ACID AND SERIOUS ENLARGED, FATTY LIVER, INCLUDING CASES RESULTING IN DEATH, HAVE BEEN REPORTED WITH THE USE OF NUCLEOSIDE ANALOGUES (MEDICINES USED FOR THE TREATMENT OF HIV) ALONE OR IN COMBINATION WITH OTHER ANTIRETROVIRALS. DOVILAMIR IS NOT INDICATED FOR TREATMENT OF CHRONIC HEPATITIS B VIRUS (HBV) INFECTION. THE SAFETY AND EFFICACY OF DOVILAMIR HAS NOT BEEN ESTABLISHED IN PATIENTS INFECTED WITH BOTH HBV AND HIV. SEVERE ACUTE WORSENING OF HEPATITIS B HAVE BEEN REPORTED IN PATIENTS WHO ARE INFECTED WITH BOTH HBV AND HIV AND HAVE STOPPED TAKING THE COMBINATION TABLET. LIVER FUNCTION SHOULD BE MONITORED CLOSELY BY A HEALTH CARE PRACTISIONER FOR AT LEAST SEVERAL MONTHS IN PATIENTS WHO ARE INFECTED WITH BOTH HIV AND HBV AND WHO STOPPED TAKING THE COMBINATION TABLET. IF APPROPRIATE, MEDICINE TO TREAT HEPTATITIS B MAY NEED TO BE PRESCRIBED.

1. What DOVILAMIR is and what it is used for:

DOVILAMIR is a triple combination therapy used to treat Human Immunodeficiency Virus-1 (HIV-1) infected adults over 18 years of age.

2. What you need to know before you take DOVILAMIR

Do not take DOVILAMIR:

- if you are hypersensitive (allergic) to dolutegravir, lamivudine or tenofovir disoproxil fumarate, or any of the other ingredients of DOVILAMIR (listed in section 6).
- If you have uncontrolled kidney failure.

- If you have moderate or severe liver disease.
- If you are pregnant or breastfeeding your baby.
- If you plan on becoming pregnant.
- If you are a woman of child bearing age and are not using effective contraceptives to prevent falling pregnant.
- If you are also taking medication for irregular heart beat containing dofetilide and pilsicainide.
- If you are taking metformin for the treatment of diabetes.
- If you are taking medication for the treatment of hepatitis B containing adefovir dipivoxil.
- If you are taking another antiretroviral medicine containing didanosine.
- If you are younger than 18 years of age.

Warnings and precautions

Tell your doctor:

- If you have abnormal metabolic processes, such as, increased cholesterol, glucose or lactate in the blood or are resistant to insulin. Your doctor may perform regular blood tests to confirm normal metabolic processes.
- If you develop changes in body fat, which may be caused by combination antiretroviral medicines, such as DOVILAMIR. These changes may include increased fat in the upper back and neck areas (“buffalo hump”), breast, and around the main part of your body (trunk). Loss of fat from the legs, arms and face may also happen.
- If you show any symptoms of infection while you are taking DOVILAMIR. Patients with advanced HIV infection (AIDS) have weak immune systems and are more likely to develop serious infections (opportunistic infections). When these patients start with the treatment, they may find that old hidden infections (such as tuberculosis) flare up, causing signs and symptoms of inflammation (such as localised swelling, area appears

red and hot, painful). These symptoms are probably caused by the body's immune system becoming stronger, so that the body starts to fight these infections.

- If you experience joint aches and pain, joint stiffness or difficulty in movement or bone fractures, you may suffer from a condition called osteonecrosis for which you may need treatment.
- If you show symptoms such as nausea, vomiting, abdominal pain, non-specific general feeling of being ill, loss of appetite, weight loss, rapid and/or deep breathing, or muscle weakness, you may be experiencing a condition called lactic acidosis (build-up of lactic acid in the body) (see "Possible side effects").
- If you are female, very overweight (obese), or have been using medicines for the treatment of HIV for a long time, as you may be more likely to get lactic acidosis.
- If your child experiences symptoms of poor growth, loss of muscle coordination, muscle weakness, visual problems, hearing problems, learning disabilities, heart disease, liver disease, kidney disease, gastrointestinal disorders, respiratory disorders, nervous system problems (brain, spine and nerves), loss of voluntary body functions (such as breathing, bladder function, heartbeat and digestive processes) and dementia (loss of memory), as these symptoms can be a sign of mitochondrial (part of the cell that creates energy) disorder. These findings should be considered for any child exposed to treatment, before being born.
- If you experience severe pain in the stomach, nausea or vomiting, as these can be symptoms of pancreatitis (swelling of the pancreas) (see "Possible side effects").
- If you suffer from kidney problems.
- If you have had bone problems in the past, your doctor may need to do tests to check your bone mineral density or may prescribe medicines to help improve your bone mineral density.

- If you suffer from liver disease, including hepatitis B or C infections, as the use of DOVILAMIR can cause deadly, unfavourable liver symptoms. Your doctor will monitor your liver enzymes through tests, as DOVILAMIR can cause liver toxicity.
- If you show signs of liver injury (yellowing of the skin and whites of the eyes, feeling generally weak or tired, loss of weight, nausea, vomiting).
- If you develop a rash, or show any general signs of allergy (rash, accompanied by fever, general feeling of being ill, tiredness, muscle or joint aches, sores, oral scrapes, eye infection, facial swelling, a serious liver infection or swelling of the skin.

Special care should be taken with DOVILAMIR:

DOVILAMIR does not reduce the risk of passing HIV on to other people through sexual contact or blood contamination. Therefore, it is important to continue to take appropriate precautions to prevent passing HIV on to others.

Even if you are receiving treatment for HIV, you are still at risk of contracting other infections and other complications of the HIV infection. Therefore, you should remain under close observation by your doctor.

Children and adolescents

DOVILAMIR should not be used in children under the age of 18 years, as safety has not been established.

Other medicines and DOVILAMIR

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

If you are taking any of the following medicines, please inform your doctor before taking DOVILAMIR:

- Other products that contain dolutegravir, lamivudine or tenofovir, either alone or as combined formulations. DOVILAMIR should not be used with these medicines because they contain the same active ingredients as DOVILAMIR.
- DOVILAMIR may hinder the breakdown of zalcitabine, also used in the treatment of HIV infections.
- Taking DOVILAMIR in combination with high doses of co-trimoxazole or trimethoprim (used for the treatment of bacterial infections) must be avoided if you have a kidney condition or disease.
- DOVILAMIR may increase the levels of abacavir, atazanavir, indinavir, lopinavir, ritonavir (also used for the treatment of HIV infection) and its dose may need to be adjusted.
- DOVILAMIR may decrease the levels of indinavir (also used for the treatment of HIV infection) and its dose may need to be adjusted.
- The use of DOVILAMIR with etravirine (also used for the treatment of HIV infection) is not recommended.
- Medicines that can cause toxicity in the kidneys, for example antibiotics e.g. vancomycin, aminoglycosides (gentamycin, amikacin, tobramycin, neomycin), antifungals, e.g. amphotericin B, antiviral, e.g. foscarnet, ganciclovir, antimicrobials, e.g. pentamidine.
- Rifampicin, used for treatment of TB (tuberculosis), can decrease blood concentrations of DOVILAMIR.
- DOVILAMIR can increase blood concentration levels of isoniazid used for treatment of TB.

- DOVILAMIR can increase levels of the following heart medicines, used for the treatment of irregular heartbeat: dofetilide and pilsicainide and should not be used together with these medicines.
- DOVILAMIR can increase blood concentrations of metformin (for the treatment of diabetes), when used together. DOVILAMIR and metformin should not be used together.
- Combination medicines for treatment of HIV containing darunavir, efavirenz, fosamprenavir, nevirapine, rifampicin or tipranavir in combination with ritonavir may decrease the blood levels of DOVILAMIR.
- Atazanavir alone or with other combination HIV medicines may increase the blood concentration of DOVILAMIR.
- Phenobarbitone, phenytoin, oxcarbazepine, carbamazepine (medicines used for the treatment of epilepsy (fits)) and St. John's Wort (used for the treatment of depression, anxiety and sleeplessness (insomnia)) may decrease the blood levels of DOVILAMIR.
- Antacids (containing magnesium, aluminium or calcium, which are used for heartburn or indigestion), calcium supplements and iron supplements, may also decrease DOVILAMIR blood levels. DOVILAMIR should be taken 2 hours before or 6 hours after taking products containing magnesium, calcium, iron or aluminium.
- Medicines used in the treatment of hepatitis B containing adefovir dipivoxil may increase levels of DOVILAMIR in the blood especially if you have kidney failure and should not be used with DOVILAMIR. Whereas medicines containing ribavirin used in the treatment for hepatitis B, is not affected and does not alter the levels of DOVILAMIR.

DOVILAMIR with food, drink and alcohol

DOVILAMIR may be taken with or without a 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 being given this medicine.

Do not take DOVILAMIR if you are pregnant or breastfeeding (see "Do not take DOVILAMIR"). DOVILAMIR could seriously harm your unborn child if you fall pregnant while on treatment or if you start taking DOVILAMIR in the first few weeks of your pregnancy.

You should ensure that you always use effective contraception while you are taking DOVILAMIR. Your healthcare professional can advise you on which contraceptives to take. Never stop taking DOVILAMIR 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 DOVILAMIR 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.

Mothers should not breastfeed their infants while taking DOVILAMIR.

Driving and using machines

DOVILAMIR may cause dizziness, impaired concentration and/or drowsiness. You should not drive or operate machinery until you are sure DOVILAMIR does not affect your ability to drive or use machines.

It is not always possible to predict to what extent DOVILAMIR may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which DOVILAMIR affects you.

DOVILAMIR contains lactose monohydrate

DOVILAMIR contains lactose monohydrate. 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 DOVILAMIR

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

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

The usual dose for DOVILAMIR is one film-coated tablet taken orally, once daily, with or without food. Film-coated tablets must be swallowed whole with water and must not be crushed or chewed.

DOVILAMIR should only be used by adults and should not be taken by patients younger than 18 years of age.

If you take more DOVILAMIR than you should

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

If you forget to take DOVILAMIR

Do not take a double dose to make up for forgotten individual doses and take your dose as soon as you remember to.

If you stop taking DOVILAMIR

Your doctor will tell you how long your treatment with DOVILAMIR will last. Do not stop treatment early because this may worsen your condition and make your body resistant to the medicine.

4. Possible side effects

DOVILAMIR can have side effects.

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

If any of the following happens, stop taking DOVILAMIR 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.
- Rash or itching.
- Fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to DOVILAMIR. 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.

- IRS (Immune reconstitution syndrome):

- People with advanced HIV infection (AIDS) have weak immune systems and are more likely to develop serious infections (opportunistic infections). When these people start treatment, they may find that old, hidden infections flare up, causing signs and symptoms of inflammation. These symptoms are probably caused by the body's immune system becoming stronger, so that the body starts to fight these infections. 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.

- Swelling (inflammation) of the liver (hepatitis), that may include the following symptoms:
  - Fatigue (tiredness).
  - Nausea and vomiting.
  - Stomach pain or discomfort, especially in the area of your liver on your right side beneath your lower ribs.
  - Clay-coloured bowel movements.
  - Loss of appetite.
  - Fever.
  - Dark urine.
  - Joint pain.
  - Yellowing of the skin and eyes (jaundice).
- Neutropenia (an abnormal low concentration of white blood cells). Symptoms include:

  - Fever.
  - Painful swallowing.
  - Pain of the gums.
  - Skin abscesses.
  - Painful ears.

- Anaemia (when you have a low red blood cell count). Symptoms include:
  - Tiredness.
  - Unusually rapid heartbeat.
  - Shortness of breath.
  - Difficulty concentrating.
  - Dizziness.
  - Pale skin.
  - Leg cramps.
  - Sleeplessness.
- If you have a blood clotting problem, symptoms include:
  - Serious bleeding.
  - Purple, red or brown bruises.
- Red blood cell aplasia (decreased number of red blood cells). Symptoms include:
  - Tiredness.
  - Lethargy (feeling without any energy).
  - Getting tired quickly when doing exercise.
  - Pale skin.
- Patients who take DOVILAMIR can develop a serious condition called lactic acidosis/hyperlactataemia (build-up of acid in the blood). Symptoms include:
  - You feel very weak or tired.
  - You have unusual (not normal) muscle pain.
  - You have trouble breathing.

- You have stomach pain with nausea and vomiting.
- You feel cold, especially in your arms and legs.
- You feel dizzy or light-headed.
- You have a fast or irregular heartbeat.

- Lipodystrophy – abnormal distribution or loss of body fat in certain areas such as:
  - Increased waist or breast size.
  - Fat accumulation around neck, jaw or upper back (referred to as “moon face” or “buffalo hump”).
  - Loss of fat under the skin, most visibly on the face (especially cheeks), arms and legs.
  - Prominent leg veins due to loss of fat under the skin.
- Pancreatitis (swelling of the pancreas). Symptoms include:
  - Stomach pain.
  - Nausea and vomiting.
  - Abnormal urine tests.
- Rhabdomyolysis (breakdown of muscle fibres that leads to the release of muscle fibre contents into the bloodstream). Symptoms include:
  - Abnormal urine colour (dark, red, or cola coloured).
  - Decreased urine production.
  - General weakness.
  - Muscle stiffness or pain (myalgia).
  - Muscle tenderness.
  - Weakness of the affected muscles.
- Kidney damage or failure that includes the following symptoms:
  - Decreased urination.
  - Fluid retention (swelling of the legs, ankles or feet).
  - Weakness and shortness of breath.

- Confusion.
- Abnormal heart rhythm.
- Loss of appetite.
- High blood pressure.

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:

- Sleeplessness.
- Headaches, dizziness.
- Abnormal dreams.
- Nausea, vomiting, diarrhoea.
- Upper abdominal pain or cramps.
- Loss of appetite, indigestion.
- Rash, itching.
- Hair loss.
- Muscle disorders, painful joints and muscles.
- Tiredness, feeling of discomfort, fever, lack of energy.
- Increase in liver enzymes in the blood (ALT & AST) (seen in a blood test).
- Passing a lot of urine and feeling thirsty (nephrogenic diabetes insipidus).

Less frequent side effects:

- Increase in an enzyme called amylase in the blood (seen in a blood test).
- Decrease in bone density, bone fractures.
- Flatulence or wind.

The following side effects have also been reported (frequency not known):

- Anxiety.
- Increase in weight.
- High blood sugar – you may experience increased thirst and a dry mouth, needing to pee frequently, tiredness, blurred vision.
- Tingly feelings in the skin (pins and needles) burning or stabbing pain, weakness, usually in back, foot, hands, thigh or face.
- Worsening of hepatitis B infection symptoms, such as fever, fatigue, abdominal pain after treatment with DOVILAMIR is stopped.
- Hives (urticaria).
- Rapid swelling under the skin (puffiness).
- Decreased phosphate in your blood (seen in a blood test).
- Low levels of potassium in the blood (seen in a blood test).
- Feeling breathless (dyspnoea).
- Muscle weakness (myopathy).

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 DOVILAMIR.

5. How to store DOVILAMIR

Store at or below 30 °C in the original container.

Keep the container tightly closed.

Do not remove desiccant.

After first opening, store at or below 25 °C in the original container and use within 180 days after first opening.

STORE ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN.

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 DOVILAMIR contains

The active substances in DOVILAMIR are dolutegravir (as dolutegravir sodium), lamivudine and tenofovir disoproxil fumarate.

The other ingredients are croscarmellose sodium, lactose monohydrate, mannitol, microcrystalline cellulose, povidone K 30, pregelatinized starch, sodium starch glycolate and sodium stearyl fumarate. The tablets are film-coated with a coating material containing polyethylene glycol, polyvinyl alcohol, talc and titanium dioxide.

What DOVILAMIR looks like and contents of the pack

DOVILAMIR are white coloured, oval shaped, biconvex, film-coated tablets, debossed with ‘LA75’ on one side and plain on the other side.

Containers containing 28 tablets: DOVILAMIR is packed in 100 cc high density polyethylene (HDPE) bottles with 38 mm continuous thread (CT) polypropylene (PP) caps and 1 g silica gel canisters.

Containers containing 30 tablets: DOVILAMIR is packed in 100 cc HDPE bottles with 38 mm child resistant (CR) PP caps and 2 g silica gel canisters.

Containers containing 84 or 90 tablets: DOVILAMIR is packed in 200 cc HDPE bottles with 38 mm CR PP caps with 2 g silica gel canisters.

Containers containing 180 tablets: DOVILAMIR is packed in 400 cc HDPE bottles with 53 mm PP screw caps with can-sorb-it 2 g canisters.

Holder of Certificate of Registration

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Access to the corresponding Professional Information

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