

## PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: 

S4
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**DOLAMVIR 50 mg/300 mg/300 mg film-coated tablets**

**Dolutegravir /Lamivudine/Tenofovir disoproxil fumarate**

**Contains sugar (145,37 mg mannitol per tablet)**

### **Read all of this leaflet carefully before you take DOLAMVIR**

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- DOLAMVIR 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 DOLAMVIR is and what it is used for
2. What you need to know before you take DOLAMVIR
3. How to take DOLAMVIR
4. Possible side effects
5. How to store DOLAMVIR
6. Contents of the pack and other information

#### **1. What DOLAMVIR is and what it is used for**

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

DOLAMVIR is used to treat HIV (human immunodeficiency virus) infection in adults and adolescents over 18 years old.

**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 (SEE “TAKE SPECIAL CARE WITH DOLAMVIR”). DOLAMVIR IS NOT INDICATED FOR TREATMENT OF CHRONIC HEPATITIS B VIRUS (HBV) INFECTION. THE SAFETY AND EFFICACY OF DOLAMVIR HAS NOT BEEN ESTABLISHED IN PATIENTS INFECTED WITH BOTH HBV AND HIV. SEVERE ACUTE WORSENING OF HEPATITIS B HAS 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 HEALTHCARE PRACTITIONER 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 HEPATITIS B MAY NEED TO BE PRESCRIBED (SEE “TAKE SPECIAL CARE WITH DOLAMVIR”).**

**2. What you need to know before you take DOLAMVIR**

**You should not take DOLAMVIR:**

- if you are hypersensitive (allergic) to dolutegravir, lamivudine or tenofovir disoproxil fumarate, or any of the other ingredients of DOLAMVIR
- if you have kidney problems

- if you are pregnant or breastfeeding your baby
- if you are a woman of child-bearing age and not using effective contraceptives to prevent falling pregnant
- if you are taking chronic medication for hepatitis B infection, containing adefovir dipivoxil
- if you are also taking heart medication for irregular heartbeat containing dofetilide and pilsicainide
- if you are taking other anti-retroviral medicine containing didanosine
- if you are taking metformin, for the treatment of type 2 diabetes
- if you are younger than 18 years of age
- if you have liver disease.

### **Warnings and precautions**

Take special care with DOLAMVIR:

Tell your doctor:

- 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).
- If you have abnormal metabolic processes, such as increased cholesterol, glucose or lactate in the blood or are resistant to insulin. Your healthcare provider may perform regular blood tests to confirm normal metabolic processes.
- If you develop changes in body fat, since changes have been seen in some patients taking DOLAMVIR and other anti-HIV medicines. These changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the main part of your body (trunk). Loss of fat from the legs, arms and face may also happen. The cause and long-term health effect of these conditions are not known at this time.
- If you develop inflammatory reactions (e.g. pain, redness, swelling, high temperature). This may resemble an infection and may be severe. Within the first few weeks of treatment with anti-HIV medicines, some

patients, particularly those that have been HIV positive for some time, have reported these symptoms. These reactions are thought to be caused by a recovery of the body's ability to fight infections, previously suppressed by HIV. If you become concerned about any new symptoms, or any changes in your health after starting HIV treatment, please discuss with your healthcare provider.

- If you experience joint aches and pain, joint stiffness or difficulty moving or bone fractures, tell your doctor as you may need to take calcium and vitamin D supplements to prevent further damage to your bones that may be caused by this medicine, when taken together with corticosteroids or alcohol, or if you have a very weak immune system and are overweight.
- If you show any symptoms of infection while you are taking DOLAMVIR. People with advanced HIV infection (AIDS) have weak immune systems and are more likely to develop serious infections (opportunistic infections). When these people 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 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.
- If you have liver problems, including hepatitis B virus (HBV) infection, as the use of antiviral medicine can cause severe or potentially fatal liver symptoms. Your doctor will monitor your liver enzymes as DOLAMVIR can cause liver toxicity.
- If you suffer from kidney disease or kidney impairment.
- If you have had bone problems in the past. Your healthcare provider may need to do tests to check your bone mineral density or may prescribe medicines to help your bone mineral density.
- If you experience joint aches and pain, joint stiffness or difficulty in movement. You may suffer from osteonecrosis.

- If you are elderly and suffer from kidney or liver damage or failure.

DOLAMVIR should be used with caution in the elderly (65 years and over), due to decreased liver and kidney function.

#### *Protect other people*

DOLAMVIR does not reduce the risk of passing HIV to others through sexual contact or blood contamination.

Therefore, it is important to continue to take appropriate precautions to prevent passing HIV 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**

DOLAMVIR should NOT be taken by children and adolescents under 18 years.

#### **Taking other medicines with DOLAMVIR:**

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 DOLAMVIR:

- Other medicines that contain dolutegravir, lamivudine or tenofovir, either alone or as combined formulations. DOLAMVIR should not be used with these medicines because they contain the same or similar active ingredients as DOLAMVIR.
- Medicine that can cause toxicity of the kidneys, for example antibiotics e.g. vancomycin, aminoglycosides (gentamycin, amikacin, tobramycin, neomycin), antifungals (e.g. amphotericin B), antivirals (e.g. foscarnet, ganciclovir), antimicrobials (e.g. pentamidine).

- Medicines that contain didanosine. DOLAMVIR may increase the amount of didanosine, used for the treatment of HIV, in your blood. You should not take didanosine and DOLAMVIR together.
- DOLAMVIR increases levels of abacavir used in the treatment of HIV and may need to be adjusted.
- DOLAMVIR is not affected and does not influence the levels of emtricitabine, lopinavir and ritonavir used in the treatment of HIV.
- DOLAMVIR increases the levels of atazanavir (also used for the treatment of HIV infection) and may need to be adjusted.
- Taking DOLAMVIR 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.
- DOLAMVIR may hinder the breakdown of zalcitabine, also used in the treatment of HIV infections.
- The use of DOLAMVIR with etravirine for HIV infections is not recommended.
- DOLAMVIR can increase blood concentration levels of isoniazid used for treatment of tuberculosis.
- Medicines used in the treatment of hepatitis B containing adefovir dipivoxil may increase levels of DOLAMVIR in the blood, especially if you have kidney failure. Whereas medicines containing ribavirin used in the treatment of hepatitis B, is not affected and does not alter the levels of DOLAMVIR.
- Other medicines used for the treatment of HIV infections that decrease DOLAMVIR levels include efavirenz, nevirapine, ritonavir, tipranavir.
- Combination medicines for treatment of HIV containing fosamprenavir and ritonavir, or darunavir and ritonavir decrease levels of DOLAMVIR.
- Phenobarbitone, phenytoin, oxcarbazepine, carbamazepine and St. John's Wort decrease levels of DOLAMVIR.
- DOLAMVIR can increase blood concentrations of metformin (for the treatment of type 2 diabetes), when used simultaneously.
- Rifampicin, used for treatment of tuberculosis, can decrease blood concentrations of

DOLAMVIR.

- DOLAMVIR is not affected and does not change levels of methadone, used in the treatment of opioid abuse.
- DOLAMVIR can increase levels of the following heart medicine for the treatment of irregular heartbeat - dofetilide and pilsicainide.
- Certain antacids can also decrease DOLAMVIR levels, that contain for example magnesium, aluminium, iron or calcium.
- DOLAMVIR must be taken 2 hours before or 6 hours after taking products containing magnesium, calcium, iron or aluminium.

#### **DOLAMVIR with food and drink**

DOLAMVIR can be taken 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 healthcare provider for advice before taking DOLAMVIR.

Do not take DOLAMVIR if you are pregnant or breastfeeding your baby.

If you are thinking of having a baby, do not stop using DOLAMVIR and contraception before you have talked to your healthcare provider. If you think you are pregnant go to your healthcare provider to get a pregnancy test and to be advised on your future HIV treatment and on a pregnancy management plan.

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). It 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.

### **Driving and using machines**

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

### **3. How to take DOLAMVIR**

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

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

#### **Adults:**

The usual dose is one tablet taken orally, once a day with or without food.

Swallow the tablet with some liquid.

Your doctor will tell you how long your treatment with DOLAMVIR will last. Do not stop treatment early because you feel better. If you have the impression that the effect of DOLAMVIR is too strong or too weak, tell your doctor or pharmacist.

**Children:** DOLAMVIR should not be used in children younger than 18 years.

#### **If you take more DOLAMVIR 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 a dose of DOLAMVIR**

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

**If you stop taking DOLAMVIR**

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

**4. Possible side effects**

DOLAMVIR can have side effects.

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

If any of the following happens, stop taking DOLAMVIR 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 DOLAMVIR. 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:

*Frequently occurring*

- swelling (inflammation) of the liver (hepatitis), that may include the following symptoms e.g. fatigue, 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, low-grade fever, dark urine and joint pain

*Less frequently occurring*

- hypersensitivity reactions which include bronchospasm, fast or irregular breathing, puffiness or swelling around the face, shortness of breath and sudden decrease in blood pressure.
- lactic acidosis/raised blood lactate concentration (hyperlactataemia). Symptoms include feeling very weak or tired, having unusual (not normal) muscle pain, trouble breathing, stomach pain with nausea and vomiting, you feel cold, especially in your arms and legs, dizzy, lightheaded and fast or irregular heartbeat.
- rhabdomyolysis (a condition affecting the muscles with symptoms such as dark urine and difficulty moving arms or legs)
- inflammation of the pancreas, which causes severe pain in the abdomen and back (pancreatitis)
- thoughts of killing or harming yourself, attempting to commit suicide

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:*

- a persistent raised blood lactate concentration
- difficulty in sleeping
- abnormal dreams

- depression
- headache
- dizziness, spinning sensation
- nausea
- loss of appetite
- Anorexia, indigestion
- diarrhoea
- vomiting
- stomach pain or cramps
- wind (flatulence)
- increase in liver enzymes
- hair loss
- muscle disorders
- joint pain
- impaired kidney function, renal function decline
- inflammation of the kidneys, passing a lot of urine and feeling thirsty
- kidney disorder where the kidneys can't respond to a hormone that regulates fluid balance
- changes to your urine and back pain caused by kidney damage or failure
- high levels of protein in your urine
- tiredness
- general feeling of being unwell, lack of energy
- fever
- painful swelling and sores inside your mouth

*Less frequent side effects:*

- an abnormally low concentration of white blood cells
- low red blood cell count (anaemia)
- decreased number of cells involved in blood clotting (thrombocytopenia)
- 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
- peripheral neuropathy (damage to nerves outside the spinal cord, affecting the normal functioning of the body’s organs and movement and/or feeling of sensation in the extremities, including your arms and legs)
- neurological disorders (e.g. epilepsy, Alzheimer's disease, Parkinson's disease, multiple sclerosis, and autism spectrum disorders) appearing later in children who were exposed to them while in the womb.
- inflammation of the pancreas, temporary liver enzymes increased
- temporary increase in liver enzymes. Symptoms include fatigue, nausea, anorexia and discomfort over the liver area (upper right quadrant of the body)
- muscle pain and weakness, inflammation in the muscles
- rapid breakdown of damaged skeletal muscle
- softening of bones and occasionally contributing to breaks, fractures
- numbness, pain and tingly feelings in the skin (pins and needles)

*Side effects with unknown frequency*

- a failure of the bone marrow to produce new red blood cells (pure red cell aplasia)
- short of breath, difficulty in breathing
- high blood sugar
- fatty liver disease (symptoms may include weight loss, fatigue and abdominal pain)

- severe allergic reaction
- hives
- weakness and fatigue in the muscles
- hypophosphatemia (an electrolyte disorder in which there is a low level of phosphate in the blood, with symptoms that may include weakness, trouble breathing, and loss of appetite)
- low blood potassium (with symptoms including muscle weakness, cramps, muscle twitches)

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

### **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. You can also report side effects 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 DOLAMVIR.

### **5. How to store DOLAMVIR**

Store all medicines out of reach of children.

Store at or below 30 °C in HDPE container packs.

Keep the desiccant sachet in the container. Do not remove the desiccant sachet. Keep the tablets in the original container. Keep HDPE containers tightly closed.

Do not use DOLAMVIR after the expiry date which is stated on the carton after “EXP”. The expiry date refers to the last day of that month.

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 DOLAMVIR contains**

DOLAMVIR contains the active substances dolutegravir, lamivudine and tenofovir disoproxil fumarate. Each film-coated tablet contains 50 mg dolutegravir (as sodium), 300 mg lamivudine and 300 mg tenofovir disoproxil fumarate which is equivalent to 245 mg of tenofovir disoproxil.

The other ingredients are colloidal silicon dioxide, croscarmellose sodium, ferric oxide, hypromellose, magnesium stearate, mannitol, microcrystalline cellulose, povidone, sodium starch glycollate, sodium stearyl fumarate.

The tablet coating consists of: Opadry II White 85F18422 (containing ferrousferrous oxide / black iron oxide, iron oxide red, macrogol/PEG, polyvinyl alcohol - part hydrolysed, talc, titanium dioxide).

### **What DOLAMVIR looks like and contents of the pack**

DOLAMVIR is a pink coloured, oval, biconvex, film coated tablet debossed with 'N33' on one side and plain on the other side.

DOLAMVIR are packed in round wide mouth white opaque 100 ml HDPE container closed with white opaque polypropylene 38 mm - 400 polypropylene child resistant closure with wad having induction sealing liner. The HDPE container also contains 3 g of silica gel sachet. This HDPE container will be further packed in preprinted carton with package leaflet.

Each container contains 30 tablets.

Pack size: 30's - one HDPE container contains 30 tablets.

### **Holder of Certificate of Registration**

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