

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S4

TRILATED 50mg/300mg/300 mg

Film-coated tablets

Dolutegravir, Lamivudine, Tenofovir disoproxil fumarate

Contains sugar (lactose monohydrate 160,84 mg and mannitol 138,30 mg per tablet)

Read all of this leaflet carefully before you are given TRILATED

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

1. What TRILATED is and what it is used for

TRILATED is an antiviral medicine that is used for the treatment of HIV-1 infection in adults aged 18 years and older.

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 WARNINGS AND PRECAUTIONS). TRILATED IS NOT INDICATED FOR TREATMENT OF CHRONIC HEPATITIS B VIRUS (HBV) INFECTION. THE SAFETY AND EFFICACY OF TRILATED 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 HEALTHCARE PROVIDER 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 (SEE WARNINGS AND PRECAUTIONS).

2. What you need to know before you take TRILATED

Do not take TRILATED

- If you are hypersensitive (allergic) to dolutegravir, lamivudine, tenofovir disoproxil fumarate or any of the other ingredients of TRILATED (listed in section 6).
- If you have uncontrolled renal kidney failure.
- If you have liver disease.
- If you are pregnant and/or breastfeeding.
- If you plan on becoming pregnant.
- If you are a woman of child bearing age and not using effective contraceptives to prevent falling pregnant.

- If you are also taking heart medication for irregular heart beat containing dofetilide and pilsicainide.
- If you are taking metformin, for the treatment of type 2 diabetes.
- If you are taking chronic medication for hepatitis B infection, containing adefovir dipivoxil.
- If you are taking other anti-retroviral medicine containing didanosine.
- If you are younger than 18 years of age.

Warnings and precautions

Take special care with TRILATED.

Tell your doctor:

- if you are taking another combination of antiretroviral medication as this could lead to metabolic abnormalities, the redistribution/accumulation of body fat, a collection of inflammatory disorder associated with the worsening of pre-existing infectious conditions, death of bone tissue due to a loss of blood supply to the bone
- 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 experience softening of bones
- if you develop new infections and other complications of HIV infection
- if you have liver problems including Hepatitis B Virus (HBV) infection or show signs of the liver injury
- if you develop liver problems with enlarged liver and with fat in the liver
- 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 process
- If you develop abdominal pain, nausea, vomiting, kidney problems (the signs include feeling tired, bruising easily and passing water (urinating) less often). If you experience pain in the

stomach, as this can be a symptom of pancreatitis (swelling of the pancreas) (see 4. Possible side effects).

- If you are 65 years and old
- If you notice any symptoms of depression (including suicidal ideation) during treatment

Children and adolescents

Do not give TRILATED to children younger than 18 years of age because it is unlikely to be safe.

Other medicines and TRILATED

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 TRILATED:

- Other products that contain dolutegravir, lamivudine or tenofovir, either alone or as combined formulations. TRILATED should not be used with these medicines because they contain the same or similar ingredients as TRILATED
- Rifampicin, used for treatment of tuberculosis, can decrease blood concentrations of TRILATED
- TRILATED can increase blood concentration of metformin (for the treatment of Type 2 Diabetes), when used simultaneously.
- Other medicine used for the treatment of HIV infections that decreases TRILATED levels includes efavirenz, nevirapine, ritonavir, tipranavir.
- TRILATED can increase levels of the following heart medicine for the treatment of irregular heartbeat – dofetilide and pilsicainide.
- TRILATED can increase blood concentration levels of isoniazid used for treatment of tuberculosis.
- Certain antacids can also decrease TRILATED levels, that contains for example magnesium, aluminium or calcium.
- TRILATED must be taken 2 hours before or 6 hours after taking products containing magnesium, calcium, iron or aluminium

- TRILATED may hinder the breakdown of zalcitabine, also used in the treatment of HIV infections.
- Taking TRILATED 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 disease.
- The use of TRILATED with etravirine for HIV infections is not recommended.
- Medicine 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.
- TRILATED increases the levels of atazanavir (also used for the treatment of HIV infection) and may need to be adjusted.
- Phenobarbitone, phenytoin, oxcarbazepine, carbamazepine and St. John's Wort decreases levels of TRILATED.
- TRILATED increases levels of abacavir used in the treatment of HIV and may need to be adjusted.
- TRILATED is not affected and does not influence the levels of emtricitabine, lopinavir and ritonavir used in the treatment of HIV.
- TRILATED is not affected and does not change levels of methadone, used in the treatment of opioid abuse.
- Combination medicines for treatment of HIV containing fosamprenavir and ritonavir or darunavir and ritonavir decreases levels of TRILATED.
- Medicines used in the treatment of hepatitis B containing adefovir dipivoxil may increase levels of TRILATED in the blood especially if you have kidney failure. Whereas medicines containing ribavirin used in the treatment for hepatitis B, is not affected and does not alter the levels of TRILATED.
- Medicines that contain didanosine: TRILATED may increase the amount of didanosine used for the treatment of HIV in your blood. You may need to be monitored more carefully if you are taking TRILATED and didanosine together. The dose of didanosine may also need to be reduced.

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 this medicine.

You should stop taking TRILATED if you plan to become pregnant. Women of childbearing age should not use TRILATED unless they are reliably using highly effective contraception.

It should be noted that the use of dolutegravir, as contained in TRILATED, was associated with a small increase in the likelihood of neural tube defects (birth defects) compared to non-dolutegravir regimens. Most neural tube defects occur within the first 4 weeks of pregnancy which is approximately 6 weeks after your last menstrual cycle (period).

A pregnancy test should be performed before you start taking TRILATED, if you are able to bear children, to exclude the unintentional use of TRILATED during the first trimester of pregnancy.

Dolutegravir, as contained in TRILATED, may be used in the second and third trimester of pregnancy when the expected benefit outweighs the potential risk to the foetus.

TRILATED should not be taken by pregnant or breastfeeding women.

Mothers should not breastfeed their infants while taking TRILATED, to avoid transmission of HIV.

Driving and using machines

TRILATED cause dizziness, impaired concentration and/or drowsiness and may affect the ability to drive and use machines.

Patients should ensure that they do not engage in driving or using machines until they know how TRILATED affects them.

TRILATED contains sugar

TRILATED contains lactose monohydrate and mannitol and may have a laxative effect. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking TRILATED.

3. How to take TRILATED

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

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

The usual dose for adults is one tablet taken orally, once daily, with or without food. TRILATED is not recommended for use in patients younger than 18 years of age.

Your doctor will tell you how long your treatment with TRILATED will last. Do

not stop treatment early because this may worsen your condition and make

your body resistant to the medicine. If you have the impression that the effect of TRILATED is too strong or too weak, tell your doctor or pharmacist.

If you take more TRILATED 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 TRILATED

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

4. Possible side effects

TRILATED can have side effects.

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

If the following happens, stop using TRILATED and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and 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 reaction to TRILATED. You may need urgent medical attention or further hospitalisation.

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

- chest pain
- angina
- changes in the way your heart beats, for example, if you notice it beating faster
- difficulty breathing
- signs of recurrent infections such as fever or sore throat
- less urine than is normal for you
- yellowing of the skin and eyes, dark urine and tiredness which may be symptoms of liver problems

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

Tell your doctor if you notice any of the following:

Frequent:

- Sleeplessness (Insomnia),
- Headaches,
- Dizziness,
- Abnormal dreams.
- Diarrhoea,
- Nausea, vomiting,
- Upper abdominal pain, abdominal pain, abdominal discomfort, abdominal swelling, cramps, flatulence or wind, loss of appetite, indigestion.
- Anorexia
- Rash, itching (pruritis),
- Hair loss (alopecia).
- Tiredness, lack of energy.
- Feeling of discomfort (malaise),
- Fever
- Increase in liver enzymes in the blood (ALT & AST).

- Muscle disorders, painful joints and muscles.
- Kidney damage or failure
- Damage to or disease affecting nerves, which may harm sensation, movement, gland or organ function, or other aspects of health, depending on the type of nerve affected (peripheral neuropathy).
- Swelling (inflammation) of the liver (hepatitis), that may include the following symptoms:
 - 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
 - Joint pain
- Yellowing of the skin and eyes (jaundice)

Less frequent:

Hypersensitivity to reactions:

- Bronchospasm (sudden constriction of the muscles in the walls of the lungs)
- Fast or irregular breathing
- Puffiness or swelling around the face
- Shortness of breath
- Sudden decrease in blood pressure
- Immune Reconstitution Syndrome (IRS)
- Neutropenia (an abnormal low concentration of white blood cells).
- Anaemia (when you have a low red blood cell count)
- Thrombocytopenia (low levels of platelets (clotting agents in your blood)).
- If you have a blood clotting problem
- Lipodystrophy – abnormal distribution or loss of body fat in certain areas

- Damage to or disease affecting nerves, which may harm sensation, movement, gland or organ function, or other aspects of health, depending on the type of nerve affected (peripheral neuropathy).
- Pancreatitis (swelling of the pancreas).
- Increased levels of amylase, an enzyme that is produced by the pancreas that help breaks down food in the intestines.
- Temporary increase in liver enzymes
- Rhabdomyolysis (breakdown of muscle fibres that leads to the release of muscle fibre contents into the bloodstream).
- Softening of bones and occasionally contributing to breaks.
- Lactic acidosis/hyperlactataemia (build-up of acid in the blood)

Frequency unknown

- Red blood cell aplasia (decreased number of red blood cells).

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 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 By reporting side effects, you can help provide more information on the safety of TRILATED.

5. How to store TRILATED

Store all medicines out of reach of children.

Store at or below 30° C.

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

6. Contents of the pack and other information

What TRILATED contains

The active substances are dolutegravir sodium, lamivudine, tenofovir disoproxil fumarate.

The other ingredients are croscarmellose sodium, lactose monohydrate, magnesium stearate, mannitol, microcrystalline cellulose (PH101, PH112), pigment yellow 42, povidone, pregelatinized starch, sodium starch glycolate and Opadry II white 85F18422 (tablet coating).

What TRILATED looks like and contents of the pack

White colour capsule shaped film coated tablets with "C7" debossed on one side and plain on other side.

The primary packaging components of TRILATED are:

- a white opaque round shaped HDPE container
- a polypropylene child resistant closure (white outer shell embossed with pictorial design and clear inner shell fitted with a heat seal and pulp liner)
- a white/translucent bead/granule silica gel

Holder of Certificate of Registration

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