APPROVED PATIENT INFORMATION LEAFLET

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

RARUDINE film-coated tablets

Dolutegravir / Lamivudine / Tenofovir disoproxil fumarate

Read all of this leaflet carefully before you start taking RARUDINE

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- RARUDINE 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 RARUDINE is and what it is used for

RARUDINE contains three active ingredients, namely dolutegravir, tenofovir disoproxil and lamivudine and belongs to a group of medicines called antiviral medicines.

RARUDINE is used is used to treat HIV (human immunodeficiency virus) infection in adults aged 18 years and older.

2. What you need to know before you take RARUDINE

Do not take RARUDINE:

- if you are hypersensitive (allergic) to dolutegravir, tenofovir disoproxil, lamivudine or any of the other ingredients of RARUDINE (see section 5)
- if you have kidney problems
- if you are pregnant or breastfeeding your baby
- if you are a women of child-bearing-age unless and are not using highly effective contraception
- if you are taking a medicine called adefovir dipivoxil (used to treat hepatitis B)

- if you are taking medicines called dofetilide or pilsicainide (to treat heart conditions)
- if you are taking medicine called didanosine (used in the treatment of HIV)
- if you are taking medicine called metformin (used to treat high blood sugar levels)
- if you are under the age of 18
- if you suffer from moderate to severe liver disease.

Warnings and precautions

WARNING

If you take RARUDINE alone or with other medicine used for the treatment of HIV/AIDS (called antiretrovirals), you may develop a condition called lactic acidosis (build-up of lactate in the body which causes symptoms like stomach discomfort, lower appetite diarrhoea) or an enlarged liver with a condition called fatty liver disease (a build-up of fat in the liver and may include symptoms like fatigue, weight loss and abdominal pain)

RARUDINE is not indicated for the treatment of chronic hepatitis B virus (HBV) infection (a serious liver infection). Your healthcare provide may advise you to discontinue the use of RARUDINE if you have both the HBV virus and HIV/AIDS, as you may experience worsening of the liver infection. Your healthcare provider

will monitor your liver function, closely. Your healthcare provider may consider giving you anti-hepatitis B therapy.

Take special care with RARUDINE:

- if you suffer from high cholesterol, increased blood sugar levels, insulin resistance or increased blood lactate levels, as these conditions may worsen if you are taking RARUDINE.
- as redistribution, accumulation or loss of body fat may occur in patients receiving combination antiretroviral therapy. Contact your healthcare provider if you notice changes in body fat. e.g. a hump forming on your back, loss of fat from your face, collection of fat around your abdomen
- as within the first few weeks of treatment with anti-HIV medicines, some people, particularly those that have been HIV positive for some time, may develop inflammatory reactions (e.g. pain, redness, swelling, high temperature) which may resemble an infection and may be severe. These reactions are thought to be caused by a recovery of the body's ability to fight infections, previously supressed 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.
- as some patients with advanced HIV infection (AIDS) and a history of AIDS-associated (opportunistic) infection, signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started, some of these conditions may include pneumonia, herpes virus infections.
- as HIV infection is spread by sexual contact, or by transfer of infected blood (for example, by sharing injection needles). You can still pass on HIV when taking this medicine, but the risk is lowered by effective antiretroviral therapy. Discuss with your health care provider the precautions needed to avoid infecting other people.
- If you experience nausea, vomiting, abdominal pain, generalised weakness, anorexia, and sudden unexplained weight loss, and difficulty breathing you should tell your doctor immediately as you may be experiencing lactic acidosis. This usually occurs after a few months of treatment with RARUDINE.
- if you took this medicine while pregnant, your infant may be anaemic with symptoms such as tiredness and a pale skin, abnormal blood test results, may have poor muscle tone, abnormal behaviour and may have seizure (fits)

- as inflammation of the pancreas (pancreatitis), with symptoms including abdominal pain, nausea and vomiting, has been observed in some patients receiving RARUDINE. However, it is unclear whether this is due to treatment with this medicine or to HIV disease.
- as RARUDINE may affect your kidneys, especially if you are taking any other medicines at the same time. Before starting this medicine, and during treatment, you may need blood tests to check how well your kidneys are working.
- if you have had kidney disease or if tests have shown problems with your kidneys, notify your health care provider. If so, the dose of tenofovir disoproxil and lamivudine may need to be reduced. In such cases, your healthcare provider may prescribe another medicine.
- as RARUDINE is not usually taken with other medicines that can damage your kidneys (see Other medicines). If this is unavoidable, you may need regular tests to check how well your kidneys are working.
- if you have a history of liver disease including hepatitis (a serious liver infection), notify your healthcare provider. If your liver disease becomes worse during treatment, your healthcare provider may discontinue your treatment with RARUDINE.

- as HIV-infected patients with liver disease, including chronic hepatitis B or C, who are treated with antiretrovirals (medicine used to treat HIV/AIDS), have a higher risk of severe and potentially fatal liver complications. If you are infected with HIV and hepatitis B virus, your healthcare provider will carefully consider the best treatment for you. If you have a history of liver disease or chronic hepatitis B infection your healthcare provider may continually conduct blood tests to monitor your liver function.
- if you have Hepatitis B (a serious liver infection), you should not stop your RARUDINE treatment without instructions for your doctor, as you may have a recurrence of your hepatitis. This recurrence may be more severe if you have serious liver disease.
- if you get any rash as it may be an indication that you are having an allergic reaction. You should stop taking RARUDINE and contact your healthcare provider immediately if you get other symptoms of an allergic reaction such as fever, fatigue, muscle or joint aches, blisters, sores in your mouth, swelling of your feet or face.
- if you are an elderly patient your healthcare provider may want to monitor your kidney function before and during treatment.

Children

RARUDINE is not suitable for children under the age of 18 years.

Other medicines and RARUDINE

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

The following medicines may affect how RARUDINE works, or RARUDINE may affect how they work:

- the antibiotic co-trimoxazole causes an increase in the level of lamivudine (which is contained in RARUDINE) in your blood
- RARUDINE will increase the levels of didanosine (medicine used to treat HIV/AIDS) in your blood if taken with medicines that contain didanosine
- atazanavir, indinavir and lopinavir/ritonavir (used in HIV treatment) will increase the effect of RARUDINE
- the effect of zidovudine will decrease when taken in combination with RARUDINE
- lamivudine, which is contained in RARUDINE, may reduce the antiviral action of zalcitabine, therefore the two medicines should not be used together.
- etravirine, efavirenz, fosamprenavir/ritonavir, nevirapine or tipranavir/ritonavir (to treat HIV infection) will decrease the effect of RARUDINE
- rifampicin (to treat tuberculosis and other bacterial infections) will decrease the effect of RARUDINE

- isoniazid (medicine used to treat tuberculosis) effect will increase when taken with RARUDINE
- pilsicainide and dofetilide (used to treat irregular heartbeats) as RARUDINE will increase the effects of these medicines
- St John's wort (*Hypericum perforatum*), an herbal remedy used for treating depression decrease the effect of RARUDINE
- phenytoin and phenobarbital (to treat epilepsy) will decrease the effect of RARUDINE
- oxcarbazepine and carbamazepine (to treat epilepsy or bipolar disorder) decrease the effect of RARUDINE
- antacids, to treat indigestion and heartburn. Do not take an antacid during the 6 hours before you take RARUDINE, or for at least 2 hours after you take it
- calcium supplements, iron supplements - do not take a calcium supplement or iron supplement during the 6 hours before you take RARUDINE, or for at least 2 hours after you take it
- RARUDINE may increase the effect of metformin (used to treat diabetes).

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare provider for advice before using RARUDINE.

Pregnancy

Taking RARUDINE at the time of becoming pregnant or during early pregnancy, may increase the risk of a type of birth defect, called neural tube defect, such as spina bifida (malformed spinal cord). You should not take RARUDINE if you are pregnant.

Breastfeeding

Lamivudine and tenofovir disoproxil are found in human breast milk, therefore you should not breastfeed your baby whilst taking RARUDINE.

Fertility

There is no data on the effects of RARUDINE on fertility.

Driving and using machines:

RARUDINE can cause dizziness.

It is not always possible to predict to what extent RARUDINE may interfere with the daily activities of a patient. Patients should ensure that they do not operate machines or drive until they are aware of the measure to which RARUDINE affects them.

RARUDINE contains lactose

RARUDINE contains 140 mg lactose and 157 mg mannitol per tablet.

If you have been told by your doctor that you have an intolerance to some sugars, contact your health care provider before taking RARUDINE.

3. How to take RARUDINE

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

Always use RARUDINE exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The usual dose is one tablet once daily.

RARUDINE can be taken with food or between meals.

Your doctor will tell you how long your treatment with RARUDINE 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 RARUDINE is too strong or too weak, tell your doctor or pharmacist.

If you take more RARUDINE 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.

There is no specific treatment for overdose, therefore if you have taken more RARUDINE than you should, have your doctor will treat you for the symptoms that you have.

If you forget to take RARUDINE:

If you forget to take RARUDINE, take a dose as soon as you remember, then continue to take RARUDINE at the usual times. Do not take a double dose to make up for forgotten individual doses.

If you stop taking RARUDINE

If you have HIV and hepatitis B virus (HBV) and stop taking RARUDINE, your hepatitis infection may become worse than it was before starting treatment.

4. Possible side effects

RARUDINE can have side effects.

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

If any of the following happens, stop using RARUDINE 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 with blisters.

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

- inflammation of the pancreas, which causes severe pain in the abdomen and back (pancreatitis)
- bleeding into the skin, bruising and slow blood clotting after an injury (thrombocytopenia)
- hepatitis (swelling and inflammation of the liver, characterised by symptoms such as, abdominal pain or distension, dark urine and pale or clay-coloured stools, fatigue, fever, general itching, yellowing of the skin or eyes, loss of appetite, nausea and vomiting), jaundice
- thoughts of killing or harming yourself, or attempting to commit suicide
- rhabdomyolysis (a condition affecting the muscles with symptoms such as dark urine and difficulty moving arms or legs)
- kidney failure
- lactic acidosis (excess lactic acid in the blood) with symptoms including deep, rapid breathing, drowsiness, nausea, vomiting and stomach pain.

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:

- Hypophosphataemia is 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
- Insomnia (difficulty sleeping), abnormal dreams (nightmares), depression, anxiety
- Headache, dizziness
- Cough, nasal discharge and congestion
- Nausea, diarrhoea, vomiting, flatulence, stomach pain or discomfort
- Skin rash, hair loss, severe itching of the skin
- Fatigue, general feeling of being unwell, fever
- Liver problems, increased enzyme levels
- Painful inflammation in the mouth
- Arthralgia
- Anorexia, indigestion.

Less frequent side effects:

- Anaemia, changes in the white blood cell counts (neutropenia), possibly resulting in an increased risk of infection
- 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)

- Tingling sensation in the hands, feet or lips (pins and needles)
- Difficulty in breathing (dyspnoea)
- Increased digestive enzyme levels
- Joint pain, muscle pain
- Changes to your urine and back pain caused by kidney problems, including kidney failure
- Abnormal physical weakness or lack of energy
- Redistribution of your body fat around your body
- Increased liver enzymes as determined by blood tests
- Decreased bone density, bone fractures

The following side effects have been reported but the frequency for them to occur is not known:

- Low blood potassium (with symptoms including muscle weakness, cramps, muscle twitches)
- Fatty liver disease (symptoms may include weight loss, fatigue and abdominal pain)
- Bone pain, muscle weakness
- Inflammation of the kidney, passing a lot of urine and feeling thirsty
- Recurrence of previous infections such as nose, throat or chest infections
- Abdominal pain and discomfort.

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 or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug 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 RARUDINE.

5. How to store RARUDINE

Store all medicines out of reach of children.

Store at or below 30 °C in original container.

Discard 90 days after first opening.

Do not use after the expiry date stated on the carton.

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 RARUDINE contains

The three active substances are dolutegravir, lamivudine and tenofovir disoproxil fumarate.

Each RARUDINE film coated tablet contains 50 mg dolutegravir, 300 mg lamivudine and 300 mg tenofovir disoproxil fumarate.

RARUDINE contains sugar lactose - 140 mg per tablet and mannitol 157 mg per tablet.

The other ingredients are:

Tablet core:

Colloidal silicone dioxide, croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate (vegetable grade), mannitol, microcrystalline cellulose (Avicel PH101), povidone, sodium starch glycolate, talc

Tablet coating: Opadry II White: Macrogol, polyvinyl alcohol, talc, titanium dioxide

What RARUDINE looks like and contents of the pack

RARUDINE is a film-coated tablet, white coloured, biconvex modified capsule shaped bevelled edge film coated tablets debossed with ‘L160’ on one side and plain on the other side.

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RARUDINE is packed into either one of the following:

Round opaque white HDPE bottle with 38 mm child resistant closure of polypropylene with HS 12335 printed liner with two molecular sieve sachet of 5 g containing 30 tablets.

Round opaque white HDPE bottle with 38 mm child resistant closure of polypropylene with HS 12335 printed liner with two molecular sieve sachets of 5 g containing 60 tablets.

Holder of Certificate of Registration

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