PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

JUXOLU film-coated tablets

Dolutegravir sodium equivalent to dolutegravir 50 mg

Lamivudine 300 mg

Tenofovir disoproxil fumarate equivalent to tenofovir disoproxil 300 mg

Contains sugar: lactose monohydrate and mannitol

Read all of this leaflet carefully before you start taking JUXOLU

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

JUXOLU is a fixed dose combination of dolutegravir, lamivudine and tenofovir disoproxil fumarate. It is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults aged 18 years and older. JUXOLU contains three active substances that are used to treat human immunodeficiency virus (HIV) infection:

- Dolutegravir is an integrase inhibitor.
- Lamivudine is a nucleoside reverse transcriptase inhibitor.
- Tenofovir disoproxil is a nucleoside reverse transcriptase inhibitor.

Each of these active substances are also known as antiretroviral medicines. Tenofovir disoproxil and lamivudine work by interfering with an enzyme (reverse transcriptase) that is essential for the virus to multiply. Dolutegravir work by reducing the amount of virus which helps to increase the CD4 cell count in your blood. CD4 cells are a type of white blood cells that are important for fighting the infection.

2. What you need to know before you take JUXOLU

Do not take JUXOLU:

- If you are hypersensitive (allergic) to dolutegravir, lamivudine, tenofovir disoproxil fumarate or any of the other ingredients of JUXOLU (listed in section 6).
- If you have moderate or severe liver disease.
- If you have kidney disease.
- If you are pregnant or breastfeeding or are a woman of child-bearing age, not using contraception.
- If you are younger than 18 years of age.
- If you are taking dofetilide or pilsicainide for a heart problem.
- If you are taking metformin to control your blood sugar.
- If you are taking chronic medication for hepatitis B infection, containing adefovir dipivoxil.

- If you are taking other anti-retroviral medicine containing didanosine.

Warnings and precautions

Special care should be taken with JUXOLU:

- If you have or have had kidney disease, or if tests have shown problems with your kidneys. JUXOLU may affect your kidneys. Before starting JUXOLU you may need blood tests to check how well your kidneys are working. Blood tests may also be required during treatment to check the health of your kidneys.
- If you have a history of liver disease, including chronic active hepatitis. Patients with liver disease including chronic hepatitis B or C, who are treated with combination antiretrovirals, have a higher risk of severe and potentially life-threatening liver problems. If you have hepatitis B infection, your health care provider will carefully consider the best treatment regimen for you. Your health care provider may conduct blood tests to check how well your liver is working.
- If you experience any signs of inflammation or infection. In some patients with advanced HIV infection (AIDS) and a history of AIDS-associated (opportunistic) infection, signs, and symptoms of inflammation from such previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms. If you notice any symptoms of infection, please tell your health care provider at once. In addition, 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. These 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, irregular heartbeats, trembling or shaking, or hyperactivity, please inform your health care

provider at once.

- 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 are female, very overweight (obese), or have been medicines used for the treatment of HIV for a long time as you may be more likely to get lactic acidosis (build-up of lactic acid in the body).
- If you experience any signs of bone problems. Some patients taking combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The duration of antiretroviral therapy, use of a corticosteroid such as dexamethasone or prednisolone, alcohol consumption, severe suppression of the immune system, and being overweight may be some of the many risk factors for developing this disease. Signs of osteonecrosis are joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you notice any of these, tell your health care provider. Bone problems (sometimes resulting in fractures) may also occur due to damage to the kidney cells. Bone fractures may also occur due a decrease in bone density.
- If you have abnormal metabolic processes, such as, increased cholesterol, glucose or lactate in the blood or are resistant to insulin. Your healthcare professional may perform regular blood tests to confirm normal metabolic processes.
- If you develop changes in body fat have been seen in some patients taking JUXOLU 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 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 pain in the stomach, as this can be a symptom of pancreatitis (swelling of the pancreas).

Children and adolescents

Safety and effectiveness in paediatric patients and patients younger than 18 years of age have not been established.

Other medicines and JUXOLU

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

It is very important to tell your health care provider if you are taking other medicines that may damage your kidneys. These include:

- aminoglycosides, pentamidine or vancomycin (for bacterial infection)
- amphotericin B (for fungal infection)
- foscarnet, ganciclovir, or cidofovir (for viral infection)
- adefovir dipivoxil (for hepatitis B virus infection)
- tacrolimus (for suppression of the immune system)
- interleukin-2 (to treat cancer)

Medicines containing didanosine (for HIV infection): Taking JUXOLU with medicines that contain didanosine can increase the amount of didanosine in your blood. Rarely, inflammation of the pancreas and lactic acidosis (excess lactic acid in the blood), sometimes causing death, has been reported when medicines containing tenofovir disoproxil and didanosine were taken together. Combining tenofovir disoproxil with didanosine can also reduce the effects of antiretroviral therapy. Your health care provider will carefully consider whether to treat you with a combination of tenofovir disoproxil and

didanosine.

If you are currently taking any of the following medicines tell your healthcare provider immediately:

- dofetilide and pilsicainide (for the treatment of irregular heartbeat)
- antacids, laxatives, or other medicines that contain aluminium, magnesium, sucralfate, or buffered medicines
- metformin (for the treatment of Type 2 Diabetes)
- rifampicin (used for the treatment of tuberculosis)
- didanosine (for HIV infections)
- etravirine, efavirenz, fosamprenavir/ritonavir, nevirapine or tipranavir/ritonavir (to treat HIV infection)
- phenytoin and phenobarbital (to treat epilepsy)
- oxcarbazepine and carbamazepine (to treat epilepsy or bipolar disorder)
- St John's wort (*Hypericum perforatum*), a herbal remedy used for treating depression
- other medicines containing tenofovir disoproxil, emtricitabine, lamivudine or zalcitabine to treat HIV infection.

Taking these medicines with JUXOLU could cause threatening side effects or stop these medicines from working properly.

Taking JUXOLU 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.

JUXOLU with food

It is recommended that JUXOLU be swallowed with water, with or without food.

Pregnancy and breastfeeding

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.

You should not take JUXOLU if you are pregnant or breastfeeding.

Driving and using machines

It is not always possible to predict to what extent JUXOLU may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which JUXOLU affects them. JUXOLU causes dizziness, impaired concentration and/or drowsiness and may affect the ability to drive and use machines.

JUXOLU contains lactose and mannitol

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking JUXOLU.

Each tablet also contains less than 1 mmol sodium (23 mg) sodium per tablet, therefore is essentially sodium-free.

3. How to take JUXOLU

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

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

The usual dose is one tablet taken orally, once daily.

JUXOLU should not be used by children younger than 18 years old.

Your doctor will tell you how long your treatment with JUXOLU will last. If you have the impression that the effect of JUXOLU is too strong or too weak, tell your doctor or pharmacist.

If you take more JUXOLU 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 JUXOLU

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

If you stop taking JUXOLU

Don't stop taking this medicine without talking to your health care provider. Stopping JUXOLU can seriously affect your response to future treatment. If JUXOLU is stopped, speak to your health care provider before you restart taking these tablets. Your health care provider may consider giving you the components of JUXOLU separately if you are having problems or need your dose adjusted.

If you have both HIV infection and hepatitis B, it is especially important not to stop your JUXOLU treatment without talking to your health care provider first. Some patients have had blood tests or symptoms indicating that their hepatitis got worse after stopping treatment. Your health care provider may recommend that you resume hepatitis B treatment if you stop JUXOLU treatment. You may require blood tests to check how your liver is working for 4 months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment is not recommended as this may lead to worsening of your hepatitis, which may be life-threatening.

Tell your health care provider immediately about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection.

4. Possible side effects

JUXOLU can have side effects.

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

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

- allergic reaction (hypersensitivity) that may cause severe skin reactions,
- swelling of the face, lips, tongue or throat.

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

Lactic acidosis (excess lactic acid in the blood) is a rare, but serious side effect that can be fatal. The following side effects may be signs of lactic acidosis:

- deep rapid breathing,
- drowsiness,
- feeling sick (nausea), being sick (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

- headache, dizziness,

- diarrhoea, feeling sick (nausea), being sick (vomiting),
- stomach pain or cramps,
- skin rashes itching,
- hair loss,
- joint pain, stiffness, and muscle problems,
- feeling weak,
- tests may also show decreases in phosphate levels in the blood,
- difficulty sleeping, abnormal dreams,
- problems with digestion resulting in discomfort after meals, feeling bloated, wind (flatulence),
- loss of appetite,
- tiredness,
- protein in the urine,
- inflammation of the kidney, passing a lot of urine and feeling thirsty,
- changes to your urine and back pain caused by kidney problems, including kidney failure,
- fever (high temperature),
- general feeling of being unwell,
- tests may also show:
    - increased fatty acids (triglycerides) or sugar levels in the blood,
    - liver and pancreas problems.

Less frequent

- allergic reactions,
- fatty liver,
- softening of the bones (with bone pain and sometimes resulting in fractures)
- breakdown of muscle, muscle pain or weakness,

- a decreased number of cells involved in blood clotting (thrombocytopenia),
- a low red blood cell count (anaemia) or low white blood cell count (neutropenia),
- increase in body fat.

Frequency unknown

- inflammation of the liver,
- red blood cell abnormalities,
- numbness, tingly feelings in the skin (pins and needles),
- difficulty breathing.

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 JUXOLU.

5. How to store JUXOLU

Store all medicines out of reach of children.

- Store at or below 30 °C.
- Do not use after the expiry date stated on the label or bottle.

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 JUXOLU contains

- The active substances are tenofovir disoproxil fumarate, lamivudine and dolutegravir. Each film-coated tablet contains dolutegravir sodium equivalent to dolutegravir 50 mg, lamivudine 300 mg and tenofovir disoproxil fumarate equivalent to of tenofovir disoproxil 300 mg.

  Contains sugar: 152,66 mg lactose monohydrate and 125 mg mannitol per tablet.
- The other ingredients are*:*

  Core tablet: croscarmellose sodium, lactose monohydrate, magnesium stearate, mannitol (E421), microcrystalline cellulose, povidone, pregelatinised starch, sodium starch glycolate, sodium stearyl fumarate.

  Film coat: D&C Yellow #10, FD&C Blue #2, macrogol/PEG, polyvinyl alcohol (partly hydrolysed), talc, titanium dioxide (E171).

What JUXOLU looks like and contents of the pack

JUXOLU tablets are green coloured, oblong shaped, film-coated tablets, debossed with ‘E22’ on one side and plain on the other side.

30 tablets packed in 100 ml white opaque HDPE container closed with a 38 mm white polypropylene child resistant closure with liner.

90 tablets packed in 250 ml white opaque HDPE container closed with a 53 mm white polypropylene child resistant closure with liner.

180 tablets packed in 500 ml white opaque HDPE container closed with a 53 mm white polypropylene screw cap.

All pack sizes contain a 1 g canister desiccant.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

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Access to the corresponding Professional Information

To be confirmed.