PROPOSED (CLEAN) PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

ODYSTRA film-coated tablets

Lamivudine/ Tenofovir disoproxil fumarate/ Dolutegravir sodium

Contains sugar: lactose monohydrate 136 mg and mannitol 131,4 mg

ODYSTRA may lead to serious problems with your liver or cause too much acid in your blood. If left untreated, this may even cause death. The safety and efficacy of ODYSTRA in patients who are infected with both human immunodeficiency virus (HIV) and hepatitis B virus (HBV) have not been established. ODYSTRA should not be used for the treatment of chronic HBV infection. You should be closely monitored by your doctor for several months if you are infected with HBV and discontinue the use of ODYSTRA.

Read all of this leaflet carefully before you start taking ODYSTRA

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

2. What you need to know before you take ODYSTRA

3. How to take ODYSTRA

4. Possible side effects

5. How to store ODYSTRA

6. Contents of the pack and other information

1. What ODYSTRA is and what it is used for

ODYSTRA belongs to a group of medicines, known as antiretrovirals.

Combination antiretroviral medicines, such as ODYSTRA, are used in the treatment of HIV-1 (human immunodeficiency virus-1) infection in adults aged 18 years and older.

ODYSTRA does not cure or prevent HIV infection; however, it helps to keep HIV from reproducing and appears to slow down the destruction of the immune system. ODYSTRA will not keep you from spreading HIV to other people. Appropriate precautions must continue to be used.

2. What you need to know before you take ODYSTRA

Do not take ODYSTRA:

- If you are hypersensitive (allergic) to tenofovir disoproxil fumarate, lamivudine, dolutegravir or any of the other ingredients in ODYSTRA tablets (listed in section 6).
- If you have uncontrolled kidney failure.
- If you are a woman of childbearing age and not using effective contraceptives.
- If you are pregnant or planning to become pregnant or breastfeeding.
- If you are taking a medicine called adefovir dipivoxil (used for the treatment of chronic hepatitis B).
- If you are taking a medicine called dofetilide and pilsicainide (used for the treatment of abnormal heartbeat – cardiac dysrhythmias).
- If you are taking a medicine called didanosine (used for the treatment of HIV infection).
- If you are taking a medicine called metformin which is used for lowering of blood sugar levels.
- If you are younger than 18 years of age.
- If you have moderate to severe liver disease.

Warnings and precautions

Take special care with ODYSTRA:

Tell your doctor:

- If you are a female, overweight or have been taking nucleoside-containing medicines for a long time, as you are more likely to get lactic acidosis (build-up of lactic acid in the body) (see information about lactic acidosis under 4. Possible side effects).

- 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.
- Before starting treatment, your doctor may order blood tests to assess your kidney function and may advise you to take ODYSTRA tablets less often. Do not reduce the prescribed dose unless your doctor has told you to do so. Your doctor may also order blood tests during treatment to monitor how your kidneys work.
- Some people taking combination medicines for HIV develop a condition called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). You must contact your doctor if you experience joint aches and pain, joint stiffness or difficulty in movement.
- Talk to your doctor if you suffer from osteoporosis, have a history of bone fracture or if you have problems with your bones. Bone problems (manifesting as persistent or worsening bone pain and sometimes resulting in fractures) may also occur due to damage to kidney tubule cells (see section 4, Possible side effects). Tell your doctor if you have bone pain or fractures. Tenofovir disoproxil may also cause loss of bone mass.
- If you have liver problems including hepatitis B virus infection.
- If you have hepatitis B or C, you are at increased risk for severe and potentially fatal liver adverse reactions.
- If you experience any signs of inflammation or infection. Signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment such as ODYSTRA is started. It is believed that these symptoms are due to an 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 inform your doctor immediately.
- If you develop abdominal pain, nausea, vomiting, contact your doctor as it could indicate problems with your pancreas.
- If you develop changes in body fat, as changes have been seen in some patients taking ODYSTRA and other anti-HIV medicines. These changes may include an increased amount of fat in the upper back and neck ("buffalo hump"), in the breasts and around the trunk. Loss of fat from the legs, arms and face may also happen. The cause and long-term health effects of these fat changes are not known.

- If you have a history of depression or mental illness as ODYSTRA may cause depression and suicidal thoughts.
- 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).
- ODYSTRA helps to control (treat) HIV infection but is not a cure. You will need to take it every day. You must not stop taking ODYSTRA without first talking to your doctor. If you are concerned that you may be developing symptoms of a hypersensitivity reaction, call your doctor immediately who will advise whether you must stop taking ODYSTRA. You may continue to develop other infections and other illnesses associated with HIV disease. You should therefore keep in regular contact with your doctor while you are taking ODYSTRA.
- Treatment with ODYSTRA has not been shown to reduce the risk of passing HIV infection to others through sexual contact or contaminated blood. If you are sexually active you should continue to use appropriate precautions to prevent this.
- To protect other people from becoming infected with HIV:
  - **A condom must be used** when you have oral or penetrative sex.
  - **Blood transfer should be avoided** – for example, needles must not be shared.

Children and adolescents

Do not give this medicine to children under the age of 18 years.

Other medicines and ODYSTRA

Always tell your health care 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 ODYSTRA:

- Other medicines that contain tenofovir disoproxil fumarate, lamivudine dolutegravir or emtricitabine, either alone, or in other formulations.

ODYSTRA should not be used with these medicines because they contain the same or similar active ingredients as ODYSTRA.

- Medicines that contain didanosine. Tenofovir disoproxil fumarate (an ingredient in ODYSTRA) may

cause the amount of didanosine in your blood to increase. You may need to be followed more carefully if you are taking ODYSTRA and didanosine together. The dose of didanosine may need to be reduced.

- Adefovir dipivoxil (used for the treatment of chronic hepatitis B).
- ODYSTRA can increase levels of the following heart medicine for the treatment of irregular heartbeat – dofetilide and pilsicainide.
- Zalcitabine (antiretroviral treatment). Lamivudine which is contained in ODYSTRA may reduce the antiviral action of zalcitabine therefore the two medicines should not be used together.
- Etravirine, efavirenz, fosamprenavir/ritonavir, darunavir/ritonavir, nevirapine or tipranavir/ritonavir (to treat HIV infection).
- Oxcarbazepine, phenytoin, phenobarbitone, carbamazepine, St. John's wort (used for treatment of fits and depression).
- Trimethoprim, as in co-trimoxazole (an antibiotic), may cause an increase in ODYSTRA plasma levels. If you have no kidney disease, a dosage adjustment is not necessary.
- Rifampicin (antibiotic used to treat several types of bacteria) may decrease the blood levels of dolutegravir.
- ODYSTRA can increase blood concentration levels of isoniazid used for treatment of tuberculosis.
- Polyvalent cation-containing antacids. Antacids which contain magnesium, aluminium or calcium are recommended to be administered 2 hours before or 6 hours after ODYSTRA.
- Calcium supplements: Recommended to be administered 2 hours before or 6 hours after ODYSTRA or taken with food.
- Iron supplements: Recommended to be administered 2 hours before or 6 hours after ODYSTRA or taken with food.
- Metformin: Co-administered with ODYSTRA may increase plasma levels of insulin.
- Oral contraceptives: ODYSTRA does not change the concentration levels of oral contraceptives.
- Methadone (a pain killer): ODYSTRA does not change the concentration levels of this painkiller.
- Some patients who are taking ODYSTRA may continue to experience infections and the use of antibiotics may have to be considered.

ODYSTRA with food and drink

ODYSTRA can be taken without regard to food.

Pregnancy, breastfeeding and fertility

Do not take ODYSTRA tablets if you are pregnant or breastfeeding (see 2. What you need to know before you take ODYSTRA). ODYSTRA could seriously harm your unborn child if you fall pregnant while on treatment or if you start taking ODYSTRA in the first few weeks of your pregnancy.

If you are pregnant or breastfeeding your baby, 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 ODYSTRA.

If you are a woman who is able to have children, you should be counselled about the potential risk of neural tube defects with dolutegravir.

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

If you plan on becoming pregnant, your doctor will need to discuss the risks and benefits of starting or continuing treatment with ODYSTRA versus another medicine regimen.

Use of dolutegravir during pregnancy was associated with a small increase in the birth defects of the brain and spine.

If a pregnancy is confirmed in the first trimester while on dolutegravir, the benefits and risks of continuing dolutegravir versus switching to another antiretroviral medicine should be discussed with you. Dolutegravir may be used during the second and third trimester of pregnancy when the expected benefit outweighs the potential risk to the foetus.

You should ensure that you always used effective contraception while you are taking ODYSTRA. Your health care professional can advise you on which contraceptives to take. Never stop taking ODYSTRA 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 ODYSTRA and contraception before you have talked to your healthcare professional. If you think you are pregnant go to your health care professional to get a pregnancy test and to be advised on your future HIV treatment and on a pregnancy management plan.

Do not breastfeed your baby if you are taking ODYSTRA.

HIV infected mothers should not breastfeed their infants in order to avoid transmission of HIV or follow appropriate guidelines.

There are no data on the effects of dolutegravir on human male or female fertility.

Driving and using machines

ODYSTRA may affect the ability to drive and use machines. ODYSTRA can make you feel dizzy or sleepy and may have other side effects and make you less alert. Make sure you know how you react to ODYSTRA before you drive, use machines, or do anything else that could be dangerous.

ODYSTRA tablets contains lactose, mannitol and sodium

ODYSTRA tablets contains lactose:

Patients with the rare hereditary conditions of lactose or galactose intolerance should not take ODYSTRA. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking ODYSTRA.

ODYSTRA tablets contains lactose monohydrate which may have an effect on the control of your blood sugar if you have diabetes mellitus.

ODYSTRA tablets contains mannitol:

ODYSTRA contains mannitol which may cause loose bowels.

ODYSTRA tablets contains sodium:

ODYSTRA contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

3. How to take ODYSTRA

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

Treatment should be prescribed and initiated by a doctor experienced in the management of HIV infection. Always take ODYSTRA exactly as your doctor has instructed you. Check with your doctor or pharmacist if you are not sure.

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

You can only take ODYSTRA if you are older than 18 years.

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

If you take more ODYSTRA 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 ODYSTRA

If you forget to take a dose of ODYSTRA, take it as soon as you remember unless it is nearly time for your next dose and then continue as before. Do not take a double dose to make up for forgotten individual doses.

If you stop taking ODYSTRA

Do not suddenly stop taking ODYSTRA without consulting with your doctor first. If you have stopped taking ODYSTRA for any reason, especially if you think you are having side effects, or for another illness, it is important that you contact your doctor before restarting.

You should not stop treatment unless your doctor instructs you to. When your ODYSTRA supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to the ingredients in ODYSTRA and become harder to treat.

If you have the impression that the effect of ODYSTRA is too strong or too weak, talk to your doctor or pharmacist.

4. Possible side effects

ODYSTRA can have side effects.

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

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

- Sudden swelling of hands, face, lips, mouth, tongue and throat or mucous membranes with difficulty breathing and/or itching and rash.

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

- Serious liver problems (hepatitis) with liver enlargement (hepatomegaly) and fat in the liver (steatosis). The following are signs of the liver problems:
  - Yellow discolouration of the skin and the white part of your eyeballs.
  - Darkening of your urine.
  - Your bowel movements turn lighter in colour.
  - You feel sick to your stomach (nausea).
  - You have stomach pain.

You may need urgent medical attention or hospitalisation.

Lactic acidosis

Some people who have taken medicines like ODYSTRA (nucleoside analogues) have developed a serious condition called lactic acidosis (build-up of acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in the hospital. Call your doctor immediately if you get the following signs or symptoms of lactic acidosis:

- 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 lightheaded.
- You have a fast or irregular heartbeat.

This side effect can cause inflammation of the pancreas, liver and kidney failure, and has occasionally been fatal. Lactic acidosis also occurs more often in women, particularly if they are overweight. If you have liver disease, you may also be more at risk of getting this condition. While you are being treated with ODYSTRA, your doctor will monitor you closely for any signs that you may be developing lactic acidosis.

Tell your doctor if you notice any of the following:

Frequent side effects:

- Headache.
- Dizziness.
- Difficulty in sleeping (insomnia), abnormal dreams.
- Nausea, vomiting.
- Stomach pain or cramps.
- Diarrhoea, flatulence.
- Rash, itching.
- Hair loss.
- Joint pain (arthralgia).
- Muscles become weak, painful and may even cause paralysis (muscle disorder).
- Feeling tired, weak (fatigue).
- Feeling of bodily discomfort (malaise).
- Fever.
- Loss of bone mass.
- Loss of appetite.
- Chronic kidney disease, of kidney failure (renal insufficiency).

Less frequent side effects:

- Depression.
- Neutropenia (low white blood cell count).
- Anaemia (low red blood cell count).
- Increased bruising or bleeding (thrombocytopenia).
- Increases in enzymes produced by the liver.
- Allergic reaction (hypersensitivity).
- Immune system begins to recover (immune reconstitution syndrome).
- Abdominal pain or discomfort.

- Hepatitis (disease of the liver).
- Redistribution/accumulation of body fat.
- Abnormal sensation of tingling, numbness or burning (paraesthesia).
- Peripheral neuropathy (when the nerves carrying messages to and from the brain are damaged).
- Inflammation of the pancreas, which causes severe pain in the abdomen and back.
- Abnormal muscle breakdown which can lead to kidney problems.
- Bones are more porous than they should be (osteopenia).
- Fractures.
- Abnormally low levels of phosphate in the blood (hypophosphataemia).
- Nose and throat infection.
- Nasal discharge and congestion.
- Increased blood sugar levels.
- Cough.

Side effects with frequency unknown:

- Inflammation of the liver (hepatitis).
- Bone marrow stops making red blood cells (pure red cell aplasia).
- Abdominal pain.
- Abdominal discomfort.
- Shortness of breath (dyspnoea).

If you notice any side effects not mentioned in this leaflet, please inform the medical practitioner 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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of ODYSTRA.

5. How to store ODYSTRA

Store all medicines out of reach of children.

Store at or below 30 °C. Store in the original container. Do not remove from the carton until required for use. Keep the bottle tightly closed.

Do not store in a bathroom.

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

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 ODYSTRA contains

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

Each ODYSTRA film-coated tablet contains lamivudine 300 mg, tenofovir disoproxil fumarate 300 mg and dolutegravir sodium equivalent to dolutegravir 50 mg.

The other ingredients are croscarmellose sodium, lactose monohydrate, mannitol, magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycolate.

Film-coating colourant:

Opadry II White: Macrogol/PEG 4000, polyvinyl alcohol – part. hydrolysed, talc, titanium dioxide.

Aqua-ll White: Polyethylene glycol, polyvinyl alcohol, talc, titanium dioxide.

What ODYSTRA looks like and contents of the pack

White to off white, film-coated, capsule-shaped, biconvex bevelled edge tablet debossed with “M” on one side and “LTD” on the other side of the tablet.

ODYSTRA is packed in a round, blue, opaque high-density polyethylene (HDPE) bottle, with blue opaque polypropylene (PP) screw closure, an aluminium induction sealing liner wad and a desiccant. Packed in an outer carton. Pack sizes of 28’s, 30’s, 84’s, 90’s and 180’s

Not all packs and pack sizes may be marketed.

Holder of Certificate of Registration

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To be advised

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