PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

DIVTRIDA (film-coated tablet)

Read all of this leaflet carefully before you start taking DIVTRIDA.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **DIVTRIDA 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.

1. WHAT DIVTRIDA CONTAINS

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

Each film-coated tablet contains dolutegravir sodium equivalent to 50 mg of dolutegravir, lamivudine 300 mg and tenofovir disoproxil fumarate 300 mg which is equivalent to 245 mg of tenofovir disoproxil.

The other ingredients of **DIVTRIDA are** colloidal silicon dioxide, croscarmellose sodium, ferric oxide, hypromellose, magnesium stearate, microcrystalline cellulose, opadry II pink 85F94172, povidone, sodium starch glycolate and sodium stearyl fumarate.

In addition opadry II pink 85F94172 contains iron oxide red (C.I. No: 77491), oxide black (C.I. No: 77499), polyethylene glycol, talc and titanium dioxide (C.I. No: 77891).

Contains sugar: 145,37 mg mannitol.

WARNING

LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS, INCLUDING FATAL CASES, HAVE BEEN REPORTED WITH THE USE OF NUCLEOSIDE ANALOGUES ALONE OR IN COMBINATION WITH OTHER ANTIRETROVIRALS.

DIVTRIDA IS NOT INDICATED FOR THE TREATMENT OF CHRONIC HEPATITIS B VIRUS (HBV) INFECTION. THE SAFETY AND EFFICACY OF DIVTRIDA HAS NOT BEEN ESTABLISHED IN PATIENTS CO-INFECTED WITH HBV AND HIV. SEVERE ACUTE EXACERBATIONS OF HEPATITIS B HAVE BEEN REPORTED IN PATIENTS WHO ARE CO-INFECTED WITH HBV AND HIV AND HAVE DISCONTINUED THE COMBINATION TABLET. HEPATIC FUNCTION SHOULD BE MONITORED CLOSELY WITH BOTH CLINICAL AND LABORATORY FOLLOW-UP FOR AT LEAST SEVERAL MONTHS IN PATIENTS WHO DISCONTINUE DIVTRIDA AND ARE CO-INFECTED WITH HIV AND HBV. IF APPROPRIATE, INITIATION OF ANTI-HEPATITIS B THERAPY MAY BE WARRANTED.

2. WHAT DIVTRIDA IS USED FOR

DIVTRIDA is a triple combination therapy used to treat human immunodeficiency virus (HIV) infection in adults aged 18 years and older.

3. BEFORE YOU TAKE DIVTRIDA

Do not take DIVTRIDA:

- If you are hypersensitive (allergic) to dolutegravir, lamivudine or tenofovir or any of the other ingredients of **DIVTRIDA.**
- If you suffer from uncontrolled kidney failure.
- If you are taking anti-arrhythmic medicines called dofetilide or pilsicainide.
- If you are taking a medicine called metformin which is used for lowering of blood sugar levels.
- If you are taking the antiretroviral medicine called didanosine.
- If you are taking a medicine called adefovir dipivoxil which is used to treat hepatitis B.
- If you have any liver disease (moderate or severe).

- If you are younger than 18 years old.
- If you are pregnant or planning to become pregnant or breastfeeding (see **Pregnancy and Breastfeeding**).

Take special care with DIVTRIDA:

- If you suffer from high cholesterol, increased blood sugar levels, insulin resistance or increased blood lactate levels, as it may worsen if you are taking **DIVTRIDA.**
- If you notice a redistribution/accumulation of fat, obesity, peripheral wasting, facial wasting and breast enlargement, inform your doctor as triple combination antiretroviral therapy often causes this.
- If you get any other symptoms of other serious infections as sometimes you may experience an inflammatory reaction that causes an existing infection to get worse. This is caused by the body's immune system becoming stronger.
- 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 **DIVTRIDA,** when taken together with corticosteroids or alcohol, or if you have a very weak immune system and are overweight.
- As it does not prevent your risk of transmitting HIV to others through sexual contact or blood contamination. You should still take appropriate precautions.
- 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 **DIVTRIDA.**
- If you experience any symptoms of anaemia such as extreme tiredness or paler skin than usual, or if you start experiencing fits, a change in your muscle tone or unusual behaviour from yourself you may be experiencing mitochondrial dysfunction and should therefore inform your doctor immediately.
- If you experience severe abdominal pain, nausea or vomiting you need to tell your doctor immediately as he may have to do blood tests to confirm if you are suffering from inflammation of your pancreas.
- If you suffer from kidney problems you should inform your doctor, as you may not be able to take **DIVTRIDA since** the dosage cannot be adjusted.

- If you are already suffering from any liver disease you should inform your doctor as your condition may worsen while taking **DIVTRIDA.**
- You should tell your doctor of any medicines that you are taking or have recently taken as some medicines cannot be taken with **DIVTRIDA as** it may damage your kidneys.
- If you suffer from chronic hepatitis B or C you should tell your doctor as you should not be taking **DIVTRIDA as** it could cause severe liver damage which could even result in death.
- If you experience an allergic reaction with symptoms such as a severe rash, fever, general weakness and tiredness, muscle or joint aches, blisters, sores in your mouth, swelling of your face or severe abdominal pain you should stop taking **DIVTRIDA** immediately.

Taking DIVTRIDA with food and drink:

DIVTRIDA can be taken with or without food.

Pregnancy and breastfeeding:

- Do not take **DIVTRIDA tablets** if you are pregnant or breastfeeding (see **Do not take DIVTRIDA tablets**). **DIVTRIDA could** seriously harm your unborn child if you fall pregnant while on treatment or if you start taking **DIVTRIDA in** the first few weeks of your pregnancy.
- If you are pregnant or breastfeeding your baby, please consult your healthcare professional for advice before taking **DIVTRIDA.** You should ensure that you always use effective contraception while you are taking **DIVTRIDA.** Your healthcare professional can advise you on which contraceptives to take. Never stop taking **DIVTRIDA without** first consulting your healthcare professional as your HIV condition may become worse.
- If you are thinking of having a baby, do not stop using **DIVTRIDA and** contraception before you have talked to your healthcare professional. If you think you are pregnant go to your healthcare professional to get a pregnancy test and to be advised on your future HIV treatment and on a pregnancy management plan.

If your pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **DIVTRIDA.**

Driving and using machinery:

You should consider the possible side effects of **DIVTRIDA before** you drive or operate machinery. You should first establish the effects of this medicine on you before driving or operating any machinery.

Important information about some of the ingredients of DIVTRIDA:

DIVTRIDA contains a type of sugar called mannitol which may have a laxative effect.

Taking other medicines with DIVTRIDA:

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

DIVTRIDA may have an effect on other medicines or other medicines may have an effect on **DIVTRIDA.**

- Lamivudine which is contained in **DIVTRIDA may** reduce the antiviral action of zalcitabine therefore the two medicines should not be used together.
- The antibiotic co-trimoxazole causes an increase in the level of lamivudine which is contained in **DIVTRIDA in** your blood.
- The following medicines will decrease the effect of **DIVTRIDA** by interacting with either of the medicines contained in the triple combination tablet: rifampicin (used in TB treatment); etravirine, efavirenz, nevirapine, tipranavir/ritonavir, fosamprenavir/ritonavir, darunavir/ritonavir (used in HIV treatment), oxcarbazepine, phenytoin, phenobarbitone, carbamazepine, St. John's wort (used for treatment of fits and depression); antacids which contain magnesium, aluminium or calcium; iron and calcium supplements.
- The following medicines will increase the effect of **DIVTRIDA** by interacting with either of the medicines contained in the triple combination tablet: Atazanavir and indinavir, lopinavir/ritonavir (used in HIV treatment)

- **DIVTRIDA** will either increase or decrease the blood levels of the following medicines if taken together: Abacavir, indinavir, atazanavir, zalcitabine (used in HIV treatment); dofetilide or pilsicainide (used to treat irregular heartbeats); and metformin used in treatment of diabetes

4. HOW TO TAKE DIVTRIDA

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

DIVTRIDA therapy should be initiated by a medical practitioner experienced in the management of HIV infection. Always take **DIVTRIDA exactly** as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The usual dose of **DIVTRIDA is** one tablet daily and is only recommended for adults 18 years and older.

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

If you take more DIVTRIDA then you should:

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

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 DIVTRIDA:

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

5. POSSIBILE SIDE EFFECTS

DIVTRIDA can have side effects.

Not all side effects reported for **DIVTRIDA are** included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

If any of the following happens, stop taking **DIVTRIDA** 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 **DIVTRIDA.** 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 which may occur frequently:

- Severe upper abdominal pain
- Yellowing of your skin, white of eyes, and nails

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

Tell your doctor if you notice any of the following which may occur frequently:

- Difficulty sleeping
- Headache
- Dizziness
- Abnormal dreams
- Diarrhoea

- Nausea
- Rash
- Itchy skin
- Tiredness
- Excess production of milk
- Increased blood sugar levels
- Feeling depressed
- Hair loss
- Painful muscles and joints
- Stomach cramps

The following side effects occur less frequently:

- Vomiting
- Flatulence
- A redistribution of your body fat around your body
- Pins and needles in hands and feet
- Nose and throat infections
- Nasal discharge and congestion
- Loss of appetite

The following side effects frequency unknown:

- Cough
- Wheezing chest

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

6. STORING AND DISPOSING OF DIVTRIDA:

Store at or below 30 °C.

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.

STORE OUT OF REACH AND SIGHT OF CHILDREN.

Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. PRESENTATION OF DIVTRIDA

Tablets are packed in white opaque round 100 ml HDPE container of 38 mm neck finish closed with white opaque polypropylene 38 mm- 400 child resistance closure with wad having induction sealing liner. The HDPE container also contains 3 g of silica gel sachet

Each container contains 30 tablets and is packed in an outer cardboard carton.

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

8. IDENTIFICATION OF DIVTRIDA

Pink coloured, oval, biconvex, film coated tablet debossed with 'N33' on one side and plain on the other side.

9. REGISTRATION NUMBER

To be allocated

10. NAME AND ADDRESS OF REGISTRATION HOLDER

Novagen Pharma (Pty) Ltd

Office 2, 100 Sovereign Drive,

Route 21 Corporate Park,

Nellmapius Drive, Irene,

0157, Pretoria,

South Africa.

11. DATE OF PUBLICATION

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