Annotated Proposed Patient Information Leaflet

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS **S4**

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

VOLUTRIP (film-coated tablet)

Dolutegravir / Lamivudine / Tenofovir disoproxil fumarate

Contains sugar: 145,37 mg mannitol.

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

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

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

VOLUTRIP 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 VOLUTRIP

Do not take VOLUTRIP:

- If you are hypersensitive (allergic) to dolutegravir, lamivudine or tenofovir or any of the other ingredients of **VOLUTRIP** (listed in section 6).
- 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 breastfeeding and fertility**).

Warnings and precautions

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.

VOLUTRIP IS NOT INDICATED FOR THE TREATMENT OF CHRONIC HEPATITIS B VIRUS (HBV) INFECTION. THE SAFETY AND EFFICACY OF VOLUTRIP 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 VOLUTRIP AND ARE CO-INFECTED WITH HIV AND HBV. IF APPROPRIATE, INITIATION OF ANTI-HEPATITIS B THERAPY MAY BE WARRANTED.

Take special care with VOLUTRIP:

Tell your doctor:

- 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 **VOLUTRIP**.
- 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 **VOLUTRIP,** 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 **VOLUTRIP.**
- 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 **VOLUTRIP** 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 **VOLUTRIP**.

- You should tell your doctor of any medicines that you are taking or have recently taken as some medicines cannot be taken with **VOLUTRIP** 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 **VOLUTRIP** 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 **VOLUTRIP** immediately.

Other medicines and VOLUTRIP:

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

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

- Lamivudine which is contained in **VOLUTRIP** 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 **VOLUTRIP[~~r~~]** in your blood.
- The following medicines will decrease the effect of **VOLUTRIP** by interacting with either of the medicines contained in the triple combination tablet: rifampicin and isoniazid (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 **VOLUTRIP** by interacting with either of the medicines contained in the triple combination tablet: Atazanavir and indinavir, lopinavir/ritonavir (used in HIV treatment)
- **VOLUTRIP** 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

Children and adolescents

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

Taking VOLUTRIP with food and drink:

VOLUTRIP can be taken with or without food.

Pregnancy, breastfeeding and fertility:

- Do not take **VOLUTRIP** tablets if you are pregnant or breastfeeding (see **Do not take VOLUTRIP tablets**). **VOLUTRIP** could seriously harm your unborn child if you fall pregnant while on treatment or if you start taking **VOLUTRIP** 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 **VOLUTRIP**. You should ensure that you always use effective contraception while you are taking **VOLUTRIP**. Your healthcare professional can advise you on which contraceptives to take. Never stop taking **VOLUTRIP** 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 **VOLUTRIP** 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 you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **VOLUTRIP**.

Driving and using machinery:

It is not always possible to predict to what extent **VOLUTRIP** may interfere with the daily activities of a patient. Dizziness, impaired concentration and drowsiness may occur when taking **VOLUTRIP**. If this happens, do not drive or use machines that require you to be alert. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which **VOLUTRIP** affects them.

Important information about some of the ingredients of VOLUTRIP:

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

3.HOW TO TAKE VOLUTRIP

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

VOLUTRIP therapy should be initiated by a medical practitioner experienced in the management of HIV infection.

Always take **VOLUTRIP** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

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

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

If you take more VOLUTRIP then you should:

There is no specific treatment for **VOLUTRIP** overdose therefore if you have taken more **VOLUTRIP** 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 VOLUTRIP:

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.

If you stop taking VOLUTRIP:

Consult your doctor if you stop or intend to stop taking **VOLUTRIP**.

4. POSSIBILE SIDE EFFECTS

VOLUTRIP can have side effects.

Not all side effects reported for **VOLUTRIP** 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 **VOLUTRIP** 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 **VOLUTRIP**. 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
- Kidney disorder in which the spaces between the kidney tubules become swollen (inflamed)- interstitial nephritis).
- excessive or an abnormally large production or passage of urine (polyuria)
- Fanconi syndrome (condition that affects how your kidneys reabsorb minerals and nutrients that you need to function).symptoms include:
    - muscle weakness.
    - low blood phosphate levels (hypophosphatemia).
    - low blood potassium levels (hypokalemia).
    - more amino acids in your pee (hyperaminoaciduria).
    - a buildup of acids in your bodily fluids (metabolic acidosis).
    - passing more urine than usual.
    - dehydration.
    - being thirstier than usual.
- hypophosphatemia (low blood phosphate levels).

The following side effects occur less frequently:

- Vomiting
- Flatulence
- A redistribution of your body fat around your body (lipodistrophy)
- Pins and needles in hands and feet
- Nose and throat infections
- Nasal discharge and congestion
- Loss of appetite
- Lactic acidosis (build-up of an acid in the blood) is a less frequent but very serious side effect that can be fatal. The following symptoms may be signs of lactic acidosis:
    - deep rapid breathing
    - drowsiness
    - feeling sick (nausea)
    - being sick (vomiting)
    - stomach pain
- Rhabdomyolysis (deterioration of skeletal muscle which causes painful muscles)
- Muscle weakness
- Osteomalacia (soft or weak bones causing pain in the bones and hips)
- Weakness and lack of energy (asthenia)

The following side effects frequency unknown:

- Cough
- Wheezing chest
- Pure red cell aplasia (type of anemia)

- Abdominal pain
- Abdominal discomfort
- Inflammation of the liver (hepatitis)

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (whoumc.org) found on SAHPRA website.

By reporting side effects, you can help provide more information on the safety of **VOLUTRIP**:

5 How to store **VOLUTRIP**

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 ALL MEDICINES OUT OF REACH OF CHILDREN.

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 VOLUTRIP contains

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

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

VOLUTRIP contains mannitol 145,37 mg per tablet

The other ingredients are

Tablet core:

Croscarmellose sodium,ferric oxide, hypromellose,magnesium stearate, mannitol, microcrystalline cellulose,opadry II pink 85F94172, povidone, sodium starch glycolate sodium stearyl fumarate.

Tablet coating: Opadry II pink 85F94172 , iron oxide red (C.I. No: 77491), oxide black (C.I. No: 77499), polyethylene glycol, talc , titanium dioxide (C.I. No: 77891)

What VOLUTRIP looks like and contents of the pack

1.Tablets are packed in white opaque round 75 ml HDPE container with 38 mm neck finish closed with white opaque polypropylene 38 mm - 400 child resistant closure with wad having induction sealing liner. The HDPE container also contains 3 g of silica gel sachet.

Each container contains 28 tablets and is packed in an outer cardboard carton.

Pack size: 28s – One HDPE container contains 28 tablets

2. Tablets are packed in white opaque round 100 ml HDPE container with 38 mm neck finish closed with white opaque polypropylene 38 mm - 400 child resistant 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

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

Each container contains 90 tablets and is packed in an outer cardboard carton.

Pack size: 90's – One HDPE container contains 90 tablets

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

Each container contains 180 tablets and is packed in an outer cardboard carton.

Pack size: 180's – One HDPE container contains 180 tablets

IDENTIFICATION OF VOLUTRIP

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

Holder of Certificate of Registration

Aurobindo Pharma (Pty) Ltd

Woodhill Office Park, Building 1

53 Phillip Engelbrecht Avenue

Meyersdal, Ext. 12, 1448

Johannesburg

South Africa

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