PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

TRIVENZ 600 mg, 200 mg, 300 mg, film-coated tablets
Efavirenz, Emtricitabine, Tenofovir disoproxil fumarate
Sugar free

Read all of this leaflet carefully before you start taking TRIVENZ

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

TRIVENZ contains three active substances that are used to treat human immunodeficiency virus (HIV) infection: efavirenz is a non-nucleoside reverse transcriptase inhibitor (NNRTI), emtricitabine is a nucleoside reverse transcriptase inhibitor (NRTI) and tenofovir is a nucleotide reverse transcriptase inhibitor (NRTI).

Each of these active substances, also known as antiretroviral medicines, work by interfering with an enzyme (reverse transcriptase) that is essential for the virus to multiply.
TRIVENZ can be used alone as a complete regimen or in combination with other anti-retroviral medicines for the treatment of HIV-1 infection in adults**.**

2. What you need to know before you take TRIVENZ

Do not take TRIVENZ:

- If you are hypersensitive (allergic) to efavirenz, emtricitabine and/or tenofovir disoproxil fumarate or any of the other ingredients of TRIVENZ (listed in section 6).
- You had a liver disorder or liver failure attributed to treatment with TRIVENZ.
- If you have moderate to severe kidney failure.
- If you are pregnant or breastfeeding.
- If you have a heart condition, such as an abnormal electrical signal called prolongation of the QT interval that puts you at high risk for severe heart rhythm problems (Torsade de Pointes).
- If any member of your family (parents, grandparents, brothers or sisters) has died suddenly

due to a heart problem or was born with heart problems.
- If your doctor has told you that you have high or low levels of electrolytes such as low potassium or low magnesium in your blood.
- If you are also taking the following medicines: antiarrhythmics of classes IA and III, neuroleptics, antidepressants, terfenadine, astemizole, bepridil, cisapride, ergot derivatives, midazolam, pimozide, triazolam, voriconazole, St. John's wort, flecainide, certain antibiotics (macrolides, fluoroquinolones, imidazole), triazole antifungals, certain antimalarial medicines and methadone.

Do not take TRIVENZ with the following related medicines:
- Medicines containing the same active ingredients as TRIVENZ such as emtricitabine, tenofovir disoproxil fumarate, emtricitabine/tenofovir disoproxil fumarate and efavirenz.
- Medicines containing lamivudine, which is similar to emtricitabine including lamivudine/zidovudine, lamivudine, abacavir sulphate/ lamivudine or abacavir sulphate/lamivudine/zidovudine (see Other medicines and TRIVENZ).

Warnings and precautions
Take special care with TRIVENZ:
- If you have been diagnosed with chronic hepatitis B or have a history of hepatitis B infections as you may experience a severe exacerbation of hepatitis upon discontinuation of treatment.
- If you have a history of liver disease or risk factors for liver disease because you may be at risk for lactic acidosis (low pH in the blood and bodily tissues accompanied by a build-up of lactic acid) and severe hepatomegaly with steatosis (enlargement of liver with fatty deposits in it). This risk is higher if you are female, obese and have had long term exposure to antiretrovirals.
- If you have kidney failure.
- If you have a history of psychiatric disorders, the use of psychiatric medication, injection medicine use or if you start experiencing psychiatric disturbance such as severe depression, suicidal thoughts, suicide attempts, aggressive behaviour, paranoid reactions and manic reactions.
- Because you may experience nervous system symptoms such as dizziness, difficulty sleeping, impaired concentration, drowsiness or a strong desire to sleep, abnormal dreams, hallucinations, being intensely happy and excited for no apparent reason, confusion, agitation, loss of memory, stupor, abnormal thinking and feeling detached from one's self. These symptoms would normally
- subside within 2 to 4 weeks of starting treatment. Beware of simultaneous intake of alcohol and other central nervous system depressants or operating hazardous machinery (see Driving and using machines).
- Tell your doctor if you develop or see signs of opportunistic infections or other complications even when you are on TRIVENZ treatment as such could be detrimental to your health.
- As the use of TRIVENZ does not eliminate the risk of HIV transmission to others through sexual contact or blood contamination, therefore you must always take appropriate

precautions when involved in activities such as sexual intercourse or handling blood.

- You may experience skin rash in the first month of treatment with TRIVENZ, tell your doctor about your skin rash if it is persistent. You must stop taking TRIVENZ if your rash becomes severe with symptoms such as fever, blistering or skin peeling.
- Tell your doctor if you are suffering from osteomalacia (bone disorder indicated by bone pain especially in the hips, bone fractures with no known cause or injury and also by muscle weakness) as TRIVENZ can aggravate your condition.
- Take TRIVENZ with caution if you have a history of seizures and let your doctor know about them.
- TRIVENZ is known to lead to fat redistribution in your body and this is usually indicated by gaining weight around the midriff, formation of buffalo hump-like structure on the trunk (also called enlargement of dorsocervical fat), facial wasting, losing weight on the arms and legs and breast enlargement.
- If you are under the age of 18 years because TRIVENZ is not recommended for use in patients under the age of 18 years.
- If you are an elderly patient over the age of 65 years as this population tends to experience decreased kidney, liver and heart functioning and are usually taking other medications.
- If you are also taking products containing St. John's wort (*Hypericum perforatum*) because St. John's wort can reduce the effect of TRIVENZ against HIV infection (see Other medicines and TRIVENZ).
- You should not use TRIVENZ if you are at increased risk of Torsade de Pointes (fast heartbeat) or if you are using medicine with a known risk for Torsade de Pointes.
- Tenofovir disoproxil may also cause loss of bone mass.
- Overall, the effects of tenofovir disoproxil on long term bone health and future fracture risk in adult and paediatric patients are uncertain.

Other medicines and TRIVENZ

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

Do not take TRIVENZ with the following medicines:

- *Voriconazole:* risk severity of side effects associated with the use of TRIVENZ is increased.
- *Astemizole, bepridil, cisapride, and pimozide*: Life-threatening adverse events such as abnormal or irregular heart rates can occur.
- *Ergot derivatives (dihydroergotamine, ergonovine, ergotamine, methylergonovine)*: effect of TRIVENZ is decreased and may lead to viral resistance of anti-HIV medicines like TRIVENZ.
- *Anti-retrovirals (efavirenz, emtricitabine, tenofovir disoproxil fumarate, lamivudine)*: efavirenz, emtricitabine and tenofovir disoproxil fumarate are already ingredients in TRIVENZ, while lamivudine is closely related to emtricitabine.
- *Benzodiazepines (midazolam, triazolam)*: prolonged or increased sedation or respiratory depression, e.g. difficulties in breathing.

TRIVENZ with food and drink
There are no studies for TRIVENZ in the presence of food but tenofovir disoproxil fumarate and efavirenz concentrations may be increased by taking them with a high fat meal and may possibly expose you to more side effects. Please see section 3. How to take TRIVENZ.

Do not take TRIVENZ with grapefruit.

Pregnancy, breastfeeding and fertility

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 healthcare provider for advice before taking TRIVENZ.

TRIVENZ should not be used during pregnancy. Studies in animals have associated efavirenz with birth defects.

Women of childbearing age who are using TRIVENZ should avoid falling pregnant and should ensure this by using a barrier method of contraception in combination with other methods of contraception.
It is recommended to use adequate contraceptive measures for 12 weeks after you have stopped using TRIVENZ.
Do not breastfeed if you are taking TRIVENZ. Studies in animals (rats) have shown that TRIVENZ may appear in milk.

Driving and using machines
It is not always possible to predict to what extent TRIVENZ may interfere with the daily activities of a patient.
Do not drive or operate tools and machinery especially while you are on TRIVENZ therapy. You may experience dizziness, drowsiness or a strong desire to sleep, impaired concentration, hallucinations, being intensely happy and excited for no apparent reason, confusion, loss of memory, stupor and abnormal thinking.
Patients should ensure that they do not engage in the above activities until they are aware of the measure to which TRIVENZ affects them.

3. HOW TO TAKE TRIVENZ
Do not share medicines prescribed for you with any other person.

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

Take one tablet daily on an empty stomach.

Taking TRIVENZ at bedtime may improve the tolerability of nervous system symptoms.

Take your dose with water.

Do not stop taking TRIVENZ unless your doctor has told you so.

Taking your dose at the same time each day will have the best effect in controlling your viral load and will help you remember when to take the tablets.

Always get more tablets before your current supply is finished in order to avoid ever skipping a dose.

Children
TRIVENZ is not recommended for use in patients under the age of 18 years.

Kidney failure
TRIVENZ should not be used by patients who need dose adjustment because it is a fixed dose tablet. If your creatinine clearance is less than 50 ml/min you may not use TRIVENZ.

If you have the impression that the effect of TRIVENZ is too strong or too weak, tell your doctor or pharmacist.

If you take more TRIVENZ 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.

If you forget to take TRIVENZ
Take a missed dose as soon as you remember it. However, if it is almost time for your next dose rather leave it and continue with your normal schedule. Do not take a double dose to make up for forgotten individual doses. If you miss more than one dose, rather leave those doses and resume with the normal schedule when the time comes to take your normal dose.

Please consult your doctor or pharmacist if you are not sure about your dosing.

4. POSSIBLE SIDE EFFECTS
TRIVENZ can have side effects.

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

If any of the following happens, stop taking TRIVENZ and tell your doctor immediately or go to the casualty department at your nearest hospital:
- Allergic reaction, e.g. skin rash, itching.
- Erythema multiforme (skin disorder occurring due to allergic reaction and its symptoms may

include fever, itching, joint aches and multiple skin lesions).
- Stevens-Johnson syndrome (life-threatening skin disorder whereby the outmost part of skin peels off).

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to TRIVENZ. 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*:*
- Suicidal thoughts or attempts.
- Increased susceptibility to infection, for example, coughing, flu-like symptoms, pneumonia.
- Diarrhoea.
- Shortness of breath.
- Irregular heartbeat.
- Seizures or fits.
- Bone pain.
- Loss of bone mass.

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

Tell your doctor if you notice any of the following:
- Anorexia (severely resisting food due to irrational fear of gaining weight).
- Aggressive behaviour.
- Impaired concentration.
- Anxiety.
- Nervousness.
- Sleeplessness.
- Euphoria (intense feeling of happiness and excitement for no apparent reason).
- Confusion.
- Depersonalisation.
- Hallucination.
- Agitation.
- Being paranoid.
- Partial loss of sensation and drowsiness.
- Forgetfulness.
- Abnormal thoughts or dreams.
- Headache.
- Fatigue.
- Increased sweating.
- Mild to severe depression, or mania.
- Feeling of tingling or prickling, or numbness.
- Vomiting.
- Flatulence.

- Breast growth in men and females.
- Indigestion.
- Constipation.
- Bloatedness.
- Abdominal pain.
- Abnormal vision.
- Back pain.
- Joint pain and muscle pain.
- Dizziness.
- Feeling weak or sickly.
- Sensation of ringing in the ears.
- Frequent urination.
- Lack of voluntary coordination of movements, speech and movements such as walking may be affected.
- Tremors.
- Changes in body fat resulting in formation of buffalo hump-like structure on the trunk, weight gain in and around the stomach area, loss of weight on the limbs and face.
- Skin discolouration.
- Photo-allergic skin reactions.

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 TRIVENZ.

5. How to store TRIVENZ
- Store all medicines out of the reach of children.
- Store at or below 30 °C.
- Store TRIVENZ in the original container.
- Keep the container tightly closed in order to protect the medicine from light and moisture.
- Do not store in a bathroom.
- Do not use after the expiry date stated on the label/carton /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 TRIVENZ contains

The active substances are: 600 mg of efavirenz; 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate.

The other ingredients are:
Tablet core: croscarmellose sodium, hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose, sodium lauryl sulphate
Film-coating: macrogol/polyethylene glycol (E1521), iron dioxide black (E172), iron oxide red (E172), polyvinyl alcohol-part hydrolysed (E1203), talc (E563b), titanium dioxide (E171).

What TRIVENZ looks like and contents of the pack

TRIVENZ is a pink coloured, capsule shaped, film-coated tablet debossed with “H” on one side and “128” on the other side.
TRIVENZ is packed as 28’s, 30’s, 60’s, 84’s, 90’s, 120’s, 180’s and 500’s in white opaque, heavy weight high density polyethylene (HDPE) bottles with child-resistant closures and a silica gel desiccant sachet.
Not all pack sizes may be marketed.

Holder of certificate of registration

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