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PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

ATROIZA 600 mg, 200 mg, 300 mg film-coated tablets

(Efavirenz, Emtricitabine, Tenofovir disoproxil fumarate)

Contains sugar: Lactose monohydrate 120 mg

Read all of this leaflet carefully before you start taking ATROIZA

- 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.
- ATROIZA 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 ATROIZA is and what it is used for.
2. What you need to know before you take ATROIZA.
3. How to take ATROIZA.
4. Possible side effects.
5. How to store ATROIZA.
6. Contents of the pack and other information.

1 What ATROIZA is and what it is used for

What ATROIZA is

ATROIZA belongs to a group of antiviral medicines, also known as antiretrovirals.

ATROIZA contains three active ingredients:

- Efavirenz is a non-nucleoside reverse transcriptase inhibitor (NNRTI).

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- Emtricitabine is a nucleoside reverse transcriptase inhibitor (NRTI).
- Tenofovir is a nucleotide reverse transcriptase inhibitor (NRTI).

Each of these active ingredients, also known as antiretroviral medicines, work by interfering with an enzyme (reverse transcriptase) that is essential for the virus to multiply.

What ATROIZA is used for

- These are used to treat Human Immunodeficiency Virus (HIV) infection.
- ATROIZA can be given alone or in combination with other antiretrovirals.

2 What you need to know before you take ATROIZA

Do not take ATROIZA

- If you are hypersensitive (allergic) to tenofovir disoproxil fumarate, emtricitabine or efavirenz or any of the other ingredients of ATROIZA (listed in section 6).
- If you have kidney problems or are undergoing kidney dialysis treatment.
- If you are pregnant or planning to become pregnant.
- If you are breastfeeding your baby.
- If you are younger than 18 years of age.
- If you are a child weighing less than 40 kg.
- If you have severe liver disease.
- If you had a liver disorder or liver failure attributed to treatment with ATROIZA.
- 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 potassium or magnesium in your blood.
- If you are currently taking any of the following medicines:
  - Bepridil (used to treat heart disease).
  - Cisapride (used to treat heart burn).
  - Ergot alkaloids (used to treat migraines and cluster headaches).

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- Midazolam and triazolam (used to help you sleep).
- Pimozide (used to treat certain mental conditions).
- St John's Wort *(Hypericum perforatum)* (a herbal remedy used for depression and anxiety).
- Voriconazole (used to treat fungal infections).
- Elbasvir/grazoprevir to treat chronic (long-lasting) hepatitis C, a viral infection of the liver.
- Flecainide, (used to treat irregular heartbeat).
- Certain antibiotics (macrolides, fluoroquinolones, imidazole).
- Triazole antifungal medicines.
- Certain antimalarial medicines.
- Methadone (used to treat opiate addiction).
- Imipramine, amitriptyline or clomipramine (used to treat certain mental conditions).
- If you are taking any of these medicines, tell your doctor immediately. Taking these medicines with ATROIZA could cause serious or life-threatening side effects or stop these medicines from working properly.

- If you are already taking lamivudine/zidovudine, lamivudine, abacavir sulphate/ lamivudine, abacavir sulphate/lamivudine/zidovudine, tenofovir disoproxil fumarate, efavirenz, emtricitabine or adefovir dipivoxil because these medicines contain the same or similar active ingredients. Discuss this with your treating doctor if you are unsure.

Warnings and precautions

ATROIZA will not cure or prevent HIV infection or AIDS; however, it helps keep HIV from reproducing and appears to slow down the destruction of the immune system. ATROIZA will not keep you from spreading HIV to other people.

To protect other people from becoming infected with HIV:

- Use a condom when you have oral or penetrative sex.
- Do not risk blood transfer – for example, do not share needles.

Take special care with ATROIZA:

- If you suffer from osteoporosis, have a history of bone fracture or if you have problems with your bones (see section – Bone problems).
- If you have liver problems, including hepatitis B infection.

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- If you have ever had mental illness or are using medicines for mental illness, including depression, or of substance or alcohol abuse. Tell your doctor immediately if you feel depressed, have suicidal thoughts or have strange thoughts (see section 4 – Possible side effects).
- If you have ever had seizures or are taking medicines for seizures such as carbamazepine, phenobarbital and phenytoin.
- If you are older than 65 years of age.
- If you are taking other medicines that contain efavirenz, emtricitabine, tenofovir disoproxil, tenofovir alafenamide or lamivudine or adefovir dipivoxil, as ATROIZA may interact with these medicines.
- If you use medicines that may affect your kidney function since use of such medicines in combination with ATROIZA will require careful monitoring of your kidney function. Speak to your doctor about this.
- If you have serious nervous system symptoms such as loss of feeling or tingling, double vision, memory loss, severe headache and psychiatric symptoms such as extreme mood changes, problems sleeping, confused thinking and excessive fears and worries.
- If you have a heart disorder, such as abnormal electrical signal called prolongation of the QT interval (see section – Do not take ATROIZA).
- Once you start taking ATROIZA look out for:
  - ***Any signs of skin rash****.* Rashes may be caused by this medicine. If you see any signs of a severe rash with blistering or fever, stop taking ATROIZA and tell your doctor at once (see section 4 – Possible side effects). If you had a rash while taking other antiviral medicines (NNRTI), you may be at higher risk of getting a rash with this medicine.
  - ***Any signs of inflammation or infection.*** In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection, signs and symptoms of inflammation from 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 doctor at once. In addition to the opportunistic infections, 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.

Autoimmune disorders 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, palpitations, tremor or hyperactivity, please inform your doctor immediately to seek necessary treatment.

- ***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 length of combination antiretroviral therapy, corticosteroid use, alcohol consumption, severe immunosuppression, higher body mass index, among others, 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 symptoms, please inform your doctor.
- Bone problems such as osteomalacia (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 (a component of ATROIZA) may also cause loss of bone mass. Overall, the effects of tenofovir disoproxil on long-term bone health and future fracture risk in adult patients are uncertain and your doctor may consider changing your treatment. The decrease in bone mass generally improves after treatment with ATROIZA is discontinued. Tell your doctor if you know you suffer from osteoporosis. Patients with osteoporosis are at a higher risk of fractures.
- ***Accumulation of body fat.*** Some patients taking combination antiretroviral therapy may develop a dorso-cervical fat enlargement (buffalo hump), facial wasting and breast enlargement. Your doctor may consider monitoring your cholesterol once you start treatment with ATROIZA.

Children and adolescents

Do not give ATROIZA to children and adolescents under 18 years of age. The use of this medicine in children and adolescents has not been studied (see section – Do not take ATROIZA).

Other medicines and ATROIZA

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

Tell your doctor if you are taking any of the following medicines:

- Other medicines which contain tenofovir disoproxil fumarate, efavirenz, emtricitabine, or lamivudine either alone or as combination pills. ATROIZA should not be used with those medicines because they contain the same or similar active ingredients as found in ATROIZA.
- Adefovir dipivoxil for the treatment of Hepatitis B infection due to the increased risk of kidney damage if combined with ATROIZA.
- Medicines that contain didanosine (another antiretroviral). Tenofovir disoproxil fumarate (a component of ATROIZA) may increase the amount of didanosine in your blood, and the risk of side effects.
- Atazanavir sulphate or atazanavir/ritonavir in a combination pill. These medicines may increase the amount of tenofovir disoproxil fumarate (a component of ATROIZA) in the blood, which could result in more side effects.
- St John's Wort and Ginkgo biloba extracts.
- Cisapride, midazolam, triazolam, or ergot derivatives as efavirenz (a component of ATROIZA) could prevent break down of these medicines and may cause side effects such as abnormal heart rhythm and breathing problems.
- Sofosbuvir/velpatasvir and sofosbuvir/velpatasvir/voxilaprevir (medicines used to treat hepatitis).
- Other medicines used for HIV infection: amprenavir, indinavir, lopinavir/ritonavir combination pill, ritonavir, or saquinavir.
- Medicines used to treat fungal infections (antifungals): itraconazole and ketoconazole since no dosage recommendations are available when used in combination with ATROIZA.
- Voriconazole.
- Metamizole (used to relieve spasms e.g. tummy cramps).
- Please tell your doctor or pharmacist if you are taking any of the following, since this may require changes in your medicine, dose changes or careful monitoring of blood medicine levels:
    - Medicines called calcium channel blockers could be affected by ATROIZA if taken together.

These include diltiazem, and other calcium channel blockers such as verapamil, felodipine, nifedipine and nicardipine.

- Medicines such as cidofovir, acyclovir, valacyclovir, ganciclovir and valganciclovir. These compete for excretion by the kidney.
- Selective serotonin reuptake inhibitors (SSRI's) for the treatment of depression.
- Medicines used to lower blood fats (also called statins): atorvastatin, simvastatin and pravastatin. ATROIZA can reduce the amount of statins in your blood.
- Medicines used to treat convulsions/seizures (anticonvulsants): carbamazepine, phenytoin and phenobarbitone. ATROIZA can reduce the amount of anticonvulsant medicine in your blood. Carbamazepine can reduce the amount of efavirenz, one of the components of ATROIZA, in your blood.
- Medicines used to treat bacterial infections, including tuberculosis and AIDs-related infections: clarithromycin, rifabutin and rifampicin.
- Immunosuppressants (used in liver and kidney transplant patients) such as tacrolimus.
- Indinavir (another antiretroviral medicine).
- Hormonal contraceptives (e.g. the pill, injection or contraceptive implant). Because the potential for efavirenz, one of the components of ATROIZA, to interact with hormonal contraceptives has not been fully studied, a reliable method of barrier contraception (e.g. a condom) should always be used in addition to the hormonal contraceptive (see section – Pregnancy and breastfeeding).
- Methadone, a medicine used to treat opiate addiction.
- Sertraline, a medicine used to treat depression.
- Warfarin, acenocoumarol (medicines used to reduce clotting of the blood).
- Taking ATROIZA with alcohol or other medicines causing similar side effects as ATROIZA, such as drowsiness, may increase those side effects (see section 4 – Possible side effects).

ATROIZA with food and drink

ATROIZA must be taken on an empty stomach preferably at bedtime.

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 healthcare provider for advice before taking this medicine.

- You should not take ATROIZA if you are pregnant or breastfeeding your baby.
- Women who are taking ATROIZA should not become pregnant.
- Serious birth defects have been seen in the babies of women who have been treated with efavirenz (a component of ATROIZA) during pregnancy: Tell your healthcare provider right away if you are pregnant.
- Women should not rely only on hormone-based birth control, such as pills, injections or implants, because ATROIZA may make these contraceptives ineffective.
- Women must use a barrier form of contraceptive, such as a condom or diaphragm, even if they also use other methods of birth control.
- Do not breastfeed if you are taking ATROIZA. It is not known whether the active ingredients in ATROIZA are excreted in breast milk.
- Because of both the potential of HIV infection and for the potential of serious side effects in breastfed babies, it is recommended that mothers should not breastfeed their babies when using ATROIZA.

Driving and using machines

It is not always possible to predict to what extent ATROIZA 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 ATROIZA affects them.

ATROIZA may cause drowsiness, dizziness and impaired concentration. If you experience these symptoms while taking ATROIZA, do not drive and do not use any tools or machinery.

Taking ATROIZA with alcohol or other medicines causing similar side effects as ATROIZA, such as drowsiness, may increase those side effects.

ATROIZA contains sugar (lactose monohydrate)

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

3 How to take ATROIZA

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

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

Treatment should be prescribed and initiated by a doctor experienced in the management of HIV infection.

The usual dose of ATROIZA tablets is one tablet once a day.

You should take ATROIZA on an empty stomach.

- Swallow the ATROIZA tablet whole with water.
- Take ATROIZA at bedtime that will make some side effects less bothersome.
- Tell your healthcare provider if you start any new medicine or change how you take the old ones. Your doses may need adjustment.

Your doctor will tell you how long your treatment with ATROIZA will last. Do not suddenly stop taking this medicine without consulting with your doctor first. If you have the impression that the effect of ATROIZA is too strong or too weak, tell your doctor or pharmacist.

If you take more ATROIZA tablets 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 ATROIZA

- Do not take a double dose to make up for forgotten individual doses.
- If you miss a dose of ATROIZA take it as soon as possible.
- However, if it is almost time for your next dose or less than 12 hours until the next day's dose, skip the missed dose and go back to your regular dosing schedule. Contact your doctor of pharmacist if you are not sure what to do.
- Do not take more than one tablet of ATROIZA in one day.

If you stop taking ATROIZA

You should not stop treatment unless your doctor instructs you to. When your ATROIZA supply starts to run low, get more from your healthcare provider or pharmacy. This is very important as 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 ATROIZA and become harder to treat.

4 Possible side effects

ATROIZA can have side effects.

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

During HIV therapy there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and lifestyle, and in the case of blood lipids sometimes to the HIV medicines themselves. Your doctor will test for these changes.

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

- A life-threatening allergic reaction referred to as anaphylaxis. Symptoms include but are not limited to, fast or irregular breathing, puffiness or swelling around the face, shortness of breath, a sudden severe decrease in blood pressure, abdominal pain and cramping, anxiety, confusion, cough, diarrhoea, difficulty in swallowing, fainting, light-headedness, dizziness, hives, itchiness, wheezing and blocked nose. These are all very serious side effects. If you have them, you may have had a serious allergic reaction to ATROIZA. You may need urgent medical attention or hospitalisation.
- Lactic acidosis (build-up of an acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in hospital. Call your doctor right away or go to the casualty department at your nearest hospital if you get any of the following signs of lactic acidosis:
  - You feel weak and tired.
  - You have unusual muscle pain.
  - You have stomach pain with nausea and vomiting.
  - You feel cold especially in your arms and legs.
  - You feel dizzy and lightheaded.
  - You have a fast and irregular heartbeat.
- Serious liver problems (hepatotoxicity), with liver enlargement (hepatomegaly) and fat in the liver (steatosis). Call your doctor right away or go to the casualty department at your nearest hospital if you get any of the following signs of liver problems:

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- 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.

- Serious psychiatric problems. Some patients may experience severe depression, strange thoughts, thoughts of suicide or angry behaviour, paranoia, unable to think clearly, mood being affected, seeing or hearing things that are not really there (hallucinations), personality change (psychosis), catatonia (a condition in which the patient is rendered motionless and speechless for a period), while taking ATROIZA. Contact your doctor right away if you think you are having these psychiatric symptoms.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- "Flare-ups" with Hepatitis B virus (HBV) infection, in which the disease returns in a worse way than before. Your doctor will monitor your condition for several months after stopping ATROIZA if you have both HIV and HBV infection and may recommend treatment for your HBV.
- Kidney problems. Should you notice blood in your urine, have difficulty or painful urination, and pain in the lower back, contact your doctor immediately.
- Changes in bone mineral density (thinning bones). It is not known whether long-term use of ATROIZA will cause damage to the bones. If you have had bone problems in the past, your doctor may need to do tests to check your bone mineral density or may prescribe medicines to help your bone mineral density.

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- Dizziness, headache, diarrhoea, feeling sick (nausea), being sick (vomiting).
- Rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions.
- Feeling weak.

- Tests may also show:
  - Decreases in phosphate levels in the blood.
  - Increased levels of creatine kinase in the blood that may result in muscle pain and weakness.
- Allergic reactions.
- Loss of bone mass.
- Disturbances of coordination and balance.
- Feeling worried or depressed.
- Difficulty sleeping, abnormal dreams, difficulty concentrating, drowsiness.
- Pain, stomach pain.
- Problems with digestion resulting in discomfort after meals, feeling bloated, wind (flatulence).
- Loss of appetite.
- Tiredness.
- Itching.
- Changes in skin colour including darkening of the skin in patches often starting on hands and soles of feet.
- Tests may also show:
  - Low white blood cell count (a reduced white blood cell count can make you more prone to infection).
  - Liver and pancreas problems.
  - Increased fatty acids (triglycerides), bilirubin or sugar levels in the blood.

Less frequent side effects:

- Breakdown of muscle, muscle pain or weakness.
- Anaemia (low red blood cell count).
- A feeling of spinning or tilting (vertigo), whistling, ringing or other persistent noise in the ears.
- Blurred vision.
- Chills.
- Breast enlargement in males.
- Decreased sexual drive.
- Flushing.

- Dry mouth.
- Increased appetite.
- Tests may also show:
  - Decreases in potassium in the blood.
  - Increases in creatinine in the blood.
  - Proteins in urine.
  - Increased cholesterol in the blood.
  - Itchy rash to the skin caused by a reaction to sunlight.
- The breakdown of muscle, softening of the bones (with bone pain and sometimes resulting in fractures), muscle pain, muscle weakness and decreases in potassium or phosphate in the blood may occur due to damage to kidney tubule cells.

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 (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of ATROIZA.

5 How to store ATROIZA

- 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.
- Protect from light/moisture.
- Do not store in bathrooms.
- 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 ATROIZA contains

The active ingredients are:

Efavirenz 600 mg

Emtricitabine 200 mg

Tenofovir disoproxil fumarate 300 mg

The other ingredients of the tablets are croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose and sodium lauryl sulfate. The film-coating consists of black iron oxide, polyethylene glycol, polyvinyl alcohol, red iron oxide, talc and titanium dioxide.

What ATROIZA looks like and contents of pack

Pink coloured, capsule shaped, film-coated tablets debossed with “M171” on one side and plain on the other side.

ATROIZA is packed in high density polypropylene (HDPE) bottle pack comprising of white opaque wide mouth HDPE bottle with a white opaque polypropylene (PP) screw closure with desiccant, packed in an outer carton in 28s and 30s.

ATROIZA is packed in high density polypropylene (HDPE) bottle pack comprising of white opaque wide mouth HDPE bottle with a white opaque polypropylene (PP) screw closure with desiccant without outer carton in pack sizes of 28s and 30s.

ATROIZA is packed in high density polypropylene (HDPE) bottle pack comprising of white opaque wide mouth HDPE bottle with a white opaque polypropylene (PP) screw closure along with wad containing aluminium induction sealing liner with desiccant sieve sachet, packed in an outer carton in 90s.

ATROIZA is packed in high density polypropylene (HDPE) bottle pack comprising of blue opaque wide mouth HDPE bottle with a blue opaque polypropylene screw closure with desiccant, packed in an outer carton in 28s and 30s.

ATROIZA is packed in high density polypropylene (HDPE) bottle pack comprising of blue opaque wide mouth HDPE bottle with a blue opaque polypropylene screw closure with desiccant sachet or desiccant canister without outer carton, packed in 28s and 30s.

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ATROIZA is packed in low density polypropylene (LDPE) bag tied close along with a sieve or canister desiccant in 70s.

ATROIZA is packed in high density polypropylene (HDPE) bottle pack comprising of white opaque wide mouth HDPE bottle with a white opaque polypropylene screw closure along with wad containing aluminium induction sealing liner with desiccant sieve sachet packed without carton, packed in 84s.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

Viatris Healthcare (Pty) Ltd

4 Brewery Street

Isando

Gauteng, 1609

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To be confirmed

Registration number

45/20.2.8/0172

Access to the corresponding Professional Information

Can be obtained on the SAHPRA website.