VIATRIS

1.3.2.1 Clean Patient Information leaflet

SCHEDULING STATUS:

S4

ERESTZ (film-coated tablets)

Tenofovir disoproxil fumarate/ Emtricitabine/ Rilpivirine hydrochloride

WARNINGS:

ERESTZ 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 ERESTZ in patients who are infected with both human immunodeficiency virus (HIV) and hepatitis B virus (HBV) have not been established. You should not use ERESTZ 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 ERESTZ.

Read all of this leaflet carefully before you start taking ERESTZ:

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

2. What you need to know before you take ERESTZ.

3. How to take ERESTZ.

4. Possible side effects.

5. How to store ERESTZ.

6. Contents of the pack and other information.

1. What ERESTZ is and what it is used for

ERESTZ contains three active substances:

- Emtricitabine, a nucleoside reverse transcriptase inhibitor (NRTI).
- Rilpivirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI).
- Tenofovir, a nucleotide reverse transcriptase inhibitor (NRTI).

Contains sugar: 243,025 mg lactose monohydrate.

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

ERESTZ reduces the amount of HIV in your body. This will improve your immune system and reduces the risk of developing illnesses linked to HIV infection.

ERESTZ is a treatment for Human Immunodeficiency Virus (HIV) infection:

- in adults over 18 years, weighing at least 35 kg who have never taken HIV-1 medicines before, and who have an amount of HIV-1 in their blood (this is called ‘viral load’) that is no more than 100 000 copies/mL before they start taking ERESTZ.
- in certain people who have a viral load that is less than 50 copies/mL when they start taking ERESTZ, to replace their current HIV-1 medicines.

2. What you need to know before you take ERESTZ

Do not take ERESTZ:

- If you are allergic (hypersensitive) to tenofovir disoproxil fumarate, emtricitabine, rilpivirine hydrochloride or any of the other ingredients in ERESTZ.
- If you are pregnant or breastfeeding.
- If you have chronic kidney disease or chronic kidney failure.
- If you have liver damage or liver failure.

If this applies to you, tell your doctor immediately.

- **If you are currently taking any of the following medicines**
  - **carbamazepine, oxcarbazepine, phenobarbitone and phenytoin** (medicines used to treat epilepsy and prevent seizures);
  - **rifampicin and rifapentine** (used to treat some bacterial infections such as tuberculosis);
  - **omeprazole, lansoprazole, rabeprazole, pantoprazole and esomeprazole** (proton pump inhibitors that are medicines used to prevent and treat stomach ulcers, heartburn, acid reflux disease);
  - **dexamethasone** (a corticosteroid used to treat inflammation and suppress the immune system) when taken by mouth or injected (except as a single dose treatment);
  - **products that contain St. John's wort** (*Hypericum perforatum*) (a herbal remedy used for depression and anxiety).

Warnings and precautions

You must remain under the care of your doctor while taking ERESTZ.

- **You can still pass on HIV** when taking this medicine. Discuss with your doctor the precautions needed to avoid infecting other people. This medicine is not a cure for

HIV infection. While taking ERESTZ you may still develop infections or other illnesses associated with HIV infection.

- **Tell your doctor if you had kidney disease**, or if tests have shown kidney problems. ERESTZ may affect your kidneys. Before and during treatment, your doctor may order blood tests to measure kidney function. ERESTZ is not recommended if you have moderate to severe kidney disease.

ERESTZ is not usually taken with other medicines that can damage your kidneys (*see Other medicines and* ERESTZ). If this is unavoidable, your doctor will monitor your kidney function once a week.

- **Talk to your doctor if you have a history of liver disease, including hepatitis**. HIV patients with liver disease (including chronic hepatitis B or C), who are treated with antiretrovirals, have a higher risk of severe and potentially fatal liver complications. If you have hepatitis B, your doctor will carefully consider the best treatment regimen for you. Two of the active substances in ERESTZ (tenofovir disoproxil and emtricitabine) show some activity against hepatitis B virus. If you have a history of liver disease, or chronic hepatitis B infection, your doctor may conduct blood tests in order to monitor liver function.

If you have hepatitis B infection, liver problems may become worse after you stop taking ERESTZ. It is important not to stop taking ERESTZ without talking to your doctor: see section 3, Do not stop taking ERESTZ.

- **Tell your doctor immediately and stop taking ERESTZ if you develop a skin rash with the following symptoms: fever, blisters, redness in your eyes and swelling of your face, mouth or body**. This may become severe or potentially life-threatening.
- **Talk to your doctor if you are over 65 years of age**. Not enough patients over the age of 65 have been studied. If you are over 65 years of age and are prescribed ERESTZ, your doctor will monitor you carefully.

While you take ERESTZ

Once you start taking ERESTZ, look out for:

- Any signs of inflammation or infection
- 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 (a component of ERESTZ) 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. Tell your doctor if you know you suffer from osteoporosis. Patients with osteoporosis are at a higher risk for fractures.

If you notice any of these symptoms, tell your doctor immediately.

Children and adolescents

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

Other medicines and ERESTZ

Always tell your health care 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:

- **Any other medicines containing:**
  - emtricitabine
  - rilpivirine
  - tenofovir disoproxil

- tenfovir alafenamide
- any other antiviral medicines that contain lamivudine or adefovir dipivoxil

ERESTZ may interact with other medicines. As a result, the amounts of ERESTZ or other medicines in your blood may be affected. This may stop your medicines from working properly or may make any side effects worse. In some cases, your doctor may need to adjust your dose or check your blood levels.

- **Medicines that may damage your kidneys**, examples include:
  - aminoglycosides (such as streptomycin, neomycin and gentamicin), vancomycin (for bacterial infections)
  - foscarnet, ganciclovir, cidofovir (for viral infections)
  - amphotericin B, pentamidine (for fungal infections)
  - interleukin-2, also called aldesleukin (to treat cancer)
  - non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pains)

- **Medicines containing didanosine (for HIV infection):** Taking ERESTZ with other antiviral medicines that contain didanosine can raise the levels of didanosine in our blood and may reduce CD4 cell counts. Inflammation of the pancreas and lactic acidosis (excess lactic acid in the blood), which sometimes caused death, have been reported rarely when medicines containing tenofovir disoproxil and didanosine were taken together. Your doctor will carefully consider whether to treat you with other medicines used for treating HIV infection (*see Other medicines used for HIV infection*).

- **Other medicines used for HIV infection:** Non-nucleoside reverse transcriptase inhibitors (NNRTIs). ERESTZ contains an NNRTI (rilpivirine) and so ERESTZ is not

to be combined with other medicines of this type. Your doctor will discuss a different medicine if required.

- **Rifabutin**, a medicine to treat some bacterial infections. This medicine can decrease the amount of rilpivirine (a component of ERESTZ) in your blood. Your doctor may need to give you an additional dose of rilpivirine to treat your HIV infection (see section 3 How to take ERESTZ)
- **Antibiotics used to treat bacterial infections** including tuberculosis containing:
  - clarithromycin
  - erythromycin

These medicines can increase the amount of rilpivirine (a component of ERESTZ) in your blood. Your doctor may need to change the dose of the antibiotic or give you a different antibiotic.

- **Medicines for stomach ulcers, heartburn of acid reflux** such as:
  - antacids (aluminium/magnesium hydroxide or calcium carbonate).
  - H_2-antagonists (famotidine, cimetidine, nizatidine or ranitidine).

These medicines can decrease the amount of rilpivirine (a component of ERESTZ) in your blood. If you are taking one of these medicines your doctor will either give you a different medicine for stomach ulcers, heartburn or acid reflux, or recommend how and when you take that medicine.

- **If you are taking an antacid** (such as medicines containing magnesium or potassium), take it at least 2 hours before or at least 4 hours after ERESTZ (*see section 3 How to take* ERESTZ*)*
- **If you are taking an H_2-antagonist** (also used to treat stomach acid or acid reflux disease), take it at least 12 hours before or at least 4 hours after ERESTZ. H2-antagonists can only be taken once a day if you take ERESTZ. H2-antagonists should not be taken in a twice a day regimen. Talk to your doctor about an alternative regimen (see section 3 How to take ERESTZ).

- **Methadone**, a medicine used to treat opiate addiction, as our doctor may need to change your methadone dose.

Tell your doctor if you are taking any of these medicines. Do not stop your treatment without contacting your doctor.

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 health care provider for advice before taking this medicine.

- **Women must not get pregnant** while taking ERESTZ.
- **Use effective contraception** while taking ERESTZ.
- **Tell your doctor immediately if you become pregnant or if you plan to become pregnant.**

Pregnant women should not take ERESTZ as the safe use of this medicine in pregnancy has not been proven.

Do not breastfeed during treatment with ERESTZ:

- This is because the active substances in this medicine pass into human breast milk.
- If you are a woman with HIV, it is recommended that you do not breastfeed, to avoid passing the virus to the baby in breast milk.

Driving and using machines

Do not drive or operate machines if you feel tired, sleepy of dizzy after taking your medicine.

ERESTZ contains lactose

- **Tell your doctor if you are lactose intolerant or intolerant to other sugars**.

ERESTZ contains lactose. Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not take ERESTZ.

3. How to take ERESTZ

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

The usual dose in adult patients weighing at least 35 kg, is one tablet taken each day by mouth. The tablet must be taken with food. This is important to get the right levels of active substance in your body. A nutritional drink alone does not replace food.

Swallow the tablet whole with water.

Do not chew, crush or split the tablet – if you do it may affect the way the medicine is released into your body.

If you are taking an antacid such as medicines containing magnesium or potassium. Take it at least 2 hours before or at least 4 hours after ERESTZ.

If you are taking an H_2-antagonist such as famotidine, cimetidine, nizatidine or ranitidine. Take it at least 12 hours before or at least 4 hours after ERESTZ. H_2-antagonists can only be taken once a day if you take ERESTZ. H_2-antagonists should not be taken twice a day. Talk to your doctor about an alternative treatment regimen.

If you are taking rifabutin. Your doctor may need to give you an additional dose of rilpivirine. Take the rilpivirine tablet at the same time you take ERESTZ. Check with your doctor or pharmacist if you are not sure.

If you take more ERESTZ 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 accidentally take more than the recommended dose of ERESTZ you may be at increased risk of experiencing possible side effects with this medicine (see section 4 Possible side effects).

If you forget to take ERESTZ

It is important not to miss a dose of ERESTZ.

If you do miss a dose:

- If you notice within 12 hours of the time you usually take ERESTZ, you must take the tablet as soon as possible. Always take the tablet with food. Then take the next dose as usual.
- **If you notice after 12 hours** or more of the time you usually take ERESTZ, then do not take the missed dose. Wait and take the next dose, with food, at your usual time.

If you vomit less than 4 hours after taking ERESTZ, take another tablet with food. **If you vomit more than 4 hours after taking ERESTZ** you do not need to take another tablet until your next regularly scheduled tablet.

Do not stop taking ERESTZ

Do not stop taking ERESTZ without talking to your doctor. Stopping ERESTZ can seriously affect your response to future treatment. If ERESTZ for any reason is stopped, speak to your doctor before you restart taking ERESTZ tablets. Your doctor may consider giving you the components of ERESTZ separately if you are having problems or need your dose adjusted.

When your supply of ERESTZ starts to run low, get more from your doctor or pharmacist. This is very important because the amount of virus may start to increase if the medicine is stopped for even a short time. The virus may then become harder to treat.

If you have HIV infection and hepatitis B, it is especially important not to stop your ERESTZ treatment without talking to your doctor first. Some patients have had blood tests or symptoms indicating that their hepatitis has got worse after stopping emtricitabine or tenofovir disoproxil (two of the three active substance of ERESTZ). If ERESTZ is stopped your doctor may recommend that you resume hepatitis B treatment. You may need blood tests to check how your liver is working for 4 months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment is not recommended as this may lead to worsening of your hepatitis, which may be life-threatening.

Tell your doctor immediately about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection.

If you have any further questions on the use of ERESTZ, ask your doctor or pharmacist.

4. Possible side effects

ERESTZ can have side effects.

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

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

- Swelling of the hands, feet, ankles, face lips and mouth or throat, which may cause difficulty in swallowing or breathing
- Rash or itching
- fainting
- **Lactic acidosis** (excess lactate in the blood) is a rare but potentially life-threatening side effect of some HIV medicines. Lactic acidosis occurs more often in women – particularly if they are overweight, and in people with liver disease. The following may be signs of lactic acidosis:
    - Deep, rapid breathing
    - Tiredness or drowsiness
    - Feeling sick (nausea), being sick (vomiting)
    - Stomach pain

If you think you may have lactic acidosis, tell your doctor immediately.

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

Any signs of inflammation or infection. In some patients with advanced HIV infection (AIDS) and a history of opportunistic infections (infections that occur in people with a weak immune system), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is thought 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.

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.

If you notice any symptoms of inflammation or infection, tell your doctor immediately.

Tell your doctor if you notice any of the following:

Very common side effects

- Diarrhoea, being sick (vomiting), feeling sick (nausea)
- Difficulty sleeping (insomnia)
- Dizziness, headache
- Rash
- 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
- Increased levels of cholesterol and/or pancreatic amylase in the blood
- Increased levels of liver enzymes in the blood

If any of the side effects get serious tell your doctor.

Common side effects

- Decreased appetite
- Depression and depressed mood
- Tiredness, feeling sleepy (somnolence)
- Pain, stomach pain or discomfort, feeling bloated, dry mouth
- Abnormal dreams, sleep disorders
- Problems with digestion resulting in discomfort after meals, wind (flatulence)
- Rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions, itching, changes in skin colour including darkening of the skin in patches
- Loss of bone mass
- Other allergic reactions, such as wheezing, swelling or feeling light-headed

Tests may also show:

- Low white blood cell count (a reduced white blood cell count can make you more prone to infection)
- Low platelet count (a type of blood cell involved in clotting blood)
- Decrease in haemoglobin in your blood (low red blood cell count)
- Increased fatty acids (triglycerides), bilirubin or sugar in the blood
- Pancreas problems

If any of the side effects get serious tell your doctor.

Uncommon side effects

- Anaemia (low red blood cell count)
- Pain in the abdomen (tummy) caused by inflammation of the pancreas
- Breakdown of muscle, muscle pain or weakness
- Swelling of the face, lips, tongue or throat
- Signs or symptoms of inflammation or infection
- Severe skin reactions including rash accompanied by fever, swelling and liver problems
- Damage to kidney tubule cells

Tests may also show:

- Decreases in potassium in the blood
- Increases in creatinine in your blood
- Changes to your urine

If any of the side effects increases or gets more frequent tell your doctor.

Rare side effects

- Lactic acidosis (see Possible side effects: tell a doctor immediately)
- Back pain caused by kidney problems, including kidney failure. Your doctor may do blood tests to see if your kidneys are working properly
- Fatty liver
- Yellow skin or eyes, itching or pain in the abdomen (tummy) caused by inflammation of the liver

- Inflammation of the kidney, passing a lot of urine and feeling thirsty
- Softening of the bone (with bone pain and sometimes resulting in fractures)

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 any of the side effects increases or gets more frequent tell your doctor.

Other effects that may be seen during HIV treatment

The frequency of the following side effects is not known (frequency cannot be estimated from the available data).

Bone problems. Some patients taking combination antiretroviral medicines such as ERESTZ may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). Taking this type of medicine for a long time, taking corticosteroids, drinking alcohol, having a very weak immune system, and being overweight, may be some of the many risk factors for developing this disease. Signs of osteonecrosis are:

- Joint stiffness
- Joint aches and pains (especially of the hip, knee and shoulder)
- Difficulty with movement

If you notice any of these symptoms tell your doctor.

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.

Depressive Disorders

Inform patients that depressive disorders (depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicidal ideation) have been reported with ERESTZ. Advise patients to seek immediate medical evaluation if they experience depressive symptoms

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 ERESTZ.

5. How to store ERESTZ

Store all medicines out of reach of children.

Store at or below 30 ºC. 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 this medicine after the expiry date which is stated on the bottle and carton after {EXP}.

The expiry date refers to the last day of that month.

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 ERESTZ contains

- **The active substances are** tenofovir disoproxil fumarate, emtricitabine and rilpivirine. Each ERESTZ film-coated tablet contains 300 mg tenofovir disoproxil fumarate; 200 mg emtricitabine and 27,5 mg rilpivirine hydrochloride equivalent to 25 mg rilpivirine.

- **The other ingredients are:**

Tablet core:

Croscarmellose sodium; lactose monohydrate, magnesium stearate; microcrystalline cellulose; polysorbate 20; povidone, corn starch.

Tablet coating:

Hypromellose; iron oxide black; iron oxide red; lactose monohydrate; polyethylene glycol; titanium dioxide; triacetin.

What ERESTZ looks like and contents of the pack

ERESTZ is a purple coloured, film-coated, capsule shaped, biconvex, bevelled edged tablet debossed with ‘M’ on one side of the tablet and ‘TER’ on the other side.

HDPE bottle pack with desiccant: HDPE bottle pack (marketable pack) comprises of round wide mouth white high-density polyethylene (HDPE) bottle white opaque polypropylene screw cap with aluminium induction sealing liner wad with desiccant. The HDPE bottle pack with desiccant may be placed in an outer cardboard carton based on commercial requirement.

HDPE bottle pack without desiccant: HDPE bottle pack (marketable pack) comprises of round wide mouth white high-density polyethylene (HDPE) bottle with white opaque polypropylene screw cap with aluminium induction sealing liner wad without desiccant. The HDPE bottle pack without desiccant may be placed in an outer cardboard carton based on commercial requirement.

Pack sizes: 28's, 30's

* Not all packs and pack sizes may be marketed

Holder of Certificate of Registration

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