PATIENT INFORMATION LEAFLET FOR

TRENVIR

SCHEDULING STATUS: S4

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

Emtricitabine, tenofovir disoproxil fumarate, efavirenz

Sugar free

Read all of this leaflet carefully before you start taking TRENVIR

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

TRENVIR is a fixed dose combination tablet with the following active ingredients: emtricitabine, tenofovir disoproxil fumarate and efavirenz. Each TRENVIR tablet contains emtricitabine 200 mg, tenofovir disoproxil fumarate 300 mg and efavirenz 600 mg. Emtricitabine, tenofovir disoproxil fumarate and efavirenz belong to a group of antiviral medicines, also known as antiretrovirals.

TRENVIR is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults. Combination antiretroviral therapy, such as TRENVIR, reduces the number of viruses in your blood and keeps it at a low level. The use of a combination of medicines rather than a single medicine helps to prevent viruses from becoming resistant to treatment.

TRENVIR is not a cure for HIV infection. You may continue to experience illnesses associated with HIV infection, including infections caused by other bacteria and viruses (germs), known as opportunistic infections. You should remain under the care of your doctor when taking TRENVIR.

Please note that treatment with TRENVIR does not reduce the risk of transmission of HIV to others through sexual contact or blood contamination. You should continue to make use of appropriate precautions against transmitting the virus to other people. Please speak to your doctor, pharmacist, or other health care provider.

2. What you need to know before you take TRENVIR

Do NOT take TRENVIR if you:

- Are hypersensitive (allergic) to emtricitabine, tenofovir disoproxil fumarate, efavirenz or any of the other ingredients of TRENVIR (listed in **section 6**).
- Suffer from impaired kidney function, since this requires dosage adjustments that are not possible with a fixed dose combination tablet such as TRENVIR.
- Are pregnant or breast feeding.

- Are receiving treatment with astemizole, cisapride, midazolam, triazolam, or ergot derivatives since potential interactions with the efavirenz in TRENVIR may cause serious or life-threatening adverse events (side effects).
- Are younger than 18 years of age, since safety and efficacy of TRENVIR in paediatric patients have not been established.
- Suffer from severe impairment of liver function.
- You had a liver disorder or liver failure attributed to treatment with TRENVIR.
- Are using voriconazole, a medicine that is used to treat fungal infections, since combination therapy with TRENVIR requires dosage adjustments that are not possible with a fixed dose combination tablet.
- Are taking other medicines containing efavirenz, tenofovir or emtricitabine, lamivudine (or other cytidine analogues) or adefovir dipivoxil for the treatment of HIV. Please discuss this with your treating doctor if you are unsure.
- Are using herbal medicinal products containing St. John's wort.
- 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).
- Have any member of your family (parents, grandparents, brothers, or sisters) who has died suddenly due to a heart problem or was born with heart problems.
- Have been told by your doctor that you have high or low levels of electrolytes such as low potassium or low magnesium in your blood.

Warnings and precautions

Take special care with TRENVIR.

Before taking TRENVIR you should speak to your doctor if you:

- Have liver problems, including hepatitis B virus infection.
- Use any medicines that may affect your kidney function, since use of such medicines in combination with TRENVIR will require careful monitoring of your kidney function. Speak to your doctor or pharmacist about other medicines you are currently taking.

- Suffer from bone disease, including previous fractures and low bone mineral density (osteopenia).
- Are older than 65 years of age, because it has not yet been established if elderly patients respond differently to TRENVIR than younger patients. Elderly patients may require dosage adjustments.
- Suffer from high blood cholesterol levels since you will require careful monitoring of your cholesterol levels.
- Take any other prescription medicines (please see **"Other medicines and TRENVIR"**).
- Have a history of seizures, let your doctor know about it.
- Taking TRENVIR, you may develop 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.

Some antiretrovirals, including TRENVIR, may cause a condition known as lactic acidosis, together with an enlarged liver. Lactic acidosis, if it occurs, usually develops after a few months. Symptoms of lactic acidosis include deep, rapid breathing, drowsiness, and non-specific symptoms, such as nausea, vomiting and stomach pain. If you are female, obese, suffer from liver disease, or if you have been using antiretrovirals for a long time, you have a greater risk of developing this condition. However, this condition has also developed in patients with no known risk factors. Your treating doctor will monitor you closely for the development of lactic acidosis. Please report any of the symptoms listed here to him/her.

TRENVIR is not indicated for the treatment of hepatitis B virus (HBV) infection. If you suffer from both HBV and HIV infection, you need to discuss this with your treating doctor before you start taking TRENVIR. Your doctor will closely monitor your liver function, especially if it is necessary for you to stop treatment with TRENVIR.

Serious nervous system and psychiatric symptoms have been reported with efavirenz, one of the active ingredients in TRENVIR. Some patients developed inappropriate behaviour (including aggressive

reactions) and psychosis. These reactions occurred predominantly in patients with a history of mental illness or substance abuse. If you suffered from mental illness in the past, including mental depression, please inform your treating doctor. If you or your family members notice abnormal behaviour or thought processes, these should immediately be reported to your treating doctor.

If you have a history of previous fractures not due to injuries or are at risk of developing osteoporosis, your doctor will regularly monitor your bone mineral density and may decide to supplement your diet with calcium and vitamin D.

Some patients who received combination antiretroviral therapy, such as TRENVIR, developed redistribution of body fat that included central (around the waist) obesity, fat pad on the back of the neck, thinning of the arms, legs and face, and breast enlargement. The mechanism and long-term consequences of these events are not known. A causal relationship with TRENVIR has not been established.

A condition known as immune reconstitution syndrome has been reported in some patients who were treated with combination antiretroviral therapy, such as TRENVIR. During the initial or early phase of treatment, patients whose immune systems responded, developed an inflammatory response to silent or residual opportunistic infections, such as tuberculosis or pneumonia. Your doctor will monitor and treat you for such conditions.

Your doctor will perform blood tests from time to time for the duration of treatment with TRENVIR. These will include tests to monitor your liver and kidney function, as well as your blood cholesterol and lipid levels.

Other medicines and TRENVIR

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

The following medicines should NOT be taken in combination with TRENVIR:

- Adefovir dipivoxil for the treatment of hepatitis B infection, due to the increased risk of kidney damage if combined with TRENVIR.
- Amprenavir, a protease inhibitor for the treatment of HIV infection, due to reduced blood levels of amprenavir when co-administered with TRENVIR.
- Atazanavir or atazanavir/ritonavir co-formulation due to the risk of increased blood levels of some of the active ingredients in TRENVIR, which may worsen the tolerability of TRENVIR (i.e., cause more side effects).
- Didanosine, another antiretroviral, due to the increased risk of didanosine-related adverse events.
- Emtricitabine or tenofovir separately, lamivudine and zidovudine co-formulation, lamivudine for HIV, lamivudine for HBV, abacavir sulphate and lamivudine co-formulation, and abacavir sulphate, lamivudine, and zidovudine co-formulation due to similarities with the active ingredients in TRENVIR.
- Itraconazole and ketoconazole for the treatment of fungal infections since no dosage recommendations are available when used in combination with TRENVIR.
- Lopinavir/ritonavir, since no dosage recommendations are available in combination with TRENVIR, and concomitant usage was not well tolerated.
- Astemizole, cisapride, midazolam, triazolam or ergot derivatives as efavirenz (component of TRENVIR) could result in the inhibition of the metabolism (break down) of these medicines and may cause potentially serious adverse events, e.g., abnormal heart rhythm, prolonged sedation, or suppression of breathing.
- Saquinavir, as the efavirenz in TRENVIR may decrease saquinavir blood levels.
- St John's wort, since this may lead to decreased blood concentrations of efavirenz that may result in loss of efficacy and the development of viruses resistant to efavirenz.
- Voriconazole (please see **section 2**).

Please inform your doctor if you take any of the following medicines, since this may require substitution, dosage adjustments or careful monitoring of blood medicine levels:

1. Calcium channel blockers, such as diltiazem, verapamil, nifedipine, etc., for hypertension (high

blood pressure), heart failure or abnormal heart rhythms.

2. Carbamazepine for the treatment of epilepsy.
3. Clarithromycin, an antibiotic.
4. HMG Co-A reductase inhibitors (also known as statins) for lowering of blood cholesterol levels.
5. Immunosuppressants, such as tacrolimus.
6. Indinavir, a protease inhibitor for the treatment of HIV infection.
7. Methadone for the treatment of opiate withdrawal.
8. Oral contraceptives (see **"Pregnancy, breastfeeding and fertility"**).
9. Anti-convulsant medicines, such as phenytoin and phenobarbital, for the treatment of epileptic fits.
10. Rifamycin (type of antibiotic) or rifampicin (used for TB).
11. Selective serotonin reuptake inhibitors (SSRI) for the treatment of depression.
12. Medicines, such as cidofovir, acyclovir, valaciclovir, ganciclovir and valganciclovir, which compete for excretion by the kidneys.

TRENVIR should not be combined with individual preparations of emtricitabine, tenofovir disoproxil fumarate or efavirenz.

The efavirenz in TRENVIR may give rise to false positive screening test results for cannabis. This has only been observed with one of the tests used for screening and not with other assays, including tests used for confirmation of positive results.

TRENVIR with food, drink, and alcohol

TRENVIR should be taken on an empty stomach, since the presence of food may enhance the absorption of some of the components of TRENVIR, causing more side effects. TRENVIR tablets should be swallowed whole with water.

Pregnancy, breastfeeding, and fertility

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 TRENVIR.

The safe and efficacious use of TRENVIR during pregnancy and breast feeding has not been established. The use of TRENVIR during pregnancy is therefore not recommended.

Women of childbearing age should use barrier contraception (e.g., condoms) in combination with other methods of birth control (e.g., oral, or other hormonal contraceptives) and should undergo pregnancy testing before they start treatment with TRENVIR.

It is recommended that HIV-infected mothers using TRENVIR should not breast feed their infants. It is not known whether the active ingredients in TRENVIR are excreted in human milk. Because of both the potential for HIV transmission and the potential for serious adverse reactions in nursing infants, it is recommended that mothers should not breast feed their babies when using TRENVIR.

Driving and using machines

TRENVIR can make you feel dizzy. If you develop such symptoms, you should avoid driving or operating machinery.

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

3. How to take TRENVIR

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

Always take TRENVIR exactly as your doctor or pharmacist has told you. You should check with your doctor or pharmacist if you are not sure.

Take one tablet once a day on an empty stomach, preferably at bedtime. TRENVIR should be swallowed whole with water.

The use of TRENVIR is not recommended in children younger than 18 years of age.

If you are older than 65 years of age, your doctor will monitor you carefully for possible side effects.

If you suffer from mild to moderate liver disease, your doctor may prescribe the normal recommended dosage of TRENVIR. The use of TRENVIR is contra-indicated in patients with severe liver disease.

If you have the impression that the effect of TRENVIR is too strong or too weak, talk to your doctor or pharmacist.

Your doctor will decide how long treatment with TRENVIR should continue.

If you take more TRENVIR than you should

Always take TRENVIR exactly as your doctor has instructed you. In the event of an overdosage, or if someone else has taken your medicine by mistake, you, or this other person, may experience side effects such as those listed below.

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 TRENVIR

Always take TRENVIR as prescribed. If you miss a dose, take it as soon as you remember, unless it is less than 12 hours until the next day's dose. In such an instance, skip the missed dose and go back to your regular dosing schedule. Do not take a double dose to compensate for the forgotten individual dose.

It is important to take TRENVIR regularly because irregular intake may increase the risk of the virus developing resistance to your medication.

4. Possible side effects

TRENVIR can have side effects.

Not all side effects reported for TRENVIR are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking TRENVIR, please consult your health care provider for advice**.**

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

- difficulty breathing,
- generalised skin rash,
- generalised itching or swelling of the face or body.

These are all very serious side effects. If you have them, you may have had a serious reaction to TRENVIR. You may need urgent medical attention or hospitalisation

Tell your doctor immediately or go to the casualty department at your nearest hospital if you develop a combination of the following symptoms:

Abdominal discomfort, decreased appetite, diarrhoea, fast shallow breathing, general feeling of discomfort, muscle pain or cramping, nausea, shortness of breath, sleepiness, and unusual tiredness or weakness, as these are symptoms associated with the development of lactic acidosis.

Should you notice blood in your urine, difficult or painful urination, and pain in the lower back, please contact your doctor immediately.

You should contact your doctor immediately if you become jaundiced (yellow discolouration of the skin and/or white part of the eyes), if your urine turns dark and your stools become light, if you lose your appetite for several days or longer or if you develop stomach pain, since TRENVIR may cause inflammation of your liver.

If you develop blisters on your skin or ulcers in your mouth, accompanied by fever, you should contact your doctor immediately, as this may indicate a serious and life-threatening side effect involving the skin and mucous membranes.

Other potential serious side effects with TRENVIR include:

- Convulsions (fits) or hallucinations (seeing things or hearing voices that are not real).
- Lung infection (pneumonia).

Check with your doctor or pharmacist as soon as possible if any of the following side effects continue or become bothersome:

- Nervous system disorders, such as headaches, tiredness, weakness, depression, dizziness, impaired concentration, sleep disturbances (abnormal dreams or sleeplessness or excessive sleepiness), anxiety, pins and needles, abnormal coordination, tremors, memory loss, decreased energy and motivation, confusion, emotional lability, extreme happiness, impotence or decreased libido, increased libido, speech disorders, vertigo, and pain in the fingers, toes, hands, or feet.
- Abnormal vision, ringing in the ears or abnormalities of taste.
- Heart and vascular system disorders, such as flushing, palpitations or rapid heart rate.
- Respiratory system disorders, such as increased cough, chest pain, shortness of breath, sinusitis, upper respiratory tract infection, and runny nose.
- Gut disorders, such as nausea, runny stomach, stomach pain, indigestion, flatulence, loss of appetite, increased appetite, reflux (heartburn), constipation, and vomiting.
- Skin disorders, such as rash, itching, and skin discolouration (increased pigmentation on the palms and/or soles), as well as acne, hair loss, eczema, dry and scaly skin, and hives.
- Muscle and bone disorders, such as muscle pain, joint pain or back pain, and muscle weakness.
- Fever, sweating, fatigue, pain, or weight loss (or weight gain) as well as alcohol intolerance, malaise (generally feeling unwell), fainting, and redistribution/accumulation of body fat, with increased fat around your trunk, back of your neck and breasts. The long term consequences and importance of these changes are not known.

You may have to undergo periodic blood tests to ensure that your bone marrow, kidneys, liver, and pancreas are still functioning properly and that your blood cholesterol and lipid levels are within normal limits.

Other side effects:

Tenofovir disoproxil

Frequency not known (cannot be estimated from the available data): Loss of bone mass.

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 or to Cipla Medpro (Pty) Ltd. by e-mail: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free). By reporting side effects, you can help provide more information on the safety of TRENVIR**.**

5. How to store TRENVIR

Store at or below 30 °C.

Keep the bottle tightly closed.

Do not use if seal over bottle opening is broken or missing.

Store all medicines out of reach of children**.**

Keep the container in the outer carton.

Do not use after the expiry date stated on the container.

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 TRENVIR contains

The active substances are emtricitabine 200 mg, tenofovir disoproxil fumarate 300 mg and efavirenz 600 mg.

The other ingredients include croscarmellose sodium, red oxide of iron, microcrystalline cellulose, Hypromellose, corn starch, magnesium stearate, sodium lauryl sulphate, hydroxy propyl cellulose. The tablet is film-coated with Flexicoat Prot Pink V5 PHA9070. (hexalake sunset yellow, kollicoat protect, sicovit red, talc and titanium dioxide)

What TRENVIR looks like and contents of the pack

Pink coloured, capsule-shaped, biconvex film-coated tablets.

TRENVIR is packed in 28s, 30s, 84s & 90s tablets supplied in a white opaque, HDPE bottle containing a silica gel bag made from non-woven fabric and closed with a white opaque HDPE grade non-child resistant screw cap, packed in a carton.

28 or 30 tablets supplied in a cylindrical milky white or white 100 mL HDPE bottle containing three (3) silica gel bags and closed with a HDPE screw cap with smooth surface on top and ribbed along the height, packed in a carton**.**

Holder of certificate of registration

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