PATIENT INFORAMTION LEAFLET

SCHEDULING STATUS

S4

EFAMAT 50 mg (film-coated tablet)

EFAMAT 100 mg (film-coated tablet)

EFAMAT 200 mg (film-coated tablet)

Efavirenz

Contains sugar: Lacose monohydrate

Read this leaflet carefully, before you start taking EFAMAT

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- EFAMAT has been prescribed for you personally or for your child or patient who you are caring for and you should not share your medicine or their medicine with other people. It may harm them, even if their symptoms are the same as yours or theirs.

What is in this leaflet

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

1. What EFAMAT is and what it is used for

What EFAMAT is:

EFAMAT contains the active substance efavirenz, which belongs to a class of antiretroviral medicines called non-nucleoside reverse transcriptase inhibitors (NNRTIs). It is an antiretroviral medicine that fights human immunodeficiency virus (HIV) infection by reducing the amount of the virus in blood.

What EFAMAT is used for:

EFAMAT tablets are used with other medicines in the treatment of infections caused by the human immunodeficiency virus (HIV). HIV is the virus that causes acquired immune deficiency syndrome (AIDS).

2. What you need to know before you take EFAMAT

Do not take EFAMAT:

- if you are hypersensitive (allergic) to efavirenz or any of the other ingredients of EFAMAT;
- if you are pregnant or breastfeeding;
- if you had a liver disorder or liver failure attributed to treatment with EFAMAT**.**
- if you have severe liver disease (Child Pugh Grade C);
- if you have a heart condition, such as changes in the rhythm or rate of the heartbeat, a slow heartbeat, or severe heart disease.
- 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:*
    - terfenadine (used to treat allergy symptoms)
    - bepridil (used to treat heart disease)
    - cisapride (used to treat heartburn)
    - ergot alkaloids (for example, ergotamine, dihydroergotamine, ergonovine, and methylergonovine) (used to treat migraine and cluster headaches)
    - midazolam or triazolam (used to help you sleep)
    - pimozide, imipramine, amitriptyline or clomipramine (used to treat certain mental conditions)
    - elbasvir or grazoprevir (used to treat hepatitis C)
    - St. John's wort (Hypericum perforatum) (a herbal remedy used for depression and anxiety)
    - flecainide, metoprolol (used to treat irregular heart beat)
    - certain antibiotics (macrolides, fluoroquinolones, imidazole)
    - triazole antifungal agents
    - certain antimalarial treatments
    - methadone (used to treat opiate addiction)

Take special care with EFAMAT:

- if you have liver problems;
- if you have a history of psychiatric disorders including inappropriate behaviour (including aggressive reactions),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 a history of convulsions (fits or seizures) or if you are being treated with anticonvulsant therapy such as carbamazepine, phenobarbital and phenytoin. If you

are taking any of these medicines, your doctor may need to check the level of anticonvulsant medicine in your blood to ensure that it is not affected while taking EFAMAT. Your doctor may give you a different anticonvulsant;

- if you have a history of liver disease, including active chronic hepatitis. Patients with chronic hepatitis B or C and treated with combination antiretroviral agents have a higher risk for severe and potentially life-threatening liver problems. Your doctor may conduct blood tests in order to check how well your liver is working or may switch you to another medicine. If you have severe liver disease, do not take EFAMAT (*see section 2 Do not take EFAMAT*);
- if you have a heart disorder, such as abnormal electrical signal called prolongation of the QT interval;

Once you start taking EFAMAT, look out for:

• *signs of dizziness,* difficulty sleeping, drowsiness, difficulty concentrating or abnormal dreaming. These side effects may start in the first 1 or 2 days of treatment and usually go away after the first 2 to 4 weeks.

• *any signs of skin rash*. If you see any signs of a severe rash with blistering or fever, stop taking EFAMAT and tell your doctor at once. If you had a rash while taking another NNRTI, you may be at a higher risk of getting a rash with EFAMAT.

• *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 an 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 immediately. 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.

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

Children and adolescents:

EFAMAT has not been studied in paediatric patients below 3 years of age or who weigh less than 13 kg.

Other medicines and EFAMAT

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

Although certain medicines should not be used together at all, in other cases two different medicines may be used together even if an interaction might occur. In these cases your doctor may want to change the dose.

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

- Indinavir, ritonavir, saquinavir (medicines used in the treatment of HIV infection)
- Clarithromycin, rifamycins (medicines used to treat bacterial infections)
- Oral contraceptives
- Methadone (medicine used to treat opiate addiction)
- St John's Wort (Hypericum perforatum)
- Ginkgo biloba
- Cisapride (medicine used to treat heartburn)
- Midazolam or triazolam (medicines used to help you sleep)
- Medicines used to treat infection with the hepatitis C virus: boceprevir, telaprevir, elbasvir/grazoprevir, simeprevir, sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir, glecaprevir/pibrentasvir.
- Medicines used to treat bacterial infections, including tuberculosis and AIDS-related mycobacterium avium complex: clarithromycin, rifabutin, rifampicin. Your doctor may consider changing your dose or giving you an alternative antibiotic.
- Medicines used to treat fungal infections (antifungals):

    voriconazole. EFAMAT may reduce the amount of voriconazole in your blood and voriconazole may increase the amount of efavirenz in your blood. Your doctor may adjust the dose of voriconazole.

    - itraconazole. EFAMAT may reduce the amount of itraconazole in your blood.

  - posaconazole. EFAMAT may reduce the amount of posaconazole in your blood.

- Medicines used to treat malaria:
  - artemether/lumefantrine: EFAMAT may reduce the amount of artemether/lumefantrine in your blood.
  - atovaquone/proguanil: EFAMAT may reduce the amount of atovaquone/proguanil in your blood.
- Medicines used to treat convulsions/seizures (anticonvulsants): carbamazepine, phenytoin, phenobarbital. EFAMAT can reduce or increase the amount of anticonvulsant in your blood. Carbamazepine may make EFAMAT less likely to work. Your doctor may need to consider giving you a different anticonvulsant.
- Medicines used to lower blood fats (also called statins): atorvastatin, pravastatin, simvastatin. EFAMAT can reduce the amount of statins in your blood. Your doctor will check your cholesterol levels and will consider changing the dose of your statin, if needed.
- Sertraline (a medicine used to treat depression): your doctor may need to change your dose of sertraline.
- Methadone, a medicine used to treat opioid addiction.
- Bupropion (a medicine used to treat depression or to help you stop smoking): your doctor may need to change your dose of bupropion.
- Diltiazem or similar medicines (called calcium channel blockers, which are medicines typically used for high blood pressure or heart problems): when you start taking EFAMAT, your doctor may need to adjust your dose of the calcium channel blocker.
- Immunosuppressants such as cyclosporine, sirolimus, or tacrolimus (medicines used to prevent organ transplant rejection): when you start or stop taking EFAMAT, your

doctor will closely monitor your plasma levels of the immunosuppressant and may need to adjust its dose.

- Warfarin or acenocoumarol (medicines used to reduce clotting of the blood): your doctor may need to adjust your dose of warfarin or acenocoumarol.
- Medicines that impact heart rhythm:
    - Medicines used to treat heart rhythm problems such as flecainide or metoprolol.
    - Medicines used to treat depression such as imipramine, amitriptyline or clomipramine.
    - Antibiotics, including the following types: macrolides, fluoroquinolones or imidazole.

EFAMAT with food and drink and alcohol

EFAMAT should be taken on an empty stomach, preferably at bedtime.

Pregnancy and breastfeeding and fertility

You should not take EFAMAT if you are pregnant or breastfeeding your baby or intend to become pregnant *(see section Do not take EFAMAT)*.

If you are pregnant or breastfeeding your baby while taking EFAMAT, please consult your doctor, pharmacist or other healthcare professional for advice.

EFAMAT has not been studied in pregnant women. Studies in pregnant animals have found that it causes birth defects in the offspring. A pregnancy test is recommended before starting treatment. It is also recommended that women with the potential to become pregnant use two methods of contraception. One method should be barrier contraception, such as condoms, and the other method should be an oral or other hormone contraceptive.

It is not known whether EFAMAT passes into breast milk. Breastfeeding is therefore not recommended in patients with HIV infection because of the risk of passing the virus on to the nursing infant.

Driving and using machinery

It is not always possible to predict to what extent EFAMAT may interfere with the daily activities of a patient. EFAMAT may cause drowsiness. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which EFAMAT affects them.

EFAMAT contains lactose

EFAMAT contains lactose, which may have an effect on the control of your blood sugar if you have diabetes mellitus. Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not take EFAMAT.

3. How to take EFAMAT

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

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

- Your doctor will prescribe the appropriate dosage in relation to your age and weight.
- Your doctor will tell you how long your treatment with EFAMAT will last.
- Do not suddenly stop taking EFAMAT without consulting your doctor first.
- EFAMAT should be taken without food on an empty stomach, preferably at bedtime.
- The central nervous system side effects (the system that controls most functions of the body and mind) that may occur with EFAMAT usually lessen after you have taken

the medicine for a while. Also, taking the medicine at bedtime, especially during the first 2 – 4 weeks, may lessen these side effects.

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

If you take more EFAMAT 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 EFAMAT

Do not take a double dose to make up for forgotten individual doses.

If you miss a dose of EFAMAT, take it as soon as possible. However, if it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule.

4. Possible side effects

EFAMAT can cause side effects.

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

During HIV therapy there may be an increase in weight and in the 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.

The most notable unwanted effects reported with EFAMAT in combination with other anti-HIV medicines are skin rash and nervous system symptoms such as memory loss, lack of coordination, severe headache and loss of sight or double vision.

You should consult your doctor if you have a rash, since some rashes may be serious; however, most cases of rash disappear without any change to your treatment with EFAMAT. Rash was more common in children than in adults treated with EFAMAT.

The nervous system symptoms such as memory loss, lack of coordination, severe headache and loss of sight or double vision tend to occur when treatment is first started, but generally decrease in the first few weeks. If you are affected your doctor may suggest that you take EFAMAT at bedtime and on an empty stomach. Some patients have more serious symptoms that may affect mood or the ability to think clearly. Some patients have actually committed suicide. These problems tend to occur more often in those who have a history of mental illness. Always notify your doctor immediately if you have these symptoms or any side effects while taking EFAMAT.

If any of the following happens, stop taking EFAMAT 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, hives
- fainting;
- tightness in the chest;
- convulsions (seizures);
- fast or abnormal heartbeat;

- fever; chills;
- skin rash; hives
- dizziness;
- liver failure, in some cases leading to death or liver transplant;
- suicidal thoughts or attempting to kill yourself.

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

- Nausea, vomiting;
- diarrhoea;
- worsening of depression;
- headache;

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

Tell your doctor if you notice any of the following:

The following side effects have been reported frequently:

- Trouble in sleeping;
- tiredness; drowsiness; difficulty to concentrate;
- taste disorders;
- itching;

Tests may show:

- Increased liver enzymes in the blood;
- increased triglycerides (fatty acids) in the blood.

The following side effects have been reported less frequently:

- Inflammation of the pancreas;
- anorexia;
- abnormal behaviour; forgetfulness; anxiety; confusion; mood changes;
- abnormal vision;
- ringing in the ears; feeling of movement (vertigo);
- flushing;
- asthma;
- heartburn;
- yellow eyes or skin (jaundice);
- hair loss or painful hair follicles;
- eczema; flaking of skin;
- joint or muscle pain;
- breast enlargement in males.

Tests may show:

- increased cholesterol in the blood

The following side effects have been reported but the frequency is unknown:

- increased appetite; changes in body or face shape due to changes in fat distribution; weight gain or loss; you may lose fat from your legs, arms and face, gain fat around the abdomen (tummy) and other internal organs, get larger breasts or fatty lumps on the back of the neck ('buffalo hump');
- abnormal dreams;
- unsteadiness;
- tingling or burning of hands, arms, feet or legs;

- speech impairment;
- tremor (shaking);
- sinusitis; upper respiratory tract infections;
- constipation; indigestion; weakness;
- liver failure;
- acne; dandruff;
- increased sweating;
- discolouration of finger or toe nails;
- increased or decreased sexual drive; impotence;
- intolerance to alcohol;
- flu-like symptoms;
- combination antiretroviral therapy may develop death of bone tissue caused by loss of blood supply to the bone (osteonecrosis). You may experience joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement;
- combination antiretroviral therapy may also cause raised lactic acid and sugar in the blood, increased fat levels in the blood (hyperlipaemia) and resistance to insulin. Your doctor will test for these changes.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions 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 EFAMAT.

5. How to store EFAMAT

- Store all medicines out of reach of children.
- Store at or below 30 °C.
- Store in the original package / container.
- Keep the bottle tightly closed.
- 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 EFAMAT contains:

- The active substance is:

  EFAMAT 50 mg:

  Efavirenz 50 mg

  EFAMAT 100 mg:

  Efavirenz 100 mg

  EFAMAT 200 mg:

  Efavirenz 200 mg

- The other ingredients are*:*

  Coscarmellose sodium, microcrystalline cellulose, hydroxy propyl cellulose-L, sodium lauryl sulphate, magnesium stearate. Film-coat: Opadry 03B52874 yellow

Contains sugar: Lactose monohydrate 21,30 mg – EFAMAT 50 mg

Lactose monohydrate 42,60 mg - EFAMAT 100 mg

Lactose monohydrate 85,20 mg – EFAMAT 200 mg

What EFAMAT looks like and contents of the pack

What EFAMAT looks like:

EFAMAT 50 mg: Peach coloured, oval, film-coated tablets, debossed with “1X” on one side and “M” on other side.

EFAMAT 100 mg: Peach coloured, oval, film-coated tablets, debossed with “2X” on one side and “M” on other side.

EFAMAT 200 mg: Peach coloured, oval, film-coated tablets, debossed with “3X” on one side and “M” on other side.

Contents of the pack:

EFAMAT 50 mg and EFAMAT 100 mg:

EFAMAT is packed in high density polyethylene (HDPE) bottle pack (marketable pack) comprising of wide mouth white HDPE bottle with a white opaque polypropylene (PP) closure with induction sealing in pack sizes of 30’s, 84’s or 90’s packed in a carton*.

*Not all pack sizes may be marketed.

EFAMAT 200 mg:

HDPE bottle pack (30’s count & 90’s count) (marketable pack) comprises of round wide mouth white high density polyethylene bottle with white opaque screw polypropylene closure with induction sealing liner.

HDPE bottle pack (84’s count) (marketable pack) comprises of round white opaque HDPE bottle with white opaque screw polypropylene closure with aluminium induction sealing liner wad.

HDPE bottle pack (84's count & 90's count) (marketable pack) comprises of Blue opaque HDPE bottle with blue opaque polypropylene screw closure with wad containing aluminium induction sealing liner.

Holder of Certificate of Registration and Manufacturer

Viatris Healthcare (Pty) Ltd

4 Brewery Street

Isando, Gauteng

1601

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Access to the corresponding Professional Information

Can be obtained on the SAHPRA website