PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

LAVEM, tablets

Dolutegravir, lamivudine and tenofovir disoproxil fumarate

Sugar content: Contains sugar (lactose monohydrate 153 mg and mannitol 184,38 mg)

Read all of this leaflet carefully before you start taking LAVEM

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

LAVEM contain 3 medicines: lamivudine tenofovir disoproxil fumarate and dolutegravir. Each of these medicines, also known as anti-retroviral medicines helps to block enzymes that are needed for the HIV virus to multiply.

LAVEM is used to treat people that are 18 years and older that are infected with the human immuno-deficiency virus (HIV). HIV is the virus that causes acquired immune deficiency syndrome (AIDS).

2. What you need to know before you take LAVEM

Do not take LAVEM:

- if you are allergic to lamivudine, tenofovir or dolutegravir or any of the ingredients of LAVEM;
- if you have uncontrolled kidney failure;
- if you are pregnant or breast-feeding your baby;
- if you are of child-bearing age and not using a highly effective contraception;
- if you are taking another medicine called adefovir dipivoxil (used to treat chronic hepatitis B);
- if you are taking another medicine called dofetilide or pilsicainide (used to treat heart conditions);
- if you are taking another medicine called didanosine (used to treat HIV infection);
- if you are taking a medicine called metformin (used to treat diabetes);
- If you are younger than 18 years of age;
- if you have moderate to severe liver disease.

Warnings and precautions

Take special care with LAVEM:

- Taking combination antiretroviral medicines may cause increased glucose, cholesterol, lactate levels or insulin resistance;
- Changes in body fat develop in some patients taking LAVEM. These changes may include an increased amount of fat in the upper back and neck (‘buffalo hump”), in the

breasts and around the trunk. Loss of fat from the legs, arms and face may also happen;

- If you get any symptoms of infection while you are taking LAVEM:

  People with advanced HIV infection (AIDS) have weak immune systems, and are more likely to develop serious infections (Opportunistic infections). When these people start treatment, they may find that old, hidden infections (such as tuberculosis) flare up, causing signs and symptoms of inflammation. These symptoms are probably caused by the body's immune system becoming stronger, so that the body starts to fight these Infections;
- If you experience joint aches, pain, stiffness or difficulty in movement, contact your doctor;
- You may continue to develop infections and other complications of HIV and therefore need to remain under close observation by your healthcare professional;
- LAVEM does not prevent the risk of infecting others by sexual contact or blood contamination. Therefore, take the necessary precautions;
- Possible signs of lactic acidosis (build-up of an acid in the blood) may occur. Lactic acidosis can be a medical emergency and may need to be treated in the hospital. Call your healthcare provider right away if you get signs of lactic acidosis. Signs include: nausea, vomiting, loss of appetite, stomach pain and shortness of breath;
- Mitochondrial dysfunction has been reported. The main signs are anaemia (shortage of iron in the body), neutropenia (too little white blood cells in the body), increased lactate and lipid levels;
- Pancreatitis (disease of the pancreas) which results in nausea, vomiting and severe stomach pain;
- If you had kidney problems in the past or take other medicines that can cause kidney problems, your doctor should do regular blood tests to check your kidneys;
- If you have liver disease, please inform your doctor;
- If you have the K65R mutation, please tell your doctor;

- 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). Tell your doctor if you have bone pain or fractures;
- Tenofovir disoproxil may also cause loss of bone mass. 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 have HIV and also hepatitis, your doctor will monitor you even after stopping treatment;
- If you get severe rashes while taking LAVEM.

Other medicines and LAVEM

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

Do not take LAVEM with these medicines:

- adefovir dipivoxil (used to treat chronic hepatitis B);
- dofetilide or pilsicainide (used to treat heart conditions);
- didanosine (used to treat HIV infection);
- metformin (used to treat diabetes).

Some medicines can affect how LAVEM works, or make it more likely that you will have side effects. These include:

- Medicines called antacids (used to treat indigestion and heartburn). Do not take an antacid 6 hours before you take LAVEM, or for at least 2 hours after you have taken it;

- Etravirine, efavirenz, nevirapine and tipranavir taken with ritonavir and zalcitabine (used to treat HIV infection);
- Rifampicin and isoniazid (used to treat tuberculosis);
- Co-trimoxazole (used to treat infections);
- Calcium and iron supplements must be taken 2 hours before or 6 hours after taking LAVEM.

LAVEM with food and drink

LAVEM can be taken with or without food.

Pregnancy, breastfeeding and fertility

Do not take LAVEM tablets if you are pregnant or breastfeeding (see section 2-Do not take LAVEM tablets).

LAVEM could seriously harm your unborn child if you fall pregnant while on treatment or if you start taking LAVEM in the first few weeks of your pregnancy.

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.

You should ensure that you always use effective contraception while you are taking LAVEM. Your healthcare professional can advise you on which contraceptives to take. Never stop taking LAVEM without first consulting your healthcare professional
as your HIV condition may become worse.

If you are thinking about having a baby, do not stop using LAVEM and contraception before you have talked to your healthcare professional. If you think you are pregnant go to your healthcare

professional to get a pregnancy test and to be advised on your future HIV treatment and on a pregnancy management plan.

Driving and using machines

Dizziness, impaired concentration and drowsiness may occur when taking LAVEM. If this happens, do not drive or use machines that require you to be alert.

LAVEM contains lactose and mannitol

Lactose: Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not take LAVEM.

LAVEM contains lactose which may have an effect on the control of your blood sugar if you have diabetes mellitus.

Mannitol: LAVEM contains mannitol which may have a mild laxative effect.

3. How to take LAVEM

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

LAVEM therapy should be initiated by a doctor experienced in the management of HIV infection.

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

For adults: The usual dose of LAVEM is one tablet once daily taken orally with or without food. Swallow LAVEM with water.

LAVEM is not recommended for use in patients less than 18 years of age.

Do not stop treatment early and when your LAVEM supply starts to run low, get more from your healthcare provider or pharmacy.

This is very important because 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 LAVEM and become more difficult to treat.

Your doctor will tell you how long your treatment with LAVEM will last.

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

If you take more LAVEM than you should

If you accidentally take too many LAVEM tablets, contact your doctor or nearest emergency department for advice. Keep the tablet bottle with you so that you can easily describe what you have taken.

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 a dose of LAVEM

If you forget to take LAVEM, take the missed dose right away, unless it is almost time for your next dose. Do not double the next dose. Carry on with your regular dosing schedule.

4. Possible side effects

LAVEM can have side effects.

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

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

- swelling, sometimes of the face, lips, mouth or throat (angioedema), causing difficulty in breathing and swallowing;
- skin rash.

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

Your doctor may decide to carry out tests on your liver, kidneys or blood and may tell you to stop taking LAVEM.

Tell your doctor as soon as possible if you notice any of the following side effects:

- High temperature (fever);
- Lack of energy (fatigue);
- Muscle or joint aches;
- Lactic acidosis (build-up of an acid in the blood) is a less frequent but very serious side effect that can be fatal. The following symptoms may be signs of lactic acidosis:
  - deep rapid breathing
  - drowsiness
  - feeling sick (nausea)
  - being sick (vomiting)
  - stomach pain
- Inflammation of the liver (hepatitis) – your skin and white of eyes become yellow;
- An inflammatory condition which may develop as the immune system becomes stronger ('IRIS'). IRIS is a reaction where your immune system begins to recover, but then responds to a previously acquired opportunistic infection with an overwhelming inflammatory response that can make the symptoms of the infection worse. Symptoms of IRIS include:

- palpitations (rapid or irregular heartbeat) or tremor
- hyperactivity (excessive restlessness and movement)
- weakness beginning in the hands and feet and moving up towards the trunk of the body.

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

Tell your doctor if you notice any of the following:

- headache;
- nausea;
- vomiting;
- upper stomach pain or cramps;
- diarrhoea;
- anorexia;
- indigestion;
- flatulence (passing wind or having gas);
- difficulty sleeping;
- abnormal dreams;
- rash;
- itchy skin;
- hair loss;
- joint pain;
- muscle disorders;
- tiredness;
- weakness and lack of energy;
- fever;
- kidney disorders;

- dizziness;
- high levels of lactate in the blood;
- lipodystrophy (redistribution of body fat);
- peripheral neuropathy (weakness, numbness and pain, usually in your hands and feet);
- paraesthesia [an abnormal sensation, typically tingling or pricking ('pins and needles')];
- inflammation of the pancreas (pain in the abdomen);
- rhabdomyolysis (deterioration of skeletal muscle which causes painful muscles);
- decrease in bone density;
- fractures;
- shortness of breath;
- wheezing chest;
- increased sugar levels;
- cough;
- nose and throat infections.

Side effects that occur less frequently and may show up in blood tests:

- anaemia (shortage of iron in the body);
- neutropenia (too little white blood cells in the body);
- thrombocytopenia (low platelet count);
- pure red cell aplasia (type of anemia);
- rise in amylase levels;
- increased liver enzyme levels;
- hypophosphataemia (low levels of phosphate).

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

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of LAVEM.

5. How to store LAVEM

Store all medicines out of reach of children.

Store at or below 30 °C.

Store in the original container. Keep the HDPE container tightly closed.

Do not use after the expiry date stated on the label/carton.

6. Contents of the pack and other information

What LAVEM contains

The active substances are:

- Lamivudine 300 mg;
- Tenofovir disoproxil fumarate 300 mg;
- Dolutegravir sodium equivalent to dolutegravir 50 mg.

The other ingredients are:

Core tablet: Microcrystalline cellulose, croscarmellose sodium, povidone, lactose monohydrate, pregelatinized starch, magnesium stearate, mannitol, sodium starch glycolate and sodium stearyl fumarate.

Film coat: Polyvinyl alcohol partially hydrolysed, titanium dioxide, macrogol/polyethylene glycol and talc.

What LAVEM looks like and contents of the pack

White to off white, capsule shaped, film-coated tablets, debossed with “HP553” on one side and plain on the other side.

28 or 30 tablets are packed in a 100 cc, white opaque, HDPE container and closed with a 38 mm, white opaque, polypropylene closure. Each HDPE container contains a HDPE canister containing silica gel.

84 or 90 tablets are packed in a 200 cc, white opaque, HDPE container and closed with a 38 mm, white opaque, polypropylene closure. Each HDPE container contains a HDPE canister containing silica gel.

180 tablets are packed in a 400 cc, white opaque, HDPE container and closed with a 53 mm, white opaque, polypropylene closure. Each HDPE container contains a HDPE canister containing silica gel.

Not all pack sizes will be marketed.

Holder of Certificate of Registration

Emcure Pharmaceuticals SA (Pty) Ltd.

Arizona House, First floor, South Wing, Aspen Business Park

1 Madison Avenue, Aspen Lakes, Extension 13

Johannesburg South

2190

Tel. no.: 011 867 7274

This leaflet was last revised in

Date of Registration: 10 October 2018

Date amended: 3 February 2025

Registration number

53/20.2.8/0090