PATIENT INFORMATION LEAFLET:

SCHEDULING STATUS:

S4

KALETRA (80 mg + 20mg) / mL Oral Solution

(lopinavir + ritonavir)

Contains sugar: Corn Syrup, High Fructose, 55 % - 168,6 mg/mL

Contains sweetener: Saccharin Sodium – 4,1 mg/mL

Acesulfame Potassium – 4,1 mg/mL

Glycerol – 59,6 mg/mL

Read all of this leaflet carefully before you start taking KALETRA

- Keep this leaflet. You may need to read it again.
- This leaflet is a summary. If you have further questions, please ask your doctor or your pharmacist.
- KALETRA 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 KALETRA is and what it is used for

KALETRA SOLUTION

- The active substance for KALETRA SOLUTION is a combination of two medicines: lopinavir and ritonavir. Each 1 mL solution contains 80 mg lopinavir and 20 mg ritonavir.

KALETRA is a type of medicine called an HIV (human immunodeficiency virus) protease inhibitor. KALETRA is always used in combination with other anti-HIV medicines to treat people with human immunodeficiency virus (HIV) infection. KALETRA is for adults and for children age 6-months and older.

HIV infection destroys CD_4 (T) cells, which are important to the immune system. After a large number of T-cells are destroyed, acquired immune deficiency syndrome (AIDS) develops.

KALETRA blocks HIV protease, which is a chemical that is needed for HIV to multiply. KALETRA reduces the amount of HIV in your blood and increases the number of CD_4 (T) cells (cells in your immune system). Patients who took KALETRA in clinical studies had significant reduction in both death and AIDS defining diseases; however KALETRA may not have these effects in all patients.

2. What you need to know before you take KALETRA

Do not take KALETRA:

- If you are allergic (hypersensitive) to lopinavir, ritonavir or to any of the other ingredients of KALETRA (see section 6).

- Do not take the following medicines with KALETRA because they can cause serious problems or death if taken with KALETRA:
  - midazolam, triazolam (used to relieve anxiety and/or trouble sleeping)
  - ergotamine, dihydroergotamine (used to treat migraine headache)

- egonovine, methylergonovine (used to treat post-partum bleeding)
- cisapride (used to relieve certain stomach problems)
- astemizole, terfenadine (commonly used to treat allergy symptoms)
- salmeterol (commonly used to treat asthma)
- Alfuzosin (used in men to treat symptoms of an enlarged prostate)
- Amiodarone, dronedarone (used to treat abnormal heartbeat)
- Fusidic acid (used to treat long-term infections of the bones and joints)
- Colchicine if you have kidney and or liver problems (used to treat gout).
- Ranolazine (used to treat chronic chest pain [angina])
- Blonanserin, Quetiapine (used to treat schizophrenia, bipolar disorder and major depressive disorder)
- Lurasidone, pimozide (used to treat abnormal thoughts or feelings)
- Product that contains St John's Wort *(Hypericum perforatum)*
- lovastatin, simvastatin (used to lower blood cholesterol)
- elbasvir/grazoprevir (used to treat chronic hepatitis C virus [HCV])
- lomitapide (used to lower blood cholesterol)
- avanafil or vardenafil (used to treat erectile dysfunction)
- sildenafil used to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery). Sildenafil used to treat erectile dysfunction may be taken under doctor's supervision (see **Other medicines and KALETRA** section).
- neratinib (used for breast cancer)
- apalutamide (used for prostate cancer)

- Do not take KALETRA with rifampin, because rifampin may lower the amount of KALETRA in your blood and make it less effective.

- Do not take KALETRA with St. John's wort *(Hypericum perforatum)*, an herbal product sold as a dietary supplement, or products containing St. John's wort. Talk to your doctor if you are taking

or planning to take St. John's wort. Taking St. John's wort may lower the amount of KALETRA and lead to increased viral load and possible resistance to KALETRA or cross-resistance to other anti-HIV medicines.

- Do not take KALETRA with the cholesterol-lowering medicines lovastatin or simvastatin because of possible serious reactions. There is also an increased risk of medicine interactions between KALETRA and atorvastatin or rosuvastatin; talk to your doctor before you take any of these cholesterol-reducing medicines with KALETRA.
- Do not take KALETRA with voriconazole as KALETRA may lower the amount of voriconazole in your blood.

Warnings and precautions

KALTERA does not cure HIV infection or AIDS. The long-term effects of KALETRA are not known at this time. People taking KALETRA may still get opportunistic infections or other conditions that happen with HIV infection.

KALETRA does not reduce the risk of passing HIV to others through sexual contact or blood contamination. Continue to practice safe sex and do not use or share dirty needles.

Take special care with KALETRA:

- If you are taking certain medicines (see **Taking KALETRA with other medicines**).
- If you have liver problems or are infected with Hepatitis B or Hepatitis C. Talk to your doctor before taking KALETRA.
- If you have diabetes. Some people taking protease inhibitors develop new or more serious diabetes or high blood sugar. Be sure to tell your doctor if you have diabetes or an increase in thirst and/or frequent urination.
- If you have haemophilia. Some people with haemophilia have had increased bleeding. It is not known whether the protease inhibitors caused these problems. Be sure to tell your doctor if you have haemophilia types A and B.

- If you are suffering from alcoholism or are recovering from alcoholism. Each 1 mL of KALETRA contains 365,3 mg of alcohol and 152,7 mg of propylene glycol. Alcohol and propylene glycol are potentially harmful when you are suffering from these conditions.
- Alcohol and propylene glycol are potentially harmful for toddler or young children and may result in significant alcohol toxicity after overdose.

Other medicines and KALETRA

Always tell your health care provider if you are taking any other prescription and non-prescription medicines. (This includes all complementary or traditional medicines). These could cause serious side-effects that could cause death.

- Talk to your doctor if you are taking or are planning to take fluticasone propionate. Taking fluticasone propionate and KALETRA can increase the levels of fluticasone in your blood and could cause serious side effects.

- Before you take avanafil (should not be used for erectile dysfunction, see “Do not take with KALETRA”) sildenafil, tadalafil or vardenafil (should not be used for erectile dysfunction, see “Do not take with KALETRA”) with KALETRA, talk to your doctor about possible drug interactions and side effects. If you take these medications and KALETRA together, you may be at risk of side effects such as low blood pressure, visual changes and penile erection lasting more than 4 hours. If an erection lasts longer than 4 hours, you should get medical help immediately to avoid permanent damage to your penis. Your doctor can explain these symptoms to you.

- If you are using birth control pills or birth control patch to prevent pregnancy, your doctor should increase the dose of your birth control or you should use a different type of birth control since KALETRA may reduce the effectiveness of these medications.

- If you are taking rifabutin, your doctor may lower the dose of rifabutin.

- If you are taking both didanosine and KALETRA, didanosine should be given one hour before or two hours after KALETRA (given with food).

- Efavirenz, nevirapine, amprenavir and nelfinavir may lower the amount of KALETRA in your blood. Your doctor may increase your dose of KALETRA if you are also taking efavirenz, nevirapine, amprenavir or nelfinavir. KALETRA should not be taken once-daily with these medicines.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

- Antibiotics: Clarithromycin, rifabutin, rifampicin
- Anticancer medicines: abemaciclib, dasatinib, encorafenib, ibrutinib, ivosidenib, nilotinib, venetoclax, vincristine and vinblastine
- Antidepressants: Trazodone, bupropion
- Anti-tuberculosis: Bedaquiline, delamanid
- Heart medicines including:
    - Digoxin
    - calcium channel antagonists (e.g. felodipine, nifedipine, nicardipine);
    - Medicine used to correct the heart rhythm: Bepridil, systemic lidocaine, quinidine, amiodarone
- Boceprevir, glecaprevir/pibrentasvir, ombitasvir/paritaprevir/ritonavir and dasabuvir, simeprevir, sofosbuvir/velpatasvir/voxilaprevir and telaprevir: antiviral medicines used to treat chronic hepatitis C virus in adults
- Fentanyl: Pain relieving medicine
- elagolix (used for moderate to severe pain associated with endometriosis)
- fostamatinib (used for low blood platelet count)
- Quetiapine: used to treat schizophrenia, bipolar and major depression
- HIV CCR5-antagonist (e.g. maraviroc)

- Anticoagulants (e.g. dabigatran etexilate, edoxaban, warfarin, rivaroxaban)
- Anti-epilepsy medicines (e.g. carbamazepine, phenytoin, phenobarbital, lamotrigine and valproate)
- Antifungals (e.g. ketoconazole, itraconazole, voriconazole)
- Anti-gout medicines (e.g. colchicine). You must not take KALETRA with colchicine if you have kidney and/or liver problems (see also '**Do not take KALETRA**' above)
- Steroids (dexamethasone, fluticasone propionate, budesonide, triamcinolone)
- medicines that cause a reaction with alcohol (e.g. disulfiram, metronidazole)
- protease inhibitors (e.g. fosamprenavir, indinavir, ritonavir, saquinavir, tipranavir)
- Antiparasitic (Atovaquone)
- medicines used to lower blood cholesterol (e.g. atorvastatin, lovastatin, rosuvastatin or simvastatin)
- medicines affecting the immune system (e.g. cyclosporin, sirolimus (rapamycin), tacrolimus)
- morphine-like medicines (e.g. methadone)
- medicines used to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery) (e.g. bosentan, sildenafil, tadalafil)
- oral contraceptive or using a patch contraceptive to prevent pregnancy. If you are currently using an oral contraceptive or using a patch contraceptive to prevent pregnancy, you should use an additional or different type of contraception (e.g. condom) as KALETRA may reduce the effectiveness of oral and patch contraceptives.

- A change in therapy should be considered if you are taking KALETRA with:
  - ⇨ Phenobarbital
  - ⇨ Phenytoin
  - ⇨ Carbamazepine
  - ⇨ Lamotrigine
  - ⇨ Valproate

These medicines may lower the amount of KALETRA in your blood and make it less effective. KALETRA should not be taken once daily with these medicines.

KALETRA can be taken with acid reducing agents (such as omeprazole and ranitidine) with no dose adjustment.

Pregnancy, breastfeeding and fertility

- If you are pregnant or planning to become pregnant: The effects of KALETRA on pregnant women or their unborn babies are not known. Ask your doctor or pharmacist for advice before taking any medicine including KALETRA.

- If you are breastfeeding: Do not breastfeed if you are taking KALETRA. You should not breastfeed if you have HIV. If you are a woman who has or will have a baby, talk with your doctor about the best way to feed your baby. You should be aware that if your baby does not already have HIV, there is a chance that HIV can be transmitted through breastfeeding. Ask your doctor or pharmacist for advice before taking any medicine including KALETRA.

- If you are pregnant or breastfeeding your baby while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

Driving and using machinery

KALETRA has not specifically been tested for its possible effects on the ability to drive a car or operate machines. Do not drive a car or operate machinery if you experience any side effects (e.g. nausea) that impact your ability to do so safely. Instead, contact your doctor.

KALETRA contains:

KALETRA solution contains alcohol. Talk with your doctor if you are taking or planning to take metronidazole of disulfiram. Severe nausea and vomiting can occur if KALETRA is taken with these medicines.

KALETRA contains sugar (fructose) up to 0,8 g per dose when taken according to the dosage recommendations. Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not take KALETRA. Due to the possibility of undetected fructose intolerance KALETRA should only be given to young children after consultation with your doctor.
As per CC Recommendation

KALETRA contains 42 % v/v alcohol and 15 % propylene glycol w/v. Each 1 mL of KALETRA oral solution contains 356,3 mg of alcohol and 152,7 mg of propylene glycol. Alcohol and propylene glycol are potentially harmful for those suffering from liver disease, kidney disease, alcoholism, epilepsy, brain injury or disease, as well as for pregnant women and children. They may modify or increase the effect of other medicines.

At the recommended adult dose(s) of this medicine, the estimated blood alcohol concentration in your body is about 0,002 – 0,01 g/dL. This is similar to an adult drinking 4-22 mL of beer or 1-4 mL of wine.

Other medicines may also contain alcohol and alcohol may be consumed in food and drinks. The combined effects may lead to increased blood alcohol levels and increase the side effects of alcohol.

KALETRA contains glycerol which is harmful in high doses. Can cause headache and stomach upset and diarrhoea.

KALETRA contains polyoxyl 40 hydrogenated castor oil. This may cause nausea, vomiting, colic, severe purgation at high doses. It should not be given when intestinal obstruction is present.

KALETRA contains potassium as acesulfame potassium, which may be harmful to people on a low potassium diet. High potassium in the blood can cause stomach upset and diarrhoea.

KALETRA contains sodium as saccharin sodium, sodium chloride and sodium citrate, which may be harmful to people on a low sodium diet.

3. HOW TO TAKE KALETRA

Always take KALETRA exactly as your doctor has told you.

Dosage:

- The usual dose for adults is 400/100 mg (5,0 mL) twice daily taken with food, in combination with other HIV medicines.

- The doctor may prescribe KALETRA as 10,0 mL of oral solution (800/200 mg) once-daily in combination with other anti-HIV medicines for some patients who have not taken anti-HIV medicines in the past.

- The dosing of KALETRA may be different for you than for other patients. Follow the directions from your doctor, exactly as written on the label.

- Children from 6-months to 12-years of age can also take KALETRA. The child's doctor will decide the right dose based on the child's height and weight.

- Take KALETRA with food if possible to help it work better.

- Be sure to set up a schedule and follow it carefully.

- When your KALETRA supply starts to run low, get more from your doctor 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 KALETRA and become harder to treat.
- Only take medicine that has been prescribed specifically for you. Do not give KALETRA to others or take medicine prescribed for someone else.

If you or your child take more KALETRA than you should

As with all medicines, KALETRA should be kept out of reach of young children. KALETRA SOLUTION contains a large amount of alcohol. If a toddler or young child accidentally drinks more than the recommended dose of KALETRA, it could make him/her sick from too much alcohol.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you or your child forget to take KALETRA

It is important that you do not miss any doses. If you miss a dose of KALETRA, take it as soon as possible and then take your next scheduled dose at its regular time. If it is almost time for your next dose, wait and take the next dose at the regular time. Do not double the next dose. Call your doctor or pharmacist if you have any questions about how to take KALETRA.

If you or your child stop taking KALETRA

- Do not change your treatment or stop treatment without first talking with your doctor. If you are not sure, you should check with your doctor.
- KALETRA should always be taken twice every day to help control your HIV infection, no matter how much better you feel.
- Taking KALETRA as recommended should give you the best chance of delaying the development of resistance to the product.

- If a side effect is preventing you from taking KALETRA as directed tell your doctor right away.
- Always keep enough KALETRA on hand so you don't run out. When you travel or need to stay in the hospital make sure you will have enough KALETRA to last until you can get a new supply.
- Continue to take this medicine until your doctor tells you otherwise

4. Possible side effects

KALETRA can have side-effects.

Not all side-effects reported for this medicine are included in this leaflet. Should your general health worsen while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

- The more frequent side-effects that are thought to be medicine-related are: diarrhoea, nausea and upper respiratory tract infections. Children taking KALETRA may sometimes get a skin rash.

- **Frequent:**
  - inflammation of the pancreas (Tell your doctor if you experience nausea, vomiting or abdominal pain as these may be suggestive of pancreatitis);
  - vomiting, enlarged abdomen, pain in the lower and upper stomach area, passing wind,
  - indigestion, decreased appetite, reflux from your stomach to your oesophagus which may cause pain;
  - swelling or inflammation of the stomach, intestines and colon;
  - increased cholesterol levels in your blood, increased triglycerides (a form of fat) levels in your blood, high blood pressure;
  - decreased ability of the body to handle sugar including diabetes mellitus, weight loss;
  - low number of red blood cells, low number of white blood cells which are usually used to fight infection;
  - rash, eczema, accumulation of scales of greasy skin;

- dizziness, anxiety, difficulty in sleeping;
- feeling tired, lack of strength and energy, headache including migraine;
- haemorrhoids;
- inflammation of the liver including increased liver enzymes;
- allergic reactions including hives and inflammation in the mouth;
- lower respiratory tract infection;
- enlargement of the lymph nodes;
- impotence, abnormally heavy or extended menstrual flow or a lack of menstruation;
- muscle disorders such as weakness and spasms, pain in the joints, muscles and back;
- damage to nerves of the peripheral nervous system;
- night sweats, itching, rash including raised bumps on the skin, infection of the skin, inflammation of skin or hair pores, accumulation of fluid in the cells or tissues.

Less frequent:

- abnormal dreams;
- hair loss;
- an abnormality in your electrocardiogram (ECG) called atrioventricular block;
- plaque building up inside your arteries which could lead to heart attack and stroke;
- inflammation of blood vessels and capillaries;
- uncontrolled shaking of the body;
- constipation;
- deep vein inflammation related to a blood clot;
- dry mouth;
- inability to control your bowels;
- inflammation of the first section of the small intestine just after the stomach, wound or ulcer in the digestive tract, bleeding from the intestinal tract or rectum;
- red blood cells in the urine;
- fatty deposits in the liver, enlarged liver;

- lack of functioning of the testes;
- a flare-up of symptoms related to an inactive infection in your body (immune reconstitution);
- increased appetite;
- abnormally high level of bilirubin (a pigment produced from the breakdown of red blood cells) in the blood;
- decreased sexual desire;
- inflammation of the kidney;
- bone death caused by poor blood supply to the area;
- mouth sores or ulcerations, inflammation of the stomach and intestine;
- kidney failure;
- breakdown of muscle fibres resulting in the release of muscle fibre contents (myoglobin) into the bloodstream;
- a sound in one ear or both ears, such as buzzing, ringing or whistling;
- tremor;
- abnormal closure of one of the valves (tricuspid valve in your heart);
- vertigo (spinning feeling);
- eye disorder, abnormal vision;
- weight gain.

Side effects where frequency is not known:

Other side effects that have been reported with KALETRA:

- yellowing of the skin or whites of eyes (jaundice);
- severe or life-threatening skin rashes and blisters (Stevens-Johnson syndrome and erythema multiforme);
- kidney stones

- Blood tests in patients taking KALETRA may show possible liver problems. People with liver disease such as Hepatitis B and Hepatitis C who take KALETRA may have worsening liver

disease. Liver problems including death have occurred in patients taking KALETRA. It is unclear if KALETRA caused these liver problems because some patients had other illnesses or were taking other medicines.

- Some patients taking KALETRA can develop serious problems with their pancreas (pancreatitis), which may cause death. You have a higher chance of developing pancreatitis if you have had it before. Tell your doctor as soon as possible if you have nausea, vomiting, or abdominal pain. These may be signs of pancreatitis.

- Some patients have large increases in triglycerides and cholesterol. The long-term chance of getting complications such as heart attacks or strokes due to increases in triglycerides and cholesterol caused by protease inhibitors is not known at this time.

- Diabetes and high blood sugar (hyperglycaemia) have occurred in patients taking protease inhibitors. Some patients had diabetes before starting protease inhibitors, others did not. Some patients need changes in their diabetes medication. Other needed new diabetes medication.

- Changes in body fat have been seen in some patients taking antiretroviral therapy. These changes may include increased amount of fat in the upper back and neck ('buffalo hump'), breast and around the trunk. Loss of fat from the legs, arms and face may also happen. The cause and long-term health effects of these conditions are not known at this time.

- Some patients with haemophilia have increased bleeding with protease inhibitors.
- Allergic reactions ranging from mild to severe have occurred in patients taking KALETRA.

There have been other side-effects noted in patients receiving KALETRA; however, these side-effects may have been due to other medicines that patients were taking or to the illness itself. Some

of these side-effects can be serious. If you have questions about side-effects, ask your doctor, or pharmacist.

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 KALETRA.

Healthcare professionals, patients and caregivers are also asked to report any suspected adverse reaction to AbbVie (Pty) Ltd via this e-mail address: MEAPV@abbvie.com

5. How to store KALETRA

Keep **KALETRA** and all other medicines out of reach of children.

KALETRA SOLUTION

- Refrigerated KALETRA SOLUTION remains stable until the expiration date printed on the label. If stored at room temperature up to 25 ºC, KALETRA SOLUTION should be used within 2-months.
- Dosing syringes are included in each carton of KALETRA oral solution. After each dose of KALETRA separate the plunger and the syringe. Wash the plunger and the syringe with dish soap and warm water immediately after use. Rinse the syringe and the plunger with clean water. Put the syringe back together and draw up and expel tap water a few times to rinse. Let the syringe dry completely before you use that syringe for dosing.

- Use KALETRA SOLUTION by the expiration date on the bottle.

Do not keep medicine that is out of date or that you no longer need. Be sure that if you throw any medicine away, it is out of reach of children.

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

KALETRA SOLUTION is a combination of two medicines: lopinavir and ritonavir. Each 1 mL solution contains 80 mg lopinavir and 20 mg ritonavir.

The other ingredients are: alcohol (42,4 % v/v), high fructose corn syrup, propylene glycol, water, glycerine, povidone, magnasweet-110 flavour, natural and artificial vanilla flavour, polyoxyl 40 hydrogenated castor oil, artificial cotton candy flavour, acesulfame potassium, saccharin sodium, sodium chloride, peppermint oil, sodium citrate, citric acid and menthol.

What KALETRA looks like and contents of the pack

KALETRA SOLUTION is a light yellow to golden coloured liquid.

KALETRA SOLUTION is supplied in amber coloured multiple-dose bottles containing 60 mL solution. Each pack contains five bottles of 60 mL (300 mL). Five 5 mL syringes (5 mL ≈ 400/100 mg dose) are provided.

Holder of Certificate of Registration

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Access to the corresponding Professional Information

For the professional information please email medicalinfo.za@abbvie.com

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