Package leaflet: Information for the user

Kaletra 200 mg/50 mg film-coated tablets
lopinavir/ritonavir

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you or your child.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you or your child only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Kaletra is and what it is used for

- Your doctor has prescribed Kaletra to help to control your Human Immunodeficiency Virus (HIV) infection. Kaletra does this by slowing down the spread of the infection in your body.
- Kaletra is not a cure for HIV infection or AIDS.
- Kaletra is used by children 2 years of age or older, adolescents and adults who are infected with HIV, the virus which causes AIDS.
- Kaletra contains the active substances lopinavir and ritonavir. Kaletra is an antiretroviral medicine. It belongs to a group of medicines called protease inhibitors.
- Kaletra is prescribed for use in combination with other antiviral medicines. Your doctor will discuss with you and determine which medicines are best for you.

2. What you need to know before you or your child takes Kaletra

Do not take Kaletra
- if you are allergic to lopinavir, ritonavir or any of the other ingredients of Kaletra (see section 6);
- if you have severe liver problems.

Do not take Kaletra with any of the following medicines:
- astemizole or terfenadine (commonly used to treat allergy symptoms – these medicines may be available without prescription);
- midazolam taken orally (taken by mouth), triazolam (used to relieve anxiety and/or trouble sleeping);
- pimozide (used to treat schizophrenia);
- quetiapine (used to treat schizophrenia, bipolar disorder and major depressive disorder);
- lurasidone (used to treat depression);
- ranolazine (used to treat chronic chest pain [angina]);
- cisapride (used to relieve certain stomach problems);
- ergotamine, dihydroergotamine, ergonovine, methylergonovine (used to treat headaches);
- amiodarone, dronedarone (used to treat abnormal heart beat);
- lovastatin, simvastatin (used to lower blood cholesterol);

- lomitapide (used to lower blood cholesterol);
- alfuzosin (used in men to treat symptoms of an enlarged prostate (benign prostatic hyperplasia (BPH));
- fusidic acid (used to treat skin infections caused by *Staphylococcus* bacteria such as impetigo and infected dermatitis). Fusidic acid used to treat long-term infections of the bones and joints may be taken under doctor's supervision (see **Other medicines and Kaletra** section);
- colchicine (used to treat gout) if you have kidney and/or liver problems (see the section on **Other medicines and Kaletra**);
- elbasvir/grazoprevir (used to treat chronic hepatitis C virus [HCV]);
- ombitasvir/paritaprevir/ritonavir with or without dasabuvir (used to treat chronic hepatitis C virus [HCV]);
- neratinib (used to treat breast cancer);
- 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);
- products that contain St John's wort (*Hypericum perforatum*).

Read the list of medicines below under 'Other medicines and Kaletra' for information on certain other medicines which require special care.

If you are currently taking any of these medicines, ask your doctor about making necessary changes either in the treatment for your other condition(s) or in your antiretroviral treatment.

Warnings and precautions

Talk to your doctor or pharmacist before taking Kaletra.

Important information

- People taking Kaletra may still develop infections or other illnesses associated with HIV disease and AIDS. It is therefore important that you remain under the supervision of your doctor while taking Kaletra.

Tell your doctor if you or your child have/had

- **Haemophilia** type A and B as Kaletra might increase the risk of bleeding.
- **Diabetes** as increased blood sugars has been reported in patients receiving Kaletra.
- A history of **liver problems** as patients with a history of liver disease, including chronic hepatitis B or C are at increased risk of severe and potentially fatal liver side effects.

Tell your doctor if you or your child experience

- Nausea, vomiting, abdominal pain, difficulty breathing and severe weakness of the muscles in the legs and arms as these symptoms may indicate raised lactic acid levels.
- Thirst, frequent urination, blurred vision or weight loss as this may indicate raised sugar levels in the blood.
- Nausea, vomiting, abdominal pain as large increases in the amount of triglycerides (fats in the blood) have been considered a risk factor for pancreatitis (inflammation of the pancreas) and these symptoms may suggest this condition.
- In some patients with advanced HIV infection 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.

- 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.
- **Joint stiffness, aches and pains** (especially of the hip, knee and shoulder) and difficulty in movement as some patients taking these medicines 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 (reduction in the activity of the immune system), higher body mass index, among others, may be some of the many risk factors for developing this disease.
- **Muscle pain,** tenderness or weakness, particularly in combination with these medicines. On rare occasions these muscle disorders have been serious.
- Symptoms of dizziness, lightheadedness, fainting or sensation of abnormal heartbeats. Kaletra may cause changes in your heart rhythm and the electrical activity of your heart. These changes may be seen on an ECG (electrocardiogram).

Other medicines and Kaletra

Tell your doctor or pharmacist if you or your child are taking, have recently taken or might take any other medicines.
- antibiotics (e.g. rifabutin, rifampicin, clarithromycin);
- anticancer medicines (e.g. abemaciclib, afatinib, apalutamide, ceritinib, encorafenib, ibrutinib, venetoclax, most tyrosine kinases inhibitors such as dasatinib and nilotinib, also vincristine and vinblastine);
- anticoagulants (e.g. dabigatran etexilate, edoxaban , rivaroxaban, vorapaxar and warfarin);
- antidepressants (e.g. trazodone, bupropion);
- 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);
- anti-tuberculosis medicine (bedaquiline, delamanid);
- antiviral medicine used to treat chronic hepatitis C virus (HCV) infection in adults (e.g. glecaprevir/pibrentasvir, simeprevir and sofosbuvir/velpatasvir/voxilaprevir);
- erectile dysfunction medicines (e.g. sildenafil and tadalafil);
- fusidic acid used to treat long-term infections of the bones and joints (e.g. osteomyelitis);
- heart medicines including:
  - digoxin;
  - calcium channel antagonists (e.g. felodipine, nifedipine, nicardipine);
  - medicines used to correct heart rhythm (e.g. bepridil, systemic lidocaine, quinidine);
- HIV CCR5-antagonist (e.g. maraviroc);
- HIV-1 integrase inhibitor (e.g. raltegravir);
- medicines used to treat low blood platelet count (e.g. fostamatinib);
- levothyroxine (used to treat thyroid problems);
- medicines used to lower blood cholesterol (e.g. atorvastatin, lovastatin, rosuvastatin or simvastatin);
- medicines used to treat asthma and other lung-related problems such as chronic obstructive pulmonary disease (COPD) (e.g. salmeterol);
- medicines used to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery) (e.g. bosentan, riociguat, sildenafil, tadalafil);
- medicines affecting the immune system (e.g. cyclosporin, sirolimus (rapamycin), tacrolimus);
- medicines used for smoking cessation (e.g. bupropion);

- pain-relieving medicines (e.g. fentanyl);
- morphine-like medicines (e.g. methadone);
- non-nucleoside reverse transcriptase inhibitors (NNRTIs) (e.g. efavirenz, nevirapine);
- oral contraceptive or using a patch contraceptive to prevent pregnancy (see section below titled **Contraceptives**);
- protease inhibitors (e.g. fosamprenavir, indinavir, ritonavir, saquinavir, tipranavir);
- sedatives (e.g. midazolam administered by injection);
- steroids (e.g. budesonide, dexamethasone, fluticasone propionate, ethinyl oestradiol, triamcinolone).

Read the list of medicines above 'Do not take Kaletra with any of the following medicines' for information on medicines that you must not take with Kaletra.

Tell your doctor or pharmacist if you or your child are taking, have recently taken or might take any other medicines, including medicines obtained without prescription.

Erectile dysfunction medicines (avanafil, vardenafil, sildenafil, tadalafil)

- **Do not take Kaletra** if you are currently taking avanafil or vardenafil.
- You must not take Kaletra with sildenafil used to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery) (see also **Do not take Kaletra** section above).
- If you take sildenafil or tadalafil and Kaletra together, you may be at risk of side effects such as low blood pressure, passing out, 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.

Contraceptives

- 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.

Pregnancy and breast-feeding

- Tell your doctor **immediately** if you are planning to have a baby, you are pregnant or think you may be pregnant.
- If you are breast-feeding, or thinking about breast-feeding, you should discuss it with your doctor as soon as possible.
- It is recommended that women living with HIV do not breast-feed their infants because there is a possibility that the baby can be infected with HIV through your breast milk.

Driving or using machines

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 sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Kaletra

It is important that Kaletra tablets are swallowed whole and not chewed, broken or crushed.

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

How much Kaletra should be taken and when?

Use in adults

- The usual adult dose is 400 mg/100 mg twice a day i.e. every 12 hours, in combination with other anti-HIV medicines. Adult patients who have not previously taken other antiviral medicines can also take Kaletra tablets once daily as an 800 mg/200 mg dose. Your doctor will advise on the number of tablets to be taken. Adult patients who have previously taken other antiviral medicines can take Kaletra tablets once daily as an 800 mg/200 mg dose if their doctor decides it is appropriate.
- Kaletra must not be taken once daily with efavirenz, nevirapine, carbamazepine, phenobarbital and phenytoin.
- Kaletra tablets can be taken with or without food.

Use in children

- For children, your doctor will decide the right dose (number of tablets) based on the child's height and weight.
- Kaletra tablets can be taken with or without food.

Kaletra is also supplied as 100 mg/25 mg film-coated tablets. Kaletra oral solution is available for patients who cannot take tablets.

If you or your child take more Kaletra than you should

- If you realise you have taken more Kaletra than you were supposed to, contact your doctor right away.
- If you cannot contact your doctor, go to the hospital.

If you or your child forget to take Kaletra

If you are taking Kaletra twice a day

– If you notice you miss a dose within 6 hours of your normal dosing time, take your missed dose as soon as possible, and then continue with your normal dose at the regular time as prescribed by your doctor.

– If you notice you miss a dose by more than 6 hours after your normal dosing time, do not take the missed dose. Take the next dose as usual. Do not take a double dose to make up for a forgotten dose.

If you are taking Kaletra once a day

– If you notice you miss a dose within 12 hours of your normal dosing time, take your missed dose as soon as possible, and then continue with your normal dose at the regular time as prescribed by your doctor.

– If you notice you miss a dose by more than 12 hours after your normal dosing time, do not take the missed dose. Take the next dose as usual. Do not take a double dose to make up for a forgotten dose.

If you or your child stop taking Kaletra

- Do not stop or change the daily dose of Kaletra without first consulting with your doctor.
- Kaletra should always be taken 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

Like all medicines, Kaletra can cause side effects, although not everybody gets them. It may be difficult to tell which side effects have been caused by Kaletra and which may occur due to other medicines you take at the same time or by the complications of the HIV infection.

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 life style, and in the case of blood lipids sometimes to the HIV medicines themselves. Your doctor will test for these changes.

The following side effects have been reported by patients who took this medicine. You should tell your doctor promptly about these or any other symptoms. If the condition persists or worsens, seek medical attention.

Very common: may affect more than 1 in 10 people
- diarrhoea;
- nausea;
- upper respiratory tract infection.

Common: may affect up to 1 in 10 people
- inflammation of the pancreas;
- 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;
  - **Tell your doctor** if you experience nausea, vomiting or abdominal pain as these may be suggestive of pancreatitis (inflammation of the pancreas).
- 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.

Uncommon: may affect up to 1 in 100 people
- abnormal dreams;
- loss or changed sense of taste;
- 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;
- inflammation of the bile duct;
- 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;
- yellowing of the skin or whites of eyes (jaundice);
- 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.

Rare: may affect up to 1 in 1,000 people
- severe or life threatening skin rashes and blisters (Stevens-Johnson syndrome and erythema multiforme).

Not known: frequency cannot be estimated from the available data
- kidney stones.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store Kaletra

- Keep this medicine out of the sight and reach of children.
- Do not use Kaletra after the expiry date which is stated on the pack.
- This medicinal product does not require any special storage conditions.
- Do not use this medicine if you notice any discolouration.

How should I dispose of any unused Kaletra?

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Kaletra contains

The active substances are lopinavir and ritonavir.
Each tablet of Kaletra contains 200 mg of lopinavir and 50 mg of ritonavir

The other ingredients are:

Tablet
Copovidone, sorbitan laurate, colloidal anhydrous silica, sodium stearyl fumarate.

Tablet coating
Hypromellose, titanium dioxide, macrogols type 400 (polyethylene glycol 400), hydroxypropyl cellulose, talc, colloidal anhydrous silica, macrogols type 3350 (polyethylene glycol 3350), red ferric oxide E172, polysorbate 80.

What Kaletra looks like and contents of the pack

Kaletra film-coated tablets are red debossed with the code “AL” on one side.

Kaletra film-coated tablets are supplied in packs containing 120 tablets (1 plastic bottle of 120 tablets) and multipacks comprising 3 plastic bottles each containing 120 tablets (360 tablets). Blister multipacks containing 120 tablets (1 pack of 120 tablets or 3 packs each containing 40 tablets) are also available.

Not all pack sizes may be marketed.

Marketing Authorisation Holder:
AbbVie Ltd, Maidenhead, SL6 4UB, UK

Manufacturer:
AbbVie Deutschland GmbH & Co. KG, Knollstrasse, 67061 Ludwigshafen, Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
AbbVie Ltd
Tel: +44 (0)1628 561090

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