

1.5.3 Patient Information Leaflet (also known as Package leaflet or PIL)

Patient Information Leaflet is enclosed overleaf.

Package leaflet: Information for the user
Lopinavir and Ritonavir Tablets USP 100 mg/ 25 mg
Lopinavir and Ritonavir Tablets USP 200 mg/ 50 mg

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 Lopinavir and Ritonavir tablets are and what it is used for
2. What you need to know before you take Lopinavir and Ritonavir tablets
3. How to take Lopinavir and Ritonavir tablets
4. Possible side effects
5. How to store Lopinavir and Ritonavir tablets
6. Contents of the pack and other information

1. What Lopinavir and Ritonavir Tablets and what it is used for

- Your doctor has prescribed Lopinavir and Ritonavir tablets to help to control your Human Immunodeficiency Virus (HIV) infection. Lopinavir and Ritonavir tablets do this by slowing down the spread of the infection in your body.
- Lopinavir and Ritonavir is not a cure for HIV infection or AIDS.
- Lopinavir and Ritonavir tablet is used by children 2 years of age or older, adolescents and adults who are infected with HIV, the virus which causes AIDS.
- Lopinavir and Ritonavir tablets contains the active substances lopinavir and ritonavir. Lopinavir and Ritonavir tablets are an antiretroviral medicine. It belongs to a group of medicines called protease inhibitors.
- Lopinavir and Ritonavir 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 • Lopinavir and Ritonavir

Do not take Lopinavir and Ritonavir if:

- you are allergic to lopinavir, ritonavir or any of the other ingredients of Lopinavir and Ritonavir tablets (see section 6);
- you have severe liver problems.

Do not take Lopinavir and Ritonavir tablets 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 Lopinavir and Ritonavir Tablets section);
- colchicine (used to treat gout) if you have kidney and/or liver problems (see the section on **Other medicines and Lopinavir and Ritonavir tablet**);
- 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 Lopinavir and Ritonavir Tablets section);
- products that contain St John’s wort (*Hypericum perforatum*).

Read the list of medicines below under ‘Other medicines and Lopinavir and Ritonavir tablet’ 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 Lopinavir and Ritonavir tablet.

Important information

- People taking Lopinavir and Ritonavir tablets 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 Lopinavir and Ritonavir tablets.
- **You can still pass on HIV when taking this medicine**, although the risk is lowered by effective antiretroviral therapy. Discuss with your doctor the precautions needed to avoid infecting other people.

Tell your doctor if you or your child have/had

- Haemophilia type A and B as Lopinavir and Ritonavir might increase the risk of bleeding.
- Diabetes as increased blood sugars has been reported in patients receiving Lopinavir and Ritonavir tablets.
- 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. Lopinavir and Ritonavir Tablets 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 Lopinavir and Ritonavir Tablets

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, ceritinib, ibrutinib, venetoclax, most tyrosine kinases inhibitors such as dasatinib and nilotinib, also vincristine and vinblastine);
- anticoagulants (e.g. warfarin, rivaroxaban, vorapaxar);
- 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 Lopinavir and Ritonavir Tablets with colchicine if you have kidney and/or liver problems (see also '**Do not take Lopinavir and Ritonavir Tablets**' 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, nifedipine);
 - 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);
- 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 Lopinavir and Ritonavir Tablets with any of the following medicines’ for information on medicines that you must not take with Lopinavir and Ritonavir Tablets .

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 Lopinavir and Ritonavir Tablets** if you are currently taking avanafil or vardenafil.
- You must not take Lopinavir and Ritonavir Tablets with sildenafil used to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery) (see also **Do not take Lopinavir and Ritonavir Tablets** section above).
- If you take sildenafil or tadalafil and Lopinavir and Ritonavir Tablets 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 Lopinavir and Ritonavir Tablets may reduce the effectiveness of oral and

patch contraceptives.

- Lopinavir and Ritonavir Tablets does not reduce the risk of passing HIV to others. Appropriate precautions (e.g. use of a condom) should be taken to prevent passing on the disease through sexual contact.

Pregnancy and breast-feeding

- Tell your doctor **immediately** if you are planning to have a baby, you are pregnant, think you may be pregnant or if you are breast-feeding.
- Breast-feeding mothers should not take Lopinavir and Ritonavir Tablets unless specifically directed by the doctor.
- It is recommended that HIV-infected women 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

Lopinavir and Ritonavir Tablets 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.

3. How to take Lopinavir and Ritonavir Tablets

It is important that Lopinavir and Ritonavir Tablets 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 Lopinavir and Ritonavir

Tablets 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 Lopinavir and Ritonavir Tablets 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 Lopinavir and Ritonavir Tablets tablets once daily as an 800 mg/200 mg dose if their doctor decides it is appropriate.
- Lopinavir and Ritonavir Tablets must not be taken once daily with efavirenz, nevirapine, carbamazepine, phenobarbital and phenytoin.
- Lopinavir and Ritonavir Tablets tablets can be taken with or without food.

Use in children of 2 years of age and above

- For children, your doctor will decide the right dose (number of tablets) based on the

child's height and weight.

- Lopinavir and Ritonavir Tablets tablets can be taken with or without food.

If you or your child take more Lopinavir and Ritonavir Tablets than you should

- If you realise you have taken more Lopinavir and Ritonavir Tablets 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 Lopinavir and Ritonavir Tablets

If you are taking Lopinavir and Ritonavir Tablets 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 Lopinavir and Ritonavir Tablets 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 Lopinavir and Ritonavir Tablets

- Do not stop or change the daily dose of Lopinavir and Ritonavir Tablets without first consulting with your doctor.
- Lopinavir and Ritonavir Tablets should always be taken every day to help control your HIV infection, no matter how much better you feel.
- Taking Lopinavir and Ritonavir Tablets 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 Lopinavir and Ritonavir Tablets as directed tell your doctor right away.
- Always keep enough Lopinavir and Ritonavir Tablets on hand so you don't run out. When you travel or need to stay in the hospital make sure you will have enough Lopinavir and Ritonavir Tablets 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, Lopinavir and Ritonavir Tablets can cause side effects, although not everybody gets them. It may be difficult to tell which side effects have been caused by Lopinavir and Ritonavir Tablets 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.
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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;
- 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 Lopinavir and Ritonavir Tablets :

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

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.

5. How to store Lopinavir and Ritonavir Tablets

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

How should I dispose of any unused Lopinavir and Ritonavir Tablets ?

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 Lopinavir and Ritonavir Tablets contains

The active substances are lopinavir and ritonavir.

Each tablet of Lopinavir and Ritonavir Tablets contains 100 mg of lopinavir and 25 mg of ritonavir.

Each tablet of Lopinavir and Ritonavir Tablets contains 200 mg of lopinavir and 50 mg of ritonavir.

The other ingredients are:

Tablet core

Colloidal silicon dioxide, Sorbitan monolaurate, Copovidone, Colloidal silicon dioxide, Colloidal silicon dioxide and Sodium Stearyl Fumarate.

Film-coating

Opadry 20C520010 Yellow and Purified water.

What Lopinavir and Ritonavir Tablets looks like and contents of the pack

Lopinavir and Ritonavir Tablets USP 100 mg/ 25 mg are yellow colored, film coated oval shaped biconvex tablets debossed with “LA59” on one side and plain on other side.

60's Count: White opaque 85cc HDPE container closed with 33 mm ARGUS CR closure with TEKNIPLEX HS 123 induction sealing wad.

Lopinavir and Ritonavir Tablets USP 200 mg/ 50 mg are yellow colored, film coated oval shaped biconvex tablets debossed with “LA58” on one side and plain on other side.

120's Count: White opaque 250CC/ 53 mm HDPE bottle closed with 53mm CR closure with TEKNIPLEX HS 123 induction sealing wad.

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