

## **Package leaflet: Information for the user**

### **Lopinavir/Ritonavir Sandoz 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.**

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

#### **1. What Lopinavir/Ritonavir Sandoz is and what it is used for**

- Your doctor has prescribed Lopinavir/Ritonavir Sandoz to help to control your Human Immunodeficiency Virus (HIV) infection. Lopinavir/Ritonavir Sandoz does this by slowing down the spread of the infection in your body.
- Lopinavir/Ritonavir Sandoz is used by children 2 years of age or older, adolescents and adults who are infected with HIV, the virus which causes AIDS.
- Lopinavir/Ritonavir Sandoz contains the active substances lopinavir and ritonavir. Lopinavir/Ritonavir Sandoz is an antiretroviral medicine. It belongs to a group of medicines called protease inhibitors.
- Lopinavir/Ritonavir Sandoz 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 take Lopinavir/Ritonavir Sandoz**

##### **Do not take Lopinavir/Ritonavir Sandoz:**

- if you are allergic to lopinavir, ritonavir or any of the other ingredients of this medicine (listed in section 6)
- if you have severe liver problems.

##### **Do not take Lopinavir/Ritonavir Sandoz 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)
- Cisapride (used to relieve certain stomach problems)
- Ergotamine, dihydroergotamine, ergonovine, methylergonovine (used to treat headaches)
- Amiodarone, dronedarone (used to treat abnormal heartbeat)
- Lovastatin, simvastatin (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/Ritonavir Sandoz' section)
- Colchicine (used to treat gout) if you have kidney and/or liver problems (see the section on '**Other medicines and Lopinavir/Ritonavir Sandoz**')
- 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 '**Take special care with Lopinavir/Ritonavir Sandoz**' section)
- Products that contain St John's wort (*Hypericum perforatum*).

**Read the list of medicines under 'Other medicines and Lopinavir/Ritonavir Sandoz'** 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 before taking Lopinavir/Ritonavir Sandoz.

### **Important information**

- Lopinavir/Ritonavir Sandoz is not a cure for HIV infection or AIDS.
- People taking Lopinavir/Ritonavir Sandoz 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/Ritonavir Sandoz.
- **You can still pass on HIV when taking this medicine**, although the risk is lowered by effective antiretroviral therapy. Discuss with your physician the precautions needed to avoid infecting other people.

### **Tell your doctor if you have/had**

- **Haemophilia** type A and B as Lopinavir/Ritonavir Sandoz might increase the risk of bleeding.
  - **Diabetes** as increased blood sugars has been reported in patients receiving lopinavir/ritonavir.
- 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 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/Ritonavir Sandoz 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/Ritonavir Sandoz**

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

- Antibiotics (e.g. rifabutin, rifampicin, clarithromycin)
- Anticancer medicines (e.g. afatinib, ceritinib, 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/Ritonavir Sandoz with colchicine if you have kidney and/or liver problems (see also '**Do not take Lopinavir/Ritonavir Sandoz**' above).
- Anti-tuberculosis medicine (bedaquiline, delamanid)
- Antiviral medicine used to treat chronic hepatitis C virus (HCV) infection in adults (e.g. boceprevir, simeprevir and telaprevir)
- 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 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. ciclosporin, 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).

**Read the list of medicines under ‘Do not take Lopinavir/Ritonavir Sandoz with any of the following medicines’** for information on medicines that you must not take with Lopinavir/Ritonavir Sandoz.

Tell your doctor or pharmacist if you 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/Ritonavir Sandoz** if you are currently taking avanafil or vardenafil.
- You must not take Lopinavir/Ritonavir Sandoz with sildenafil used to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery) (see also ‘**Do not take Lopinavir/Ritonavir Sandoz**’ section).
- If you take sildenafil or tadalafil and Lopinavir/Ritonavir Sandoz 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/Ritonavir Sandoz may reduce the effectiveness of oral and patch contraceptives.
- Lopinavir/Ritonavir Sandoz 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/Ritonavir Sandoz 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 and using machines**

Lopinavir/Ritonavir Sandoz 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/Ritonavir Sandoz**

It is important that Lopinavir/Ritonavir Sandoz Film-coated 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 much Lopinavir/Ritonavir Sandoz 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/Ritonavir Sandoz film-coated tablets once daily as an 800 mg/200 mg dose. Your doctor will advise on the number of film-coated tablets to be taken. Adult patients who have previously taken other antiviral medicines can take Lopinavir/Ritonavir Sandoz film-coated tablets once daily as an 800 mg/200 mg dose if their doctor decides it is appropriate.
- Lopinavir/Ritonavir Sandoz must not be taken once daily with efavirenz, nevirapine, carbamazepine, phenobarbital and phenytoin.
- Lopinavir/Ritonavir Sandoz 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.
- Lopinavir/Ritonavir Sandoz Film-coated tablets can be taken with or without food.
- Lopinavir/Ritonavir oral solution may be available for patients who cannot take film-coated tablets.

### **If you take more Lopinavir/Ritonavir Sandoz than you should**

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

### **If you forget to take Lopinavir/Ritonavir Sandoz**

#### **If you are taking Lopinavir/Ritonavir Sandoz 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/Ritonavir Sandoz 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 stop taking Lopinavir/Ritonavir Sandoz**

- Do not stop or change the daily dose of Lopinavir/Ritonavir Sandoz without first consulting with your doctor.
- Lopinavir/Ritonavir Sandoz should always be taken every day to help control your HIV infection, no matter how much better you feel.
- Using Lopinavir/Ritonavir Sandoz 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/Ritonavir Sandoz as directed tell your doctor right away.
- Always keep enough Lopinavir/Ritonavir Sandoz 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/Ritonavir Sandoz 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, this medicine can cause side effects, although not everybody gets them. It may be difficult to tell which side effects have been caused by Lopinavir/Ritonavir Sandoz 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
- 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.

#### **Further information about nausea, vomiting or abdominal pain**

Tell your doctor if you experience nausea, vomiting or abdominal pain as these may be suggestive of pancreatitis (inflammation of the pancreas).

#### **Uncommon:** may affect up to 1 in 100 people

- Abnormal dreams
- Loss or changed sense of taste
- Hair loss
- An abnormality in your electrocardiogram 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 fibers resulting in the release of muscle fiber 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.

Other side effects that have been reported with lopinavir/ritonavir: yellowing of the skin or whites of eyes (jaundice), severe or life-threatening skin rashes and blisters (Stevens-Johnson syndrome and erythema multiforme). It is not known how frequently these effects may occur.

### **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie). By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store Lopinavir/Ritonavir Sandoz**

Keep this medicine out of the sight and reach of children.

This medicinal product does not require any special storage conditions.

Do not use this medicine after the expiry date which is stated on the pack after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. 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/Ritonavir Sandoz contains**

The active substances are lopinavir and ritonavir.

Each film-coated tablet of Lopinavir/Ritonavir Sandoz contains 200 mg of lopinavir and 50 mg of ritonavir.

The other ingredients are:

Tablet: Copovidone K30, Sorbitan laurate, Silica colloidal anhydrous, Sodium stearyl fumarate.

Tablet coating: HPMC 2910/Hypromellose 6 cP (E464), titanium dioxide (E171), macrogol 400, hydroxypropyl cellulose (E463), HPMC 2910/Hypromellose 15 cP (E464), talc (E553b), Silica colloidal anhydrous (E551), macrogol 3350, yellow ferric oxide (E172), polysorbate 80 (E433).

### **What Lopinavir/Ritonavir Sandoz looks like and contents of the pack**

Lopinavir/Ritonavir Sandoz tablets are yellow, oval, biconvex, film-coated tablets (19.00 x 10.20mm),



debossed with “H” on one side and “L3” on other side.

This medicine is available in HDPE container (White high density polyethylene bottle containing a canister with 2 grams silica gel as desiccant) closed with white propylene screw caps packs containing 1 bottle of 120 film-coated tablets or 3 bottles of 120 film-coated tablets (360 film-coated tablets)

This medicine is available in PVC/PVDC-AL blisters in a carton packs containing: 30, 40, 60, 120, 120 (3x40) or 360 (3x120) film-coated tablets.

Not all pack sizes may be marketed.

#### **Marketing Authorisation Holder and Manufacturer**

##### **Marketing Authorisation Holder**

Rowex Ltd., Bantry, Co. Cork, Ireland.

##### **Manufacturer**

Salutas Pharma GmbH, Otto-von-Guericke-Allee 1, Sachsen-Anhalt, 39179 Barleben, Germany.

#### **This medicinal product is authorised in the Member States of the EEA under the following names:**

The Netherlands:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg, filmomhulde tabletten
Austria:	Lopinavir/ Ritonavir Sandoz 200 mg/ 50 mg – Filmtabletten
Belgium:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg filmomhulde tabletten
Germany:	Lopinavir/Ritonavir HEXAL 200 mg/50 mg Filmtabletten
Estonia:	Lopinavir /Ritonavir Sandoz
Spain:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg comprimidos recubiertos con película EFG
Finland:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg kalvopäällysteiset tabletit
France:	LOPINAVIR / RITONAVIR Sandoz 200 mg / 50 mg, comprimé pelliculé
Croatia:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg filmom obložene tablete
Ireland:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg Film-coated tablets
Italy:	Lopinavir e ritonavir Sandoz
Lithuania:	Liponavir/Ritonavir Sandoz 200 mg/50 mg plėvele dengtos tabletės
Luxembourg:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg comprimés pelliculés
Latvia:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg apvalkotās tabletes
Poland:	Lopinavir+Ritonavir Sandoz
Portugal:	Lopinavir + Ritonavir Sandoz
Romania:	Lopinavir/Ritonavir Sandoz 200 mg/50 mg comprimate filmate
Slovenia:	Lopinavir/Ritonavir Sandoz 200 mg /50 mg filmsko obložene tablete

**This leaflet was last revised in 05/2017.**