

**PATIENT INFORMATION LEAFLET**

## PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER

### Ritonavir 25 mg Tablets <sup>1</sup>

**Read all of this leaflet carefully before you start taking this medicine because it contains important information for your child.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your health care provider.
- This medicine has been prescribed for your child. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If your child gets any side effects, talk to your healthcare provider. This includes any possible side effects not listed in the leaflet.

#### What is in this leaflet

1. What Ritonavir 25 mg Tablets is and what it is used for
2. What you need to know before you take Ritonavir 25 mg Tablets
3. How to take Ritonavir 25 mg Tablets
4. Possible side effects
5. How to store Ritonavir 25 mg Tablets
6. Contents of the pack and other information

### 1. WHAT RITONAVIR 25 MG TABLETS IS AND WHAT IT IS USED FOR

Ritonavir 25 mg Tablets contains the active substance ritonavir. It is taken in combination with protease inhibitors and acts as a booster (pharmacokinetic enhancer) to help improve their effect. It does this by slowing down the breakdown of the protease inhibitors which will make them stay in the body for longer.

Your healthcare provider will discuss with you the best combination of medicines for your child.

*This product is intended for use in children. Safety information on use in adults is also provided.*

### 2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE RITONAVIR 25 MG TABLETS

#### Do not use Ritonavir 25 mg Tablets:

- if your child is allergic to ritonavir or any of the other ingredients of Ritonavir 25 mg Tablets (see section 6).
- if he/she has severe liver disease.
- if you he/she is currently taking any of the following medicines:
  - astemizole or terfenadine (commonly used to treat allergy symptoms – these medicines may be available without prescription);
  - amiodarone, bepridil, encainide, flecainide, propafenone, quinidine (used to correct irregular heartbeats);
  - dihydroergotamine, ergotamine (used to treat migraine headache);
  - ergonovine, methylergonovine (used to stop excessive bleeding that may occur following childbirth or an abortion);
  - clorazepate, diazepam, estazolam, flurazepam, triazolam or oral (taken by mouth) midazolam (used to help you sleep and/or relieve anxiety);

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<sup>1</sup> Trade names are not prequalified by WHO. This is the national medicines regulatory authority's responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

- clozapine, pimozide, (used to treat abnormal thoughts or feelings);
- pethidine, piroxicam, propoxyphene (used to relieve pain);
- cisapride (used to relieve certain stomach problems);
- rifabutin (used to prevent/treat certain infections)\*;
- voriconazole (used to treat fungal infections)\*;
- simvastatin, lovastatin (used to lower blood cholesterol);
- alfuzosin (used to treat enlarged prostate gland);
- fusidic acid (used to treat bacterial infections);
- sildenafil if one suffers from a lung disease called pulmonary arterial hypertension that makes breathing difficult. Patients without this disease may use sildenafil for impotence (erectile dysfunction) under their health care provider's supervision (see the section on "Other medicines and Ritonavir 25 mg Tablets");
- avanafil or vardenafil (used to treat erectile dysfunction in adult patients)
- products containing St John's wort (*Hypericum perforatum*) as this may stop Ritonavir 25 mg Tablets from working properly. St John's wort is often used in herbal medicines that you can buy yourself.

\* Your healthcare provider may decide whether your child can take rifabutin and/or voriconazole with Ritonavir 25 mg Tablets.

If you are currently taking any of the above medicines, ask your healthcare provider about switching to a different medicine while you are taking Ritonavir 25 mg Tablets. Often, there are other medicines you can take instead.

Also read the list of medicines under 'Other medicines and Ritonavir 25 mg Tablets for use with certain other medicines which require special care.

### Warnings and precautions

Talk to your healthcare provider before taking Ritonavir 25 mg Tablets.

### Important information

- If Ritonavir 25 mg Tablets is taken in combination with other antiretroviral medicines, it is important that you also carefully read the leaflets that are provided with these other medicines. There may be additional information in those leaflets about situations when Ritonavir 25 mg Tablets should be avoided. If you have any further questions about Ritonavir 25 mg Tablets or the other medicines prescribed, please ask your health care provider.
- Ritonavir 25 mg Tablets is not a cure for HIV infection or AIDS.
- People taking Ritonavir 25 mg Tablets may still develop infections or other illnesses associated with HIV infection or AIDS. It is therefore important that your child remains under the supervision of your healthcare provider while taking Ritonavir 25 mg Tablets.
- Your child can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your health care provider the precautions needed to avoid infecting other people.

### Tell your healthcare provider if your child has/had:

- A history of **liver disease**.
- **Hepatitis B or C** and are being treated with a combination of antiretroviral agents, as your child is at a greater risk of a severe and potentially life threatening reaction because of the effect on the liver. Regular blood tests may be required to check the liver is working properly.
- **Haemophilia**, as there have been reports of increased bleeding in patients with haemophilia who are taking this type of medicine (protease inhibitors). The reason for this is not known.

Your child may need additional medicine to help your blood clot (factor VIII), in order to control any bleeding.

- **Erectile Dysfunction (in adult patients)**, as the medicines used to treat erectile dysfunction can cause hypotension and prolonged erection.
- **Diabetes**, as there have been reports of worsening of or the development of diabetes (diabetes mellitus) in some patients taking protease inhibitors.
- **Kidney (renal) disease**, since your health care provider may need to check the dose of the other medicines (such as protease inhibitors) your child is taking.

#### **Tell your healthcare provider if you experience:**

- **Diarrhoea or vomiting** that is not improving (persistent), as this may reduce how well the medicines your child is taking work.
- **Feeling sick** (nausea), **vomiting** or have **stomach pain**, because these may be signs of inflammation of the pancreas (pancreatitis). Some patients taking Ritonavir 100 mg Tablets can develop serious problems with their pancreas. Tell your health care provider as soon as possible if this applies to you.
- **Symptoms of infection** – inform your health care provider immediately. Some patients with advanced HIV infection (AIDS) who then start anti-HIV treatment may develop the symptoms of infections they have had in the past even if they didn't know they had had them. It is believed that this happens because the body's immune response improves and helps the body to fight these infections.

In addition to the opportunistic infections, autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after your child starts 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 health care provider immediately to seek necessary treatment.

- **Joint stiffness, aches and pains** (especially of the hip, knee and shoulder) and difficulty moving, tell your health care provider, as this may be a sign of a problem that can destroy bone (osteonecrosis). Some patients taking a number of antiretroviral medicines may develop this disease.
- **Muscle pain, tenderness or weakness**, particularly in combination with antiretroviral therapy including protease inhibitors and nucleoside analogues. On rare occasions these muscle disorders have been serious. (See section 4 **Possible side effects**)
- **Dizziness, lightheadedness, fainting spells or abnormal heartbeat**. Some patients taking Ritonavir 100 mg Tablets may experience changes in the electrocardiogram (ECG). Tell your healthcare provider if your child has a heart defect or conduction defect.

If you have any other health concerns, discuss these with your healthcare provider as soon as you can.

#### **Other medicines and Ritonavir 25 mg Tablets**

Please tell your healthcare provider if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription. There are some medicines your child cannot take at all with Ritonavir 25 mg Tablets. These are listed earlier in Section 2, under 'Do not use Ritonavir 25 mg Tablets'. There are some other medicines that can only be used under certain circumstances, as described below.

**Tell your healthcare provider if your child is taking any of the medicines listed below, as special care should be taken.**

- Colchicine (for gout) as Ritonavir 25 mg Tablets may raise the blood levels of this medicine. Your child must not take Ritonavir 25 mg Tablets with colchicine if he/she has kidney and/or liver problems (see also ‘Do not use Ritonavir 25 mg Tablets’ above).
- **Digoxin** (heart medicine). Your health care provider may need to adjust the dose of digoxin and monitor your child while he/she is taking digoxin and Ritonavir 25 mg Tablets in order to avoid heart problems.
- **Hormonal contraceptives** containing ethinyl oestradiol as Ritonavir 25 mg Tablets may reduce the effectiveness of these medicines. It is recommended that a condom or other non-hormonal method of contraception is used instead. One may also notice irregular uterine bleeding if one is taking this type of hormonal contraceptive with Ritonavir 25 mg Tablets.
- **Atorvastatin or rosuvastatin** (for high cholesterol) as Ritonavir 25 mg Tablets may raise the blood levels of these medicines. Talk to your healthcare provider before your child takes any cholesterol-reducing medicines with Ritonavir 25 mg Tablets (see also ‘**Do not use Ritonavir 25 mg Tablets**’ above).
- **Steroids** (eg dexamethasone, fluticasone propionate, prednisolone) as Ritonavir 25 mg Tablets may raise the blood levels of these medicines which may lead to Cushing’s syndrome (development of a rounded face) and reduce production of the hormone cortisol. Your healthcare provider may wish to reduce the steroid dose or monitor the side effects of your child more closely.
- **Trazodone** (a medicine for depression) as, unwanted effects like nausea, dizziness, low blood pressure and fainting can occur when taken with Ritonavir 25 mg Tablets.
- **Rifampicin and saquinavir** (used for tuberculosis and HIV, respectively) as serious liver damage can occur when taken with Ritonavir 25 mg Tablets.
- **Bosentan, riociguat** (used for pulmonary arterial hypertension) as Ritonavir 25 mg Tablets may increase the blood levels of this medicine.
- **Sildenafil or tadalafil** for impotence in adult patients.  
The dose and/or frequency of use of these medicines may need to be reduced to avoid hypotension and prolonged erection. Your child must not take Ritonavir 25 mg Tablets with sildenafil for the treatment of pulmonary arterial hypertension (see also section 2.). Tell your healthcare provider if your child is taking tadalafil for pulmonary arterial hypertension.

There are medicines that may not mix with Ritonavir 25 mg Tablets because their effects could increase or decrease when taken together. In some cases your healthcare provider may need to perform certain tests, change the dose or monitor you regularly. This is why you should tell your healthcare provider if your child is taking any medicines, including those you have bought yourself or herbal products, but it is especially important to mention these:

- amphetamine or amphetamine derivatives;
- antibiotics (e.g. erythromycin, clarithromycin);
- anticancer treatments (e.g. afatinib, ceritinib, dasatinib, nilotinib, vincristine, vinblastine);
- anticoagulants (e.g. rivaroxaban, warfarin);
- antidepressants (eg amitriptyline, desipramine, fluoxetine, imipramine, nefazodone, nortriptyline, paroxetine, sertraline, trazodone);
- antifungals (eg ketoconazole, itraconazole);
- antihistamines (eg loratidine, fexofenadine);
- antiretroviral medicines including HIV-protease inhibitors (amprenavir, atazanavir, darunavir, fosamprenavir, indinavir, saquinavir, tipranavir), non-nucleoside reverse transcriptase inhibitors (NNRTI) (delavirdine, efavirenz, nevirapine), and others (didanosine, maraviroc, raltegravir, zidovudine); anti-tuberculosis medicine (bedaquiline and delamanid);
- antiviral medicine used to treat chronic hepatitis C virus (HCV) infection in adults (simeprevir);
- anxiety medicine, buspirone;

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- asthma medicine, theophylline, salmeterol;
- atovaquone, a medicine used to treat a certain type of pneumonia and malaria;
- buprenorphine, a medicine used for the treatment of chronic pain;
- bupropion, a medicine used to help you stop smoking;
- epilepsy medicines (eg carbamazepine, divalproex, lamotrigine, phenytoin);
- heart medicines (eg disopyramide, mexiletine and calcium channel antagonists such as amlodipine, diltiazem and nifedipine);
- immune system (eg cyclosporine, tacrolimus, everolimus);
- morphine and morphine-like medicines used to treat severe pain (eg methadone, fentanyl);
- sleeping pills (eg alprazolam, zolpidem) and also midazolam administered by injection;
- tranquillisers (eg haloperidol, risperidone, thioridazine);
- colchicine, a treatment for gout

### **Taking Ritonavir 25 mg Tablets with food and drink**

Ritonavir 25 mg Tablets should be taken with food.

### **Pregnancy**

A woman who is pregnant or contemplating pregnancy should discuss this with her healthcare provider, so that the benefits and risks of treatment are clear.

### **Breast feeding**

If a mother wants to breast-feed her baby, she should discuss the risks and benefits with her healthcare provider.

### **Driving and using machines**

Ritonavir 25 mg Tablets can cause sleepiness and dizziness. If the ability to drive or use machines seems to be affected then one should not drive or use machinery.

### **Important information about some of the ingredients of Ritonavir 25 mg Tablets**

This medicine contains sodium. To be taken into consideration by patients on a controlled sodium diet

## **3. HOW TO TAKE RITONAVIR 25 MG TABLETS**

Always give Ritonavir 25 mg Tablets exactly as your healthcare provider has told you. You should check with your healthcare provider if you are not sure.

Ritonavir Tablets 25 mg is used to boost the effects of certain other anti-HIV medicines. The ritonavir dose varies depending on the co-administered protease inhibitor and ranges from two to four tablets per day. Ritonavir 25 mg Tablets should be taken with food as this can affect the way in which Ritonavir 25 mg Tablets is absorbed into your body. For more detailed dose recommendations, including those for children, see the Patient Information Leaflets of the other anti-HIV medicines that are being given in the combination.

It is important that Ritonavir 25 mg Tablets are swallowed whole and not chewed, broken or crushed.

Ritonavir 25 mg tablets should only be used in children who can swallow tablets whole. Other, more suitable formulations may be available for children less than 5 years of age or other children not able to swallow tablets whole.

Your health care provider will advise you on the dosage to be taken.

Ritonavir 25 mg Tablets should be taken every day to help control your HIV, no matter how much better you feel. If a side effect is preventing your child from taking Ritonavir 25 mg Tablets as directed, tell your healthcare provider straight away. During episodes of diarrhoea your healthcare provider may decide that extra monitoring is needed.

Always keep enough Ritonavir 25 mg Tablets on hand so you don't run out. When you travel with your child or when your child needs to stay in the hospital, make sure you have enough Ritonavir 25 mg Tablets to last until you can get a new supply.

### **If your child takes more Ritonavir 25 mg Tablets than he/she should**

Numbness, tingling, or a "pins and needles" sensation may occur if one takes too much Ritonavir 25 mg Tablets. If you realise your child has taken more Ritonavir 25 mg Tablets than he/she were supposed to, contact your health care provider or the Emergency Department of your nearest hospital straight away.

### **If you forget to give Ritonavir 25 mg Tablets**

If you forget to miss a dose, take the missed dose as soon as possible. If it is nearly time for the next dose, just give that one. Do not give a double dose to make up for a forgotten dose.

### **If your child stops taking Ritonavir 25 mg Tablets**

Even if your child feels better, do not stop giving Ritonavir 25 mg Tablets without talking to your health care provider. Giving Ritonavir 25 mg Tablets as recommended should give your child the best chance of delaying resistance to the medicines.

## **4. POSSIBLE SIDE EFFECTS**

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 health care provider will test for these changes.

Like all medicines, Ritonavir 25 mg Tablets can cause side effects, although not everybody gets them. Also, the side effects of Ritonavir 25 mg Tablets when used with other antiretroviral medicines are dependent on the other medicines. It is important that you carefully read the side effects section of the leaflets that are provided with these other medicines.

The frequency of possible side effects listed below is defined using the following convention:

very common	affects more than 1 user in 10
common	affects 1 to 10 users in 100
uncommon	affects 1 to 10 users in 1,000
rare	affects 1 to 10 users in 10,000
very rare	affects less than 1 user in 10,000
not known	frequency cannot be estimated from the available data.

### **Very common side effects:**

- Upper or lower stomach ache
- vomiting
- diarrhoea (may be severe)
- feeling sick (nausea)
- headache
- a tingling sensation or numbness in the hands, feet or around the lips and mouth
- feeling weak/tired
- bad taste in the mouth
- damage to the nerves that can cause

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- flushing, feeling hot
- dizziness
- pain in the throat
- cough
- upset stomach or indigestion
- weakness and pain
- itching
- rash
- joint pain and back pain

**Common side effects:**

- allergic reactions including skin rashes (may be red, raised, itchy), severe swelling of the skin and other tissues
- inability to sleep (insomnia)
- anxiety
- increase in cholesterol
- increase in triglycerides
- gout
- stomach bleeding
- inflammation of the liver and yellowing of skin or whites of the eyes
- increase in urination
- reduced kidney function
- low level of blood platelets
- seizures (fits)
- thirst (dehydration)
- abnormally heavy periods
- wind (flatulence)
- loss of appetite
- mouth ulcer
- muscle aches (pain), tenderness or weakness
- fever
- weight loss
- laboratory test results (such as blood chemistry and blood count)
- confusion
- difficulty paying attention
- fainting
- blurred vision
- swelling of the hands and feet
- high blood pressure
- low blood pressure and feeling faint when getting up
- coldness in the hands and feet
- acne

**Uncommon side effects:**

- heart attack
- diabetes
- kidney failure

**Rare side effects:**

- severe or life threatening skin reaction including blisters (Stevens Johnson syndrome, toxic epidermal necrolysis)
- serious allergic reaction (anaphylaxis)
- high levels of sugar in the blood

Tell your health care provider if your child feels sick (nauseous), if he/she is vomiting, or has stomach pain, because these may be signs of an inflamed pancreas. Also tell your health care provider if your child experiences joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty moving, as this may be a sign of osteonecrosis. See also section 2 **What you need to know before you take Ritonavir 25 mg Tablets.**

In patients with haemophilia type A and B, there have been reports of increased bleeding while taking this treatment or another protease inhibitor. Should this happen to your child, seek immediate advice from your health care provider.

Abnormal liver function tests, hepatitis (inflammation of the liver), and rarely jaundice, have been reported in patients taking Ritonavir 25 mg Tablets. Some people had other illnesses or were taking other medicines. People with liver disease or hepatitis may have worsening of liver disease.



There have been reports of muscle pain, tenderness or weakness, particularly when taking medicines to lower cholesterol in combination with antiretroviral therapy, including protease inhibitors and nucleoside analogues. On rare occasions these muscle disorders have been serious (rhabdomyolysis). In the event of unexplained or continual muscle pain, tenderness, weakness or cramps, stop giving the medicine, contact your health care provider as soon as possible or take your child to the Emergency Department of your nearest hospital.

Inform your health care provider as soon as possible if your child experiences any symptoms that suggest an allergic reaction after taking Ritonavir 25 mg Tablets such as rash, hives or breathing difficulties.

**If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, contact your health care provider or Emergency department.**

## **5. HOW TO STORE RITONAVIR 25 MG TABLETS**

Keep out of the reach and sight of children.

Do not store above 30°C, store in the original container

Do not use Ritonavir 25 mg Tablets after the expiry date on the label. The expiry date refers to the last day of that month.

## **6. FURTHER INFORMATION CONTENTS OF THE PACK AND OTHER INFORMATION**

### **What Ritonavir 25 mg Tablets contains**

- The active substance is ritonavir. Each film-coated tablet contains 25 mg ritonavir.
- The other tablet ingredients are: colloidal silicon dioxide, sodium chloride, copovidone, sorbitan monolaurate, sodium stearyl fumarate
- The tablet coating (Opadry White 20C580015) is composed of: hypromellose, titanium dioxide, polyethylene glycol , polysorbate, talc, colloidal anhydrous silica, hydroxypropyl cellulose

### **What Ritonavir 25 mg Tablets looks like and contents of the pack**

White, film-coated, round, biconvex, bevelled edge tablets debossed with “RT” on one side of the tablet and “25” on the other side.

Round, wide mouth, white HDPE bottle with white opaque polypropylene screw cap with aluminium induction sealing liner wad and containing a desiccant comprising of a plastic canister with perforation for breathing, containing silica gel.

Pack size: 30 tablets

### **Supplier**

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### **Manufacturer**

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For any information about this medicine, contact the local representative of the supplier:

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Detailed information on this medicine is available on the World Health Organization (WHO) web site:  
<https://extranet.who.int/prequal>