

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrORKAMBI®

Lumacaftor / Ivacaftor Tablets, and Lumacaftor / Ivacaftor Granules

Read this carefully before you start taking **ORKAMBI** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ORKAMBI**.

What is **ORKAMBI** used for?

ORKAMBI is used to treat cystic fibrosis (CF) in children and adults (1 year of age and older) who have two copies of the *F508del* mutation in the *cystic fibrosis transmembrane conductance regulator (CFTR)* gene (*F508del/F508del*).

How does **ORKAMBI** work?

ORKAMBI belongs to a group of medicines known as “*CFTR* modulators”, and is a combination of two medicinal ingredients, lumacaftor and ivacaftor. It works to treat CF by affecting the *CFTR* protein in the body. This protein helps move chloride ions in and out of the cells in many organs of the body. In patients with CF, the *CFTR* protein is in lower amounts and/or the *CFTR* protein does not work properly causing mucus build-up in the lungs and many organs. Each ingredient in ORKAMBI works as follows:

- **Lumacaftor** (a *CFTR* corrector): Increases the amount of the *CFTR* protein on the surface of the cell.
- **Ivacaftor** (a *CFTR* potentiator): Makes the *CFTR* protein at the cell surface work better.

What are the ingredients in **ORKAMBI**?

Medicinal ingredients: lumacaftor and ivacaftor.

Non-medicinal ingredients:

- **Tablets:** ammonium hydroxide, carmine, croscarmellose sodium, FD&C Blue #1, FD&C Blue #2, hypromellose acetate succinate, iron oxide black, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, povidone, propylene glycol, shellac, sodium lauryl sulfate, talc, and titanium dioxide.
- **Granules:** croscarmellose sodium, hypromellose acetate succinate, microcrystalline cellulose, povidone, and sodium lauryl sulfate.

ORKAMBI comes in the following dosage forms:

- **Tablets:** 100 mg/125 mg, and 200 mg/125 mg of lumacaftor/ivacaftor.
- **Granules:** 75 mg/94 mg, 100 mg/125 mg, and 150 mg/188 mg of lumacaftor/ivacaftor.

Do not use **ORKAMBI** if:

- You are allergic to lumacaftor, ivacaftor, or any of the other ingredients in ORKAMBI.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ORKAMBI. Talk about any health conditions or problems you may have, including if you:

- have liver problems. Taking ORKAMBI when you already have severe liver disease can cause serious life-threatening problems. Your healthcare professional should closely monitor you and may adjust your dose of ORKAMBI.
- have had an organ transplant.
- have high blood pressure, a low heart rate, or other heart problems.
- have kidney problems.
- are using birth control (e.g., hormonal contraceptives including oral, injectable, transdermal, or implantable types). Hormonal contraceptives should not be used as a method of birth control when taking ORKAMBI.
- are pregnant or plan to become pregnant. It is not known if ORKAMBI will harm your unborn baby. You and your healthcare professional should decide if you will take ORKAMBI while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if ORKAMBI passes into your breast milk. You and your healthcare professional should decide if you will take ORKAMBI while you are breastfeeding.

Other warnings you should know about:

Menstrual irregularities: Women taking ORKAMBI may have irregular or abnormal periods. They may also have more bleeding during their periods. This happened mainly in women taking hormonal birth control.

Testing and check-ups: Your healthcare professional will regularly monitor your health throughout your treatment. They may do this by performing certain tests before and during your treatment. These may be used to monitor your health including your:

- **Blood pressure and heart rate:** An increase in blood pressure and/or a decrease in heart rate has been reported in patients taking ORKAMBI. Your healthcare professional may monitor your blood pressure and heart rate during your treatment.
- **Eyes (e.g., for cataracts):** Cataracts (cloudiness of the eye lens) has been reported in children and adolescents taking ORKAMBI. Your healthcare professional may do an eye exam before you start taking ORKAMBI and during your treatment.
- **Lungs:** When you first start taking ORKAMBI, you may have shortness of breath or tightness in your chest. This is more likely to occur if you already have poor lung function. Your healthcare professional may monitor your lung function throughout your treatment.
- **Liver:** ORKAMBI can cause an increase in liver enzymes leading to serious liver problems, especially if you already have a liver problem. Your healthcare professional will order blood tests to check your liver function:
 - before you take ORKAMBI,
 - every 3 months of the first year while you are taking ORKAMBI, and
 - every year while you are taking ORKAMBI.

Additional blood tests may be required if you have had abnormal blood tests of the liver in the past.

Liver problems: ORKAMBI can cause serious liver problems. Tell your healthcare professional right away if you have any of these symptoms, which may be a sign of liver

problems

- Pain or discomfort in the upper right stomach (abdominal) area
- Yellowing of your skin or the white part of your eyes
- Loss of appetite
- Nausea or vomiting
- Dark urine
- Confusion
- Pale stools

Driving and using machines: It is not known if ORKAMBI can cause dizziness. You should know how you react to ORKAMBI before driving or using heavy machinery.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ORKAMBI:

- Antifungal medicines (used for the treatment of fungal infections) such as ketoconazole, itraconazole, posaconazole, voriconazole, and fluconazole.
- Antibiotic medicines (used for the treatment of bacterial infections) such as clarithromycin, rifabutin, rifampicin, levofloxacin, and erythromycin.
- Anticonvulsant medicines (used for the treatment of epileptic seizures) such as phenobarbital, carbamazepine, and phenytoin.
- Ranitidine (used to treat peptic ulcers and gastroesophageal reflux disease).
- St. John's wort (*Hypericum perforatum*), an herbal medicine.
- Benzodiazepines (used for the treatment of anxiety, insomnia, agitation, etc.) such as midazolam and triazolam.
- Antidepressants (used for the treatment of depression) such as citalopram, escitalopram, and sertraline.
- Anti-allergics (used for the treatment of allergy symptoms) such as montelukast.
- Anti-inflammatories (used to reduce pain, inflammation, and fever) such as ibuprofen.
- Immunosuppressants (used after an organ transplantation) such as cyclosporine, everolimus, sirolimus, and tacrolimus.
- Cardiac glycosides (used for the treatment of mild to moderate congestive heart failure and an abnormal heart rhythm called atrial fibrillation) such as digoxin.
- Anticoagulants (used to prevent blood clots from forming or growing larger in blood and blood vessels) such as warfarin.
- Hormonal contraceptives (used to prevent pregnancy) including oral, injectable, skin patches (transdermal), and implantable products such as ethinylestradiol, norethindrone, and other progestogens. These should not be relied upon as an effective method of birth control when given with ORKAMBI.
- Glucocorticoids (used to treat inflammation) such as methylprednisolone, and prednisone.
- Proton pump inhibitors (used to treat acid reflux disease and ulcers) such as omeprazole, esomeprazole, and lansoprazole.
- Antimycobacterial medicines (used to treat a certain type of bacterial infection caused by *Mycobacterium*).

Know the medicines you take. Keep a list of them to show your healthcare professional when you get a new medicine.

How to take ORKAMBI:

- Take ORKAMBI exactly as your healthcare professional tells you to, even if you feel well. Check with your healthcare professional if you are not sure. Do not change the dose or stop taking ORKAMBI without first talking to your healthcare professional.
- **Always take ORKAMBI with a fat-containing food.** This helps to ensure that you get the right amount of medicine in your body. Meals and snacks recommended in CF guidelines contain acceptable amounts of fat. This includes meals that have been prepared with butter or oils, meals that have eggs, nuts, whole milk dairy products (such as whole milk, breastmilk, infant formula, cheese, and yogurt), or meats.

ORKAMBI tablets:

Each ORKAMBI box contains 4 cartons (i.e., a 4 week supply). Each carton contains 7 blister strips, one for each day. Each blister strip contains 4 tablets (i.e., 2 morning doses and 2 evening doses).

1. To separate your prescribed dose from the blister strip, you may cut along the dotted line.
2. Unpeel the paper backing from the blister strip. Do **NOT** push the tablet through the paper backing because the tablet could break.
3. Remove your dose and swallow the tablet(s) whole with food that contains fat. Do **NOT** break, crush, or chew the tablet(s).
4. Take your evening dose 12 hours after your morning dose.

ORKAMBI granules:

Each ORKAMBI box contains 4 individual wallets (i.e., a 4 week supply). Each wallet contains 14 packets of granules (i.e., 7 morning doses and 7 evening doses for a total of 7 days). Finish the entire wallet (i.e., all 7 days' doses) before starting a new wallet. Each packet is for single use only.

1. Remove 1 packet from the wallet.
2. Hold the packet with cut line on top.
3. Shake the packet gently to settle the granules to the bottom of the packet.
4. Tear or cut packet completely open along cut line.
5. Pour all the granules of the packet into 5 mL (1 teaspoon) of soft food or liquid that is between 5°C to 25°C and mix until granules are dissolved. Some examples of soft foods or liquids include puréed fruits or vegetables, flavoured yogurt or pudding, applesauce, milk, or juice (except grapefruit).
6. **After mixing, give within 1 hour and do NOT store for future use. Make sure all medicine is taken. This is very important for it to work properly and be effective.**
7. In addition to the granule mixture, fat-containing food must be ingested just **before** or just **after** the granules dose. This helps the body better absorb the medicine.
8. Take your evening dose 12 hours after your morning dose.

Refilling your prescription: Remember to get a new prescription from your healthcare professional, or a refill from your pharmacy before all your tablets or granules are taken.

Usual dose:

Your healthcare professional will determine the right dose of ORKAMBI tablets or ORKAMBI granules for you. This may depend on your health condition, other medicines you are taking, your weight, your age, and how you respond to ORKAMBI.

The usual dose for ORKAMBI is as follows:

- **ORKAMBI Tablets**
 - **6 to 11 years of age:** Two tablets (ORKAMBI 100 mg/125 mg) every 12 hours in the morning and in the evening.
 - **12 years of age and older:** Two tablets (ORKAMBI 200 mg/125 mg) every 12 hours in the morning and in the evening.
- **ORKAMBI Granules (1 to 5 years of age):** Based on weight and age, as seen in the table below.

Age	Weight	Product	Dose	
			Morning	Evening
1 to <2 years	7 kg to <9 kg	ORKAMBI 75 mg/94 mg granules per packet	1 packet	1 packet
	9 kg to <14 kg	ORKAMBI 100 mg/125 mg granules per packet		
	≥14 kg	ORKAMBI 150 mg/188 mg granules per packet		
2 to 5 years	<14 kg	ORKAMBI 100 mg/125 mg granules per packet	1 packet	1 packet
	≥14 kg	ORKAMBI 150 mg/188 mg granules per packet		

Overdose:

If you think you, or a person you are caring for, have taken too much ORKAMBI, contact a healthcare professional, hospital emergency department, or regional Poison Control Centre immediately, even if there are no symptoms. If possible, have your medicine and this leaflet with you.

Missed Dose:

If you miss a dose of ORKAMBI and:

- **it is within 6 hours** of when you usually take it, take your dose of ORKAMBI as prescribed as soon as possible with fat-containing food.
- **it is more than 6 hours** after the time you usually take it, skip the missed dose and take the next dose at your regularly scheduled time. Do **NOT** double your dose to make up for the missed dose.

What are possible side effects from using ORKAMBI?

These are not all the possible side effects you may feel when taking ORKAMBI. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- shortness of breath and/or chest tightness
- increase in blood pressure
- decrease in heart rate
- upper respiratory tract infection (common cold), including sore throat, stuffy or runny nose
- nausea
- diarrhea
- passing gas
- rash
- fatigue
- flu or flu like symptoms
- irregular, abnormal, or painful periods (menses) and increase in the amount of menstrual bleeding

Additional side effects in children may include:

- headache
- upper abdominal pain
- increased cough and/or mucus in the lungs or airways

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
UNCOMMON			
Liver problems: pain or discomfort in the upper right stomach (abdominal) area, yellowing of the skin or eyes (jaundice), loss of appetite, nausea, vomiting, dark urine, confusion, unusual tiredness, itchy skin, anorexia or pale stools.		√	
Liver disease (worsening of liver function): confusion, coma, death.			√
Increased creatine phosphokinase levels in the blood: muscle pain, or dark urine.		√	
Pulmonary exacerbations: new or increased cough or sputum production, change in sputum appearance, fever, fatigue, increased shortness of breath.		√	
Pneumonia (infection in the lungs): chest pain when you breath or cough, cough which may produce phlegm, fatigue, fever, sweating and shaking chills, or shortness of breath.		√	
Hemoptysis: coughing up blood.	√		
Coughing	√		
UNKNOWN FREQUENCY			
Allergic reaction: rash; hives; swelling of the face, lips, tongue, or throat; difficult swallowing; drop in blood pressure; or difficult breathing.			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

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

Store at or below 30°C.

Keep out of reach and sight of children.

You may need to read this leaflet again. Please do not throw this away.

If you want more information about ORKAMBI:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (<http://www.vrtx.com/canada>), or by calling 1-877-634-8789.

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