

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION**

**PrORKAMBI®
Lumacaftor/Ivacaftor tablets**

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 for the chronic treatment of cystic fibrosis (CF). It is used for patients aged 6 years and older who have two copies of the *F508del* mutation in the *cystic fibrosis transmembrane conductance regulator* (CFTR) gene (*F508del/F508del*).

ORKAMBI should not be used in patients other than those who have two copies of the *F508del* mutation in their *CFTR* gene.

It is not known if ORKAMBI is safe and effective in children under 6 years of age.

How does ORKAMBI work?

- The CFTR protein helps bring chloride ions out of the cells in many organs.
- People who have two copies of the *F508del* mutation in the *CFTR* gene have a lower amount of CFTR protein at the surface of their cells.
- ORKAMBI is a type of medicine called a “*cystic fibrosis transmembrane conductance regulator corrector and potentiator*.”
- The two ingredients in ORKAMBI help bring more chloride ions out of the cells in many organs:
 - Lumacaftor, a CFTR corrector, increases the amount of the CFTR proteins at the cell surface.
 - 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: cellulose, microcrystalline; croscarmellose sodium; hypromellose acetate succinate; magnesium stearate; povidone; and sodium lauryl sulfate. The tablet film coat contains carmine, FD&C Blue #1, FD&C Blue #2, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide. The printing ink contains ammonium hydroxide, iron oxide black, propylene glycol, and shellac.

ORKAMBI comes in the following dosage forms:

Tablet: 100 mg lumacaftor /125 mg ivacaftor

Tablet: 200 mg lumacaftor/125 mg ivacaftor

Do not use ORKAMBI if:

You are hypersensitive (allergic) to this drug or to any ingredient in the formulation or component of the container.

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 disease, as your doctor may need to adjust the dose of ORKAMBI.
- have had an organ transplant.
- have high blood pressure, a low heart rate, or other heart conditions
- have kidney disease.
- are using birth control (hormonal contraceptives including oral, injectable, transdermal, or implantable forms). 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 doctor should decide if you will take ORKAMBI while you are pregnant.
- are breastfeeding or planning to breastfeed. It is not known if ORKAMBI passes into your breast milk. You and your doctor should decide if you will take ORKAMBI while you are breastfeeding.

Other warnings you should know about:Cataracts

A problem with the lens of the eye (cataract) has been seen in some children and adolescents while taking ivacaftor, an ingredient in ORKAMBI. Your doctor may perform eye examinations before you start taking ORKAMBI and during treatment with ORKAMBI to look for cataracts.

Abnormal test results

Abnormal blood tests of the liver have been seen in some people receiving ORKAMBI.

Your doctor will order some blood tests to check your liver:

- before you take ORKAMBI,
- every 3 months of the first year while you are taking ORKAMBI, and
- every year while you are taking ORKAMBI.

If you have had abnormal blood tests of the liver in the past, your doctor may order blood tests to check your liver more often.

Tell your doctor 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

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.

Children

ORKAMBI is not for use in children under the age of 6 years. It is not known if ORKAMBI is safe and effective in children under 6 years of age.

Respiratory

You may experience shortness of breath or tightness in your chest when you first start taking ORKAMBI. Your doctor may monitor you more closely if you have poor lung function.

Blood Pressure and Heart Rate (number of heart beats per minute)

An increase in blood pressure has been seen in some patients treated with ORKAMBI. Your doctor may monitor your blood pressure periodically during treatment with ORKAMBI.

A decrease in heart rate has been seen in some patients treated with ORKAMBI.

Tell your doctor if you are taking medicines that affect your blood pressure or heart rate.

Driving and using machines

It is not known if ORKAMBI causes 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, fluconazole
- Antibiotic medicines (used for the treatment of bacterial infections) such as telithromycin, clarithromycin, rifabutin, rifampicin, levofloxacin, erythromycin
- Anticonvulsant medicines (used for the treatment of epileptic seizures) such as phenobarbital, carbamazepine, phenytoin
- Ranitidine, a medication 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, triazolam

- Antidepressants such as citalopram, escitalopram, sertraline
- Anti-allergics such as montelukast
- Anti-inflammatories such as ibuprofen
- Immunosuppressants (used after an organ transplantation) such as cyclosporine, everolimus, sirolimus, 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) such as oral, injectable, skin patches (transdermal), and implantable products. 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, prednisone
- Proton pump inhibitors (used to treat acid reflux disease and ulcers) such as omeprazole, esomeprazole, lansoprazole

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How to take ORKAMBI:

- **Do not** break, crush, or chew the tablet. Swallow the tablet **whole**.
- Take it exactly as your doctor tells you to take it, even if you feel well.
- Check with your doctor if you are not sure about your dose.
- Do not change the dose or stop taking ORKAMBI without first talking to your doctor.
- Your doctor may need to adjust your dose if you have liver disease or if you are taking medications that may interact with ORKAMBI.

ORKAMBI should always be taken with a fat-containing food:

- Taking ORKAMBI with fat-containing food is important to get the right amount of medicine in your body.
- Each dose should be taken just before or just after eating fat-containing food.
- Meals and snacks recommended in CF guidelines contain acceptable amounts of fat.
- Examples of meals that contain fat are:
 - Meals that have been prepared with butter or oils.
 - Meals that have eggs, nuts, whole-milk dairy products (such as whole-milk, cheese, and yogurt), or meats.
- Each box contains a 4 week supply of ORKAMBI
- Each carton contains 7 daily blister strips (1 strip per day)
- Each blister strip contains 4 tablets: 2 for the morning dose and 2 for the evening dose.
- You may cut along the dotted line to separate your doses from the blister strip.
- Peel back the paper backing from a blister strip to remove the tablets. **Do not** push tablet through paper backing.

Usual dose:

Patients aged 6 through 11 years: take 2 of the 100 mg/ 125 mg tablets every 12 hours (morning and evening) just before or just after eating fat-containing food.

Patients aged 12 years and over: take 2 of the 200 mg/ 125 mg tablets every 12 hours (morning and evening) just before or just after eating fat-containing food.

Overdose:

If you think you have taken too much ORKAMBI, contact your 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 with fat-containing food as soon as possible.
- If you miss a dose of ORKAMBI and it is **more than 6 hours** after the time you usually take it, **skip** that dose only and take the next dose when you usually take it.
- Do **not** take 2 doses at the same time to make up for your missed dose.

Refilling your prescription:

Remember to get a new prescription from your doctor or a refill from your pharmacy before all your tablets are taken.

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. Please also see Warnings and Precautions.

Like all medicines, this medicine can cause side effects, although not everybody gets them.

- 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
- gastrointestinal symptoms, including nausea, diarrhea, and gas
- rash
- fatigue
- flu or flu-like symptoms
- increase in muscle enzyme levels
- irregular, abnormal, or painful periods (menses) and increase in the amount of menstrual bleeding

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 Abnormal blood tests of the liver: pain or discomfort in the upper right stomach (abdominal) area, yellowing of the skin or eyes, loss of appetite, nausea or vomiting, dark urine, confusion, pale stools		√	
Increased blood creatine phosphokinase: muscle pain, dark urine		√	
Pneumonia (lung infection)		√	
Hemoptysis (cough up blood)	√		
Cough	√		
UNKNOWN Allergic reaction: rash; hives; swelling of the face, lips, tongue, or throat; difficult swallowing or 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, talk to your healthcare professional.

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
 - By calling 1-866-234-2345 (toll-free);
 - By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 0701E
Ottawa, ON
K1A 0K9
- Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](#).

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

Storage:

Store 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](#); the manufacturer's website <http://www.vrtx.ca>, or by calling 1-877-634-VRTX (8789).

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