ORKAMBI®
(lumacaftor/ivacaftor)
200 mg / 125 mg tablets

Your Guide to the Possible Side Effects of ORKAMBI®

When taking ORKAMBI, it's important to know the possible side effects. This guide will help to explain the possible serious side effects and Important Safety Information. You'll also learn about the most common side effects of ORKAMBI and how many people experienced them in two, 24-week clinical trials.

Remember, this guide is for informational purposes only and is not intended to be a substitute for professional medical advice. You should talk to your healthcare provider about the possible side effects of ORKAMBI and whether ORKAMBI is right for you.

What is ORKAMBI?

ORKAMBI is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 12 years and older who have two copies of the *F508del* mutation (*F508del/F508del*) in their *CFTR* gene.

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 12 years of age.

How the safety of ORKAMBI was studied in clinical trials

Two, 24-week trials were done to evaluate the safety and efficacy of ORKAMBI in people age 12 years and older with 2 copies of the *F508del* mutation.

Across both trials, a total of 369 people took ORKAMBI every 12 hours with fat-containing food, and 370 received placebo. Both groups continued to take all of their other prescribed CF therapies.

The safety data from the 2 clinical trials were combined and reviewed together, or "pooled," to arrive at the results.

You should talk to your healthcare provider about this information and if ORKAMBI is right for you.

Who should not take ORKAMBI?

Do not take ORKAMBI if you take certain medicines or herbal supplements, such as:

- antibiotics: rifampin (Rifamate®, Rifater®) or rifabutin (Mycobutin®)
- seizure medicines: phenobarbital, carbamazepine (Tegretol®, Carbatrol®, and Equetro®), or phenytoin (Dilantin®, Phenytek®)
- sedatives/anti-anxiety medicines: triazolam (Halcion®) or midazolam (Dormicum®, Hypnovel®, and Versed®)
- immunosuppressant medicines: everolimus (Zortress®), sirolimus (Rapamune®), or tacrolimus (Astagraf XL®, Envarsus XR®, Prograf®, and Protopic®)
- St. John's wort (*Hypericum perforatum*)

Talk to your doctor before taking ORKAMBI if you take any of the medicines or supplements listed above.

Please click the following links to see full Prescribing Information, including Patient Information.

On the next page, review the serious side effects of ORKAMBI. →

ORKAMBI® can cause serious side effects.

High liver enzymes in the blood, which can be a sign of liver injury, have been reported in patients receiving ORKAMBI. In two, 24-week clinical trials, less than 1% of people taking ORKAMBI experienced serious side effects related to high liver enzymes.

Your healthcare provider will do blood tests to check your liver:

- Before you start ORKAMBI
- At 3, 6, 9, and 12 months after starting treatment
- Every year thereafter while you are taking ORKAMBI

You may be able to get these tests done during your regular CF Center visits. Talk to your healthcare provider about how best to schedule these tests.

Call your healthcare provider right away if you have any of the following symptoms 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, amber-colored urine
- Confusion

Respiratory events such as shortness of breath or chest tightness were observed in patients when starting ORKAMBI. The majority of respiratory events began during the first week of treatment and were more common in people who had poor lung function. **If you have poor lung function, your healthcare provider may monitor you more closely when you start ORKAMBI.**

In two, 24-week clinical trials, 9% of people experienced chest tightness compared with 6% taking placebo. 13% of people experienced shortness of breath compared with 8% taking placebo.

For people who had respiratory events within 1 to 2 days after starting ORKAMBI and who continued treatment, these events generally resolved within the first 2 to 3 weeks of taking ORKAMBI.

If you experience any of these side effects, talk to your healthcare provider right away.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents receiving ivacaftor, a component of ORKAMBI.

Your healthcare provider should perform eye examinations prior to and during treatment with ORKAMBI to look for cataracts.

Please click the following links to see full Prescribing Information, including Patient Information.

On the next page, review the common side effects of ORKAMBI. →

What are the most common side effects of ORKAMBI®?

Below are the most common side effects of ORKAMBI and percentage of people who experienced them during two, 24-week clinical trials.*

	SIDE EFFECT	PEOPLE TAKING ORKAMBI	PEOPLE TAKING PLACEBO
Respiratory events	Shortness of breath	13%	8%
	Chest tightness	9%	6%
Respiratory tract infections	Common cold	13%	11%
	Upper respiratory tract infection	10%	5%
	Runny nose	6%	4%
Gastrointestinal events	Nausea	13%	8%
	Diarrhea	12%	8%
	Gas	7%	3%
Other events	Irregular, missed, or abnormal periods and increase in the amount of menstrual bleeding†	10%	2%
	Fatigue	9%	8%
	Elevated muscle enzymes	7%	5%
	Rash	7%	2%
	Flu or flu-like symptoms	5%	2%

*Both groups continued to take all of their other prescribed CF therapies.
†These events occurred more frequently in women taking ORKAMBI who were using hormonal contraceptives (27%) than those not using hormonal contraceptives (3%).

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of ORKAMBI. For more information, ask your healthcare provider or pharmacist. Call your healthcare provider for medical advice about side effects. You are encouraged to report side effects to the FDA at **1-800-FDA-1088.**

Please click the following links to see full Prescribing Information, including Patient Information.

On the next page, review additional Important Safety Information.

What should I tell my doctor before taking ORKAMBI®?

Before you take ORKAMBI, tell your doctor if you:

- have or have had liver problems
- have kidney problems

- 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. Talk to your doctor about the best birth-control method you should use while 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.

ORKAMBI may affect the way other medicines work, and other medicines may affect how ORKAMBI works. **Tell your doctor about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements, because the dose of ORKAMBI may need to be adjusted when taken with certain medicines.

Especially tell your doctor if you take:

- antifungal medicines, such as ketoconazole (e.g., Nizoral®), itraconazole (e.g., Sporanox®), posaconazole (e.g., Noxafil®), or voriconazole (e.g., Vfend®)
- antibiotics, such as telithromycin (e.g., Ketek®), clarithromycin (e.g., Biaxin®), or erythromycin (e.g., Ery-Tab®)

What should I know when taking ORKAMBI?

Tell your doctor if you stop ORKAMBI for more than 1 week. Your doctor may need to change your dose of ORKAMBI or other medicines you take.

It is unknown if ORKAMBI causes dizziness. Do not drive a car, use machinery, or do anything that needs you to be alert until you know how ORKAMBI affects you.

Please click the following links to see full Prescribing Information, including Patient Information.