ORKAMBI®
(lumacaftor/ivacaftor)
100 / 125 mg • 150 / 188 mg oral granules

GET TO KNOW ORKAMBI®

A resource for caregivers of children age 2 through 5 years with 2 copies of the F508del-CFTR mutation

WHAT IS ORKAMBI® (lumacaftor/ivacaftor)?

ORKAMBI is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 2 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 2 years of age.

IMPORTANT SAFETY INFORMATION

Your child should not take ORKAMBI if he or she takes 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 and anti-anxiety medicines: triazolam (Halcion®) or midazolam (Dormicum®, Hypnovel®, and Versed®)
- immunosuppressant medicines: cyclosporine, everolimus (Zortress®), sirolimus (Rapamune®), or tacrolimus (Astagraf XL®, Envarsus XR®, Prograf®, and Protopic®)
- St. John's wort *(Hypericum perforatum)*

Talk to your child's doctor before taking ORKAMBI if he or she takes any of the medicines or supplements listed above.

All photos are of people with CF who have 2 copies of the F508del mutation in their CFTR gene or their caregivers. The people with CF may or may not be taking ORKAMBI.

Please see additional Important Safety Information throughout brochure, and full Prescribing Information, including Patient Information.

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ORKAMBI® WAS STUDIED IN CHILDREN AGE 2 THROUGH 5 YEARS

SAFETY STUDY

The primary purpose of the 24-week study of 60 children age 2 through 5 years with 2 copies of the F508del-CFTR mutation was to determine the safety of ORKAMBI.

This study also evaluated sweat chloride levels, which are a measure of the amount of salt in a child's sweat (mmol/L). Sweat chloride level measurement is used to help diagnose cystic fibrosis (CF). High sweat chloride levels are a hallmark of CF. After 24 weeks, there was a 2-week period when the children stopped ORKAMBI in order to observe any changes in sweat chloride.

HOW ORKAMBI WAS GIVEN

Children who weighed **less than ~31 pounds** (less than 14 kg) received ORKAMBI oral granules (lumacaftor 100 mg/ivacaftor 125 mg) every 12 hours.

Children who weighed **~31 pounds or more** (14 kg or more) received ORKAMBI oral granules (lumacaftor 150 mg/ivacaftor 188 mg) every 12 hours.

All children took one packet of ORKAMBI oral granules mixed with **1 teaspoon of soft food or liquid** every 12 hours. All children ate fat-containing food just before or just after taking the oral granules dose. No children in the study took placebo. All children continued to take their other prescribed CF treatments throughout the full study, including the 2-week period when they stopped taking ORKAMBI.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Before taking ORKAMBI, tell your child's doctor about all of your child's medical conditions, including if he or she:

- has or has had liver problems
- has had an organ transplant
- has kidney problems
- is 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 the doctor about the best birth control method to use while taking ORKAMBI
- is pregnant or plans to become pregnant. It is not known if ORKAMBI will harm an unborn baby. Patients and their doctor should decide whether ORKAMBI should be taken during pregnancy
- is breastfeeding or planning to breastfeed. It is not known if ORKAMBI passes into breast milk. Patients and their doctor should decide whether ORKAMBI should be taken while breastfeeding

STUDY RESULTS

SAFETY

The safety in this study was similar to what was observed in studies of ORKAMBI® in older patients. See the possible side effects of ORKAMBI on the next page.

During the study, 3 children taking ORKAMBI stopped permanently because of high liver enzymes.

SWEAT CHLORIDE

Sweat Chloride

At Week 24:
Decreased 31.7 mmol/L on average
(average mmol/L at beginning of study was 105.8)

At Week 26, after ORKAMBI was stopped for 2 weeks:
Increased 33.0 mmol/L on average

STUDY CONSIDERATIONS

- Comparisons with placebo could not be made because all people in the study received ORKAMBI. **Therefore, it is not known if changes in sweat chloride levels were due to ORKAMBI**
- Changes in sweat chloride levels are not related to changes in lung function

Additional studies of ORKAMBI were conducted in different age groups. For more information, please go to ORKAMBI.com.

IMPORTANT SAFETY INFORMATION (CONTINUED)

ORKAMBI may affect the way other medicines work, and other medicines may affect how ORKAMBI works.

Tell your child's doctor about all the medicines he or she takes, 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 child's doctor if he or she takes:

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

Tell your child's doctor if he or she stops ORKAMBI for more than 1 week. Your child's doctor may need to change the dose of ORKAMBI or other medicines your child takes.

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IMPORTANT SAFETY INFORMATION (CONTINUED)

What are the possible side effects of ORKAMBI®?

ORKAMBI can cause serious side effects, including:

Worsening of liver function in people with severe liver disease. The worsening of liver function can be serious or cause death. Talk to your child's doctor if you have been told that he or she has liver disease as your child's doctor may need to adjust the dose of ORKAMBI.

High liver enzymes in the blood, which can be a sign of liver injury in people receiving ORKAMBI. Your child's doctor will do blood tests to check your child's liver:

- before starting ORKAMBI
- every 3 months during the first year of taking ORKAMBI
- every year while taking ORKAMBI

Call your child's doctor right away if he or she has any of the following symptoms of liver problems:

- pain or discomfort in the upper right stomach (abdominal) area
- yellowing of the skin or the white part of the eyes
- loss of appetite
- nausea or vomiting
- dark, amber-colored urine
- confusion

Breathing problems such as shortness of breath or chest tightness in patients when starting ORKAMBI, especially in patients who have poor lung function. If your child has poor lung function, your child's doctor may monitor him or her more closely when starting ORKAMBI.

An increase in blood pressure in some people receiving ORKAMBI. Your child's doctor should monitor your child's blood pressure during treatment with ORKAMBI.

Abnormality of the eye lens (cataract) in some children and adolescents receiving ORKAMBI. Your child's doctor should perform eye examinations before and during treatment with ORKAMBI to look for cataracts.

The most common side effects of ORKAMBI include:

- breathing problems such as shortness of breath and chest tightness
- nausea
- diarrhea
- fatigue
- increase in a certain blood enzyme called creatine phosphokinase
- rash
- gas
- common cold, including sore throat, stuffy or runny nose
- flu or flu-like symptoms
- irregular, missed, or abnormal periods (menses) and increase in the amount of menstrual bleeding

Side effects seen in children are similar to those seen in adults and adolescents. Additional common side effects seen in children include:

- cough with sputum
- stuffy nose
- headache
- stomach pain
- increase in sputum

These are not all the possible side effects of ORKAMBI. Call your child's doctor for medical advice about side effects. You are encouraged to report side effects to FDA at 1-800-FDA-1088.

Please see additional Important Safety Information throughout brochure, and full Prescribing Information, including Patient Information.

Learn how to take ORKAMBI oral granules

Visit ORKAMBI.com for:

- A video demonstrating how to give your child ORKAMBI oral granules
- Suggestions for fat-containing foods

If you have any questions about ORKAMBI, be sure to talk with your or your child's healthcare provider.

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