

Consumer Medicine Information

What is in this leaflet

This leaflet answers some of the more common questions about ORKAMBI.

It does not contain all of the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking ORKAMBI against the benefits he/she expects it will have for you.

If you have any concerns or questions about taking this medicine, ask your doctor or pharmacist.

Keep this leaflet with your medicine.

You may need to read it again.

What ORKAMBI is used for

ORKAMBI is for the chronic treatment of cystic fibrosis (CF) in patients age 2 years and older who have two copies of the F508del mutation in the CFTR gene.

What is cystic fibrosis?

Cystic fibrosis is caused by genetic defects that limit the flow of chloride and water through cell membranes. As a result, the mucus in the lungs (and other organs) becomes thick and sticky, clogs the lungs and makes it easier for germs to grow. ORKAMBI is a medicine that works by improving the flow of chloride and water in patients with

cystic fibrosis who have a certain genetic defect.

How ORKAMBI works

ORKAMBI belongs to a group of medicines called “cystic fibrosis transmembrane conductance regulator (CFTR) modulators.”

The CFTR protein is a chloride ion channel that is normally present at the cell surface of epithelial cells where it transports chloride ions out of the cell in multiple organs. In people who have two copies of the F508del mutation in the CFTR gene, the amount of CFTR protein at the cell surface is much lower than normal. The small amount of CFTR protein that reaches the cell surface does not function properly, as the chloride ion channel remains closed more often than normal.

ORKAMBI is a combination product that contains:

- a CFTR corrector (lumacaftor), which increases the amount of working CFTR at the cell surface
- and a CFTR potentiator (ivacaftor), which makes the CFTR protein at the cell surface function better because the chloride ion channel is open more often.

ORKAMBI therefore allows more chloride ions to get transported out of cells in multiple organs.

ORKAMBI is not addictive.

Before you take ORKAMBI

When you must not take it

Do not take ORKAMBI if you have an allergy to:

- any medicine containing lumacaftor or ivacaftor, the active ingredients in ORKAMBI.
- any of the other ingredients listed at the end of this leaflet.

Some of the symptoms of an allergic reaction may include:

- shortness of breath
- wheezing or difficulty breathing
- swelling of the face, lips, tongue or other parts of the body
- rash, itching or hives on the skin

Do not take this medicine after the expiry date printed on the pack or if the packaging is torn or shows signs of tampering.

If the medicine has expired or the packaging is damaged, return it to your pharmacist for disposal.

Before you start to take it

Tell your doctor if you have allergies to any other medicines, foods, preservatives, or dyes.

Talk to your doctor if you have been told you have liver disease.

Worsening of liver function has been seen in patients with severe liver disease and can be serious or fatal.

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

Respiratory events such as shortness of breath or chest tightness were seen in patients when starting ORKAMBI, especially in patients who have poor lung function. If you have poor lung function, your doctor may monitor you more closely when you start ORKAMBI.

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

If you are pregnant or plan to become pregnant, ask your doctor for advice before taking this medicine.

Your doctor will help you decide what is best for you.

If you are breast-feeding or plan to breast-feed, ask your doctor for advice before taking this medicine.

It is unknown whether ORKAMBI is excreted in human milk. If you plan to breast-feed, ask your doctor for advice before taking ORKAMBI.

If you are using or plan to use hormonal birth control (oral, injectable, skin patches, and implantable products), ask your doctor for advice before taking this medicine.

This type of birth control may not work while taking ORKAMBI.

Do not give ORKAMBI to children under 2 years of age.

The safety and efficacy of this medicine in children under 2 years of age have not been established.

Abnormality of the eye lens (cataract) without any effect on vision has been noted in some children receiving ORKAMBI.

Your doctor may perform eye examinations before and during treatment with ORKAMBI.

Taking other medicines

Tell your doctor or pharmacist if you are taking any other medicines, including:

- all prescription medicines
- all medicines, vitamins, herbal supplements, or natural therapies you buy without a prescription from a pharmacy, supermarket, naturopath, or health food shop.

Some medicines may be affected by ORKAMBI or may affect how well it works. You may need different amounts of your medicines, or you may need to take different medicines. Your doctor will advise you.

Take ORKAMBI with fat-containing food.

Tell your doctor or pharmacist if you are taking any of the following:

- Antifungal medicines (used for the treatment of fungal infections): ketoconazole, itraconazole, posaconazole, voriconazole, fluconazole
- Antibiotic medicines (used for the treatment of bacterial infections): telithromycin, clarithromycin, erythromycin, rifampicin, rifabutin
- Anticonvulsant medicines (used for the treatment of epileptic seizures): phenobarbital, carbamazepine, phenytoin
- Herbal medicines: St. John's wort (*Hypericum perforatum*)
- Benzodiazepines (used for the treatment of anxiety, insomnia, agitation, etc.): midazolam, triazolam
- Immunosuppressants (used after an organ transplantation): ciclosporin, everolimus, sirolimus, tacrolimus

- Cardiac glycosides (used for the treatment of mild to moderate congestive heart failure and an abnormal heart rhythm called atrial fibrillation): digoxin
- Anticoagulants (used to prevent blood clots from forming or growing larger in blood and blood vessels): warfarin
- Hormonal contraceptives (used to prevent pregnancy): 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): prednisone
- Antidepressants (used to treat depression): citalopram, escitalopram, sertraline
- Oral hypoglycaemics (used to treat type 2 diabetes): repaglinide, sulfonyleurea
- Proton pump inhibitors (used to treat acid reflux disease and ulcers): omeprazole, esomeprazole, lansoprazole

Your doctor or pharmacist has more information on medicines to be careful with or to avoid while taking ORKAMBI.

Ask your doctor or pharmacist if you are not sure about this list of medicines.

Laboratory Testing

Your doctor will do some blood tests to check your liver prior to and while you are taking ORKAMBI, particularly during the first year (every 3 months), and once a year after that.

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

If you have had abnormal blood tests of the liver in the past, your

doctor may order blood tests to test your liver more often.

Talk to your doctor if you have been told you have liver or kidney disease or if you are taking any other medicine, as your doctor may need to adjust the dose of ORKAMBI.

How to take ORKAMBI

Follow all directions given to you by your doctor and pharmacist carefully.

These directions may differ from the information contained in this leaflet.

How much to take

Your doctor will tell you how much ORKAMBI you need to take each day. This may depend on your condition and whether or not you are taking any other medicines.

The recommended dose for patients 2 years and over are as follows:

- **Patients aged 2 to 5 years and weighing less than 14 kg:**
One sachet of 100 mg lumacaftor/125 mg ivacaftor granules taken orally every 12 hours (total daily dose of 200mg lumacaftor/ 250mg ivacaftor).
- **Patients aged 2 to 5 years and weighing greater than 14 kg:**
One sachet of 150 mg lumacaftor/ 188 mg ivacaftor granules taken orally every 12 hours (total daily dose of 300 mg lumacaftor/ 376 mg ivacaftor).
- **Patients aged 6 to 11 years:**
Two tablets (100 mg lumacaftor/125 mg ivacaftor in each tablet) taken orally every 12 hours (total number of tablets is 4 per day for a total of 400 mg lumacaftor/500 mg ivacaftor).
- **Patients aged 12 years and older:**
Two tablets (200 mg lumacaftor/125 mg ivacaftor in each tablet) taken orally every

12 hours (the total number of tablets is 4 per day for a total of 800 mg lumacaftor/500 mg ivacaftor).

If you have liver problems, your doctor may need to reduce the dose.

How to take it

Orkambi is for oral use.

Tablets

Take 2 tablets of ORKAMBI every 12 hours by mouth with a fat-containing meal or snack.

Granules

Each sachet is for single use only. Take one sachet of ORKAMBI every 12 hours.

Giving ORKAMBI to your child:

- Hold sachet of granules with cut line on top.
- Shake sachet gently to settle contents.
- Tear or cut sachet open along cut line.
- Mix the entire content of a sachet with 5 mL of age-appropriate soft food or liquid. Food or liquid should be at room temperature or below. Some examples of age-appropriate soft foods or liquids include puréed fruits or vegetables, yogurt, applesauce, water, milk, or juice.
- Once mixed, give the product to your child immediately. If this is not possible, give it within one hour after mixing. Ensure that the mixture is completely and immediately consumed.
- A fat-containing meal or snack should be given to your child just before or just after dosing.

Meals and snacks recommended in CF guidelines or meals recommended in standard nutritional guidelines contain adequate amounts of fat. Examples of meals or snacks that contain fat are those prepared with butter or oils or those containing eggs, cheeses, nuts, chocolate, whole milk, whole-milk dairy products,

meats, avocados, oily fish, and soy-based products (tofu).

Taking ORKAMBI with fat-containing food is important to get the right levels of medicine in your body.

ORKAMBI is always given in combination with the medicines you usually use.

You must keep using all your medicines unless your doctor tells you to stop using any of them.

How long to take it

Take ORKAMBI for as long as your doctor tells you.

Your doctor will determine if your treatment should be stopped.

If you forget to take it

Take the missed dose if less than 6 hours have passed since the time you should have taken the dose. Otherwise, wait until your next scheduled dose as you normally would.

Do not take a double dose to make up for the dose that you missed.

This may increase the chance of you getting an unwanted side effect.

If you are not sure what to do, talk to your doctor or pharmacist.

If you take too much (overdose)

Immediately telephone your doctor or the Poisons Information Centre (telephone Australia 13 11 26) for advice, or go to the Emergency Department at the nearest hospital, if you think that you or anyone else may have taken too much ORKAMBI. Do this even if there are no signs of discomfort or poisoning.

You may need urgent medical attention.

While you are taking ORKAMBI

Things you must do

Keep all of your doctor's appointments so that your progress can be checked.

Use ORKAMBI exactly how your doctor has prescribed.

Take ORKAMBI with fat-containing food.

Tell all doctors, dentists, and pharmacists who are treating you that you are using ORKAMBI.

Tell your doctor if you become pregnant while using ORKAMBI.

Tell your doctor if, for any reason, you have not used ORKAMBI exactly as prescribed.

Things you must not do

Do not stop using ORKAMBI or change the dose without first checking with your doctor.

Do not let yourself run out of medicine over the weekend or on holidays.

Do not give ORKAMBI to anyone else even if they have the same condition as you.

Do not use ORKAMBI to treat other complaints unless your doctor tells you to.

Do not take any other medicines whether they require a prescription or not without first telling your doctor or consulting a pharmacist.

Things to be careful of

Be careful driving or operating machinery until you know how ORKAMBI affects you.

Side effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking ORKAMBI.

All medicines can have side effects. Sometimes they are serious, most of

the time they are not. You may need medical treatment if you get some of the side effects.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor or pharmacist if you notice any of the following and they worry you:

Very common side effects (may affect more than 1 in 10 people)

- shortness of breath
- diarrhoea
- nausea

Common side effects (may affect up to 1 in 10 people)

- chest tightness
- sore throat
- upper respiratory tract infection
- gas
- rash
- stuffy or runny nose
- vomiting
- irregular periods (menses) or pain with menses

Uncommon side effects (may affect up to 1 in 100 people)

- abnormal periods, including the absence or infrequent menses, or more frequent or heavier menstrual bleeding
- increase in blood pressure

Additional side effects in children

Very common side effects (may affect more than 1 in 10 people):

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

Tell your doctor immediately or go to the Emergency Department at your nearest hospital if you notice any of the following:

- significant 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

These may be indicative of serious side effects. You may need urgent medical attention. Serious side effects are uncommon (may affect up to 1 in 100 people).

This is not a complete list of all possible side effects. Your doctor or pharmacist has a more complete list. Others may occur in some people and there may be some side effects not yet known.

Tell your doctor if you notice anything else that is making you feel unwell, even if it is not on this list.

Other side effects not listed above may also occur in some people.

After taking ORKAMBI

Storage

Store below 30°C. Keep this medicine out of the sight and reach of children.

Disposal

If your doctor tells you to stop using ORKAMBI or ORKAMBI has passed its expiry date, ask your pharmacist what to do with any medicine that is left over.

Product description

Availability

Tablets

ORKAMBI tablets are available in the following pack sizes:

- 112-count tablet box (contains a 4-week supply in 4 weekly cartons of 7 daily blister strips with 4 tablets per strip)

ORKAMBI tablets are available in the following strength:

- 200 mg of lumacaftor and 125 mg of ivacaftor

- 100 mg of lumacaftor and 125 mg of ivacaftor

Granules

ORKAMBI granules are available in the following pack size:

- 56 sachets (containing 4 individual wallets with 14 sachets per wallet)

ORKAMBI granules are available in the following strengths:

- 100 mg of lumacaftor and 125 mg of ivacaftor
- 150 mg of lumacaftor and 188 mg of ivacaftor

What does ORKAMBI look like

ORKAMBI 200/125 mg Tablets

Pink, oval-shaped tablets, printed with "2V125" in black ink on one side and plain on the other.

ORKAMBI 100/125 mg Tablets

Pink, oval-shaped tablets, printed with "1V125" in black ink on one side and plain on the other.

Granules

White to off-white granules enclosed in unit dose sachets

Ingredients

Active ingredients

ORKAMBI 200/125 mg Tablets

- lumacaftor 200 mg
- ivacaftor 125 mg

ORKAMBI 100/125 mg Tablets

- lumacaftor 100 mg
- ivacaftor 125 mg

ORKAMBI 100/125 mg Granules (per sachet)

- lumacaftor 100 mg
- ivacaftor 125 mg

ORKAMBI 150/188 mg Granules (per sachet):

- lumacaftor 150 mg
- ivacaftor 188 mg

Inactive ingredients

Tablets

- microcrystalline cellulose;
- croscarmellose sodium;

hypromellose acetate succinate; povidone; sodium lauryl sulfate; magnesium stearate; Opadry II Pink 85F140026 (PI# 110227); Opacode monogramming ink S-1-17823 BLACK (PI# 12108)

Granules

- microcrystalline cellulose;
- croscarmellose sodium;
- hypromellose acetate succinate;
- povidone; sodium lauryl sulfate.

Sponsor

Vertex Pharmaceuticals (Australia) Pty Ltd
Suite 3, Level 3
601 Pacific Highway
St Leonards NSW 2065
Australia

ARTG Number

200/125 mg film-coated tablets
blister pack
AUST R 235759

100/125 mg film-coated tablets
blister pack
AUST R 289715

100/ 125mg granules in sachet
AUST R 305011

150/188mg granules in sachet
AUST R 305012

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