

Package leaflet: Information for the patient

Kalydeco 75 mg film-coated tablets Kalydeco 150 mg film-coated tablets ivacaftor

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Kalydeco is and what it is used for
2. What you need to know before you take Kalydeco
3. How to take Kalydeco
4. Possible side effects
5. How to store Kalydeco
6. Contents of the pack and other information

1. What Kalydeco is and what it is used for

Kalydeco contains the active ingredient ivacaftor. Ivacaftor acts at the level of the cystic fibrosis transmembrane conductance regulator (CFTR), a protein that forms a channel at the cell surface that allows the movement of particles such as chloride in and out of the cell. Due to mutations in the *CFTR* gene (see below), chloride movement is reduced in those with cystic fibrosis (CF). Ivacaftor helps certain abnormal CFTR proteins open more often to improve chloride movement in and out of the cell.

Kalydeco tablets are indicated:

- As monotherapy for patients aged 6 years and older and weighing 25 kg or more with cystic fibrosis (CF) who have an *R117H* *CFTR* mutation or one of the following gating mutations in the *CFTR* gene: *G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *S1251N*, *S1255P*, *S549N* or *S549R*.
- In combination with tezacaftor/ivacaftor tablets for patients aged 6 years and older with CF who have two *F508del* mutations in the *CFTR* gene (homozygous for the *F508del* mutation) or who have an *F508del* mutation and certain other second mutations that result in reduced amount and/or function of the CFTR protein (heterozygous for the *F508del* mutation with a residual function (RF) mutation). If you have been prescribed Kalydeco to be taken with tezacaftor/ivacaftor, read the package leaflet of the latter. It contains important information about how to take these two medicines.
- In combination with ivacaftor/tezacaftor/elexacaftor tablets for patients aged 12 years and over who have CF, with at least one *F508del* mutation in the *CFTR* gene. If you have been prescribed Kalydeco to be taken with ivacaftor/tezacaftor/elexacaftor, read the package leaflet of the latter. It contains important information about how to take these two medicines.

2. What you need to know before you take Kalydeco

Do not take Kalydeco

- if you are allergic to ivacaftor or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- Talk to your doctor if you have liver problems or have previously had them. Your doctor may need to adjust your dose.
- Increased liver enzymes in the blood have been seen in some people receiving Kalydeco (alone or in combination with tezacaftor/ivacaftor or ivacaftor/tezacaftor/elexacaftor). 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 the skin or the white part of the eyes
 - Loss of appetite
 - Nausea or vomiting
 - Dark urine

Your doctor will do some blood tests to check your liver before and during treatment, particularly during the first year and especially if your blood tests showed high liver enzymes in the past.

- Talk to your doctor if you have kidney problems or have previously had them.
- Kalydeco (alone or in combination with tezacaftor/ivacaftor or ivacaftor/tezacaftor/elexacaftor) is not recommended if you have undergone an organ transplant.
- Talk to your doctor if you are using hormonal contraception – for example, women using the contraceptive pill. This may mean you are more likely to get a rash while taking Kalydeco in combination with ivacaftor/tezacaftor/elexacaftor.
- Abnormality of the eye lens (cataract) without any effect on vision has been noted in some children and adolescents treated with Kalydeco (alone or in combination with tezacaftor/ivacaftor or ivacaftor/tezacaftor/elexacaftor). Your doctor may perform some eye examinations prior to and during treatment.
- Kalydeco (alone or in combination with tezacaftor/ivacaftor or ivacaftor/tezacaftor/elexacaftor) should only be used if you have one of the mutations in the *CFTR* gene indicated in section 1 (What Kalydeco is and what it is used for).

Children and adolescents

Do not give this medicine to children under 4 months of age as it is not known if ivacaftor is safe and effective in these children.

Do not give this medicine in combination with tezacaftor/ivacaftor to children under 6 years of age or in combination with ivacaftor/tezacaftor/elexacaftor to children under 12 years of age as it is not known if they are safe and effective for them.

Other medicines and Kalydeco

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. Some medicines can affect how Kalydeco works or make side effects more likely. In particular, tell your doctor if you are taking any of the medicines listed below. Your doctor may decide to adjust your dose or that you need extra check-ups.

- **Antifungal medicines** (used for the treatment of fungal infections). These include fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole.
- **Antibiotic medicines** (used for the treatment of bacterial infections). These include clarithromycin, erythromycin, rifabutin, rifampicin, and telithromycin .
- **Epilepsy medicines** (used for the treatment of epileptic seizures or fits). These include carbamazepine, phenobarbital, and phenytoin.
- **Herbal medicines.** These include St. John's wort (*Hypericum perforatum*).
- **Immunosuppressants** (used after an organ transplantation). These include ciclosporin, everolimus, sirolimus, and tacrolimus.
- **Cardiac glycosides** (used for the treatment of some heart conditions). These include digoxin.
- **Anticoagulant medicines** (used to prevent blood clots). These include warfarin.
- **Medicines for diabetes.** These include glimepiride and glipizide.
- **Medicines for lowering blood pressure.** These include verapamil.

Kalydeco with food and drink

Avoid food or drink containing grapefruit during treatment with Kalydeco as they may increase the side effects of Kalydeco by increasing the amount of ivacaftor in your body.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. It may be better to avoid using Kalydeco during pregnancy, if possible, and your doctor will help you decide what is best for you and your child.

It is unknown whether ivacaftor is excreted in human milk. If you plan to breast-feed, ask your doctor for advice before taking Kalydeco. Your doctor will decide whether to recommend that you stop breast-feeding or for you to stop ivacaftor therapy. Your doctor will take into account the benefit of breast-feeding for the child and the benefit of therapy for you.

Driving and using machines

Kalydeco can make you dizzy. If you feel dizzy, do not drive, cycle or use machines.

Important information about the contents of Kalydeco

Kalydeco contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Kalydeco contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to take Kalydeco

Always take this medicine exactly as your doctor has told you to. Check with your doctor if you are not sure.

Your doctor will determine which medicine and dose is right for you.

Kalydeco dosing recommendations are provided in Table 1.

Table 1: Dosing recommendations

	Morning	Evening
Kalydeco as monotherapy		
6 years and older, ≥ 25 kg	One Kalydeco 150 mg tablet	One Kalydeco 150 mg tablet
Kalydeco in combination with tezacaftor/ivacaftor		
6 years to less than 12 years, < 30 kg	One tezacaftor 50 mg/ivacaftor 75 mg tablet	One Kalydeco 75 mg tablet
6 years to less than 12 years, ≥ 30 kg	One tezacaftor 100 mg/ivacaftor 150 mg tablet	One Kalydeco 150 mg tablet
12 years and older	One tezacaftor 100 mg/ivacaftor 150 mg tablet	One Kalydeco 150 mg tablet
Kalydeco in combination with ivacaftor/tezacaftor/elexacaftor		
12 years and older	Two ivacaftor 75 mg/tezacaftor 50 mg/elexacaftor 100 mg tablets	One Kalydeco 150 mg tablet

Take the morning and evening doses approximately 12 hours apart with food that contains fat.

You must keep using all other medicines you use, unless your doctor tells you to stop using any.

If you have liver problems, either moderate or severe, your doctor may need to reduce the dose of your tablets, because your liver will not clear the medicine as fast as in people who have normal liver function.

This medicine is for oral use.

Swallow the tablet whole. Do not break, chew or dissolve the tablets. Take Kalydeco tablets with food that contains fat.

Meals or snacks that contain fat include those prepared with butter or oils or those containing eggs.

Other fat-containing foods are:

- Cheese, whole milk, whole-milk dairy products, yogurt, chocolate
- Meats, oily fish
- Avocados, hummus, soy-based products (tofu)
- Nuts, fat-containing nutritional bars or drinks

If you take more Kalydeco than you should

You may experience side effects, including those mentioned in section 4 below. If so, contact your doctor or pharmacist to ask for advice. If possible, have your medicine and this leaflet with you.

If you forget to take Kalydeco

Take the missed dose if less than 6 hours have passed since the time you missed the dose. Otherwise, wait until your next scheduled dose as you normally would. Do not take a double dose to make up for a forgotten dose.

If you stop taking Kalydeco

Take Kalydeco for as long as your doctor recommends. Do not stop unless your doctor advises you to. If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

Serious side effects

Stomach (abdominal) ache and increased liver enzymes in the blood.

Possible signs of liver problems

Increased liver enzymes in the blood are common in patients with CF. These may be signs of liver problems:

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

Tell your doctor straight away if you get any of these.

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

- Upper respiratory tract infection (the common cold), including sore throat and nasal congestion
- Headache
- Dizziness
- Diarrhoea
- Stomach or abdominal pain
- Changes in the type of bacteria in mucus
- Increased liver enzymes (signs of stress on the liver)
- Rash

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

- Runny nose
- Ear pain, ear discomfort
- Ringing in the ears
- Redness inside the ear
- Inner ear disorder (feeling dizzy or spinning)
- Sinus problems (sinus congestion)
- Redness in the throat
- Breast mass
- Feeling sick (nausea)
- Flu
- Low blood sugar (hypoglycaemia)
- Abnormal breathing (shortness of breath or difficulty breathing)
- Wind (flatulence)
- Spots (acne)
- Itchy skin
- Increased creatine phosphokinase (sign of muscle breakdown) seen in blood tests

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

- Ear congestion
- Breast inflammation
- Enlargement of the breast in males
- Nipple changes or pain
- Wheezing
- Increased blood pressure

Additional side effects in children and adolescents

Side effects seen in children and adolescents are similar to those observed in adults. However, increased liver enzymes in the blood are more frequently seen in young children.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting systems:

Ireland

HPRA Pharmacovigilance

Website: www.hpra.ie

United Kingdom (Northern Ireland)

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Kalydeco

Keep this medicine out of the sight and reach of children.

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

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Kalydeco contains

The active substance is ivacaftor.

Kalydeco 75 mg film-coated tablets

Each 75 mg film-coated tablet contains 75 mg of ivacaftor.

Kalydeco 150 mg film-coated tablets

Each 150 mg film-coated tablet contains 150 mg of ivacaftor.

The other ingredients are:

- Tablet core: cellulose microcrystalline, lactose monohydrate, hypromellose acetate succinate, croscarmellose sodium, sodium laurilsulfate (E487), silica, colloidal anhydrous, and magnesium stearate.
- Coating: polyvinyl alcohol, titanium dioxide (E171), macrogol (PEG 3350), talc, indigo carmine aluminium lake (E132) and carnauba wax.
- Printing ink: shellac, iron oxide black (E172), propylene glycol (E1520) and ammonia solution, concentrated.

See the end of section 2 - Important information about the contents of Kalydeco.

What Kalydeco looks like and contents of the pack

Kalydeco 75 mg film-coated tablets are light blue, capsule-shaped, 12.7 mm x 6.8 mm, and printed with “V 75” in black ink on one side and plain on the other side.

The following pack sizes are available:

- Blister card pack containing 28 film-coated tablets

Kalydeco 150 mg film-coated tablets are light blue, capsule-shaped, 16.5 mm x 8.4 mm, and printed with “V 150” in black ink on one side and plain on the other.

The following pack sizes are available:

- Blister card pack containing 28 film-coated tablets
- Blister pack containing 56 film-coated tablets
- Bottle containing 56 film-coated tablets

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website:

<http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.