

Package leaflet: Information for the patient

Kalydeco 25 mg granules in sachet
Kalydeco 50 mg granules in sachet
Kalydeco 75 mg granules in sachet
ivacaftor

Read all of this leaflet carefully before your child starts taking this medicine because it contains important information for your child.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your child's doctor or pharmacist.
- This medicine has been prescribed for your child only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as your child's.
- If your child gets any side effects, talk to your child's 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 your child takes 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 granules are indicated for the treatment of babies and children aged 4 months and older and weighing 5 kg to less than 25 kg 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*.

2. What you need to know before your child takes Kalydeco

Do not take Kalydeco

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

Warnings and precautions

- Talk to your child's doctor if your child has liver problems or has had them previously. Your child's doctor may need to adjust your child's dose.
- Increased liver enzymes in the blood have been seen in some people receiving Kalydeco. Tell your child's doctor right away if your child has 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 child's doctor will do some blood tests to check your child's liver before and during treatment, particularly during the first year and especially if blood tests showed high liver enzymes in the past.

- Talk to your child's doctor if you have been told your child has kidney problems or has previously had them.
- Kalydeco is not recommended for patients who have undergone an organ transplant.
- Abnormality of the eye lens (cataract) without any effect on vision has been noted in some children and adolescents during treatment.
Your child's doctor may perform some eye examinations prior to and during treatment with ivacaftor.

Children

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.

Other medicines and Kalydeco

Tell your child's doctor or pharmacist if your child is using, has 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 child's doctor if your child is taking any of the medicines listed below. Your child's doctor may decide to adjust your child's dose or if extra check-ups are needed.

- **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 giving your child 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 child's body.

Driving and using machines

Kalydeco can make your child dizzy. If your child feels dizzy, it is advised that your child does not ride his/her bike or do anything else that needs his/her full attention.

Important information about the contents of Kalydeco

Kalydeco contains lactose. If you have been told by your child's doctor that your child has an intolerance to some sugars, contact your child's doctor before your child takes 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 give your child this medicine exactly as your child's doctor has told you to. Check with your child's doctor if you are not sure.

Your child's doctor will determine the correct dose for your child. Your child must keep using all other medicines, unless your child's doctor tells him/her to stop using any.

Kalydeco dosing recommendations are provided in Table 1.

Table 1: Dosing recommendations for children aged 4 months and older

Age	Weight	Dose	Total daily dose
4 months to less than 6 months	5 kg or more	One sachet of 25 mg granules taken orally every 12 hours with fat-containing food	50 mg
6 months and older	5 kg to less than 7 kg	One Kalydeco sachet of 25 mg granules taken orally every 12 hours with fat-containing food	50 mg
	7 kg to less than 14 kg	One Kalydeco sachet of 50 mg granules taken orally every 12 hours with fat-containing food	100 mg
	14 kg to less than 25 kg	One Kalydeco sachet of 75 mg granules taken orally every 12 hours with fat-containing food	150 mg
	25 kg or more	Please refer to Kalydeco tablets Package Leaflet	

If your child has liver problems, your child's doctor may need to reduce the dose of Kalydeco as your child's liver will not clear the medicine as fast as in children who have normal liver function.

- **Moderate liver problems in children 6 months of age or older:** the dose may be reduced to one half of the indicated dose in the table above, that is one sachet once daily.
- **Severe liver problems in children 6 months of age or older:** the use is not recommended but your child's doctor will decide if it is appropriate for your child to use this medicine in which case the dose (as indicated in the table above) must be reduced to one sachet every other day.
- **Liver problems in children between 4 months and 6 months of age:** the use is not recommended but your child's doctor will decide if it is appropriate for your child to use and what dose your child should have.

Kalydeco is for oral use.

Each sachet is for single use only.

Giving Kalydeco 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, breast milk, infant formula, or juice.
- Once mixed, give the product to your child immediately. If this is not possible, give it within the following 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 (some examples are provided below).

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, breast milk, infant formula, chocolate
- Meats, oily fish
- Avocados, hummus, soy-based products (tofu)
- Nuts, fat-containing nutritional bars or drinks

If your child takes more Kalydeco than he/she should

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

If you forget to give your child Kalydeco

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

If you stop giving your child Kalydeco

Give Kalydeco to your child for as long as your child's doctor recommends. Do not stop unless your child's doctor advises you to. If you have any further questions on the use of this medicine, ask your child's 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 child's doctor straight away if he/she gets 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
- Rash
- Changes in the type of bacteria in mucus

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 congestion
- Redness in the throat
- Breast mass

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

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 your child gets any side effects, talk to your child's 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.

Once mixed, the mixture has been shown to be stable for one hour.

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

Kalydeco 25 mg granules in sachet:

The active substance is ivacaftor. Each sachet contains 25 mg of ivacaftor.

Kalydeco 50 mg granules in sachet:

The active substance is ivacaftor. Each sachet contains 50 mg of ivacaftor.

Kalydeco 75 mg granules in sachet:

The active substance is ivacaftor. Each sachet contains 75 mg of ivacaftor.

The other ingredients are: silica, colloidal anhydrous, croscarmellose sodium, hypromellose acetate succinate, lactose monohydrate, magnesium stearate, mannitol, sucralose and sodium laurilsulfate (E487).

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

What Kalydeco looks like and contents of the pack

Kalydeco 25 mg granules in sachet are white to off-white granules.

Kalydeco 50 mg granules in sachet are white to off-white granules.

Kalydeco 75 mg granules in sachet are white to off-white granules.

The granules are supplied in sachets.

- Pack size of 56 sachets (contains 4 individual wallets with 14 sachets per wallet)

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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.