

Package leaflet: Information for the patient

Zykadia® 150 mg hard capsules ceritinib

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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

1. What Zykadia is and what it is used for

What Zykadia is

Zykadia is a cancer medicine that contains the active substance ceritinib. It is used to treat adults with advanced stages of a form of lung cancer called non-small cell lung cancer (NSCLC). Zykadia is only given to patients whose disease is due to a defect in a gene called ALK (anaplastic lymphoma kinase).

How Zykadia works

In patients with ALK defects, an abnormal protein is produced that stimulates the growth of the cancer cells. Zykadia blocks the action of this abnormal protein and thus slows down the growth and spread of NSCLC.

If you have any questions about how Zykadia works or why this medicine has been prescribed for you, ask your doctor or pharmacist.

2. What you need to know before you take Zykadia

Do not take Zykadia:

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

Warnings and precautions

Talk to your doctor or pharmacist before taking Zykadia:

- if you have problems with your liver.
- if you have problems with your lungs or problems breathing.
- if you have problems with your heart, including reduced heart rate, or if the results of an electrocardiogram (ECG) have shown that you have an abnormality of the electrical activity of

- your heart known as “prolonged QT interval”.
- if you have diabetes (high level of sugar in your blood).
 - if you have problems with your pancreas.
 - if you are currently taking steroids.

Tell your doctor or pharmacist immediately if you get any of the following signs or symptoms during treatment with Zykadia:

- tiredness, itchy skin, yellowing of your skin or the whites of your eyes, nausea (feeling sick) or vomiting, decreased appetite, pain on the right side of your abdomen (belly), dark or brown urine, bleeding or bruising more easily than normal. These may be signs or symptoms of liver problems.
- new or worsening cough with or without mucus, fever, chest pain, trouble breathing or shortness of breath. These may be symptoms of lung problems.
- chest pain or discomfort, changes in your heartbeat (fast or slow), light-headedness, fainting, dizziness, blue discoloration of your lips, shortness of breath, swelling of your lower limbs or skin. These may be signs or symptoms of heart problems.
- severe diarrhoea, nausea or vomiting. These are symptoms of digestive problems.
- excessive thirst or increased frequency of urination. These may be symptoms of a high level of sugar in the blood.

Your doctor may need to adjust your treatment or stop Zykadia temporarily or permanently.

Blood tests during treatment with Zykadia

Your doctor should perform blood tests before you start treatment, every 2 weeks during the first three months of treatment and monthly thereafter. The purpose of these tests is to check your liver function. Your doctor should also perform blood tests to check the functioning of your pancreas and the level of sugar in your blood before you start treatment with Zykadia and regularly during treatment.

Children and adolescents

The use of Zykadia in children and adolescents up to 18 years of age is not recommended.

Other medicines and Zykadia

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription such as vitamins or herbal supplements, because they might interact with Zykadia. It is particularly important that you mention any of the following medicines.

Medicines which may increase the risk of side effects with Zykadia:

- medicines used to treat AIDS/HIV (e.g. ritonavir, saquinavir).
- medicines used to treat infections. These include medicines that treat fungal infections (antifungals such as ketoconazole, itraconazole, voriconazole, posaconazole) and medicines that treat certain types of bacterial infection (antibiotics such as telithromycin).

The following medicines may reduce the effectiveness of Zykadia:

- St. John’s Wort, a herbal medicine used to treat depression.
- medicines used to stop seizures or fits (anti-epileptics such as phenytoin, carbamazepine, or phenobarbital).
- medicines used to treat tuberculosis (e.g. rifampicin, rifabutin).

Zykadia may increase the side effects associated with the following medicines:

- medicines used to treat irregular heartbeat or other heart problems (e.g. amiodarone, disopyramide, procainamide, quinidine, sotalol, dofetilide, ibutilide and digoxin).
- medicines used to treat stomach problems (e.g. cisapride).
- medicines used to treat mental health problems (e.g. haloperidol, droperidol, pimozide).
- medicines used to treat depression (e.g. nefazodone).
- midazolam, a medicine used to treat acute seizures or as a sedative before or during surgery or

- medical procedures.
- warfarin and dabigatran, medicines used to prevent blood clots.
 - diclofenac, a medicine used to treat joint pain and inflammation.
 - alfentanil and fentanyl, medicines used to treat severe pain.
 - ciclosporin, sirolimus and tacrolimus, medicines used in organ transplantation to prevent transplant organ rejection.
 - dihydroergotamine and ergotamine, medicines used to treat migraine.
 - domperidone, a medicine used to treat nausea and vomiting.
 - moxifloxacin and clarithromycin, medicines used to treat bacterial infections.
 - methadone, a medicine used to treat pain and for the treatment of opioid dependence.
 - chloroquine and halofantrine, medicines used to treat malaria.
 - topotecan, a medicine used to treat certain types of cancer.
 - colchicine, a medicine used to treat gout.
 - pravastatine and rosuvastatine, medicines used to reduce cholesterol levels.
 - sulfasalazine, a medicine used to treat inflammatory bowel disease or rheumatoid arthritis.

Ask your doctor or pharmacist if you are not sure whether your medicine is one of the medicines listed above.

These medicines should be used with care or may need to be avoided during your treatment with Zykadia. If you are taking any of these, your doctor might need to prescribe an alternative medicine for you.

You should also tell your doctor if you are already taking Zykadia and you are prescribed a new medicine that you have not already taken at the same time as Zykadia.

Oral contraceptives

If you take Zykadia whilst using oral contraceptives, the oral contraceptives may become ineffective.

Zykadia with food and drink

You should not eat grapefruit or drink grapefruit juice during treatment. It may make the amount of Zykadia in your blood increase to a harmful level.

Pregnancy and breast-feeding

You must use a highly effective method of birth control during treatment with Zykadia and for 3 months after stopping treatment. Talk to your doctor about the birth control methods that may be right for you.

Zykadia is not recommended during pregnancy unless the potential benefit outweighs the potential risk to the baby. If you are pregnant, think you might be pregnant or plan to become pregnant, ask your doctor for advice. Your doctor will discuss with you the potential risks of taking Zykadia during pregnancy.

Zykadia should not be used during breast-feeding. You and your doctor will decide together whether you should breast-feed or take Zykadia. You should not do both.

Driving and using machines

You should take special care when driving and using machines when taking Zykadia as you may experience visual disturbances or tiredness.

3. How to take Zykadia

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

How much to take

The recommended dose is 450 mg (three capsules) taken once daily with food, although your doctor could modify this recommendation if needed. Your doctor will tell you exactly how many capsules you need to take. Do not change the dose without talking to your doctor.

- Take Zykadia once a day at about the same time each day with food (for example a snack or a full meal). If you cannot eat food while taking Zykadia, talk to your doctor.
- Swallow the capsules whole with water. Do not chew or crush them.
- If you vomit after you swallow the Zykadia capsules, do not take any more capsules until your next scheduled dose.

How long to take Zykadia

- Continue taking Zykadia for as long as your doctor tells you.
- This is a long-term treatment, possibly lasting for months. Your doctor will monitor your condition to see that the treatment is having the desired effect.

If you have questions about how long to take Zykadia, talk to your doctor or pharmacist.

If you take more Zykadia than you should

If you accidentally take too many capsules, or if someone else accidentally takes your medicine, contact a doctor or hospital for advice immediately. Medical treatment may be necessary.

If you forget to take Zykadia

What to do if you forget to take a dose depends on how long it is until your next dose.

- If your next dose is in 12 hours or more, take the missed capsules as soon as you remember. Then take the next capsules at the usual time.
- If your next dose is in less than 12 hours, skip the missed capsules. Then take the next capsules at the usual time.

Do not take a double dose to make up for a forgotten dose.

If you stop taking Zykadia

Do not stop taking this medicine before talking to your doctor. If you have any questions contact your doctor right away.

4. Possible side effects

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

STOP taking Zykadia and seek medical help immediately if you experience any of the following, which may be signs of an allergic reaction:

- Difficulty in breathing or swallowing
- Swelling of the face, lips, tongue or throat
- Severe itching of the skin, with a red rash or raised bumps

Some side effects could be serious

If you experience any of the following side effects, tell your doctor or pharmacist immediately:

- Chest pain or discomfort, changes in your heartbeat (fast or slow), light-headedness, fainting, dizziness, blue discoloration of your lips, shortness of breath, swelling of your lower limbs or skin (potential signs or symptoms of heart problems)
- New or worsening cough with or without mucus, fever, chest pain, trouble breathing or shortness of breath (potential signs of lung problems)
- Tiredness, itchy skin, yellowing of your skin or the whites of your eyes, nausea (feeling sick) or vomiting, decreased appetite, pain on the right side of your abdomen (belly), dark or brown urine, bleeding or bruising more easily than normal (potential signs or symptoms of liver problems)

- Severe diarrhoea, nausea or vomiting
- Excessive thirst, increased frequency of urination (symptoms of high level of glucose in the blood)
- Severe upper stomach pain (sign of inflammation of the pancreas, also known as pancreatitis)

Other possible side effects

Other side effects are listed below. If these side effects become severe, please tell your doctor or pharmacist.

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

- Tiredness (fatigue and asthenia)
- Abnormal results of blood tests to check liver function (high levels of enzymes called alanine aminotransferase and/or aspartate aminotransferase and/or gamma glutamyltransferase and/or blood alkaline phosphatase, high levels of bilirubin)
- Abdominal pain
- Decreased appetite
- Weight decreased
- Constipation
- Rash
- Abnormal results of blood tests to check kidney function (high level of creatinine)
- Heartburn (potential sign of a disorder of the digestive tract)
- Reduction in the number of red blood cells, known as anaemia

Common (may affect up to 1 in 10 people):

- Vision problems
- Low level of phosphate in the blood (this would be detected during blood tests)
- High level of enzymes called lipase and/or amylase in the blood (this would be detected during blood tests)
- Significantly decreased urine flow (potential sign of a kidney problem)

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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Ireland:	HPRA Pharmacovigilance Earlsfort Terrace IRL - Dublin 2 Tel: +353 1 6764971 Fax: +353 1 6762517 Website: www.hpra.ie e-mail: medsafety@hpra.ie
Malta:	ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal
United Kingdom	Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store Zykadia

- 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 carton and blister after EXP. The expiry date refers to the last day of that month.
- This medicine does not require any special storage conditions.
- Do not use this medicine if you notice any damage to the packaging or if there are any signs of tampering.

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 protect the environment.

6. Contents of the pack and other information

What Zykadia contains

- The active substance of Zykadia is ceritinib. Each hard capsule contains 150 mg of ceritinib.
- The other ingredients are:
 - Capsule contents: silica, colloidal anhydrous; hydroxypropylcellulose, low-substituted; sodium starch glycolate (type A); magnesium stearate; cellulose, microcrystalline.
 - Capsule shell: gelatin, indigotine (E132) and titanium dioxide (E171).
 - Printing ink: Shellac (bleached, de-waxed) glaze 45%, iron oxide black (E172), propylene glycol and ammonium hydroxide 28%.

What Zykadia looks like and contents of the pack

Zykadia hard capsules have a white opaque body and blue opaque cap, with “LDK 150MG” imprinted on the cap and “NVR” on the body. They contain white to almost white powder.

The capsules are provided in blisters and are available in packs containing 40, 90 or 150 (3 packs of 50) capsules. Not all pack sizes may be marketed in your country.

Marketing Authorisation Holder

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>