

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr ZYKADIA®

Ceritinib Capsules

Read this carefully before you start taking ZYKADIA® and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about ZYKADIA.

Serious Warnings and Precautions

ZYKADIA should be prescribed and used only under the supervision of a healthcare professional experienced with drugs used to treat cancer.

Serious side effects with ZYKADIA include:

- Heart problems (QT interval prolongation).
- Lung disorders, such as interstitial lung disease or pneumonitis. These may result in death.
- Liver problems.
- Gastrointestinal Reactions: Stomach and intestinal problems.

ZYKADIA has not been studied in patients with severe kidney problems who require dialysis.

What is ZYKADIA used for?

ZYKADIA is used to treat adult patients with anaplastic lymphoma kinase (ALK)-positive locally advanced (a cancer that cannot be surgically removed for cure) or metastatic (a cancer that has spread to other parts of the body) non-small cell lung cancer (NSCLC) who have progressed on (their cancer got worse) or who were intolerant to (unable to take) the drug crizotinib. Refer to the NOC/c summary box below for additional detail.

ZYKADIA is also used to treat adult patients with anaplastic lymphoma kinase (ALK)-positive locally advanced (a cancer that cannot be surgically removed for cure) or metastatic (a cancer that has spread to other parts of the body) non-small cell lung cancer (NSCLC).

It is not known whether ZYKADIA is safe and effective in children.

For the following indication ZYKADIA has been approved with conditions (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

- the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive locally advanced (a cancer that cannot be surgically removed for cure) or metastatic (a cancer that has spread to other parts of the body) non-small cell lung cancer (NSCLC) who have progressed on (their cancer got worse) or who were intolerant to (unable to take) the drug crizotinib.

For the following indication ZYKADIA has been approved without conditions. This means it has passed Health Canada's review and can be bought and sold in Canada.

- for the first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive locally advanced (a cancer that cannot be surgically removed for cure) or metastatic (a cancer that has spread to other parts of the body) non-small cell lung cancer (NSCLC).

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How does ZYKADIA work?

ZYKADIA belongs to a group of anti-tumor medicines which stop cancer from making new cells if the cancer is caused by a defect in a gene called anaplastic lymphoma kinase (ALK). ZYKADIA may slow down the growth and spread of non-small cell lung cancer (NSCLC).

What are the ingredients in ZYKADIA?

Medicinal ingredients: Ceritinib

Non-medicinal ingredients: black iron oxide; colloidal anhydrous silica; gelatin; indigotine; hydroxypropylcellulose, low-substituted; magnesium stearate; microcrystalline cellulose; sodium starch glycolate; titanium dioxide

ZYKADIA comes in the following dosage forms:

Capsules; 150 mg

Do not use ZYKADIA if:

- are allergic to ceritinib, or any non-medicinal ingredients in the formulation.
- have congenital long QT syndrome – a heart disorder that you were born with.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ZYKADIA. Talk about any health conditions or problems you may have, including if you:

- have/had problems with your liver.
- have/had diabetes or high blood sugar.
- have/had problems with your lungs or problems breathing.
- have/had problems with your heart, including a condition called long QT syndrome.
- have/had problems with your pancreas.
- have a history of fainting.

- have a family history of sudden cardiac death at less than 50 years of age.
- have electrolyte disturbances such as hypokalemia (low potassium in the blood), hypomagnesemia (low magnesium in the blood) or hypocalcemia (low calcium in the blood) or suffer from excessive vomiting or an eating disorder.
- are currently taking steroid medications.
- are pregnant, think you may be pregnant, or plan to become pregnant.
- are breast-feeding or plan to breast-feed.

Other warnings you should know about:

Women who might get pregnant (women of child-bearing age) and Males

Both men and women must use a highly effective method of birth control during treatment with ZYKADIA and for 3 months after stopping ZYKADIA. Talk to your healthcare professional about the birth control methods that may be right for you.

Pregnancy and breast-feeding

• **Pregnant women**

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

• **Breast-feeding mothers**

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

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ZYKADIA:

- Medicines used to treat irregular heart beat such as anti-arrhythmics: quinidine, amiodarone, disopyramide, procainamide, sotalol, ibutilide, dronedarone, flecainide, propafenone;
- Medicines used to stabilize thinking and behaviour, such as chlorpromazine, droperidol, haloperidol, ziprasidone;
- Medicines used to treat mood disorder such as fluoxetine, citalopram, venlafaxine, tricyclic/tetracyclic antidepressants (e.g. amitriptyline, imipramine, maprotiline, nefazodone) or medicines used to treat psychosis such as pimozide;
- Medicines used to prevent and treat pneumocystis carinii pneumonia such as pentamidine;
- Medicines used to treat malaria such as quinine, chloroquine;
- Medicines used to treat AIDS/HIV such as ritonavir or saquinavir;
- Medicines used to treat infections. These include medicines which treat fungal infections, such as antifungals like ketoconazole, itraconazole, fluconazole, voriconazole or posaconazole, or medicines which treat certain types of bacterial infections, such as antibiotics like azithromycin, moxifloxacin, levofloxacin, ciprofloxacin, erythromycin, clarithromycin, telithromycin, tacrolimus;
- Medicines that decrease electrolyte levels (water pills, laxatives);
- Pentamidine;
- Methadone;

- Medicines for nausea and vomiting such as ondansetron or medicines that may increase the motility in the upper gastrointestinal tract such as domperidone;
- Other cancer medicines such as vorinostat, sunitinib, nilotinib, lapatinib, and vandetanib;
- Medicines used to treat asthma such as formoterol and salmeterol;
- Arsenic trioxide- a natural product used to treat certain types of cancers;
- St. John's Wort - an herbal product used to treat depression and other conditions, also known as Hypericum perforatum;
- Medicines which stop seizures or fits (anti-epileptics such as phenytoin, carbamazepine, or phenobarbital);
- Medicines used to treat tuberculosis such as rifampin or rifabutin;
- Midazolam, a medicine used to treat acute seizures, or as a sedative before or during surgery or medical procedures;
- Warfarin, an anticoagulant medicine used to prevent blood clots;
- Diclofenac, a medicine used to treat joint pain and inflammation;
- Cyclosporine, tacrolimus and sirolimus, medicines used in organ transplantation to prevent transplant organ rejection;
- Dihydroergotamine and ergotamine, medicines used to treat migraine;
- Medicines used to treat heartburn and indigestion such as antacids and H2 blockers;
- Alfentanil and fentanyl, medicines used to treat severe pain.

Ask your healthcare professional if you are not sure whether your medicine is one of the medicines listed above.

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

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 healthcare professional might need to prescribe an alternative medicine for you.

You should also tell your healthcare professional if you are already taking ZYKADIA and you are prescribed a new medicine that you have not taken previously during treatment with ZYKADIA.

How to take ZYKADIA:

- Exactly as your healthcare professional has told you.
- Once a day at the same time each day.
- Take with food (for example a snack or full meal).
- Swallow whole with water. Do NOT chew or crush capsules.
- If vomiting occurs after you swallow ZYKADIA capsules, do not take any more until your next scheduled dose.

How long to take ZYKADIA

- Continue for as long as your healthcare professional tells you.
- This is a long-term treatment that might last for months. Your healthcare professional will monitor your condition to be sure that the treatment is having the desired effect.

If you have questions about how long to take ZYKADIA, talk to your healthcare professional.

Usual dose:

Maximum Recommended Dose: 450 mg once a day with food.

Do not change the dose without talking to your healthcare professional.

If you have certain side effects your healthcare professional may interrupt, decrease or stop ZYKADIA.

Dosing for Patients with Gastrointestinal Reactions: If you have diarrhea, nausea or vomiting your healthcare professional may lower your dose. This may help to decrease these problems.

Overdose:

If you think you, or a person you are caring for, have taken too much ZYKADIA, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose of ZYKADIA, take it as soon as you remember. If your next dose is due within 12 hours, then skip the missed dose. Just take the next dose at your regular time.

What are possible side effects from using ZYKADIA?

These are not all the possible side effects you may have when taking ZYKADIA. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- Diarrhea
- Nausea
- Vomiting
- Abdominal pain
- Tiredness, fatigue
- Decreased appetite
- Weight loss
- Constipation
- Heartburn, indigestion
- Difficulty swallowing
- Pain in the back or extremities (hands, arms, feet and legs)
- Rash
- Numbness and tingling in the hands and/or feet
- Vision problems

ZYKADIA can cause abnormal test results. You can especially get high blood sugar, bilirubin or liver enzymes. These can include alanine aminotransferase (ALT), aspartate aminotransferase (AST) gamma glutamyltransferase (GGT), or blood alkaline phosphatase.

Your healthcare professional should do tests, before you start and regularly during your treatment. They can monitor your blood pressure, heart rate by ECG. Blood tests can be used to check on your health and on the blood, liver and kidneys. Your healthcare professional will decide when to perform tests and will interpret the results.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Liver Disorder: yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite, itching skin			√
Anemia: fatigue, loss of energy, weakness, shortness of breath		√	
COMMON			
Heart disorders (Bradycardia, QT prolongation): ECG changes, irregular or slow heartbeat, heart palpitations, dizziness, fainting or loss of consciousness			√
Lung disorders (pneumonia, pneumonitis), respiratory failure: Cough, difficult or painful breathing, wheezing, pain in chest when breathing, fever. Increased breathing rate, sudden worsening of shortness of breath, bluish colour on skin, lips and fingernails. Irregular heartbeats, feel sleepy, loss of consciousness			√
Kidney Disorder: change in frequency of urination, nausea, vomiting, swelling of extremities, fatigue		√	
Increased blood sugar (hyperglycemia): frequent urination, thirst, and hunger		√	
Decreased levels of phosphate in the blood: muscle pain and weakness, altered mental state		√	
Convulsion: seizure, spasms, shaking or fits			√
Pericardial Effusion, pericarditis (fluid around the heart, inflammation of the lining surrounding the heart): Chest pain or pressure, shortness of breath, nausea, abdominal fullness,			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
difficulty swallowing, sharp, stabbing chest pain that gets worse when you cough, swallow, breathe deeply or lie flat			
Chest pain or discomfort		√	
Severe nausea, vomiting and/or diarrhea, dehydration: Thirst, headache, general discomfort, loss of appetite, decreased urine, confusion, unexplained tiredness		√	
Headache		√	
General Physical Health Deterioration		√	
UNCOMMON:			
Gastrointestinal Bleeding in the stomach or bowels: Black, tarry stool, blood in the stool		√	
Inflammation of the pancreas (Pancreatitis): abdominal pain that lasts and gets worse when you lie down; nausea, vomiting			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Do not take ZYKADIA after the expiry date stated on the box.

Store in the original package. Do not store above 30°C.

Do not take this medicine if you notice any damage to the packaging or if there are any signs of tampering. Ask your pharmacist how to throw away medicines you no longer use.

Keep out of reach and sight of children.

If you want more information about ZYKADIA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>; the manufacturer's website www.novartis.ca or by calling 1-800-363-8883.

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

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ZYKADIA is a registered trademark.