Package leaflet: Information for the user

XALKORI 200 mg hard capsules
XALKORI 250 mg hard capsules
crizotinib

The words "you" and "your" are used to refer to both the adult patient and to the caregiver of the paediatric patient.

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, pharmacist, or nurse.
- 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, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What XALKORI is and what it is used for

XALKORI is an anticancer medicine containing the active substance crizotinib used to treat adults with a type of lung cancer called non-small cell lung cancer, that presents with a specific rearrangement or defect in either a gene called anaplastic lymphoma kinase (ALK) or a gene called ROS1.

XALKORI can be prescribed to you for the initial treatment if your disease is at an advanced stage of lung cancer.

XALKORI can be prescribed to you if your disease is at an advanced stage and previous treatment has not helped to stop your disease.

XALKORI may slow or stop the growth of lung cancer. It may help shrink tumours.

XALKORI is used to treat children and adolescents (age ≥ 6 to < 18 years) with a type of tumour called anaplastic large cell lymphoma (ALCL) or a type of tumour called inflammatory myofibroblastic tumour (IMT) that present with a specific rearrangement or defect in a gene called anaplastic lymphoma kinase (ALK).

XALKORI can be prescribed to children and adolescents to treat ALCL if previous treatment has not helped to stop the disease.

XALKORI can be prescribed to children and adolescents to treat IMT if surgery has not helped to stop the disease.

You should only be given this medicine and supervised by a doctor who has experience with cancer treatment. If you have any questions about how XALKORI works or why this medicine has been prescribed for you, ask your doctor.

2. What you need to know before you take XALKORI

Do not take XALKORI

- If you are allergic to crizotinib or any of the other ingredients of this medicine (listed in Section 6, "What XALKORI contains").

Warnings and precautions

Talk to your doctor before taking XALKORI:

- If you have moderate or severe liver disease.
- If you have ever had any other lung problems. Some lung problems may get worse during treatment with XALKORI, as XALKORI may cause inflammation of the lungs during treatment. Symptoms may be similar to those from lung cancer. Tell your doctor right away if you have any new or worsening symptoms including difficulty in breathing, shortness of breath, or cough with or without mucous, or fever.
- If you have been told that you have an abnormality of your heart tracing after an electrocardiogram (ECG) known as prolonged QT interval.
- If you have reduced heart rate.
- If you have ever had stomach or intestine problems such as holes (perforation), or if you have conditions causing inflammation inside the abdomen (diverticulitis), or if you have spread of cancer inside the abdomen (metastasis).
- If you have vision disorders (seeing flashes of light, blurred vision, and double vision).
- If you have severe kidney disease.
- If you are currently treated with any of the medicines listed in section "Other medicines and XALKORI".

If any of the above conditions apply to you, tell your doctor.

Talk to your doctor right away after having taken XALKORI:

- If you are experiencing severe stomach or abdominal pain, fever, chills, shortness of breath, fast heartbeat, partial or complete loss of vision (in one or both eyes) or changes in bowel habits.

Most of the available information is available in adult patients with some specific histology type of ALK-positive or ROS1-positive NSCLC (adenocarcinoma). Limited information is available in the other histologies.

Children and adolescents

The indication for non-small cell lung cancer does not cover children and adolescents. Do not give this medicine to children younger than 6 years of age with ALK-positive ALCL or ALK-positive IMT. Children and adolescents should be assessed for their ability to swallow intact capsules before prescribing XALKORI. XALKORI should be given to children and adolescents under adult supervision.

Other medicines and XALKORI

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including herbal medicines and medicine obtained over the counter.

In particular, the following medicines may increase the risk of side effects with XALKORI:

- Clarithromycin, telithromycin, erythromycin, antibiotics used to treat bacterial infections.
- Ketoconazole, itraconazole, posaconazole, voriconazole, used to treat fungal infections.
- Atazanavir, ritonavir, cobicistat, used to treat HIV infections/AIDS.

The following medicines may reduce the effectiveness of XALKORI:

- Phenytoin, carbamazepine or phenobarbital, anti-epileptics used to treat seizures or fits.
- Rifabutin, rifampicin, used to treat tuberculosis.

- St. John's wort (*Hypericum perforatum*), a herbal product used to treat depression.

XALKORI may increase side effects associated with the following medicines:
- Alfentanil and other short acting opiates such as fentanyl (painkillers used for surgical procedures).
- Quinidine, digoxin, disopyramide, amiodarone, sotalol, dofetilide, ibutilide, verapamil, diltiazem used to treat heart problems.
- Medicines for high blood pressure called beta-blockers such as atenolol, propranolol, labetolol.
- Pimozide, used to treat mental illness.
- Metformin, used to treat diabetes.
- Procainamide, used to treat cardiac arrhythmia.
- Cisapride, used to treat stomach problems.
- Ciclosporin, sirolimus and tacrolimus used in transplant patients.
- Ergot alkaloids (e.g., ergotamine, dihydroergotamine), used to treat migraine.
- Dabigatran, anticoagulant used to slow down clotting of the blood.
- Colchicine, used to treat gout.
- Pravastatin, used to reduce cholesterol levels.
- Clonidine, guanfacine, used to treat hypertension.
- Mefloquine, used for the prevention of malaria.
- Pilocarpine, used to treat glaucoma (a severe eye disease).
- Anticholinesterases, used to restore muscle function.
- Antipsychotics, used to treat mental illness.
- Moxifloxacine, used to treat bacterial infections.
- Methadone, used to treat pain and for the treatment of opioid dependence.
- Bupropion, used to treat depression and smoking cessation.
- Efavirenz, raltegravir, used to treat HIV infection.
- Irinotecan, a chemotherapy medicine used to treat cancer of the colon and rectum.
- Morphine, used to treat acute and cancer pain.
- Naloxone, used to treat opiate medicine addiction and withdrawal.

These medicines *should be avoided* during your treatment with XALKORI.

Oral contraceptives
If you take XALKORI whilst using oral contraceptives, the oral contraceptives may be ineffective.

XALKORI with food and drink
You can take XALKORI with or without food; however, you should avoid drinking grapefruit juice or eating grapefruit while on treatment with XALKORI as they may change the amount of XALKORI in your body.

Sun protection
Avoid spending prolonged time in sunlight. XALKORI can make your skin sensitive to the sun (photosensitivity), and you may burn more easily. You should wear protective clothing and/or use sunscreen that covers your skin to help protect against sunburn if you have to be in the sunlight during treatment with XALKORI.

Pregnancy and breast-feeding
Talk to your doctor or pharmacist before taking this medicine if you are pregnant, may become pregnant or are breast-feeding.

It is recommended that women avoid becoming pregnant and that men do not father children during treatment with XALKORI because this medicine could harm the baby. If there is any possibility that the person taking this medicine may become pregnant or father a child, they must use adequate contraception during treatment, and for at least 90 days after completing therapy as oral contraceptives may be ineffective while taking XALKORI.

Do not breast-feed during treatment with XALKORI. XALKORI could harm a breast-fed baby.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
You should take special care when driving and using machines as patients taking XALKORI may experience visual disturbances, dizziness, and tiredness.

XALKORI contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 200 mg or 250 mg capsule, that is to say essentially 'sodium-free'.

3. How to take XALKORI

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

- The recommended dose for adults with NSCLC is one capsule of 250 mg taken orally twice daily (total amount 500 mg).
- The recommended dose for children and adolescents with ALK-positive ALCL or ALK-positive IMT is 280 mg/m^2 orally twice daily. The recommended dose will be calculated by the child's doctor and depends on the child's body surface area (BSA). The maximum daily dosage in children and adolescents should not exceed 1000 mg. XALKORI should be given under adult supervision.
- Take the recommended dose once in the morning and once in the evening.
- Take the capsules at about the same time each day.
- You can take the capsules with or without food always avoiding grapefruit.
- Swallow the capsules whole and do not crush, dissolve or open the capsules.

If necessary, your doctor may decide to reduce the dose to be taken orally. Your doctor may decide to permanently discontinue XALKORI treatment if you are unable to tolerate XALKORI.

If you take more XALKORI than you should
If you accidentally take too many capsules, tell your doctor or pharmacist right away. You may require medical attention.

If you forget to take XALKORI
What to do if you forget to take a capsule depends on how long it is until your next dose.
- If your next dose is in **6 hours or more**, take the missed capsule as soon as you remember. Then take the next capsule at the usual time.
- If your next dose is in **less than 6 hours**, skip the missed capsule. Then take the next capsule at the usual time.

Tell your doctor about the missed dose at your next visit.

Do not take a double dose (two capsules at the same time) to make up for a forgotten capsule.

If you vomit after taking a dose of XALKORI, do not take an extra dose; just take your next dose at your regular time.

If you stop taking XALKORI
It is important to take XALKORI every day, as long as your doctor prescribes it to you. If you are not able to take the medicine as your doctor prescribed, or you feel you do not need it anymore, contact your doctor right away.

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.

If you experience any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet.

Although not all adverse reactions identified in the adults with NSCLC have been observed in children and adolescents with ALCL or IMT, the same side effects for adult patients with lung cancer should be considered for children and adolescents with ALCL or IMT.

Some side effects could be serious. You should immediately contact your doctor if you experience any of the following serious side effects (see also section 2 "What you need to know before you take XALKORI"):

- **Liver failure**
  Tell your doctor right away if you feel more tired than usual, your skin and whites of your eyes turn yellow, your urine turns dark or brown (tea colour), you have nausea, vomiting, or decreased appetite, you have pain on the right side of your stomach, you have itching, or if you bruise more easily than usual. Your doctor may do blood tests to check your liver function, and if the results are abnormal, your doctor may decide to reduce the dose of XALKORI or stop your treatment.

- **Lung inflammation**
  Tell your doctor right away if you experience difficulty in breathing, especially if associated with cough or fever.

- **Reduction in the number of white blood cells (including neutrophils)**
  Tell your doctor right away if you experience fever or infection. Your doctor may do blood tests and if the results are abnormal, your doctor may decide to reduce the dose of XALKORI.

- **Light-headedness, fainting, or chest discomfort**
  Tell your doctor right away if you experience these symptoms which could be signs of changes in the electrical activity (seen on electrocardiogram) or abnormal rhythm of the heart. Your doctor may perform electrocardiograms to check there are no problems with your heart during treatment with XALKORI.

- **Partial or complete loss of vision in one or both eyes**
  Tell your doctor right away if you experience any new vision problems, loss of vision or any change in vision such as difficulty seeing out of one or both eyes. Your doctor may hold or permanently stop XALKORI treatment and refer you to an ophthalmologist.

  For children and adolescents taking XALKORI to treat ALK-positive ALCL or ALK-positive IMT: Your doctor should refer you to an ophthalmologist before starting XALKORI, and within 1 month of starting XALKORI to check for vision problems. You should have an eye examination every 3 months during treatment with XALKORI and more often if there are any new vision problems.

- **Severe stomach and intestine (gastrointestinal) problems in children and adolescents with ALK-positive ALCL or ALK-positive IMT**
  XALKORI may cause severe diarrhoea, nausea or vomiting. Tell your doctor right away if problems with swallowing, vomiting, or diarrhoea develop during treatment with XALKORI. Your doctor may give medicines as needed to prevent or treat diarrhoea, nausea, and

vomiting. Your doctor may recommend drinking more fluids or may prescribe electrolyte supplements or other kinds of nutritional support if severe symptoms develop.

Other side effects of XALKORI in adults with NSCLC may include:

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

- Visual effects (seeing flashes of light, blurred vision, light sensitivity, floaters or double vision, often beginning soon after starting treatment with XALKORI).
- Stomach upset, including vomiting, diarrhoea, nausea.
- Oedema (excess fluid in body tissue, causing swelling of the hands and feet).
- Constipation.
- Abnormalities in liver blood tests.
- Decreased appetite.
- Tiredness.
- Dizziness.
- Neuropathy (feeling of numbness or pins and needles in the joints or extremities).
- Alteration in sense of taste.
- Pain in the abdomen.
- Reduction in the number of red blood cells (anaemia).
- Skin rash.
- Reduced heart rate.

*Common side effect*s (may affect up to 1 in 10 people)

- Indigestion.
- Increased blood levels of creatinine (may indicate that kidneys are not functioning properly).
- Increased levels of the enzyme alkaline phosphatase in the blood (an indicator of organ malfunction or injury, particularly liver, pancreas, bone, thyroid gland, or gall bladder).
- Hypophosphataemia (low blood phosphate levels that can cause confusion or muscle weakness).
- Closed pouches of fluid within the kidneys (kidney cysts).
- Fainting.
- Inflammation of the oesophagus (swallowing tube).
- Decreased levels of testosterone, a male sex hormone.
- Heart failure.

*Uncommon side effect*s (may affect up to 1 in 100 people)

- Hole (perforation) in stomach or intestine.
- Sensitivity to sunlight (photosensitivity).
- Increased blood levels of tests that check for muscle damage (high creatine phosphokinase levels).

Other side effects of XALKORI in children and adolescents with ALK-positive ALCL or ALK-positive IMT may include:

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

- Abnormalities in liver blood tests.
- Visual effects (seeing flashes of light, blurred vision, light sensitivity, floaters or double vision, often beginning soon after starting treatment with XALKORI).
- Pain in the abdomen.
- Increased blood levels of creatinine (may indicate that kidneys are not functioning properly).
- Anaemia (reduction in the number of red blood cells).
- Low platelet counts in blood tests (may increase the risk of bleeding and bruising).
- Tiredness.
- Decreased appetite.
- Constipation.

- Oedema (excess fluid in body tissue, causing swelling of the hands and feet).
- Increased levels of the enzyme alkaline phosphatase in the blood (an indicator of organ malfunction or injury, particularly liver, pancreas, bone, thyroid gland, or gall bladder).
- Neuropathy (feeling of numbness or pins and needles in the joints or extremities).
- Dizziness.
- Indigestion.
- Alteration in sense of taste.
- Hypophosphataemia (low blood levels of phosphate that can cause confusion or muscle weakness).

*Common side effect*s (may affect up to 1 in 10 people)
- Skin rash.
- Inflammation of the oesophagus (swallowing tube).

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: 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 XALKORI

- 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 bottle or blister foil and carton 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 any pack that is damaged or shows 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 XALKORI contains
– The active substance in XALKORI is crizotinib.
XALKORI 200 mg: each capsule contains 200 mg crizotinib
XALKORI 250 mg: each capsule contains 250 mg crizotinib

– The other ingredients are (see also section 2 "XALKORI contains sodium"):
Capsule content: colloidal anhydrous silica, microcrystalline cellulose, anhydrous calcium hydrogen phosphate, sodium starch glycolate (Type A), magnesium stearate.
Capsule shell: gelatin, titanium dioxide (E171), and red iron oxide (E172).
Printing ink: shellac, propylene glycol, potassium hydroxide, and black iron oxide (E172).

What XALKORI looks like and contents of the pack
XALKORI 200 mg is supplied as hard gelatin capsules with pink cap and white body, printed with black ink "Pfizer" on the cap, "CRZ 200" on the body.

XALKORI 250 mg is supplied as hard gelatin capsules with pink cap and body, printed with black ink "Pfizer" on the cap, "CRZ 250" on the body.

It is available in blister packs of 60 hard capsules and in plastic bottles of 60 hard capsules.

Not all pack sizes may be marketed.

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