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Xalkori (*crizotinib*)

An overview of Xalkori and why it is authorised in the EU

What is Xalkori and what is it used for?

Xalkori is a cancer medicine used on its own to treat adults with a type of lung cancer called non-small cell lung cancer (NSCLC), when the disease is advanced. It can be used if the NSCLC is 'ALK-positive', which means that the cancer cells contain certain changes affecting the gene responsible for a protein called ALK (anaplastic lymphoma kinase). It is also used when the NSCLC is 'ROS1-positive'. This means that the cancer cells contain changes affecting the gene responsible for the protein ROS1.

Xalkori can also be used to treat children and adolescents from 6 to less than 18 years of age with ALK-positive anaplastic large cell lymphoma (ALCL), a type of blood cancer, or with ALK-positive inflammatory myofibroblastic tumour (IMT) that cannot be removed by surgery. IMT is a usually benign tumour affecting a type of muscle cells called myofibroblasts, which play an important role in the wound healing process.

Xalkori contains the active substance crizotinib.

How is Xalkori used?

Treatment with Xalkori should be started and supervised by a doctor who is experienced in using cancer medicines. The presence of the genetic changes affecting ALK ('ALK-positive' status) or ROS1 ('ROS1-positive' status) has to be confirmed before starting treatment with Xalkori.

Xalkori is available as capsules and the recommended dose in adults with ALK-positive or ROS1-positive advanced NSCLC is 250 mg twice per day. The recommended dose in children and adolescents with ALK-positive ALCL or ALK-positive IMT depends on the body surface area (calculated using the patient's height and weight). If certain side effects develop the doctor may decide to interrupt or reduce the dose. Treatment may have to be stopped altogether if the patient develops certain severe side effects. Doses may need to be adjusted in patients with severely reduced kidney or liver function.

For more information about using Xalkori, see the package leaflet or contact your doctor or pharmacist.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000
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How does Xalkori work?

ALK and ROS1 belong to a family of proteins called receptor tyrosine kinases (RTKs), which are involved in the growth of cells. In tumours either 'ALK-positive' or 'ROS1-positive', the ALK or ROS1 protein is abnormally active and can promote the uncontrolled growth of cells and the development of new blood vessels that supply them.

The active substance in Xalkori, crizotinib, is an RTK inhibitor. It works mainly by blocking the activity of ALK or ROS1, including when the genetic change is present, thereby reducing the growth and spread of the cancer in ALK-positive ALCL and IMT and both ALK- and ROS1-positive NSCLC.

What benefits of Xalkori have been shown in studies?

ALK-positive NSCLC

A study in 347 previously treated ALK-positive adult patients showed that those taking Xalkori lived on average for nearly 8 months without their disease getting worse compared with 3 months in patients who were treated with either pemetrexed or docetaxel.

In another study in 343 adult patients who had not received previous treatment for their NSCLC before, patients treated with Xalkori lived on average for nearly 11 months without their disease getting worse compared with 7 months in patients who were treated with pemetrexed-containing therapy.

ROS1-positive NSCLC

A study in 53 ROS1-positive adult patients with advanced disease showed that around 70% of patients taking Xalkori (37 out of 53) responded completely or partially to treatment. This is considered a favourable response when compared with response rates of around 20 to 30% to previous treatments, in those patients who had been given them. For the previously untreated patients, 6 out of 7 responded to treatment.

ALK-positive ALCL and ALK-positive IMT

A study investigated Xalkori in 36 children and adolescents with ALK-positive ALCL or IMT that cannot be removed by surgery. Among the 22 patients with ALK-positive ALCL, 86% (19 out of 22) achieved a complete (17 patients) or partial response (2 patients) which lasted on average for 3.6 months.

Among the 14 patients with ALK-positive IMT, 86% (12 out of 14) achieved a complete (5 patients) or partial response (7 patients) which lasted on average for 14.8 months.

What is the risk associated with Xalkori?

The most common side effects with Xalkori (which may affect more than 1 in 4 patients) in adults with ALK- or ROS1-positive NSCLC are vision problems, nausea (feeling sick), diarrhoea, vomiting, oedema (swelling), constipation, increases in liver enzymes in the blood, tiredness, decreased appetite, dizziness and neuropathy (pain due to nerve damage). The most serious side effects are liver damage, pneumonitis (lung inflammation), neutropenia (low blood levels of neutrophils, a type of white blood cell) and prolonged QT interval (a problem with the electrical activity of the heart).

In children and adolescents with ALK-positive ALCL or IMT, the most common side effects with Xalkori (which may affect more than 8 in 10 patients) are increases in liver enzymes in the blood, vomiting,

neutropenia, nausea, diarrhoea and leucopenia (low levels of leucocytes, a type of white blood cell). The most frequent serious side effect is neutropenia.

For the full list of side effects and restrictions of Xalkori, see the package leaflet.

Why is Xalkori approved?

The European Medicines Agency concluded that treatment with Xalkori increases the time adults with ALK-positive NSCLC live without the disease getting worse, whether they are previously treated or not. For patients with ROS1-positive NSCLC, the Agency noted the evidence of a high response rate, in particular for patients who had previously received other cancer treatments.

Xalkori was also shown to be effective in the treatment of children with ALK-positive ALCL or ALK-positive IMT that cannot be removed by surgery. Although the study was small, given the rarity of these diseases, the results were considered very good and promising.

Therefore the Agency decided that Xalkori's benefits are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe and effective use of Xalkori?

The company that markets Xalkori will ensure that doctors who are expected to prescribe Xalkori receive a pack containing the medicine's summary of product characteristics and a patient alert card to be given to patients.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Xalkori have also been included in the summary of product characteristics and the package leaflet.

Other information about Xalkori

Xalkori received a marketing authorisation valid throughout the EU on on 23 October 2012.

Further information on Xalkori can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/xalkori

This overview was last updated in 11-2022.