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Krazati (*adagrasib*)

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

What is Krazati and what is it used for?

Krazati is a medicine for treating adults with advanced non-small cell lung cancer (NSCLC) when the cancer cells have a particular genetic change (mutation) known as *KRAS* G12C. It is used in patients whose disease got worse after at least one systemic treatment (a treatment given by injection or by mouth and affecting the whole body).

Krazati contains the active substance adagrasib.

How is Krazati used?

The medicine can only be obtained with a prescription and should be started by a doctor experienced in the use of cancer medicines.

Krazati is available as tablets to be taken twice a day. Treatment should continue until the disease gets worse or until the side effects become unmanageable. The doctor may delay or reduce the dose, or stop treatment, if certain side effects occur. Before starting treatment with Krazati, the presence of the *KRAS* G12C mutation must be confirmed by an appropriate test.

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

How does Krazati work?

Genetic changes to the *KRAS* gene can produce an altered form of the KRAS protein, which causes the uncontrolled growth of cancer cells. The active substance in Krazati, adagrasib, attaches to the altered protein inside cancer cells, stopping the protein from functioning and thereby slowing the growth and spread of the cells. It also encourages processes that kill the cancer cells.

What benefits of Krazati have been shown in studies?

Krazati was investigated in a main study involving 116 adults with advanced NSCLC with a *KRAS* G12C mutation whose disease got worse after previously being treated with other cancer medicines; Krazati was not compared with any other medicine or placebo (a dummy treatment). Overall, 41.4% of

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patients (48 out of 116) in the study responded partially or completely to treatment with Krazati (as measured by shrinkage in the size of the cancer). On average, the response lasted for 8.5 months.

What are the risks associated with Krazati?

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

The most common side effects with Krazati (which may affect more than 1 in 5 people) include diarrhoea, nausea (feeling sick), vomiting, tiredness, anaemia (low levels of red blood cells), increased blood levels of creatinine or liver enzymes (a sign of possible liver problems), decreased appetite, peripheral oedema (swelling especially of the ankles and feet), dizziness and hyponatraemia (low blood sodium levels).

Krazati must not be used together with certain medicines known as 'CYP3A substrates with a narrow therapeutic index' (alfuzosin, amiodarone, cisapride, pimozide, quinidine, ergotamine, dihydroergotamine, quetiapine, lovastatin, simvastatin, sildenafil, sirolimus, midazolam, triazolam, ticagrelor and tacrolimus), as this may increase the risk of serious and life-threatening side effects.

Why is Krazati authorised in the EU?

Krazati was shown to be of benefit for patients with NSCLC with a *KRAS* G12C mutation and to have an acceptable safety profile. Although the main study did not compare Krazati with another cancer treatment, it showed that the medicine was effective at treating the cancer including in patients whose disease got worse after several different treatments.

Krazati has been given 'conditional authorisation'. This means that the European Medicines Agency decided that the benefits of Krazati are greater than its risks, but the company will have to provide additional evidence after authorisation.

Conditional authorisation is granted on the basis of less comprehensive data than are normally required. It is granted for medicines that fulfil an unmet medical need to treat serious diseases and when the benefits of having them available earlier outweigh any risks associated with using the medicines while waiting for further evidence. Every year, the Agency will review any new information that becomes available until data become comprehensive and this overview will be updated as necessary.

Since Krazati was given conditional authorisation, at the time of approval the company was required to provide the final results of an ongoing study comparing Krazati with docetaxel (another cancer medicine) in patients with NSCLC with a *KRAS* G12C mutation who have received at least one prior treatment.

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

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

As for all medicines, data on the use of Krazati are continuously monitored. Suspected side effects reported with Krazati are carefully evaluated and any necessary action taken to protect patients.

Other information about Krazati

Krazati received a conditional marketing authorisation valid throughout the EU on 5 January 2024.

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

This overview was last updated in 01-2024.