10 November 2023
EMA/497823/2023
EMEA/H/C/006013

Approval of the marketing authorisation for Krazati (adagrasib)

Re-examination leads to recommendation to approve

After re-examining its initial opinion, the European Medicines Agency has recommended approving the conditional marketing authorisation for the medicine Krazati (adagrasib) for treating advanced non-small cell lung cancer (NSCLC) with a *KRAS* G12C mutation.

The Agency had initially refused the marketing authorisation application for Krazati on 20 July 2023.

The company that applied for authorisation is Mirati Therapeutics B.V.

What is Krazati and what is it to be 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 to be 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 and is to be available as tablets to be taken by mouth.

How does Krazati work?

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

What did the company present to support its application?

The company presented results from 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. The study looked at the number of patients whose cancer responded partially or completely to treatment (as measured by shrinkage in the size of the cancer) and did not compare Krazati to any other treatment.

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What were the main reasons for initially refusing the marketing authorisation?

The Agency's human medicines committee (CHMP) noted that comprehensive data for this medicine were not yet available and that there were uncertainties on whether the medicine would lead to longer survival of patients compared with medicines already authorised.

Although the company applied for a conditional marketing authorisation, the medicine did not meet the criteria for granting this type of authorisation. The company could not show that Krazati fulfils an unmet need and could not justify making the medicine immediately available to patients while further data were still awaited. The Agency therefore recommended refusing the conditional marketing authorisation.

What happened during the re-examination?

During the re-examination, the CHMP re-assessed the data submitted by the company and consulted a group of experts in the field of cancer treatment.

What were the conclusions of the re-examination?

In its previous refusal, the CHMP took into account preliminary results from a study (CodeBreaK 200) with a similar medicine, sotorasib, that cast doubt on the potential benefits of Krazati.

On further consideration, the Committee noted that although sotorasib and adagrasib (the active substance in Krazati) work in a similar way, there are differences between the two medicines. Therefore the results of the CodeBreaK 200 study are not necessarily relevant for Krazati. In addition, the main study showed that Krazati is of benefit for patients with NSCLC with a *KRAS* G12C mutation, despite it being a small study with no comparator.

The CHMP also concluded that Krazati's different safety profile and the fact that the medicine is taken by mouth provide advantages over the medicine docetaxel, which is given by infusion into a vein and is considered the standard of care for patients with NSCLC whose disease worsened after previous treatment.

Although comprehensive data for Krazati are not yet available, the existing data were considered sufficient to justify granting a conditional marketing authorisation while further data were still awaited.

To further confirm the effectiveness and safety of Krazati, the company that markets the medicine will provide the final results of an ongoing study comparing Krazati with docetaxel in patients with NSCLC with a *KRAS* G12C mutation who have received at least one prior treatment.