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Questions and answers

Withdrawal of the marketing authorisation application for Tekinex (omacetaxine mepesuccinate)

On 11 January 2011, ChemGenex Europe SAS officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Tekinex intended to be used to treat patients with Philadelphia chromosome-positive chronic myeloid leukaemia who have the 'Bcr-Abl T315I kinase domain' mutation and whose previous treatment with imatinib had failed.

What is Tekinex?

Tekinex is a medicine that contains the active substance omacetaxine mepesuccinate. It was to be available as a powder to be made up into a solution for injection.

What was Tekinex expected to be used for?

Tekinex was expected to be used to treat adults with 'Philadelphia chromosome positive' (Ph+) chronic myeloid leukaemia (CML, a cancer of a type of white blood cells called granulocytes). Ph+ means that some of the patient's genes have rearranged themselves to form a special chromosome called the Philadelphia chromosome which produces an enzyme, Bcr-Abl kinase that leads to the development of leukaemia.

It was to be used in patients whose previous treatment with imatinib (another anticancer medicine) had failed, possibly due to a mutation in the gene for the Bcr-Abl kinase called the 'T315I mutation'.

Because the number of patients with CML is low, the disease is considered 'rare', and Tekinex was designated an 'orphan medicine' (a medicine used in rare diseases) on 2 September 2004.

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How is Tekinex expected to work?

The active substance in Tekinex, omacetaxine, is an inhibitor of protein synthesis. It is derived from harringtonine, a substance extracted from a Chinese evergreen. The way it works is unclear, but it is thought to disrupt the production of the Bcr-Abl tyrosine kinase enzyme.

Other medicines known as tyrosine kinase inhibitors, including imatinib, act in CML by attaching directly to the Bcr-Abl tyrosine kinase enzyme. The T315I mutation changes certain properties of the enzyme, making it harder for these medicines to attach to it. Because omacetaxine does not act in this way, its action is not affected by the T315I mutation. Tekinex was therefore expected to work in Ph+ patients with the T315I mutation.

What did the company present to support its application?

The effects of Tekinex were first tested in experimental models before being studied in humans. The company presented results from a main study involving 66 patients with Philadelphia-positive CML and the T315I mutation, whose previous treatment with imatinib had failed. Tekinex was not compared directly with any other treatment. The study looked at how the patients responded to treatment based on results of blood tests taken to measure how active the cancer was.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn at 'day 120'. This means that the CHMP had evaluated the initial documentation provided by the company and formulated a list of questions. The company had not yet responded to the questions at the time of the withdrawal.

What was the recommendation of the CHMP at that time?

Based on the review of the data, at the time of the withdrawal the CHMP had some concerns and was of the provisional opinion that Tekinex could not have been approved.

The CHMP was of the view that the medicine's benefits were uncertain. There was also insufficient follow-up of the patients following treatment and the Committee was doubtful about the medicine being safe enough to be self-administered by patients as intended by the company. The CHMP also had concerns about the doses used in the study and the criteria used for measuring the medicine's effectiveness. Finally, following an inspection of the study sites, the Committee noted that there were some inconsistencies in the application that could have affected the reliability of the study results.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Tekinex did not outweigh its risks.

What were the reasons given by the company for withdrawing the application?

The letter from the company notifying the Agency of the withdrawal of the application is available under the tab 'All documents'.

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that clinical trials with Tekinex will continue.

The summary of the opinion of the Committee for Orphan Medicinal Products for Tekinex can be found on the Agency's website ema.europa.eu/Find medicine/Human medicines/Rare disease designations.