05 October 2012
EMA/608075/2012
EMEA/H/C/000558/II/0043

Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Erbitux (cetuximab)

On 17 September 2012, Merck KGaA officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a change to the marketing authorisation for Erbitux, to extend its use in the treatment of non-small cell lung cancer.

What is Erbitux?

Erbitux is an anticancer medicine which has been authorised in the European Union (EU) since 29 June 2004. It is used to treat adults with colorectal cancer (a cancer of the large intestine) when the cancer is metastatic (has spread to other parts of the body). Erbitux is used in patients whose tumour cells have a protein on their surface called epidermal growth factor receptor (EGFR) and contain a 'wild-type' (non-mutated) gene called 'KRAS'. In colorectal cancer it can be used in combination with chemotherapy (medicines to treat cancer) or on its own.

Erbitux is also used to treat squamous cell cancers of the head and neck. In locally advanced cancer (when the tumour has grown but has not spread), Erbitux is given in combination with radiotherapy (treatment with radiation). In cancer that is recurrent (has come back after previous treatment) or metastatic, Erbitux is used with a 'platinum-based' anticancer medicine combination.

What was Erbitux expected to be used for?

Erbitux was also expected to be used to treat advanced or metastatic non-small cell lung cancer, when the tumour cells have high levels of EGFR on their surface. It was to be used in combination with platinum-based chemotherapy in patients who had not been treated before.

How is Erbitux expected to work?

In non-small cell lung cancer, Erbitux was expected to work in the same way as it does in its existing indications. The active substance in Erbitux, cetuximab, is a monoclonal antibody, a type of protein

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that has been designed to recognise and attach to EGFR, which can be found on the surface of some tumour cells. When it attaches to EGFR, the tumour cells can no longer receive the messages needed for growth, progression and spread.

What did the company present to support its application?

The applicant presented a re-analysis of the data from one main study involving 1,125 patients with advanced or metastatic non-small cell lung cancer with EGFR. The study had been previously used to support an application for the use of Erbitux in non-small cell lung cancers, but this application had been refused. In the study, patients were given cisplatin and vinorelbine (two chemotherapy medicines) with or without Erbitux. The main measure of effectiveness was overall survival (the length of time the patients lived). The company presented an analysis of the study data, comparing the survival of patients whose tumour cells had high levels of EGFR on their surface, with the survival of patients whose tumours had low levels of EGFR.

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

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated lists of questions. After the CHMP had assessed the company's responses to the questions, there were still some unresolved issues.

What was the recommendation of the CHMP at that time?

Based on the review of the data and the company's response to the questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Erbitux could not have been approved for the treatment of non-small cell lung cancer.

The Committee was concerned that, although the re-analysis of the data indicated that there might be a beneficial effect on survival for patients whose tumour cells had high levels of EGFR, there were some concerns, particularly over the way that patients had been categorised into high or low EGFR level groups in the retrospective analysis, as well as the fact that the effect seen in patients with high EGFR levels in the main study had not been confirmed in another study. Therefore, at the time of the withdrawal, the CHMP concluded that the medicine could not have been approved based on the data presented by the company and that further studies were required to confirm the benefit of Erbitux in patients whose tumour cells have high EGFR levels.

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

In its official letter, the company stated that its decision to withdraw the application was based on the CHMP's view that the data provided so far are not sufficient to address CHMP's concerns and that more data will be needed.

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 there were no ongoing clinical trials with Erbitux in non-small cell lung cancer at the time of the withdrawal.

What is happening with Erbitux for the treatment of other diseases?

There are no consequences on the use of Erbitux in its authorised indications.

The full European Public Assessment Report for Erbitux can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.