European Medicines Agency

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Questions and answers on the recommendation for the refusal of a change to the marketing authorisation for Erbitux
cetuximab

On 23 July 2009, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of a change to the marketing authorisation for the medicinal product Erbitux. The change concerned an extension of indication to add the treatment of non-small cell lung cancer.
The applicant requested a re-examination of the opinion. After considering the grounds for this request, the CHMP re-examined the initial opinion, and confirmed the refusal of the marketing authorisation on 19 November 2009.

What is Erbitux?
Erbitux is a solution for infusion (drip into a vein) that contains the active substance cetuximab. Erbitux has been authorised since June 2004. It is already used to treat the following types of cancer:

- metastatic cancer of the colon or rectum (large intestine). 'Metastatic' means that the cancer has spread to other parts of the body;
- 'squamous cell' cancers of the head and neck. These types of cancer affect the cells of the lining of the mouth or the throat, or of organs such as the larynx (voice box). Erbitux can be used when the cancer is locally advanced (when the tumour has grown but has not spread), recurrent (when it has come back after previous treatment) or metastatic.

What was Erbitux expected to be used for?
Erbitux was also expected to be used to treat 'non-small cell' lung cancer that was advanced (had started to spread) or metastatic. It was to be used in patients who had not been treated before, when the tumour cells had a protein on their surface called epidermal growth factor receptor (EGFR). Erbitux was to be used in combination with platinum-based chemotherapy (a combination of anticancer medicines that includes a medicine such as cisplatin or carboplatin).

How is Erbitux expected to work?
In lung cancer, Erbitux is 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 monoclonal antibody is an antibody (a type of protein) that has been designed to recognise and attach to a specific structure (called an antigen) in the body. Cetuximab has been designed to attach to EGFR, which can be found on the surface of some tumour cells. As a result, the tumour cells can no longer receive the messages needed for growth, progression and spread.

What documentation did the company present to support its application to the CHMP?
The company presented the results of two main studies involving a total of 1,801 adults with advanced, metastatic or recurrent non-small cell lung cancer who had not been treated before. In both studies, the combination of Erbitux with platinum-based chemotherapy was compared with platinum-

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based chemotherapy without Erbitux. The main measures of effectiveness were how long the patients survived and how long they lived without their cancer getting worse.

What were the major concerns that led the CHMP to recommend the refusal of the change to the marketing authorisation?
In July 2009, the CHMP was concerned that the benefits of adding Erbitux to standard platinum-based chemotherapy were modest in terms of survival times, and that the medicine did not have a convincing effect on how long patients lived without their cancer getting worse. Severe side effects were seen in some lung cancer patients who received Erbitux - these were similar to the side effects seen in patients treated with Erbitux for other types of cancer.
In November 2009, following the re-examination, the CHMP added a further concern over the ways in which the studies' results were analysed after they can been completed. These 'subgroup analyses' attempted to identify a group of patients that would benefit from treatment. The CHMP was also concerned over discrepancies in the studies' findings between the two main measures of effectiveness. Therefore, the CHMP was of the opinion that the benefits of Erbitux in the treatment of non-small cell lung cancer did not outweigh its risks. Hence, the CHMP recommended that the change to the marketing authorisation be refused.

What are the consequences of the refusal for patients in clinical trials using Erbitux?
The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Erbitux. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening with Erbitux for the treatment of cancer of the colon or rectum and cancers of the head and neck?
There are no consequences on the use of Erbitux in its authorised indications, for which the balance of benefits and risks remains unchanged.

The full European Public Assessment Report for Erbitux is available here.