21 November 2013
EMA/702774/2013
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (post authorisation)

Erbitux

cetuximab

On 21 November 2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending a variation to the terms of the marketing authorisation for the medicinal product Erbitux.

Amended use of Erbitux

The CHMP changed the indication for use in metastatic colorectal cancer (cancer of the lower bowel or rectum that has spread to other parts of the body) to clarify the particular genetic makeup of the cancer that must be present before treatment with Erbitux, which is described as epidermal growth factor receptor (EGFR)-expressing, RAS wild-type disease. Previously, use was indicated in those with EGFR-expressing, KRAS-wild type metastatic colorectal cancer. The full indication will now be[2]:

"**Erbitux is indicated for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing, *RAS* wild-type metastatic colorectal cancer**

- **in combination with irinotecan-based chemotherapy,**
- **in first-line in combination with FOLFOX,**
- **as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan.**

Erbitux is indicated for the treatment of patients with squamous cell cancer of the head and neck

- in combination with radiation therapy for locally advanced disease,
- in combination with platinum-based chemotherapy for recurrent and/or metastatic disease".

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued within 44 days (Type II variations) and 67 days (Annex II applications) from adoption of the opinion.
[2] The text in bold represents the amended indication

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Amended contraindication

The CHMP also recommended that the contraindications for Erbitux against use with oxaliplatin-containing chemotherapy in patients who have certain mutations (genetic changes) in their cancer should be amended to state that Erbitux must not be used in patients whose tumours carry mutations in RAS genes. Previously, use of Erbitux with oxaliplatin-containing chemotherapy was prohibited in patients whose tumours carried the KRAS gene (one type of RAS gene). The full contraindications for Erbitux will be as follows[3]:

> "Erbitux is contraindicated in patients with known severe (grade 3 or 4) hypersensitivity reactions to cetuximab.
>
> **The combination of Erbitux with oxaliplatin-containing chemotherapy is contraindicated for patients with mutant *RAS* metastatic colorectal cancer (mCRC) or for whom *RAS* mCRC status is unknown.**
>
> Before initiation of combination treatment, contraindications for concomitantly used chemotherapeutic agents or radiation therapy must be considered".

An assessment report containing details of the CHMP's evaluation and its conclusions on the amended benefit-risk balance of Erbitux will be available on the EMA website after the European Commission has issued a decision.

The updated EU product information containing the CHMP's full recommendations on how Erbitux should be used will be published on the EMA website after the European Commission has granted a marketing authorisation. The updated EU product information, which includes the summary of product characteristics (SmPC) and the package leaflet, will be available in all official languages of the EU.

The marketing authorisation holder for this medicinal product is Merck KGaA. They may request a re-examination of the CHMP opinion, provided that they notify the European Medicines Agency in writing of their intention within 15 days of receipt of the opinion.

[3] The text in bold represents the new or the amended contraindication