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EPAR summary for the public

Erbitux

cetuximab

This is a summary of the European public assessment report (EPAR) for Erbitux. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Erbitux.

What is Erbitux?

Erbitux is a solution for infusion (drip into a vein) that contains the active substance cetuximab.

What is Erbitux used for?

Erbitux is used to treat metastatic cancer of the colon or rectum (large intestine). 'Metastatic' means that the cancer 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 'wild-type' (non-mutated) versions of a family of genes called 'RAS'. Erbitux is given in the following ways:

- together with anticancer treatments containing irinotecan;
- together with the oxaliplatin-containing treatment FOLFOX in patients who have not been treated before;
- on its own when previous treatment containing oxaliplatin and irinotecan has failed and the patient cannot receive irinotecan.

Erbitux is also used to treat '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). 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 (when it has come back after previous treatment) or metastatic, Erbitux is used with a 'platinum-based' anticancer medicine combination (including medicines such as cisplatin or carboplatin).

The medicine can only be obtained with a prescription.

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How is Erbitux used?

Erbitux should only be given under the supervision of a doctor who has experience in the use of anticancer medicines in a setting where facilities for resuscitation are available. Before receiving Erbitux, the patient must be given an antihistamine and a corticosteroid to prevent an allergic reaction. Patients must also be closely observed for any signs of allergic reaction for at least one hour after the end of the infusion.

Erbitux is given once a week. The first infusion is given at a dose of 400 mg per square metre body surface area (calculated using the patient's height and weight) over two hours. The following infusions are 250 mg/m2 given over one hour. When it is used on its own or with other anticancer medicines, Erbitux is continued for as long as the patient responds. When it is used with radiotherapy, Erbitux is started one week before the radiotherapy starts and continued until the radiotherapy has finished.

How does Erbitux work?

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. EGFR is involved in switching on genes called RAS that are involved in the growth of cells; by attaching to EGFR, cetuximab prevents this from happening in the tumour cells and helps stop them growing. Between 79 and 89% of colorectal cancers and more than 90% of squamous cell cancers of the head and neck have EGFR on their cell surfaces.

How has Erbitux been studied?

For metastatic cancer of the colon or rectum, Erbitux was studied in six main studies:

- two studies involved 1,535 patients who had not received chemotherapy before, looking at the effects of adding Erbitux to a treatment combination containing either irinotecan or oxaliplatin (FOLFOX); a third study looked also at the effects of adding Erbitux to two treatment combinations containing oxaliplatin (one of which was similar to FOLFOX) in 1,630 patients.
- three studies involved 2,199 patients whose disease had got worse while they were on previous treatment including irinotecan, oxaliplatin or both, or who could not receive these medicines.

For cancers of the head and neck, Erbitux was investigated in two main studies:

- the first study involved 424 patients with locally advanced cancer, looking at the effects of adding Erbitux to radiotherapy;
- the second study involved 442 patients with recurrent or metastatic cancer, looking at the effects of adding Erbitux to a platinum-based anticancer medicine combination.

All of the studies looked at how long the patients lived without their cancer getting worse or how long they survived. Most of the studies looked at the results separately in patients whose tumours had wild-type KRAS (one of the types of RAS genes) and patients whose tumours had mutated KRAS. One of the studies also looked at the results separately in patients whose tumours carried wild-type forms of all RAS genes and patients with mutated forms of any RAS gene. When RAS genes (such as KRAS) are mutated they can stimulate the tumour cells to grow without being switched on by EGFR, so Erbitux would not be expected to be of much help.

What benefit has Erbitux shown during the studies?

In the studies of cancer of the colon or rectum, Erbitux was shown overall to increase the time patients lived without their cancer getting worse or how long they survived:

- in patients who had not received chemotherapy before, patients who had wild-type KRAS in their tumours lived for longer without their disease getting worse when they received Erbitux in addition to chemotherapy including irinotecan (9.9 months compared with 8.4 months, on average). In patients receiving Erbitux in combination with oxaliplatin-containing chemotherapy (FOLFOX) patients with wild-type RAS lived for longer without their disease getting worse compared with patients on FOLFOX alone (12.0 months compared with 5.8 months, on average). However, in the third study, patients with wild-type KRAS only survived overall for 16.3 months when Erbitux was added to the another oxaliplatin-based treatment similar to FOLFOX, compared with 18.2 months when the oxaliplatin-based treatment was used alone.
- the first study in patients who had taken chemotherapy before did not look at RAS mutations, but in the other two studies, patients with wild-type KRAS in their tumours lived for longer without their disease getting worse when Erbitux was added to their treatment. Patients who had failed both oxaliplatin and irinotecan treatment lived for an average of 3.6 months without their disease getting worse with Erbitux, compared with 1.9 months in those receiving best supportive care alone (the treatment of symptoms but not the cancer itself). Patients who had failed oxaliplatin treatment lived for an average of 4.0 months without their disease getting worse with Erbitux plus irinotecan, compared with 2.6 months in those receiving irinotecan alone.

In locally advanced head and neck cancers, the patients lived for longer without their disease getting worse when Erbitux was added to radiotherapy (24.4 months compared with 14.9 months, on average). In recurrent or metastatic head and neck cancer, survival was longer when Erbitux was added to a platinum-based anticancer medicine combination (10.1 months compared with 7.4 months, on average).

What is the risk associated with Erbitux?

The most common side effects with Erbitux (seen in more than 1 patient in 10) are skin reactions such as rash, hypomagnesaemia (low blood magnesium levels), mild or moderate reactions linked to the infusion (such as fever, chills, dizziness and difficulty breathing), mucositis (inflammation of the lining of the mouth) and raised levels of some liver enzymes. Skin reactions are seen in more than 80% of patients. For the full list of all side effects reported with Erbitux, see the package leaflet.

Erbitux must not be used with oxaliplatin-containing chemotherapy for metastatic colorectal cancer in patients with mutated RAS or for whom RAS status is unknown. For the full list of restrictions, see the package leaflet.

Erbitux can be associated with severe reactions during the infusion, so the patients must be monitored carefully while the medicine is being given.

Why has Erbitux been approved?

The CHMP decided that Erbitux's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Erbitux

The European Commission granted a marketing authorisation valid throughout the European Union for Erbitux on 29 June 2004.

The full EPAR for Erbitux can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Erbitux, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 12-2013.