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Questions and answers

Refusal of a change to the marketing authorisation for Vectibix (panitumumab)

On 17 March 2011, 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 Vectibix. The change concerned an extension of indication to add its use in combination with other anti-cancer medicines in the treatment of patients with metastatic cancer of the colon or rectum, both as 'first-line' treatment (in patients who had not been treated before) and as 'second-line' treatment (in patients who had been treated before).

The company that applied for the change to the authorisation is Amgen Europe B.V. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Vectibix?

Vectibix is a concentrate that is made up into a solution for infusion (drip into a vein). It contains the active substance panitumumab.

Vectibix is used to treat 'non-mutated (wild-type) *KRAS* metastatic colorectal carcinoma'. This is a cancer of the large intestine (bowel) that has spread to other parts of the body. Vectibix is used on its own after treatment has stopped working with combinations of anti-cancer medicines that include a 'fluoropyrimidine' (such as 5-fluorouracil), oxaliplatin and irinotecan.

Vectibix has been authorised in the EU since December 2007. It is marketed in all EU Member States, as well as Iceland and Norway.

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What was Vectibix expected to be used for?

Vectibix was also expected to be used in combination with chemotherapy (medicines to treat cancer) in both patients who have and those who have not been treated before.

How is Vectibix expected to work?

Vectibix in combination with chemotherapy is expected to work in the same way as it does on its own.

The active substance in Vectibix, panitumumab, 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) that is found on certain cells in the body. Panitumumab has been designed to attach to a receptor called the epidermal growth factor receptor (EGFR), which can be found on the surface of certain cells, including cells in some tumours. As a result, these tumour cells can no longer receive the messages transmitted via EGFR that they need for growth, progression and spreading (metastasis).

Panitumumab does not seem to work in tumour cells that contain mutated *KRAS* gene. This is because their growth is not controlled by signals transmitted via EGFR and they continue to grow even when the EGFR is blocked.

What did the company present to support its application?

The company presented data from two main studies involving a total of 2,369 patients with metastatic colorectal carcinoma. In the first study, Vectibix in combination with chemotherapy (oxaliplatin, 5-fluorouracil and folinic acid) was compared with chemotherapy alone in patients who had not been treated before for their metastatic cancer. The main measure of effectiveness was progression-free survival (how long the patients lived without their disease getting worse). The second study compared Vectibix in combination with chemotherapy (irinotecan, 5-fluorouracil and folinic acid) with chemotherapy alone in patients who had been treated before. The main measures of effectiveness were progression-free survival and overall survival (the length of time the patients lived).

What were the CHMP's main concerns that led to the refusal of the change to the marketing authorisation?

Although both studies showed a modest increase in progression-free survival, the CHMP questioned its clinical relevance, particularly given the lack of improvement in overall survival or other clinical endpoints such as quality of life. The Committee was also concerned over the increased toxicity of the combination of Vectibix with chemotherapy.

In addition, the CHMP noted that there was a negative effect on progression-free survival and overall survival in patients with mutated *KRAS* gene who took part in the first of the two main studies. This is a concern because of the uncertainty about the current reliability of KRAS testing (which is used to identify patients with the non-mutated *KRAS* gene) in clinical practice.

Therefore, at that point in time, the CHMP was of the opinion that the benefits of Vectibix in combination with chemotherapy did not outweigh its risks. Hence, the CHMP recommended that the change to the marketing authorisation be refused.

What consequences does this refusal have for patients in clinical trials?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Vectibix. 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 the use of Vectibix in its authorised indication?

There are no consequences for the use of Vectibix on its own in patients whose previous treatment has stopped working.

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