



London, 20 September 2007
Doc. Ref. EMEA/405113/2007

**QUESTIONS AND ANSWERS ON THE MARKETING AUTHORISATION
for
VECTIBIX**

International non-proprietary name (INN): *panitumumab*

On 20 September 2007, the Committee for Medicinal Products for Human Use (CHMP) recommended the granting of a conditional marketing authorisation for the medicinal product Vectibix 20 mg/ml concentrate for solution for infusion intended for the treatment of metastatic carcinoma of the colon or rectum, in patients whose tumour contains a non-mutated 'KRAS'. KRAS is a gene that, when mutated in tumour cells, stimulates tumour growth. The company that applied for authorisation is Amgen Europe B.V.

On 24 May 2007, the CHMP had originally adopted a negative opinion for Vectibix. At the request of the applicant, the Committee started a re-examination of its opinion. Following the re-examination, the CHMP adopted a final positive opinion on 20 September 2007, but only for use in patients whose tumours do not have a genetic mutation in KRAS.

What is Vectibix?

Vectibix is a solution for infusion (drip into a vein), which contains the active substance panitumumab.

What is Vectibix to be used for?

Vectibix is to be used to treat metastatic carcinoma of the colon or rectum. This is cancer of the lower intestine (large bowel) that has spread to other parts of the body. Vectibix is to be used on its own after treatment with a combination of anticancer medicines that includes 5-fluorouracil, irinotecan or oxaliplatin has stopped working.

How does Vectibix work?

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 bind to a specific structure (called an antigen) that is found on certain cells in the body.

Panitumumab has been designed to bind to the epidermal growth factor receptor (EGFR), which can be found on the surface of certain tumour cells. As a result of this binding, the tumour cells can no longer receive the messages they need for growth, progression and spreading (metastasis).

What documentation did the company present to support its application to the CHMP?

The effects of Vectibix were first tested in experimental models before being studied in humans. Its effectiveness in colon and rectum cancer was studied in one main study involving 463 patients, where the effects of Vectibix in addition to 'best supportive care' (any medicines or techniques to help patients, such as antibiotics, painkillers, transfusions and surgery, but not other anticancer medicines) were compared with best supportive care alone. The main measure of effectiveness was the time taken before the disease started to get worse or the patient died. The patients receiving best supportive care alone had the option to start receiving Vectibix once their disease had started to get worse.

What were the major concerns that initially led the CHMP to recommend the refusal of the marketing authorisation?

The CHMP was concerned that there was not sufficient evidence to show a benefit of Vectibix, due to the way the main study was designed. In the first few weeks of the study, many of the patients originally receiving best supportive care alone started to receive Vectibix after their disease had got worse, making it difficult to compare the effects of Vectibix and best supportive care alone. In addition, Vectibix only had a very small effect in increasing the time until the disease got worse or the patient died, in comparison with best supportive care. Studies also showed that patients receiving Vectibix had increases in side effects. These included skin reactions, which resulted in poorer quality of life in the patients reporting them.

Therefore, at that point in time, the CHMP was of the opinion that the benefits of Vectibix in the treatment of metastatic carcinoma of the colon or rectum did not outweigh its risks. Hence, the CHMP recommended that Vectibix be refused marketing authorisation.

What happened during the re-examination?

During the re-examination, the CHMP looked at information and additional analyses supplied by the company and took advice from a group of experts specialising in the treatment of cancer. As part of the re-examination, the Committee looked at the results of the main study separately in patients whose tumours contained KRAS that had not mutated, and those where the KRAS gene contained a mutation.

What were the conclusions of the CHMP following the re-examination?

The CHMP accepted that the additional methods of analysis allowed the main study's results to be treated with more confidence, despite the way the study was designed. In the patients whose tumours contains KRAS without any mutation, the Committee saw that treatment with Vectibix brought about a small increase in the time until the disease got worse or the patient died. In contrast, there was no effect of the treatment in the patients with mutated KRAS in their tumours. The Committee also concluded that the side effects of Vectibix were not a major concern and appeared to be similar to those seen with other medicines in the same class.

Overall, the CHMP concluded that the benefits of Vectibix outweigh its risks in patients whose tumours do not have mutations in KRAS and recommended that it be given a marketing authorisation for use in these patients. The Committee recommended a 'Conditional Approval', since there is more information to come about the medicine, in particular its safety and effectiveness in patients whose tumours do not contain mutations in KRAS.