European Medicines Agency

London, 19 December 2008
Doc. Ref. EMEA/651597/2008

# Questions and answers on the withdrawal of the marketing application for Theraloc

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

On 1 December 2008, Oncoscience AG officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Theraloc, for the treatment of children and adolescents with resistant or recurrent high-grade glioma. Theraloc was designated as an orphan medicinal product on 2 September 2004.

**What is Theraloc?**
Theraloc is a concentrate that is made up into a solution for infusion (drip into a vein). It contains the active substance nimotuzumab.

**What was Theraloc expected to be used for?**
Theraloc was expected to be used to treat adolescents and children from the age of three years with high-grade glioma. Glioma is a type of brain tumour that begins in 'glial' cells (the cells that surround and support nerve cells). Theraloc was to be used when the glioma was 'resistant' (it did not respond to other treatments) or 'recurrent' (it had come back after previous treatment).

**How is Theraloc expected to work?**
The active substance in Theraloc, nimotuzumab, 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. Nimotuzumab binds to an antigen called epidermal growth factor receptor (EGFR), a protein that can be found on the surface of certain tumour cells. When activated, EGFR helps the tumour cells grow, multiply and spread. By blocking EGFR, nimotuzumab was expected to slow down the progression of glioma.

**What documentation did the company present to support its application to the CHMP?**
The effects of Theraloc were first tested in experimental models before being studied in humans. Theraloc has been studied in one main study involving 47 children and adolescents with glioma who had no treatments available that could cure their disease. Theraloc was not compared with any other treatment. The main measure of effectiveness was the number of patients who responded to treatment. A patient was classified as a responder if the tumours disappeared, shrank or stayed the same size.

**How far into the evaluation was the application when it was withdrawn?**
The application was at day 173 when the company withdrew. After the CHMP had assessed the responses from the company to a list of questions, there were still some unresolved issues outstanding. The CHMP normally takes up to 210 days to evaluate a new application. Based on the review of the initial documentation, the CHMP prepares a list of questions at day 120, which is sent to the company. Once the company has supplied responses to the questions, the CHMP reviews them and may, before giving an opinion, ask any remaining questions at day 180. Following the CHMP's opinion, it usually takes around two months for the European Commission to grant a licence.

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 71 29
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

**What was the recommendation of the CHMP at that time?**
Based on the review of the data and the company's response to the CHMP list of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Theraloc could not have been approved for the treatment of children and adolescents with recurrent high-grade glioma.

**What were the main concerns of the CHMP?**
The CHMP was concerned that the company had not supplied sufficient evidence to demonstrate that Theraloc could be made in a reliable manner, and that insufficient information was provided on the way the product was treated by the body.
The Committee had concerns that the benefits of Theraloc had not been demonstrated, because the main study did not show a benefit in terms of survival and none of the patients treated with Theraloc showed a complete disappearance of the tumours. In addition, it was not clear whether all the patients included in the study had resistant or recurrent disease.
The CHMP was also concerned about the medicine's safety. No information was provided on whether the body would produce antibodies against the medicine and there was a high rate of serious side effects.
Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of Theraloc had not been sufficiently demonstrated and any benefits did not outweigh the identified risks.

**What were the reasons given by the company to withdraw the application?**
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

**What are the consequences of the withdrawal for patients undergoing clinical trials or compassionate use programmes with Theraloc?**
The company informed the CHMP that there are no consequences for patients currently included in clinical trials or compassionate use programmes with Theraloc.
If you are in a clinical trial or compassionate use programme and need more information about your treatment, contact the doctor who is giving it to you.