European Medicines Agency

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Questions and answers on the recommendation for the refusal of a change to the marketing authorisation for Avastin

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

On 19 November 2009, 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 Avastin. The change concerned an extension of indication to add the treatment of glioblastoma after relapse.
The company that applied for the change to the authorisation is Roche Registration Limited. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Avastin?
Avastin is a concentrate that is made up into a solution for infusion (drip into a vein). It contains the active substance bevacizumab.
Avastin has been authorised since January 2005. It is already used in combination with other medicines to treat cancer of the colon or rectum (large intestine), breast cancer, non-small cell lung cancer and kidney cancer.

What was Avastin expected to be used for?
Avastin was also expected to be used to treat another type of cancer called glioblastoma. It was to be used when the disease had relapsed (come back after previous treatment). Glioblastoma is a type of brain tumour that affects the 'glial' cells (the cells that surround and support the nerve cells). Avastin was to be used in on its own or in combination with irinotecan (another anticancer medicine).

How is Avastin expected to work?
In glioblastoma, Avastin is expected to work in the same way as it does in its existing indications. The active substance in Avastin, bevacizumab, 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 in the body. Bevacizumab has been designed to attach to vascular endothelial growth factor (VEGF), a protein that circulates in the blood and makes blood vessels grow. By attaching to VEGF, Avastin stops it having an effect. As a result, the cancer cells cannot develop their own blood supply and are starved of oxygen and nutrients, helping to slow down the growth of tumours.

What documentation did the company present to support its application to the CHMP?
The company presented the results of one main study involving 167 patients with glioblastoma that had come back after one or two previous courses of treatment. Half of the patients received Avastin alone and the other half received Avastin together with irinotecan. There were two main measures of effectiveness: the number of patients whose tumours had responded to treatment ; and 'progression-free survival' (the number of patients who were still alive and whose disease had not got worse) after six months of treatment. The study also looked at how long the patients survived.

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What were the major concerns that led the CHMP to recommend the refusal of the change to the marketing authorisation?
The CHMP was concerned that the company had not provided sufficient evidence of the medicine's benefits, because the number of patients who responded to treatment was not dramatic and because response rates may not be a suitable measure of the medicine's effectiveness. In addition, the CHMP could not interpret the findings on survival because the study did not compare Avastin directly with any other treatments.
Therefore, at that point in time, the CHMP was of the opinion that the balance of benefits and risks of Avastin in the treatment of glioblastoma after relapse could not be established. Hence, the CHMP recommended that the change to the marketing authorisation be refused.

What are the consequences of the refusal for patients in clinical trials using Avastin?
The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Avastin for glioblastoma. 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 Avastin for the treatment of colorectal, breast, lung and kidney cancer?
There are no consequences on the use of Avastin in its authorised indications, for which the balance of benefits and risks remains unchanged.

The full European Public Assessment Report for Avastin is available here.