European Medicines Agency

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QUESTIONS AND ANSWERS ON THE WITHDRAWAL OF THE MARKETING APPLICATION for LENALIDOMIDE CELGENE EUROPE

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

On 30 May 2008, Celgene Europe Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Lenalidomide Celgene Europe, for the treatment of anaemia due to myelodysplastic syndromes. Lenalidomide Celgene Europe was designated as an orphan medicinal product on 8 March 2004.

What is Lenalidomide Celgene Europe?
Lenalidomide Celgene Europe is a medicine containing the active substance lenalidomide. Lenalidomide has been authorised in the European Union since June 2007 under the name Revlimid, for the treatment of multiple myeloma. Multiple myeloma is a cancer of the plasma cells in the bone marrow.

What was Lenalidomide Celgene Europe expected to be used for?
Lenalidomide Celgene Europe was expected to be used to treat anaemia (low red blood cell counts) caused by myelodysplastic syndromes, a group of conditions where too few blood cells are produced by the bone marrow. In some cases, myelodysplastic syndromes can lead to the development of acute myeloid leukaemia (a type of cancer affecting the white blood cells).
Lenalidomide Celgene Europe was to be used in patients who were dependent on receiving blood transfusions to treat their anaemia and whose myelodysplastic syndromes were associated with a specific genetic mutation (deletion of part of chromosome number 5), and with a low to intermediate risk of progressing to leukaemia or death.

How is Lenalidomide Celgene Europe expected to work?
The active substance in Lenalidomide Celgene Europe, lenalidomide, is an immunomodulating agent. This means that it affects the activity of the immune system (the body's natural defences). The exact way that lenalidomide works in myelodysplastic syndromes is not known, but it is thought that it blocks the growth of tumour cells in the bone marrow, while allowing the growth of normal bone marrow cells, including the cells that produce red blood cells.

What documentation did the company present to support its application to the CHMP?
The effects of Lenalidomide Celgene Europe were first tested in experimental models before being studied in humans.
Its effectiveness was studied in one main study, carried out in a number of hospitals and clinics ('sites') in the United States of America and Germany. The study involved 148 patients with transfusion-dependent anaemia, low or intermediate (level 1) risk myelodysplastic syndromes and a deletion of part of chromosome 5 ('5q deletion'). The study looked at the effects of treatment with a daily dose of 10 mg Lenalidomide Celgene Europe either given continuously or as a repeated cycle of three weeks on treatment followed by one week off. The main measure of effectiveness was the proportion of patients who became 'transfusion independent', meaning that their anaemia was controlled without the need for a blood transfusion over an eight-week period.

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How far into the evaluation was the application when it was withdrawn?
The evaluation had finished and the CHMP had given a negative opinion, which had been confirmed following a re-examination procedure. The company withdrew its application before the European Commission had adopted a formal decision.

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 given a negative opinion and did not recommend a marketing authorisation for Lenalidomide Celgene Europe for the for the treatment of anaemia due to myelodysplastic syndromes.

What were the main concerns of the CHMP?
The CHMP had concerns over the way the main study was carried out, which meant that the safety of Lenalidomide Celgene Europe was difficult to assess. In particular, because the study did not compare the medicine to any other treatment, it was difficult to determine if treatment with Lenalidomide Celgene Europe increased the risk of progression to acute myeloid leukaemia. In addition, an inspection of one of the sites where the main study was carried out raised some concerns over the way the results were recorded, which could have further affected the reliability of the main study. Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of Lenalidomide Celgene Europe 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 Lenalidomide Celgene Europe?
The company informed the CHMP that it will continue to make lenalidomide available for patients included in clinical trials or compassionate use programmes. 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.

What is happening with Revlimid used for the treatment of multiple myeloma?
There are no consequences of this withdrawal on the use of Revlimid, which also contains lenalidomide, in its authorised indication. The balance of benefits and risks for Revlimid remains unchanged.