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Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Revlimid (lenalidomide)

On 20 June 2012, Celgene Europe Ltd. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a change to the marketing authorisation for Revlimid, to extend its use to the treatment of patients with newly diagnosed multiple myeloma.

What is Revlimid?

Revlimid is an anticancer medicine. It is used in combination with dexamethasone (an anti-inflammatory medicine) to treat adults with multiple myeloma whose disease has been treated at least once in the past (second-line treatment). Multiple myeloma is a cancer of the plasma cells in the bone marrow.

Revlimid was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 12 December 2003 for multiple myeloma.

Revlimid has been authorised in the European Union (EU) since 14 June 2007 and is marketed in 21 EU Member States[1].

What was Revlimid expected to be used for?

Revlimid was also expected to be used for the maintenance treatment of newly diagnosed multiple myeloma patients who have not progressed following initial treatment with Revlimid, melphalan, and prednisone (other medicines to treat multiple myeloma), or following autologous stem cell transplant (a transplant of the patient's own blood-producing cells).

[1] Revlimid is marketed in Austria, Belgium, Cyprus, the Czech Republic, Denmark, Finland, France, Germany, Greece Ireland, Italy, Luxembourg, Malta, the Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

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How is Revlimid expected to work?

In newly diagnosed multiple myeloma, Revlimid was expected to work in the same way as it does in its existing indication. The active substance in Revlimid, lenalidomide, is an immunomodulating agent. This means that it affects the activity of the immune system (the body's natural defences). Lenalidomide works in a number of different ways in multiple myeloma: it blocks the development of tumour cells, prevents the growth of blood vessels within tumours and also stimulates some of the specialised cells of the immune system to attack the cancerous cells.

What did the company present to support its application?

The applicant presented data from two main studies involving 1073 patients with newly diagnosed multiple myeloma. In the first study, patients were given melphalan and prednisone together with either Revlimid or placebo (a dummy treatment) during an initial phase, followed by a maintenance phase where patients received Revlimid or placebo. The main measure of effectiveness was how long the patients survived without their disease getting worse. The second study compared Revlimid with placebo in patients who had received an autologous stem cell transplant. This study looked at how long patients survived after the transplant without their disease getting worse.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated lists of questions. After the CHMP had assessed the company's responses to the questions, there were still some unresolved issues.

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 lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Revlimid could not have been approved to treat newly diagnosed multiple myeloma patients.

The Committee was concerned that, while there was a clear benefit in terms of delaying the progression of the disease in newly diagnosed multiple myeloma patients, this did not lead to a meaningful improvement of symptoms and longer survival. Furthermore, since Revlimid was associated with an increased risk of developing new cancers, the CHMP could not rule out that the lack of a longer survival could be due to death caused by new cancers. Therefore, more mature survival data and follow-up would be needed to conclude on the benefit-risk balance for this indication.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Revlimid in newly diagnosed multiple myeloma patients did not outweigh its risks.

What were the reasons given by the company for withdrawing the application?

In its official letter, the company stated that its decision to withdraw the application was based on the CHMP's view that the data provided so far require follow-up with more mature data to allow the Committee to reach a clear conclusion on the benefit-risk balance.

The letter from the company notifying the Agency of the withdrawal of the application is available here.

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that clinical trials or compassionate use programmes will not be interrupted and patients will continue to be carefully monitored with respect to overall survival and development of new cancers.

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 for the treatment of multiple myeloma?

There are no consequences on the use of Revlimid in its authorised indication, as Revlimid has a positive benefit-risk balance when used in patients with multiple myeloma who have already had one or more other types of treatment before[2].

The summary of the opinion of the Committee for Orphan Medicinal Products for Revlimid can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

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

[2] http://www.ema.europa.eu/docs/en_GB/document_library/Medicine_QA/2011/09/WC500112820.pdf