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Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Velcade (bortezomib)

On 2 July 2012, Janssen-Cilag International N.V. 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 of Velcade, which would have extended its use to patients with relapsed follicular non-Hodgkin lymphoma.

What is Velcade?

Velcade is a medicine given by injection that contains the active substance bortezomib. It has been authorised in the EU since April 2004. It is used to treat patients with multiple myeloma (a cancer of the plasma cells in the bone marrow). It is given in combination with melphalan and prednisone (other medicines for multiple myeloma) to patients who have not been treated before and who are not suitable for high-dose chemotherapy with a bone marrow transplant. It is also used on its own in patients whose disease is progressive and who have failed to respond to at least one other treatment and have already had, or cannot undergo, a bone marrow transplant.

What was Velcade expected to be used for?

Velcade was also expected to be used in follicular non-Hodgkin lymphoma (a cancer of the lymph tissue (part of the immune system) that affects a type of white blood cell called B lymphocytes, or B cells), in combination with another medicine called rituximab in patients whose disease had relapsed (returned after treatment).

How was Velcade expected to work?

In relapsed follicular non-Hodgkin lymphoma, Velcade was expected to work in the same way as it does in its existing indications. The active substance in Velcade, bortezomib, is a proteasome inhibitor.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7129
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

It blocks the proteasome, which is a system within cells that breaks down proteins when they are no longer needed. When the proteins in cancer cells, such as the proteins that control the growth of the cells, are not broken down, the cells are affected and eventually die.

What did the company present to support its application?

The applicant presented the results of a study involving 676 patients with follicular non-Hodgkin lymphoma that had relapsed or progressed despite previous treatments, designed to assess the effects of using Velcade in combination with rituximab compared with using rituximab alone in these patients. The main measure of effectiveness was progression free survival (how long the patients lived 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 its first round of 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's questions, at the time of the withdrawal the CHMP had some concerns and was of the provisional opinion that Velcade could not have been approved for the treatment of patients with relapsed follicular non-Hodgkin lymphoma.

The CHMP questioned the relevance of the study results which showed that, overall, patients treated with Velcade plus rituximab lived without their disease getting worse for an average of 1.8 months longer than patients treated with rituximab alone (12.8 months compared with 11 months). The Committee considered that this difference was unlikely to be relevant and was not convinced that a sub-group of patients had been identified who would benefit more from the addition of Velcade to rituximab. The CHMP had concerns about the methodology used to analyse the results, which left some uncertainties about the size of the effect seen. The CHMP was also concerned that the combination of Velcade and rituximab caused more side effects than rituximab alone.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Velcade in the treatment of relapsed follicular non-Hodgkin lymphoma 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 it decided to withdraw the application because the CHMP considered that the data provided did not support a positive benefit-risk balance.

The withdrawal letter is available here.

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

The company informed the CHMP that there are no consequences for patients currently included in clinical trials using Velcade. 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 Velcade for the treatment of multiple myeloma?

There are no consequences on the use of Velcade in its authorised indications.

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