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## EPAR summary for the public

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# Velcade

bortezomib

This document is a summary of the European public assessment report (EPAR) for Velcade. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Velcade.

## What is Velcade?

Velcade is a cancer medicine that contains the active substance bortezomib. It is available in vials (1 and 3.5 mg) as a powder to be made up into a solution for injection.

## What is Velcade used for?

Velcade is used to treat multiple myeloma, a blood cancer, in the following groups of patients:

- previously untreated adults who cannot have high-dose chemotherapy with a blood stem-cell transplant. In these patients, Velcade is used in combination with melphalan and prednisone;
- previously untreated patients who are going to receive high-dose chemotherapy followed by a blood stem-cell transplant. In this group of patients, Velcade is used in combination with dexamethasone, or with dexamethasone plus thalidomide;
- adults whose disease is getting worse after at least one other treatment and who have already had, or cannot undergo, a blood stem-cell transplant. Velcade is either used on its own in these patients or in combination with pegylated liposomal doxorubicin or dexamethasone.

Velcade is also used to treat mantle cell lymphoma, another blood cancer, in untreated adults who cannot have blood stem-cell transplantation. For mantle cell lymphoma, Velcade is used in combination with rituximab, cyclophosphamide, doxorubicin and prednisone.

The medicine can only be obtained with a prescription.



## How is Velcade used?

Treatment with Velcade should only be started and given under the supervision of a doctor who has experience in the use of cancer chemotherapy. Velcade 1 mg must only be given by injection into a vein, while Velcade 3.5 mg is only given either by injection into a vein or under the skin. Velcade must not be given by other routes.

The recommended starting dose is 1.3 mg per square metre body surface area (calculated using the patient's height and weight). When given into a vein, the solution is given as a three- to five-second injection through a catheter (a thin sterile tube). At least 72 hours must pass between two consecutive doses of Velcade. When injected under the skin, it is given in the thigh or abdomen (tummy).

Doses of Velcade are given intermittently, with rest periods in between doses, in treatment cycles of three to six weeks depending on whether Velcade is given alone or in combination with other medicines. If a patient develops severe side effects after a treatment cycle, the treatment must be suspended, delayed or the dose adjusted.

Patients with moderate or severe liver problems should be treated with lower doses. For more information on the use of Velcade, see the summary of product characteristics (also part of the EPAR).

## How does Velcade work?

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

## How has Velcade been studied?

In multiple myeloma, Velcade has been evaluated in 10 main studies involving over 4,339 adults, which evaluated the benefits of Velcade alone or in combination with other treatments. The main measures of effectiveness in these studies were the number of patients who responded to treatment and how long the patients lived without their disease getting worse.

In mantle cell lymphoma, Velcade was evaluated in a main study involving 487 previously untreated adults who were not considered suitable for blood stem-cell transplantation. In this study, Velcade together with rituximab, cyclophosphamide, doxorubicin and prednisone was compared with the same combination containing another medicine, vincristine, in place of Velcade. The main measure of effectiveness was how long the patients lived without their disease getting worse.

## What benefit has Velcade shown during the studies?

Studies in multiple myeloma showed Velcade and combinations containing Velcade to be beneficial in several patient groups. The following is a list of main benefits shown in these studies:

- Previously untreated patients lived for an average of 20.7 months without their disease getting worse when they received Velcade together with melphalan and prednisone, compared with 15.0 months in the patients receiving only melphalan and prednisone.
- Previously patients receiving Velcade lived for an average of 6.2 months without their disease getting worse, compared with 3.5 months in those receiving dexamethasone.
- Around 34% of the patients responded partially or completely to treatment with Velcade (in a study in which Velcade was not compared with any other medicine)

- The study that compared Velcade given under the skin with Velcade given into a vein showed that the percentage of patients who responded partially or completely to treatment was the same (42%) when using either route of administration.
- Around 15% of patients who were candidates for high-dose chemotherapy and a blood stem-cell transplant responded to treatment with Velcade plus dexamethasone, compared with 6% of those given standard combinations. In addition, 49% of these patients responded to Velcade plus thalidomide and dexamethasone, compared with about 26% who responded to treatment containing Velcade plus other anticancer drugs, and 17% who responded to thalidomide and dexamethasone alone.
- patients given Velcade with pegylated liposomal doxorubicin whose disease was getting worse after having failed to respond to at least one other treatment, lived for 9.3 months without their disease getting worse compared to 6.5 months for patients receiving Velcade alone.
- Among patients with worsening disease that had come back or failed to respond to at least one other treatment, around 70% responded to treatment with the Velcade-dexamethasone combination.

In mantle cell lymphoma, patients treated with a combination of Velcade plus rituximab, cyclophosphamide, doxorubicin and prednisone lived longer without their disease getting worse (24.7 months) than those given the same combination but with vincristine in place of Velcade (14.4 months).

## **What is the risk associated with Velcade?**

The most commonly reported side effects during treatment with Velcade are nausea (feeling sick), diarrhoea, constipation, vomiting, fatigue (tiredness), pyrexia (fever), thrombocytopenia (low blood platelets count), anaemia (low red blood cell counts), neutropenia (low levels of neutrophils, a type of white blood cell that fights infection), peripheral neuropathy (nerve damage in the hands and feet), headache, paraesthesia (unusual sensations like pins and needles), decreased appetite, dyspnoea (difficulty breathing), rash, herpes zoster (shingles) and myalgia (muscle pain).

The most serious adverse reactions include heart failure, tumour lysis syndrome (complications due to breakdown of cancer cells), pulmonary hypertension (high blood pressure in the arteries of the lungs), posterior reversible encephalopathy syndrome (a reversible brain disorder), acute diffuse infiltrative pulmonary disease (a severe lung problem), and autonomic neuropathy (damage to nerves controlling organs such as the bladder, eyes, gut, heart and blood vessels). For the full list of all side effects reported with Velcade, see the package leaflet.

Velcade must not be used in people who are hypersensitive (allergic) to bortezomib, boron or to any of the other ingredients. It must not be given to patients with acute diffuse infiltrative pulmonary disease or pericardial disease (disease affecting the sac that surrounds the heart). When Velcade is used with other medicines the restrictions for those medicines must also be taken into account, including the requirements for pregnancy testing and prevention with thalidomide.

## **Why has Velcade been approved?**

The CHMP decided that Velcade's benefits are greater than its risks and recommended that it be given marketing authorisation.

Velcade was originally authorised under 'exceptional circumstances', because, for scientific reasons, limited information was available at the time of approval. As the company had supplied the additional information requested, the 'exceptional circumstances' ended on 19 March 2012.

## **What measures are being taken to ensure the safe and effective use of Velcade?**

A risk management plan has been developed to ensure that Velcade is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Velcade, including the appropriate precautions to be followed by healthcare professionals and patients. In addition, the company that markets Velcade will ensure that healthcare professionals receive educational material explaining how to calculate the dose and how to prepare and administer the medicine.

## **Other information about Velcade:**

The European Commission granted a marketing authorisation valid throughout the European Union for Velcade on 26 April 2004.

The full EPAR for Velcade can be found on the Agency's website: [ema.europa.eu/Find\\_medicine/Human medicines/European Public Assessment Reports](http://ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports). For more information about treatment with Velcade, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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