Summary of risk management plan for Bortezomib 3.5 mg and 1 mg powder for solution for injection (Bortezomib)

This is a summary of the risk management plan (RMP) for Bortezomib 3.5 mg and 1 mg powder for solution for injection. The RMP details important risks of Bortezomib 3.5 mg and 1 mg powder for solution for injection, how these risks can be minimised, and how more information will be obtained about Bortezomib 3.5 mg and 1 mg powder for solution for injection's risks and uncertainties (missing information).

Bortezomib 3.5 mg and 1 mg powder for solution for injection's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Bortezomib 3.5 mg and 1 mg powder for solution for injection should be used.

Important new concerns or changes to the current ones will be included in updates of Bortezomib 3.5 mg and 1 mg powder for solution for injection's RMP.

I. The medicine and what it is used for

Bortezomib powder for solution for injection is authorized for the treatment of multiple myeloma as monotherapy or in combination with pegylated liposomal doxorubicin or dexamethasone in adult patients with progressive multiple myeloma who have received at least 1 prior therapy and who have already undergone or are unsuitable for haematopoietic stem cell transplantation, in combination with melphalan and prednisone adult patients with previously untreated multiple myeloma who are not eligible for high-dose chemotherapy with haematopoietic stem cell transplantation, for the induction treatment in combination with dexamethasone, or with dexamethasone and thalidomide in adult patients with previously untreated multiple myeloma who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation.

Bortezomib powder for solution for injection is also indicated in combination with rituximab, cyclophosphamide, doxorubicin and prednisone for adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation (see SmPC for the full indication). It contains Bortezomib as the active substance and it is given by intravenous route.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Bortezomib 3.5 mg and 1 mg powder for solution for injection, together with measures to minimise such risks and the proposed studies for learning more about Bortezomib 3.5 mg and 1 mg powder for solution for injection's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Important advice on the medicine's packaging;

- The authorised pack size - the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

- The medicine's legal status - the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In the case of Bortezomib 3.5 mg and 1 mg powder for solution for injection, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below under section II.B.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment and signal management activity, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Bortezomib 3.5 mg and 1 mg powder for solution for injection (Bortezomib) is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Bortezomib 3.5 mg and 1 mg powder for solution for injection are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Bortezomib 3.5 mg and 1 mg powder for solution for injection. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	• Heart failure • Hepatotoxicity • Acute hypersensitivity reaction • Tumour lysis syndrome • Peripheral motor neuropathy (including paralysis) • Autonomic neuropathy • Acute diffuse infiltrative pulmonary disease • Pericardial disease • Pulmonary hypertension • Herpes zoster infection • Posterior reversible encephalopathy syndrome • Optic neuropathy and different degrees of visual impairment (up to blindness) • Thrombocytopenia and thrombocytopenia with associated bleeding • Neutropenia and neutropenia with associated infection
Important potential risks	• Progressive multifocal leukoencephalopathy • Ventricular rhythm abnormalities • Guillain-Barré syndrome • Other central nervous system disorders • Medication/dispensing errors
Missing information	<u>Routine risk minimisation measures:</u> Sections 4.2, 4.4 and 6.6 of Bortezomib SmPC have information on this safety concern. Section 3 of Bortezomib PIL has information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. <u>Additional risk minimisation measures:</u> Bortezomib Educational Programme to the HCPs, pharmacists and other specialized healthcare personnel involved in prescribing, dispensing and/or reconstitution of Bortezomib.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Bortezomib 3.5 mg and 1 mg powder for solution for injection.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Bortezomib 3.5 mg and 1 mg powder for solution for injection.