Part VI: Summary of the risk management plan

Summary of risk management plan for Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion (Bendamustine hydrochloride)

This is a summary of the risk management plan (RMP) Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion. The RMP details important risks of Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion, how these risks can be minimised, and how more information will be obtained about Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion's risks and uncertainties (missing information).

Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion's summary of product characteristics (SmPC) and their package leaflets give essential information to healthcare professionals and patients on Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion should be used.

Important new concerns or changes to the current ones will be included in updates of Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion's RMP.

I. The medicine and what it is used for

Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion are indicated as:

First-line treatment of chronic lymphocytic leukaemia (Binet stage B or C) in patients for whom fludarabine combination chemotherapy is not appropriate.

Indolent non-Hodgkin's lymphomas as monotherapy in patients who have progressed during or within 6 months following treatment with rituximab or a rituximab containing regimen.

Front line treatment of multiple myeloma (Durie-Salmon stage II with progress or stage III) in combination with prednisone for patients older than 65 years who are not eligible for autologous stem cell transplantation and who have clinical neuropathy at time of diagnosis precluding the use of thalidomide or bortezomib containing treatment.

It contains bendamustine hydrochloride as the active substance and given by intravenous infusion.

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

Important risks of Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion, together with measures to minimise such risks and the proposed studies for learning more about Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion'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 'Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion', these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

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

II.A List of important risks and missing information

Important risks of Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion for infusion 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 Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion. 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).

Important identified risk(s)	• Myelosuppression • Infections (including opportunistic infections of herpes zoster, cytomegalovirus, *Pneumocystis jirovecii* pneumonia) • Hepatitis B reactivation
Important potential risk(s)	• Medication error (for 25 mg/ml concentrate for solution for infusion)
Missing information	• None

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Important Identified Risk: Myelosuppression	
Risk minimisation measures	Sections 4.2, 4.3, 4.4, 4.5, 4.8 and 4.9 of Accord Bendamustine SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. Additional risk minimisation measures: DHPC letter.
Important Identified Risk: Infections (including opportunistic infections of herpes zoster, cytomegalovirus, *Pneumocystis jirovecii* pneumonia)	
Risk minimisation measures	Sections 4.3, 4.4, 4.5 and 4.8 of Accord Bendamustine SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. Additional risk minimisation measures: DHCP communication letter.
Important Identified Risk: Hepatitis B reactivation	
Risk minimisation measures	Sections 4.4 and 4.8 of Accord Bendamustine SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. Additional risk minimisation measures: DHPC letter.

Important Potential risk: Medication error (for 25 mg/ml concentrate for solution for infusion)	
Risk minimisation measures	Section 6.6 of Accord Bendamustine SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. Additional risk minimisation measures: DHCP communication letter.

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 authorization or specific obligation of Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion.

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

There are no studies required for Bendamustine hydrochloride 2.5 mg/ml powder for concentrate for solution for infusion and Bendamustine hydrochloride 25 mg/ml concentrate for solution for infusion as post-authorisation development plan.