Summary of risk management plan for Pepaxti (melphalan flufenamide)

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

Pepaxti's summary of product characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals and patients on how Pepaxti should be used.

This summary of the RMP of Pepaxti should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European public assessment report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Pepaxti's RMP.

I. The medicine and what it is used for

Pepaxti is indicated, in combination with dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least 3 prior lines of therapies, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapy. For patients with a prior autologous stem cell transplantation, the time to progression should be at least 3 years from transplantation (see SmPC for the full indication). It contains melphalan flufenamide as the active substance, and it is given by intravenous infusion after reconstitution and dilution.

Further information about the evaluation of Pepaxti's benefits can be found in Pepaxti's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage https://www.ema.europa.eu/en/medicines/human/EPAR/pepaxti

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

Important risks of Pepaxti, together with measures to minimise such risks and the proposed studies for learning more about melphalan flufenamide'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 PL 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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including periodic safety update report (PSUR) assessment, 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 Pepaxti is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Pepaxti are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 Pepaxti. 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. use in patients with severely impaired kidney function).

List of important risks and missing information	
Missing information	Use in patients with severely impaired kidney function

II.B Summary of important risks

Use in patients with severe renal impairment	
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.2 stating that there are insufficient data in patients with estimated kidney function/glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 to support a dose recommendation. Additional risk minimisation measures: • None
Additional pharmacovigilance activities	Study OP-107 (BRIDGE): Pharmacokinetics, safety, and tolerability of melflufen in patients with relapsed-refractory multiple myeloma and impaired kidney function (eGFR <45 mL/min). See section II.C of this summary for an overview of the postauthorisation development plan.

II.C Postauthorisation development plan

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

There are no planned studies which are conditions of the marketing authorisation or specific obligation of Pepaxti.

II.C.2 Other studies in postauthorisation development plan

BRIDGE (OP-107)