Part VI: Summary of the risk management plan

Summary of risk management plan for Mitoxantron "Ebewe" (mitoxantrone hydrochloride)

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

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

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

I. The medicine and what it is used for

Mitoxantron "Ebewe" is authorized for:

- Treatment of metastatic breast cancer.
- Treatment of non-Hodgkin's lymphoma (NHL).
- Treatment of acute myeloid leukemia (AML) in adults.
- In combination regimens is indicated in the remission induction treatment of blast crisis in chronic myeloid leukemia.
- In combination with corticosteroids for palliation (e.g. pain relief) related to advanced castrate-resistant prostate cancer.
- Treatment of patients with highly active relapsing multiple sclerosis (MS) associated with rapidly evolving disability where no alternative therapeutic options exist.

It contains mitoxantrone as an active substance and is administered intravenously as concentrate for solution for infusion (2 mg/ml).

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of Mitoxantron "Ebewe", together with measures to minimize such risks and the proposed studies for learning more about mitoxantrone, concentrate for solution for infusion's risks are outlined below.

Measures to minimize 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 authorized 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 minimize its risks.

Together, these measures constitute *routine risk minimization measures.*

In the case of mitoxantrone, concentrate for solution for infusion, these measures are supplemented with *additional risk minimization measures* mentioned under relevant important risks below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including Periodic Safety Update Report (PSUR) assessment 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 Mitoxantron "Ebewe" are risks that need special risk management activities to further investigate or minimize 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 Mitoxantron "Ebewe". 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).

Table 6 Part VI: List of important risks and missing information

Important identified risks	Risk on cardiotoxicity: Cardiac function/ myocardial toxicity
	Risk on hematotoxicity: Secondary acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS)
Important potential risks	None
Missing information	None

II.B: Summary of important risks

Table 7 Part VI: Important identified risk: Risk on cardiotoxicity: Cardiac function/ myocardial toxicity

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.2, 4.4, 4.5, 4.8 and 5.1 Package leaflet sections 2, 3 and 4 Legal status: Prescription only **Additional risk minimization measures:** • Guide for prescribing physician

	• Checklist for prescribing physician • Medication guide for patients • Patient alert card

Table 8 Part VI: Important identified risk: Risk on hematotoxicity: Secondary AML and MDS

Risk minimization measures	**Routine risk minimization measures:** SmPC sections, 4.2, 4.4, 4.5 and 4.8 Package leaflet sections 2, 3 and 4 Legal status: Prescription only **Additional risk minimization measures:** • Guide for prescribing physician • Checklist for prescribing physician • Medication guide for patients • Patient alert card

II.C: Post-authorization development plan

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

There are no studies which are conditions of the marketing authorization or specific obligation of Mitoxantron “Ebewe”.

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

There are no studies required for Mitoxantron “Ebewe”.