Summary of risk management plan for MOZOBIL (Plerixafor)

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

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

This summary of the RMP for MOZOBIL 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 MOZOBIL's RMP.

1.1. THE MEDICINE AND WHAT IT IS USED FOR

MOZOBIL is authorized in combination with Granulocyte-Colony Stimulating Factor (G-CSF) to enhance mobilisation of hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in adult patients with lymphoma and multiple myeloma whose cells mobilise poorly. The proposed indication for MOZOBIL is as follows:

Adult patients

MOZOBIL is indicated in combination with G-CSF to enhance mobilisation of hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in adult patients with lymphoma or multiple myeloma whose cells mobilise poorly.

Paediatric patients (1 to less than 18 years)

MOZOBIL is indicated in combination with G-CSF to enhance mobilisation of hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children with lymphoma or solid malignant tumours and either:

- pre-emptively, when circulating stem cell count on the predicted day of collection after adequate mobilization with G-CSF (with or without chemotherapy) is expected to be insufficient with regards to desired hematopoietic stem cells yield or
- who previously failed to collect sufficient hematopoietic stem cells. (see SmPC for the full indication).

It contains plerixafor as the active substance and it is given by subcutaneous injection

Refer to EPAR ref. European Medicines Agency (EMA)/H/C/1030 dated June 2009 available on the EMA website at the following link:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001030/human_med_000910.jsp&mid=WC0b01ac058001d124

1.2. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERIZE THE RISKS

Important risks of MOZOBIL, together with measures to minimize such risks and the proposed studies for learning more about MOZOBIL's risks, are outlined in the next sections.

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 (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

If important information that may affect the safe use of MOZOBIL is not yet available, it is listed under "missing information" outlined in the next section.

1.2.1. List of important risks and missing information

Important risks of MOZOBIL 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 MOZOBIL. 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 (eg, on the long-term use of the medicine).

Table 1 - List of important risks and missing information

Important identified risk	Splenomegaly and splenic rupture
Important potential risks	Interstitial lung disease Myocardial Infarction Tumor cell mobilization Drug level NOS increased Anxiety, hallucination (including hallucination, visual hallucination, and auditory hallucination)

	Effect on embryo-fetal development (including teratogenicity and fetal growth restriction)
Missing information	Safety profile in paediatric under 2 years of age

NOS: Not Otherwise Specified.

1.2.2. Summary of important risks

Table 2 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any - Important identified risk: Splenomegaly and splenic rupture

Important identified risk: Splenomegaly and splenic rupture	
Evidence for linking the risk to the medicine	Clinical data, postmarketing data, literature and NEUPOGEN® Prescribing Information.[a]
Risk factors and risk groups	All patients receiving G-CSF plus plerixafor.
Risk minimization measures	**Routine risk minimization measures:** Labelled in Sections 4.4 and 4.8 of the SmPC **Additional risk minimization measures:** None

a NEUPOGEN® (filgrastim). Prescribing Information. Amgen Inc. 2007.

G-CSF: Granulocyte-Colony Stimulating Factor; SmPC: Summary of Product Characteristics.

Table 3 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any - Important potential risk: Interstitial lung disease

Important potential risk: Interstitial lung disease	
Evidence for linking the risk to the medicine	Clinical data and postmarketing data.
Risk factors and risk groups	Interstitial lung disease has been reported in patients receiving G-CSF.[a, b, c, d]
Risk minimization measures	No risk minimization measure

a Gertz MA, Lacy MQ, Bjornsson J, Litzow MR. Fatal pulmonary toxicity related to the administration of granulocyte colony-stimulating factor in amyloidosis: a report and review of growth factor-induced pulmonary toxicity. J Hematother Stem Cell Res. 2000 Oct;9(5):635-43.

b Takahashi S, Oshima Y, Okamoto S, Nishiwaki K, Nagayama H, Inoue T, et al. Recombinant human granulocyte colony stimulating factor (G-CSF) combined conditioning regimen for allogeneic bone marrow transplantation (BMT) in standard-risk myeloid leukemia. Am J Hematol. 1998;57(4):303-8.

c Yamashiki M, Nishimura A, Nobori T, Nakabayashi S, Takagi T, Inoue K, et al. In vitro effects of sho-saiko-to on production of granulocyte colony-stimulating factor by mononuclear cells from patients with chronic hepatitis C. Int J Immunopharmacol. 1997;19(7):381-5.

d Niitsu N, Iki S, Muroi K, Motomura S, Murakami M, Takeyama H,et al. Interstitial pneumonia in patients receiving granulocyte colony stimulating factor during chemotherapy: survey in Japan 1991-96. Br J Cancer. 1997;76(12):1661-6.

G-CSF: Granulocyte-Colony Stimulating Factor.

Table 4 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any - Important potential risk: Myocardial infarction

Important potential risk: Myocardial infarction	
Evidence for linking the risk to the medicine	Clinical data and postmarketing data.
Risk factors and risk groups	Patients with cardiovascular risk factors.
Risk minimization measures	**Routine risk minimization measures:** Labelled in Section 4.8 of the SmPC **Additional risk minimization measures:** None

SmPC: Summary of Product Characteristics.

Table 5 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any - Important potential risk: Tumor cell mobilization

Important potential risk: Tumor cell mobilization	
Evidence for linking the risk to the medicine	Tumor Mobilization Position Paper, clinical data and postmarketing data.
Risk factors and risk groups	Patients receiving stem cell mobilization.
Risk minimization measures	**Routine risk minimization measures:** Labelled in Section 4.4 of the SmPC **Additional risk minimization measures:** None

SmPC: Summary of Product Characteristics.

Table 6 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any - Important potential risk: Drug level NOS increased

Important potential risk: Drug level NOS increased	
Evidence for linking the risk to the medicine	Clinical study report AMD3100-1101
Risk factors and risk groups	Patients with reduced renal clearance.
Risk minimization measures	**Routine risk minimization measures:** Labelled in Section 4.2 of the SmPC (Posology and method of administration) **Additional risk minimization measures:** None

NOS: Not Otherwise Specified; SmPC: Summary of Product Characteristics.

Table 7 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any - Important potential risk: Anxiety, hallucination (including hallucination, visual hallucination, and auditory hallucination)

Important potential risk: Anxiety, hallucination (including hallucination, visual hallucination, and auditory hallucination)	
Evidence for linking the risk to the medicine	Clinical data, postmarketing data and literature.
Risk factors and risk groups	In the general population, risk of anxiety is higher in younger people, women, and people from lower socioeconomic groups. Among cancer patients, demographic differences are less relevant, although association with sex remains in multivariate analyses.[a] In addition, patients with newly diagnosed cancer are at higher risk for anxiety, as are those with functional deficits.[a] Sleep disturbances in patients undergoing HSCT have been associated with physical functioning, fatigue, and treatment-specific distress.[b] Cancer patients receiving certain treatments (eg, opioids for pain management) may be at higher risk for hallucinations and nightmares.
Risk minimization measures	No risk minimization measure

a Stark D, Kiely M, Smith A, Velikova G, House A, Selby P. Anxiety Disorders in Cancer Patients: Their Nature, Associations, and Relation to Quality of Life. Journal of Clinical Oncology, 2002 July 15;20(14):3137-48.

b Rischer J, Scherwath A, Zander AR, Koch U and Schulz-Kindermann F. Sleep disturbances and emotional distress in the acute course of hematopoietic stem cell transplantation. Bone Marrow Transplantation, 2009;44:121-8.

HSCT: Hematopoietic Stem Cell Transplantation.

Table 8 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any - Important potential risk: Effect on embryo-fetal development (including teratogenicity and fetal growth restriction)

Important potential risk: Effect on embryo-fetal development (including teratogenicity and fetal growth restriction)	
Evidence for linking the risk to the medicine	Clinical data and postmarketing data.
Risk factors and risk groups	Women who are pregnant and require stem cell mobilization.
Risk minimization measures	**Routine risk minimization measures:** Labelled in Sections 4.6 and 5.3 of the SmPC. **Additional risk minimization measures:** None

SmPC: Summary of Product Characteristics.

Table 9 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any – Missing information: Safety profile in paediatric under 2 years of age

Missing information: Safety profile in paediatric under 2 years of age	
Risk minimization measures	**Routine risk minimization measures:** Labelled in section 5 (pharmacological properties) of the SmPC

Missing information: Safety profile in paediatric under 2 years of age	
	Additional risk minimization measures: None

1.2.3. Post-authorization development plan

1.2.3.1 Studies which are conditions of the marketing authorization

There is no study which is condition of the marketing authorization or specific obligation of MOZOBIL.

1.2.3.2 Other studies in post-authorization development plan

Not applicable.