Summary of Risk Management Plan for Vimizim® (elosulfase alfa)

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The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of Vimizim is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g., by mentioning risks occurring in populations or indications not included in the Swiss authorisation.
Please note that the reference document which is valid and relevant for the effective and safe use of Vimizim in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

DRAC AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Vimizim.

Summary of Risk Management Plan for Vimizim (elosulfase alfa)

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

Vimizim's Information for healthcare professionals (summary of product characteristics / SmPC) give essential information to healthcare professionals on how Vimizim should be used.

This summary of the RMP for Vimizim should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of 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 Vimizim's RMP.

I. The medicine and what it is used for

Vimizim is authorized for mucopolysaccharidosis type IVA (MPS IVA, Morquio A Syndrome) (see Information for Professionals for the full indication). It contains elosulfase alfa as the active substance and it is given by intravenous administration.

Further information about the evaluation of Vimizim's benefits can be found in Vimizim's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage:
https://www.ema.europa.eu/en/documents/overview/vimizim-epar-summary_public_en.pdf

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

Important risks of Vimizim, together with measures to minimise such risks and the proposed studies for learning more about Vimizim'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 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 minimise its risks.

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

In the case of Vimizim, 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, 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 Vimizim is not yet available, it is listed under 'missing information' below.

II.A. List of important risks and missing information

Important risks of Vimizim 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 Vimizim. 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	• Infusion reactions (including anaphylaxis and severe allergic reactions)
Important potential risks	• Immunogenicity • Spinal/Cervical Cord Compression (including laxity and unmasking myelopathic symptoms) • Medication errors
Important missing information	• Long-term Safety and Tolerability • Safety in patients with hepatic impairments, safety in patients with renal impairments, safety in patients with cardiac impairments, and safety in pregnancy and lactation

II.B. Summary of important risks

Important identified risk: Infusion Reactions (including anaphylaxis and severe allergic reactions)	
Evidence for linking the risk to the medicine	Clinical studies and post-marketing data
Risk factors and risk groups	None identified
Risk minimisation measures	<u>Routine risk minimisation measures:</u> Information for Professionals, Section Posology/Administration, Warnings and precautions, and Undesirable effects. Legal status: Restricted medical prescription. Treatment should be supervised by a physician experienced in the management of

	patients with MPS IVA or other inherited metabolic diseases Additional risk minimisation measures: Healthcare provider educational materials
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Morquio A Registry Study (MARS) See Section II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Immunogenicity:	
Evidence for linking the risk to the medicine	Clinical studies
Risk factors and risk groups	No risk factors or at-risk populations have been identified for the development of anti-drug antibodies, as all patients treated with Vimizim in the clinical trial program to date have developed sustained anti-drug antibodies
Risk minimisation measures	Routine risk minimisation measures: Information for Healthcare Professionals, Section Undesirable effects Legal status: Restricted medical prescription. Treatment should be supervised by a physician experienced in the management of patients with MPS IVA or other inherited metabolic diseases. Additional risk minimisation measures: No risk minimisation measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Morquio A Registry Study (MARS) See Section II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Spinal/Cervical Cord Compression (including laxity and unmasking myelopathic symptoms)	
Evidence for linking the risk to the medicine	Clinical studies and post-marketing data
Risk factors and risk groups	No known risk groups or risk factors
Risk minimisation measures	Routine risk minimisation measures: Information for Professionals, Section, Warnings and precautions.

	Legal status: Medicinal product subject to restricted medical prescription. Treatment should be supervised by a physician experienced in the management of patients with MPS IVA or other inherited metabolic diseases. Additional risk minimisation measures: No risk minimisation measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Morquio A Registry Study (MARS) See Section II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Medication Errors	
Evidence for linking the risk to the medicine	Clinical studies and post-marketing data
Risk factors and risk groups	Not applicable
Risk minimisation measures	Routine risk minimisation measures: Legal status: Medicinal product subject to restricted medical prescription. Treatment should be supervised by a physician experienced in the management of patients with MPS IVA or other inherited metabolic diseases. Additional risk minimisation measures: Healthcare provider educational materials
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Morquio A Registry Study (MARS) See Section II.C of this summary for an overview of the post-authorisation development plan.

Important missing information: Long-term Safety and Tolerability	
Risk minimisation measures	Legal status: Medicinal product subject to restricted medical prescription. Treatment should be supervised by a physician experienced in the management of patients with MPS IVA or other inherited metabolic diseases.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Morquio A Registry Study (MARS) See Section II.C of this summary for an overview of the post-

	authorisation development plan.

Important missing information: Safety in patients with hepatic impairments, safety in patients with renal impairments, safety in patients with cardiac impairments, and safety in pregnancy and lactation	
Risk minimisation measures	Routine risk minimisation measures: Information for Healthcare Professionals, Section pregnancy and lactation Legal status: Medicinal product subject to restricted medical prescription. Treatment should be supervised by a physician experienced in the management of patients with MPS IVA or other inherited metabolic diseases. Additional risk minimisation measures: No risk minimisation measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Morquio A Registry Study (MARS) See Section II.C of this summary for an overview of the post-authorisation development plan.

II.C. Post-authorisation development plan

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

The following studies are conditions of the marketing authorisation: **Study**

Short Name: Morquio A Registry Study (MARS) (110-504)

Purpose of the study:

- To characterize and describe the MPS IVA population as a whole, including the heterogeneity, progression, and natural history of MPS IVA.
- To evaluate the long-term effectiveness and safety of Vimizim, including, but not limited to, the occurrence of serious hypersensitivity reactions, anaphylaxis, and changes in antibody status.
- To help the medical community with the development of recommendations for monitoring MPS IVA patients and reports on patient outcomes to optimize patient care.
- To collect data on other treatments and evaluate the prevalence of their use and their effectiveness.
- To characterize the effects and safety of Vimizim treatment up to 5 years from enrolment in the Registry for patients under 5 years of age.
- To monitor pregnancy exposure, including maternal, neonatal, and infant outcomes.

- To monitor patients who have completed the MOR-005 and MOR-007 clinical trials. These patients will be encouraged to enroll in the applicable Registry Sub-study and will be monitored using the MOR-005 and MOR-007 assessment schedules respectively.

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

There are no other studies in the post-authorisation development plan.