PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

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 summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients 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.

1 THE MEDICINE AND WHAT IT IS USED FOR

Vimizim is authorised for mucopolysaccharidosis type IVA (MPS IVA, Morquio A Syndrome) (see SmPC 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

2 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 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 (eg, 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.

2.1 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 (eg, on the long-term use of the medicine).

Table 2-1 List of important risks and missing information

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

2.2. Summary of important risks

Table 2-2 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 postmarketing data
Risk factors and risk groups	None identified
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Section 4.2, 4.4, and 4.8 PL Section 2 and 4 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 <u>Additional risk minimisation measures:</u> Healthcare provider educational materials
Additional pharmacovigilance activities	<u>Additional pharmacovigilance activities:</u> Morquio A Registry Study (MARS) See Section 2.3 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	<u>Routine risk minimisation measures:</u> SmPC Section 4.8 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. <u>Additional risk minimisation measures:</u> No risk minimisation measures
Additional pharmacovigilance activities	<u>Additional pharmacovigilance activities:</u> Morquio A Registry Study (MARS) See Section 2.3 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 postmarketing data
Risk factors and risk groups	No known risk groups or risk factors
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 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 2.3 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 postmarketing 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 2.3 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 2.3 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: SmPC Section 4.6 (for pregnancy and lactation) PL Section 2 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 2.3 of this summary for an overview of the post-authorisation development plan.

PL=Patient Leaflet; SmPC=Summary of Product Characteristics

2.3 Post-authorisation development plan

2.3.1 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 characterise 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 elosulfase alfa.
- To help the MPS IVA medical community with the development of recommendations for monitoring subjects and reports on subject outcomes to optimize subject care.

- To collect data on other treatment paradigms, evaluate the prevalence of their use and their effectiveness.
- To characterize the effects of elosulfase alfa treatment 5 years from enrollment date on subjects under 5 years of age.

2.3.2 Other studies in post-authorisation development plan

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