PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of Risk Management Plan for Naglazyme (galsulfase)

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

Naglazyme's SmPC and its package leaflet give essential information to healthcare professionals and patients on how Naglazyme should be used.

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

I. The medicine and what it is used for

Naglazyme is authorised for the treatment of mucopolysaccahridosis VI (MPS VI; N-acetylgalactosamine 4-sulfatase deficiency; Maroteaux-Lamy syndrome) disease (see SmPC for the full indication). It contains galsulfase as the active substance and it is given by intravenous infusion.

Further information about the evaluation of Naglazyme's benefits can be found in Naglazyme'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/naglazyme

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

Important risks of Naglazyme, together with measures to minimise such risks and the proposed studies for learning more about Naglazyme'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 Naglazyme, 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 Naglazyme is not yet available, it is listed under 'missing information' below.

II.A. List of important risks and missing information

Important risks of Naglazyme 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 Naglazyme. 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).

List of important risks and missing information	
Important identified risks	Hypersensitivity reactions/Infusion-associated reactions
Important potential risks	• Acute cardio-respiratory failure in patients susceptible to fluid volume overload • Allo-immune membranous glomerulonephritis
Missing information	Subgroup experience: • patients with hepatic insufficiency • patients with renal insufficiency

II.B. Summary of important risks

Important identified risk #1: Hypersensitivity reactions/Infusion-associated reactions	
Evidence for linking the risk to the medicine	Clinical trial, Clinical Surveillance Program (CSP), and Post-marketing data
Risk factors and risk groups	None identified.
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.2, 4.4, 4.8. PIL Sections 2.0, 4.0. Legal status: Medicinal product subject to restricted medical prescription. Naglazyme treatment should be supervised by a physician experienced in the management of patients with MPS VI or other inherited metabolic diseases. Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None.

Important potential risk #2: Acute cardio-respiratory failure in patients susceptible to fluid volume overload	
Evidence for linking the risk to the medicine	Clinical trial, Clinical Surveillance Program (CSP), and Post-marketing data
Risk factors and risk groups	None identified
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.2, 4.4, and 6.6. PIL Section 2.0. Legal status: Medicinal product subject to restricted medical prescription. Naglazyme treatment should be supervised by a physician experienced in the management of patients with MPS VI or other inherited metabolic diseases. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None.

Important potential risk #3: Allo-immune membranous glomerulonephritis	
Evidence for linking the risk to the medicine	Clinical trial, Clinical Surveillance Program (CSP), and Post-marketing data
Risk factors and risk groups	None identified
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4 and 4.8 PIL Section 4.0. Legal status: Medicinal product subject to restricted medical prescription. Naglazyme treatment should be supervised by a physician experienced in the management of patients with MPS VI or other inherited metabolic diseases. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None.

Missing information #1: Use in patients with hepatic insufficiency	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.2 and 5.2. Legal status: Medicinal product subject to restricted medical prescription. Naglazyme treatment should be supervised by a physician experienced in the management of patients with MPS VI or other inherited metabolic diseases. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None.

Missing information #2: Use in patients with renal insufficiency	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.2 and 5.2. Legal status: Medicinal product subject to restricted medical prescription. Naglazyme treatment should be supervised by a physician experienced in the management of patients with MPS VI or other inherited metabolic diseases. Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None.

II.C. Post-authorisation development plan

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

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

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

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