## Summary of risk management plan for FABRAZYME (Agalsidase beta)

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

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

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

### 1. THE MEDICINE AND WHAT IT IS USED FOR

FABRAZYME contains the active substance agalsidase beta and is used as enzyme replacement therapy in Fabry disease, where the level of α-galactosidase enzyme activity is absent or lower than normal. If you suffer from Fabry disease a fat substance, called globotriaosylceramide (GL-3), is not removed from the cells of your body and starts to accumulate in the walls of the blood vessels of your organs.

FABRAZYME is indicated for use as long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency). FABRAZYME is indicated in adults, children and adolescents aged 8 years and older. It contains agalsidase beta as the active substance and it is given by intravenous infusion.

Further information about the evaluation of FABRAZYME's benefits can be found in FABRAZYME's EPAR, including in its plain-language summary, available on the European Medicine's Agency (EMA) website, under the medicine's webpage:

https://www.ema.europa.eu/en/medicines/human/EPAR/fabrazyme

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

Important risks of FABRAZYME, together with measures to minimize such risks and the proposed studies for learning more about FABRAZYME'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 PL and SmPC addressed to patients and HCPs;

- 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.

In the case of FABRAZYME, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, outlined in the next sections.

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.

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

## 2.1. LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of FABRAZYME 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 FABRAZYME. 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** | Hypersensitivity reactions |
| **Important potential risk** | Medication errors in the home infusion setting |
| **Missing information** | Use in pregnant and lactating women |

## 2.2. Summary of important risks

**Table 2 - Important risk and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any – Important identified risk: Hypersensitivity reactions**

| **Hypersensitivity reactions** | |
|---|---|
| **Evidence for linking the risk to the medicine** | Clinical trials and postmarketing experience. |

| Hypersensitivity reactions | |
|---|---|
| **Risk factors and risk groups**. | Patients with IgG antibodies to r-hαGAL have a greater potential to experience infusion associated reactions, and possibly hypersensitivity reactions. These patients should be treated with caution when re-administering FABRAZYME. Antibody status should be regularly monitored. Conversely, not all patients with symptoms of hypersensitivity have detectable anti- r-hαGAL IgG antibodies. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Sections 4.3, 4.4 and 4.8 of SmPC<br>Section 2 and 4 of the PL<br>Legal status<br>**Additional risk minimization measures:**<br>HCP guide:<br>Educational material for HCPs administering FABRAZYME.<br>Patient/Caregiver guide:<br>Educational material for patients/caregivers receiving and/or administering FABRAZYME in the home setting. |
| **Additional pharmacovigilance activities:** | Additional Pharmacovigilance activities<br>New evaluation to measure effectiveness of the updated additional risk minimization measures. |

IgG: Immunoglobulin G; SmPC: Summary of Product Characteristics; PL: Package Leaflet; r-hαGAL: Recombinant Human Alpha-Galactosidase.

**Table 3 - Important risk and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any – Important potential risk: Medication errors in the home infusion setting**

| Medication errors in the home infusion setting | |
|---|---|
| **Evidence for linking the risk to the medicine** | Clinical trials and postmarketing data. |
| **Risk factors and risk groups**. | Patients who infuse themselves or with the help of non-HCP, ie, caregivers or family members. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Legal status<br>**Additional risk minimization measures:**<br>HCP guide:<br>Educational material for HCPs prescribing home infusions and HCPs administering FABRAZYME.<br>Patient/Caregiver guide:<br>Educational material for patients/caregivers receiving and/or administering FABRAZYME in the home setting (as part of key element regarding the reconstitution and administration instructions). |
| **Additional pharmacovigilance activities** | **Additional pharmacovigilance activities:**<br>New evaluation to measure effectiveness of the updated additional risk minimization measures. |

HCP: Healthcare Professional.

**Table 4 - Important risk and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any – Missing information: Use in pregnant and lactating women**

| **Use in pregnant and lactating women** | |
|---|---|
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Section 4.6 of SmPC<br>Section 2 of the PL<br>Legal status<br>**Additional risk minimization measures:**<br>None |
| **Additional pharmacovigilance activities** | **Additional pharmacovigilance activities**<br>Study MSC12868 (AGAL02603) (Lactation study).<br>Study AGAL19211 (FU2 057.4) (FABRY Registry/Pregnancy sub-registry). |

PL: Package Leaflet; SmPC: Summary of Product Characteristics.

## 2.3. Post-authorization development plan

### *2.3.1. Studies which are conditions of the marketing authorization*

There are no studies which are conditions of the marketing authorization or specific obligation of FABRAZYME.

### *2.3.2. Other studies in post-authorization development plan*

**Table 5 - Other studies in post-authorization development plan**

| **FABRAZYME home infusion educational materials effectiveness evaluation (Category 3)** |
|---|
| Purpose and objectives to be defined |
| **Lactation Study MSC12868 (AGAL02603) (Category 3)** |
| The objectives of this study are to determine whether α-GAL activity is present in the breast milk of mothers with Fabry disease who are being treated with FABRAZYME during lactation, to measure breast milk production and composition (volume, protein and fat content) in women with Fabry disease who receive FABRAZYME during lactation, and to determine whether FABRAZYME affects the growth, development, and immunologic response of infants born to mothers with Fabry disease who receive FABRAZYME during lactation. |
| **FABRY Registry/Pregnancy sub-registry, AGAL19211 (FU2 057.4) (Category 3)** |
| The rationale of the Fabry Registry Pregnancy Sub-Registry is to evaluate the safety of agalsidase beta use during pregnancy. The primary objective of this Sub-Registry is to track pregnancy outcomes in women with Fabry disease who receive agalsidase beta during pregnancy and in women with Fabry disease who do not receive agalsidase beta during pregnancy. Additionally, this Sub-Registry is designed to follow infants born to women with Fabry disease for 3 years post-partum. |

α-GAL: Alpha-Galactosidase.