Swiss Summary of the Risk Management Plan (RMP)

for

Galafold® (Migalastat)

Version: 5.0
Date: 1 April 2022
Based on EU RMP for migalastat (v7.0)
Marketing authorisation holder: Amicus Therapeutics Switzerland GmbH

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 Galafold® 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 Galafold in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic.

Amicus Therapeutics Switzerland GmbH is fully responsible for the accuracy and correctness of the content of the published summary RMP of Galafold.

Summary of risk management plan for GALAFOLD® (migalastat)

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

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

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

I. The medicine and what it is used for

GALAFOLD is authorized for long-term treatment of Fabry disease in adult and adolescents 12 years and older who have a certain genetic mutations (changes).

Further information about the evaluation of GALAFOLD's benefits can be found in GALAFOLD's EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage: https://www.ema.europa.eu/en/documents/overview/galafold-epar-summary-public_en.pdf.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of GALAFOLD, together with measures to minimize such risks and the proposed studies for learning more about GALAFOLD's risks, are outlined below.

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.

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 GALAFOLD is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of GALAFOLD 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 GALAFOLD. 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	• None
Important potential risks	• Lack of efficacy in case of use in patients with non-amenable mutations • Male infertility (reversible)
Missing information	• Use in pregnant or breast-feeding women • Use in older patients > 74 years • Use in patients with severe renal impairment (GFR < 30 mL/min/1.73 m^2) • Long-term treatment (> 1 year) • Use in the pediatric population aged 12 to < 16 years

Abbreviation: GFR = glomerular filtration rate.

II.B Summary of important risks

Important potential risk: Lack of efficacy in case of use in patients with non-amenable mutations

Evidence for linking the risk to the medicine	GALAFOLD (migalastat) is only indicated for treatment of patients with Fabry disease who have an amenable *GLA* (gene encoding α-galactosidase A) mutation. The efficacy of migalastat has only been established in patients with amenable mutations. A comprehensive reference table listing the "amenable" mutations is included in the Summary of Product Characteristics (SmPC), amenable and non-amenable mutations are listed on the website that is referenced in the SmPC. Not all mutations have been tested. The reference tables are updated with newly categorized mutations as they are identified
Risk factors and risk groups	No risk groups or risk factors have been identified.
Risk minimization measures	Routine risk communication: • SmPC Sections 4.1, 4.4, and 5.1; • PL Section 1; • Amenable mutations are listed in Section 5.1; amenable and non-amenable mutations are listed on the website that is referenced in Section 5.1. Other routine risk minimization measures beyond the Product Information: • Prescription only.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • AT1001-030 (patient registry). See **Section II.C** of this summary for an overview of the post-authorization development plan.

Abbreviation: PL = package leaflet; SmPC = Summary of Product Characteristics.

Important potential risk: Male infertility (reversible)

Evidence for linking the risk to the medicine	Transient and fully reversible infertility in male rats was associated with migalastat treatment at all doses assessed. Complete reversibility was seen after 4 weeks off-dose. Similar findings have been noted preclinically following treatment with other iminosugars. It is not yet known if GALAFOLD affects fertility in men. The effects of GALAFOLD on fertility in humans have not been studied.
Risk factors and risk groups	Male patients
Risk minimization measures	Routine risk communication: • SmPC Sections 4.6 and 5.3; • PL Section 2. Other routine risk minimization measures beyond the Product Information: • None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • AT1001-030 (patient registry). See **Section II.C** of this summary for an overview of the post-authorization development plan.

Abbreviations: PL = package leaflet; SmPC = Summary of Product Characteristics.

Important missing information: Use in pregnant or breast-feeding women

Risk minimization measures	Routine risk communication: • SmPC Section 4.6; • PL Section 2; • Recommendations not to use Galafold during pregnancy or in women of childbearing potential not using contraception is included in SmPC Section 4.6 and PL Section 2; • Recommendation regarding decision to discontinue breast-feeding or to discontinue Galafold is described in SmPC Section 4.6 and PL Section 2. Other routine risk minimization measures beyond the Product Information: • Prescription only.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • AT1001-030 (patient registry). See **Section II.C** of this summary for an overview of the post-authorization development plan.

Abbreviations: PL = package leaflet; SmPC = Summary of Product Characteristics.

Important missing information: Use in older patients > 74 years

Risk minimization measures	Routine risk communication: • SmPC Sections 4.2 and 5.2. Other routine risk minimization measures beyond the Product Information: • Prescription only.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • AT1001-030 (patient registry). See **Section II.C** of this summary for an overview of the post-authorization development plan.

Abbreviation: SmPC = Summary of Product Characteristics.

Important missing information: Use in patients with severe renal impairment (GFR < 30 mL/min/ 1.73 m^2)

Risk minimization measures	Routine risk communication: • SmPC Sections 4.2, 4.4, and 5.2. • Recommendation not to use Galafold in patients with eGFR < 30 mL/min/1.73 m^2 is included in SmPC Sections 4.2 and 4.4. Other routine risk minimization measures beyond the Product Information: • Prescription only.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • AT1001-030 (patient registry). See **Section II.C** of this summary for an overview of the post-authorization development plan.

Abbreviations: eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; SmPC = Summary of Product Characteristics.

Important missing information: Long-term treatment (> 1 year)

Risk minimization measures	Routine risk communication: • None. Other routine risk minimization measures beyond the Product Information: • Prescription only.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • AT1001-030 (patient registry). See **Section II.C** of this summary for an overview of the post-authorization development plan.

Abbreviation: SmPC = Summary of Product Characteristics.

Important missing information: Use in the pediatric population aged 12 to < 16 years

Risk minimization measures	Routine risk communication: • SmPC Sections 4.4, 4.8, 5.1, and 5.2; • PL Section 2; • Recommendation not to use Galafold in children > 12 years-old weighing < 45 kg is included in SmPC Section 4.4 and PL Section 2. Other routine risk minimization measures beyond the Product Information: • Prescription only.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • AT1001-030 (patient registry). See **Section II.C** of this summary for an overview of the post-authorization development plan.

Abbreviation: SmPC = Summary of Product Characteristics.

II.C Post-authorization development plan

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

There are no studies that are conditions of the marketing authorization or specific obligation of GALAFOLD.

Study name	Purpose of the study
None	Not applicable

II.C.2 Other studies in the post-authorization development plan

Study name	Purpose of the study
AT1001-030: A prospective, observational registry of patients with Fabry disease	The purpose of this study is to evaluate the effects of treatment on long-term safety, effectiveness, and health-related quality of life. Study objectives include: • Safety: To assess the long-term safety of migalastat in migalastat-treated Fabry disease patients as determined by the occurrence of all serious adverse events (SAEs) over the 5-year period; To obtain data on the background incidence of SAEs; • Effectiveness: To evaluate the occurrence of Fabry-associated cardiac, cerebrovascular, and renal events; To assess overall survival among all patients enrolled, by recorded patient death(s) due to any cause; • Patient-reported outcomes (PROs): To assess the quality of life of Fabry disease patients using PROs and health preference measures. • The following safety concerns will be addressed: • Use in non-amenable patients; • Male infertility (reversible); • Use in pregnant or breast-feeding women; • Use in patients with severe renal impairment (GFR < 30 mL/min/ 1.73 m^2); • Use in older patients > 74 years; • Long-term treatment (> 1 year); • Use in the pediatric population aged 12 to < 16 years.