Part VI: Summary of the risk management plan

Summary of risk management plan for Opfolda (miglustat)

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

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

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

I. The medicine and what it is used for

Opfolda is authorised for use in the treatment of late-onset Pompe disease in adults. Opfolda is always used with another medicine called "Pombiliti" (cipaglucosidase alfa), a type of enzyme replacement therapy (ERT). Pombiliti is given as an intravenous infusion and Opfolda is given orally.

Further information about the evaluation of Opfolda's benefits can be found in Opfolda'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/medicines/human/EPAR/opfolda.

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

Important risks of Opfolda, together with measures to minimise such risks and the proposed studies for learning more about Opfolda'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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, 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 Opfolda is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Opfolda 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 Opfolda. 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	• None
Missing information	• Use in pregnant and lactating women • Long-term use (> 24 months)

II.B Summary of important risks

Missing information: Use in pregnant and lactating women

Risk minimisation measures	Routine risk minimisation measures: • SmPC Sections 4.6 and 5.3; • PL Section 2; • Recommendations regarding use in pregnant women and use in breastfeeding women are provided in the SmPC (Section 4.6) and PL (Section 2); • As stated in the SmPC (Section 4.6) and PL (Section 2), female patients of childbearing potential are advised to maintain reliable contraceptive methods prior, during, and for 4 weeks after stopping Opfolda in combination with cipaglucosidase alfa; • As stated in the PL (Section 2), Opfolda in combination with cipaglucosidase alfa should not be used during pregnancy, and patients are instructed to tell their doctor if they are pregnant, may be pregnant, or are planning to become pregnant; • As stated in the PL (Section 2), Opfolda in combination with cipaglucosidase alfa should not be used in breastfeeding women, and patients are instructed to tell their doctor if they are breastfeeding. Other routine risk minimisation measures beyond the Product Information: • Prescription only.
Additional pharmacovigilance activities:	Additional pharmacovigilance activities: • Prospective observational registry. See Section II.C of this summary for an overview of the post-authorisation development plan.

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

Missing information: Long-term use (> 24 months)

Risk minimisation measures	Routine risk minimisation measures: • None. Other routine risk minimisation measures beyond the Product Information: • Prescription only.
Additional pharmacovigilance activities:	Additional pharmacovigilance activities: • ATB200-02; • ATB200-07; • Prospective observational registry. 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

Not applicable.

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

Study name	Purpose of the study
ATB200-02 – A Phase 1/2 open-label, fixed-sequence, ascending-dose, first-in-human study to assess the safety, tolerability, PK, pharmacodynamics, and efficacy of intravenous infusions of cipaglucosidase alfa co-administered with oral miglustat in adult subjects with Pompe disease	Objectives from the open-label extension portions of the study (ie, Stage 3 and Stage 4) include evaluations of long-term efficacy, safety, and tolerability of cipaglucosidase alfa/miglustat in all subjects from Stage 3. This study will help to characterise the impact of the missing information of Long-term use (> 24 months) on the safety profile of miglustat.
ATB200-07 – A Phase 3, open-label extension study to assess the long-term safety and efficacy of intravenous cipaglucosidase alfa co-administered with oral miglustat in adult subjects with late-onset Pompe disease	The primary objective is to assess the long-term safety and tolerability of cipaglucosidase alfa/miglustat. Secondary objectives include assessments of long-term efficacy (as measured by various parameters), long-term effect on biomarkers of muscle injury and disease substrate, and immunogenicity. This study will help to characterise the impact of the missing information of Long-term use (> 24 months) on the safety profile of miglustat
Prospective observational registry – A prospective observational registry of patients with Pompe disease	The goal of the registry is to assess long-term safety and effectiveness of Pompe disease treatments in patients with late-onset Pompe disease (LOPD) and infantile-onset Pompe disease (IOPD). Eligible patients include those who are currently receiving a medical therapy for Pompe disease (regardless of dose/dosing frequency) and those who are not currently receiving any medical therapy for Pompe disease. The objectives are to evaluate long-term safety of Pompe disease treatments through collection of adverse events (AEs) and serious adverse events (SAEs) occurring in patients with Pompe disease, including infusion-associated reactions (IARs), hypersensitivity reactions (including anaphylaxis), immune complex related reactions, and pregnancy exposures; to evaluate long-term real-world effectiveness of Pompe disease treatments through collection of functional outcomes assessments; to evaluate long-term real-world impact of Pompe disease treatments on quality of life (QOL) using patient reported outcome measures. This study will help to characterise the impact of the missing information of Use in pregnant and lactating women and Long-term use (> 24 months) on the safety profile of cipaglucosidase alfa and miglustat, and to help better characterise the important risks for cipaglucosidase alfa associated with IARs, hypersensitivity, anaphylaxis, immune complex related reactions, and medication errors in the home infusion setting.