EU Risk Management Plan

for

Miglustat Dipharma 100 mg hard capsules

(Miglustat)

RMP version number: 2.0

Data lock point for this RMP: 21 June 2026

Date of final sign off: 07 July 2026

Rationale for submitting an updated RMP: Update to align with reference medicinal product, update MAH due to name change.

Summary of significant changes in this RMP:

Update MAH due to name change

Safety concerns:

Update of the list of safety concerns to remove all Important identified risks, Important potential risks and Missing information in order to align with the reference medicinal product.

Details of the currently approved RMP:

Version number: 0.2

Approved with procedure: EMEA/H/C/004904

Date of approval (opinion date): 18 February 2019

QPPV name:	Dr Angela van der Salm
QPPV signature:	The final version has been signed by the QPPV, the electronic signature is kept on file.

Table of Contents:

List of abbreviations

eCTD	Electronic Common Technical Document
EEA	European Economic Area
EU	European Union
INN	International Non-proprietary Names
MAH	Marketing Authorisation Holder
RMP	Risk Management Plan

Part I – Product(s) Overview

Active substance(s) (INN or common name)	Miglustat
Pharmacotherapeutic group(s) (ATC Code)	Other alimentary tract and metabolism products (A16AX06)
Marketing Authorisation Holder	Dipharma Arzneimittel GmbH
Medicinal product(s) to which this RMP refers	One
Invented name(s) in the European Economic Area (EEA)	Miglustat Dipharma 100 mg hard capsules
Marketing Authorisation procedure	Centralised
Brief description of the product	<u>Chemical class</u> Miglustat belongs to the pharmacotherapeutic class "Other alimentary tract and metabolism products".
	<u>Summary of mode of action</u> Gaucher disease is an inherited metabolic disorder caused by a failure to degrade glucosylceramide resulting in lysosomal storage of this material and widespread pathology. Miglustat is an inhibitor of glucosylceramide synthase, the enzyme responsible for the first step in the synthesis of most glycolipids. *In vitro*, glucosylceramide synthase is inhibited by miglustat with an IC50 of 20-37 µM. In addition, inhibitory action on a non-lysosomal glycosylceramidase has been demonstrated experimentally *in vitro*. The inhibitory action on glucosylceramide synthase forms the rationale for substrate reduction therapy in Gaucher disease. Niemann-Pick type C disease is a very rare, invariably progressive and eventually fatal neurodegenerative disorder characterised by impaired intracellular lipid trafficking. The neurological manifestations are considered secondary to the abnormal accumulation of glycosphingolipids in neuronal and glial cells. Overall, the data show that treatment with miglustat can reduce the progression of clinically relevant neurological symptoms in patients with Niemann-Pick type C disease.

	<u>Important information about its composition</u> Not applicable.
Hyperlink to the Product Information	The product information is included in Module 1.3.1 of the eCTD sequence.
Indication(s) in the EEA	Current: Miglustat Dipharma is indicated for the oral treatment of adult patients with mild to moderate type 1 Gaucher disease. Miglustat Dipharma may be used only in the treatment of patients for whom enzyme replacement therapy is unsuitable. Miglustat Dipharma is indicated for the treatment of progressive neurological manifestations in adult patients and paediatric patients with Niemann-Pick type C disease.
	Proposed: Not applicable.
Dosage in the EEA	Current: <u>*Dosage in type 1 Gaucher disease*</u> *Adult* The recommended starting dose for the treatment of adult patients with type 1 Gaucher disease is 100 mg three times a day. Temporary dose reduction to 100 mg once or twice a day may be necessary in some patients because of diarrhoea. *Paediatric population* The efficacy of Miglustat in children and adolescents aged 0-17 years with type 1 Gaucher disease has not been established. No data are available. <u>*Dosage in Niemann-Pick type C disease*</u> *Adult* The recommended dose for the treatment of adult patients with Niemann-Pick type C disease is 200 mg three times a day. *Paediatric population* The recommended dose for the treatment of adolescent patients (12 years of age and above) with Niemann-Pick type C disease is 200 mg three times a day.
	Proposed: Not applicable.

Pharmaceutical form(s) and strengths	Current: 100 mg hard capsules
	Proposed: Not applicable
Is / will the product be subject to additional monitoring in the EU?	No

Part II – Safety specification

Part II: Module SI – Epidemiology of the indication(s) and target population(s)

Since this RMP concerns a generic medicinal product, this section is not applicable.

Part II: Module SII – Non-clinical part of the safety specification

Since this RMP concerns a generic medicinal product, this section is not applicable.

Part II: Module SIII – Clinical trial exposure

Since this RMP concerns a generic medicinal product, this section is not applicable.

Part II: Module SIV – Populations not studied in clinical trials

Since this RMP concerns a generic medicinal product, this section is not applicable.

Part II: Module SV – Post-authorisation experience

Since this RMP concerns a generic medicinal product, this section is not applicable.

Part II: Module SVI – Additional EU requirements for the safety specification

Since this RMP concerns a generic medicinal product, this section is not applicable.

Part II: Module SVII – Identified and potential risks

Since this RMP concerns a generic medicinal product, for which an RMP is available for the reference medicinal product, this section is not applicable.

Part II: Module SVIII – Summary of the safety concerns

Since this RMP concerns a generic medicinal product for which an RMP is available for the reference medicinal product, this section is based on the RMP from the originator.

Table SVIII.1: Summary of safety concerns

Important identified risks	None
Important potential risks	None
Missing information	None

Part III – Pharmacovigilance Plan (including post-authorisation safety studies)

III.1: Routine pharmacovigilance activities

There are no routine pharmacovigilance activities beyond adverse reactions reporting and signal detection.

III.2: Additional pharmacovigilance activities

Not applicable, as no additional pharmacovigilance activities such as Post Authorisation Safety Studies are planned by the MAH.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV – Plans for post-authorisation efficacy studies

There are no imposed post-authorisation efficacy studies planned or on-going for Miglustat. Therefore, this Part is not applicable.

Part V – Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

The safety information in the proposed product information is aligned to the reference medicinal product.

V.1. Routine Risk Minimisation Measures

Not applicable.

V.2 Additional Risk Minimisation Measures

Not applicable.

V.3 Summary of risk minimisation measures

Not applicable.

Part VI – Summary of the risk management plan

Summary of risk management plan for Miglustat Dipharma 100 mg hard capsules (Miglustat)

This is a summary of the risk management plan (RMP) for Miglustat Dipharma 100 mg hard capsules. The RMP details important risks of Miglustat Dipharma 100 mg hard capsules, and how more information will be obtained about Miglustat Dipharma 100 mg hard capsules' risks and uncertainties (missing information).

Miglustat Dipharma 100 mg hard capsules' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Miglustat Dipharma 100 mg hard capsules should be used.

This summary of the RMP for Miglustat Dipharma 100 mg hard capsules 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 Miglustat Dipharma 100 mg hard capsules' RMP.

I. The medicine and what it is used for

Miglustat Dipharma 100 mg hard capsules is authorised for the oral treatment of adult patients with mild to moderate type 1 Gaucher disease. Miglustat Dipharma may be used only in the treatment of patients for whom enzyme replacement therapy is unsuitable.

Miglustat Dipharma 100 mg hard capsules is also indicated for the treatment of progressive neurological manifestations in adult patients and paediatric patients with Niemann-Pick type C disease (see SmPC for the full indication).

It contains Miglustat as the active substance and it is taken orally.

Further information about the evaluation of Miglustat Dipharma 100 mg hard capsules' benefits can be found in Miglustat Dipharma 100 mg hard capsules' 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/miglustat-dipharma

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

Important risks of Miglustat Dipharma 100 mg hard capsules, together with measures to minimise such risks and the proposed studies for learning more about Miglustat Dipharma 100 mg hard capsules' 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 (e.g., 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 so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of important risks and missing information

Important risks of Miglustat Dipharma 100 mg hard capsules are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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 Miglustat Dipharma 100 mg hard capsules. 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 (e.g., 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	None

For Miglustat Dipharma 100 mg hard capsules, no important risks or missing information have been identified.

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product Zavesca.

II.C Post-authorisation development plan

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

There are no studies which are conditions of the marketing authorisation or specific obligation of Miglustat Dipharma 100 mg hard capsules.

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

There are no studies required for Miglustat Dipharma 100 mg hard capsules.

Part VII – Annexes

Annex 4 – Specific adverse drug reaction follow-up forms

Not applicable.

Annex 6 – Details of proposed additional risk minimisation activities (if applicable)

Not applicable.