EU Risk Management Plan

for
Sugammadex–Amomed®
(sugammadex)

RMP version to be assessed as part of this application:

RMP Version number:	2.0
Data lock point for this RMP:	20-Mar-2025
Date of final sign-off:	electronic signature and date are available on the last page
Rationale for submitting an updated RMP:	Authority request for harmonization with the Originator RMP
Summary of significant changes in this RMP:	Harmonization of the paediatric indication with the Originator RMP in line with PRAC recommendation

Other RMP versions under evaluation:

RMP Version number:	N.A.
Submitted on:	N.A.
Procedure number:	N.A.

Details of the currently approved RMP:

Version number:	1.0
Approved with procedure:	CP EMEA/H/C/005935/0000
Date of approval (opinion date):	10.01.2023

QPPV name:	Dr. Juri Hodisch AOP Orphan Pharmaceuticals GmbH Leopold-Ungar Platz 2, 1190 Vienna, Austria

QPPV oversight declaration: The content of this RMP has been reviewed and approved by the marketing authorisation holder´s QPPV. The electronic signature is available on the last page.

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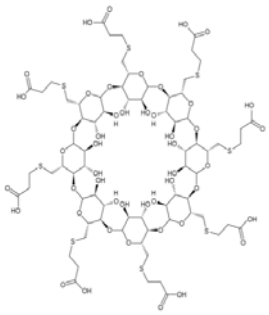
Part I: Product Overview

Table 1: Part I - Product Overview

Active substance(s) (INN or common name)	Sugammadex
Pharmacotherapeutic group(s) (ATC Code)	V03AB35
Marketing Authorisation Holder or Applicant	AOP Orphan Pharmaceuticals GmbH Leopold-Ungar-Platz 2 1190 Vienna Austria
Medicinal product to which this RMP refers	One (1)
Invented name(s) in the European Economic Area (EEA)	Sugammadex-Amomed®
Marketing authorisation procedure	Centralised
Brief description of the product	Chemical class: Sugammadex is a modified γ-cyclodextrin, with a lipophilic core and a hydrophilic periphery. This gamma cyclodextrin has been modified from its natural state by placing eight carboxyl thio ether groups at the sixth carbon positions. These extensions extend the cavity size allowing greater encapsulation of the rocuronium molecule. Sugammadex is used to reverse rocuronium or vecuronium induced neuromuscular blockade. Molecular Formula C72H112O48S8 Molecular weight: 2002.2 Structural formula: 
	Summary of mode of action: Sugammadex is a modified gamma cyclodextrin used to reverse neuromuscular blockade induced by vecuronium bromide and rocuronium bromide which are agents used for anesthesia.
	Important information about its composition: Each vial of 2 mL contains sugammadex sodium equivalent to 200 mg sugammadex. Each vial of 5 mL contains sugammadex sodium equivalent to 500 mg sugammadex. Clear and slightly yellow solution. The pH is between 7 and 8 and osmolality is between 300 and 500 mOsm/kg

Hyperlink to the Product Information	Please refer to eCTD Module 1.3.1 SmPC, Labelling and Package Leaflet
Indication(s) in the EEA	Current: Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults. For the paediatric population: sugammadex is only recommended for routine reversal of rocuronium induced blockade in children and adolescents aged 2 to 17 years.
	Proposed: Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults. For the paediatric population: sugammadex is only recommended for routine reversal of rocuronium induced blockade in paediatric patients from birth to 17 years..
Dosage in the EEA	Current: Sugammadex should only be administered by, or under the supervision of an anaesthetist. The use of an appropriate neuromuscular monitoring technique is recommended to monitor the recovery of neuromuscular blockade (see section 4.4 of SmPC). The recommended dose of sugammadex depends on the level of neuromuscular blockade to be reversed. The recommended dose does not depend on the anaesthetic regimen. Sugammadex can be used to reverse different levels of rocuronium or vecuronium induced neuromuscular blockade: Adults Routine reversal: A dose of 4 mg/kg sugammadex is recommended if recovery has reached at least 1-2 post-tetanic counts (PTC) following rocuronium or vecuronium induced blockade. Median time to recovery of the T4/T1 ratio to 0.9 is around 3 minutes A dose of 2 mg/kg sugammadex is recommended if spontaneous recovery has occurred up to at least the reappearance of T2 following rocuronium or vecuronium induced blockade. Median time to recovery of the T4/T1 ratio to 0.9 is around 2 minutes
	Proposed: Sugammadex should only be administered by, or under the supervision of an anaesthetist. The use of an appropriate neuromuscular monitoring technique is recommended to monitor the recovery of neuromuscular blockade. The recommended dose of sugammadex depends on the level of neuromuscular blockade to be reversed. The recommended dose does not depend on the anaesthetic regimen. Sugammadex can be used to reverse different levels of rocuronium or vecuronium induced neuromuscular blockade: *Adults* Routine reversal A dose of 4 mg/kg sugammadex is recommended if recovery has reached at least 1-2 post-tetanic counts (PTC) following rocuronium or vecuronium induced blockade. Median time to recovery of the T4/T1 ratio to 0.9 is around 3 minutes.

	A dose of 2 mg/kg sugammadex is recommended, if spontaneous recovery has occurred up to at least the reappearance of T2 following rocuronium or vecuronium induced blockade. Median time to recovery of the T4/T1 ratio to 0.9 is around 2 minutes. Using the recommended doses for routine reversal will result in a slightly faster median time to recovery of the T4/T1 ratio to 0.9 of rocuronium when compared to vecuronium induced neuromuscular blockade. Immediate reversal of rocuronium-induced blockade If there is a clinical need for immediate reversal following administration of rocuronium a dose of 16 mg/kg sugammadex is recommended. When 16 mg/kg sugammadex is administered 3 minutes after a bolus dose of 1.2 mg/kg rocuronium bromide, a median time to recovery of the T4/T1 ratio to 0.9 of approximately 1.5 minutes can be expected (see section 5.1). There is no data to recommend the use of sugammadex for immediate reversal following vecuronium induced blockade. Re-administration of sugammadex In the exceptional situation of recurrence of neuromuscular blockade post-operatively (see section 4.4) after an initial dose of 2 mg/kg or 4 mg/kg sugammadex, a repeat dose of 4 mg/kg sugammadex is recommended. Following a second dose of sugammadex, the patient should be closely monitored to ascertain sustained return of neuromuscular function. Re-administration of rocuronium or vecuronium after sugammadex For waiting times for re-administration of rocuronium or vecuronium after reversal with sugammadex, see section 4.4. *Additional information on special population* Renal impairment The use of sugammadex in patients with severe renal impairment (including patients requiring dialysis (CrCl < 30 ml/min)) is not recommended. Studies in patients with severe renal impairment do not provide sufficient safety information to support the use of sugammadex in these patients. For mild and moderate renal impairment (creatinine clearance $\geqslant$ 30 and < 80 ml/min): the dose recommendations are the same as for adults without renal impairment. Elderly patients After administration of sugammadex at reappearance of T2 following a rocuronium induced blockade, the median time to recovery of the T4/T1 ratio to 0.9 in adults (18-64 years) was 2.2 minutes, in elderly adults (65-74 years) it was 2.6 minutes and in very elderly adults (75 years or more) it was 3.6 minutes. Even though the recovery times in elderly tend to be slower, the same dose recommendation as for adults should be followed (see section 4.4). Obese patients In obese patients, including morbidly obese patients (body mass index $\geqslant$ 40 kg/m2), the dose of sugammadex should be based on actual body weight. The same dose recommendations as for adults should be followed. Hepatic impairment

	Studies in patients with hepatic impairment have not been conducted. Caution should be exercised when considering the use of sugammadex in patients with severe hepatic impairment or when hepatic impairment is accompanied by coagulopathy (see section 4.4). For mild to moderate hepatic impairment: as sugammadex is mainly excreted renally no dose adjustments are required. *Paediatric population (birth to 17 years of age)* Sugammadex may be diluted to 10 mg/ml to increase the accuracy of dosing in the paediatric population. Routine reversal A dose of 4 mg/kg sugammadex is recommended for reversal of rocuronium induced blockade if recovery has reached at least 1-2 PTC. A dose of 2 mg/kg is recommended for reversal of rocuronium induced blockade at reappearance of T2 (see section 5.1). Immediate reversal Immediate reversal has not been investigated in the paediatric population. Method of administration Sugammadex should be administered intravenously as a single bolus injection. The bolus injection should be given rapidly, within 10 seconds, into an existing intravenous line (see section 6.6). Sugammadex has only been administered as a single bolus injection in clinical trials.
Pharmaceutical form(s) and strengths	Current: Solution for injection, 100 mg/ ml.
	Proposed: Not applicable
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety Specification

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

N/A for generic products according to GVP Module V Rev 2.

Module SII – Non-clinical part of the safety specification

N/A for generic products according to GVP Module V Rev 2.

Module SIII – Clinical trial exposure

N/A for generic products according to GVP Module V Rev 2.

Module SIV – Populations not studied in clinical trials

N/A for generic products according to GVP Module V Rev 2.

Module SV – Post-authorisation experience

N/A for generic products according to GVP Module V Rev 2.

Module SVI – Additional EU requirements for the safety specification

N/A for generic products according to GVP Module V Rev 2.

Module SVII – Identified and potential risks

N/A for generic products according to GVP Module V Rev 2, since the Originator (Bridion, MAH: Merck Sharp & Dohme B.V.) has published RMP on the EMA website with identical safety concerns.

Module SVIII - Summary of the safety concerns

Table 2: SVIII - Summary of the safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

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

The Marketing Authorisation Holder (MAH) has a pharmacovigilance system at its disposal, which is based on the current European legislation. Routine pharmacovigilance activities are considered sufficient to monitor the safety profile of the product. Detailed information on the pharmacovigilance system is available in the current Pharmacovigilance System Master File (PSMF).

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance practices in accordance with Good Pharmacovigilance Practice, including adverse reaction reporting and signal detection are considered sufficient based on the well characterised safety profile of the reference medicinal product. Detailed information on the pharmacovigilance system is available in the current Pharmacovigilance System Master File (PSMF).

III.2 Additional pharmacovigilance activities

No additional pharmacovigilance activities are proposed.

III.3 Summary Table of additional Pharmacovigilance activities

No additional pharmacovigilance activities are proposed.

Part IV: Plans for post-authorisation efficacy studies

No post-authorisation efficacy studies are planned or ongoing.

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

Risk Minimisation Plan

V.1. Routine Risk Minimisation Measures

The safety information in the proposed Product Information is aligned to the reference medicinal product. There are no routine pharmacovigilance activities planned beyond adverse reactions reporting and signal detection.

V.2. Additional Risk Minimisation Measures

No additional risk minimisation measures activities are proposed.

V.3 Summary of risk minimisation measures

The safety information in the proposed Product Information is aligned to the reference medicinal product. There are no routine pharmacovigilance activities planned beyond adverse reactions reporting and signal detection. No additional risk minimisation activities are proposed.

Part VI: Summary of the risk management plan

Summary of risk management plan for Sugammadex-Amomed® (sugammadex)

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

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

This summary of the RMP for Sugammadex-Amomed® 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 EPAR.

Important new concerns or changes to the current ones will be included in updates of Sugammadex-Amomed®'s RMP.

I. The medicine and what it is used for

Sugammadex-Amomed® is authorised for reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults, children and adolescents (see SmPC for the full indication). It contains sugammadex sodium as the active substance and it is given by solution for injection.

Further information about the evaluation of Sugammadex-Amomed®'s benefits can be found in Sugammadex-Amomed®'s EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

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

Important risks of Sugammadex-Amomed®, together with measures to minimise such risks and the proposed studies for learning more about Sugammadex-Amomed®'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 (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, including PSUR assessment, 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 Sugammadex-Amomed®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 Sugammadex-Amomed®. 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);

Table 3: VI.II.A - Important risks and missing information

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

II.B Summary of important risks

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

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 Sugammadex-Amomed®.

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

There are no studies required for Sugammadex-Amomed®.

Part VII: Annexes

Annex 1 - EudraVigilance Interface

Not applicable.

Annex 2 - Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme

Not applicable

Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan

Not applicable.

Annex 4 - Specific adverse drug reaction follow-up forms

Not applicable.

Annex 5 - Protocols for proposed and on-going studies in RMP part IV

Not applicable.

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

Not applicable.

Annex 7 - Other supporting data (including referenced material)

Not applicable.

Annex 8 - Summary of changes to the risk management plan over time

Version	Approval date Procedure	Change
V1.0	10-Jan-2023 CP EMEA/H/C/005935/0000	Initial version
V2.0	pending	According to the CHMP, extension of the existing indication with the paediatric indication for Sugammadex and PRAC recommendation to update RMP in accordance with Originatior's RMP, the following parts were updated: Part I: Product Overview: Updated indication to include all paediatric patients (birth to 17 years) Part VI: Summary of the risk management plan: Updated indication to include all paediatric patients Annex 8 - Summary of changes to the risk management plan over time: the table was added

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