Public Assessment Report

Scientific discussion

Sugammadex Gebro 100 mg/ml oldatos injekció

(sugammadex)

HU/H/0812/001/DC

Applicant: Gebro Pharma GmbH

Date: 05-05-2023

This module reflects the scientific discussion for the approval of Sugammadex Gebro 100 mg/ml solution for injection. The procedure was finalised at 22/11/2022. For information on changes after this date please refer to the module 'Update'.

I. Introduction

In accordance with the Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 *on the Community code relating to medicinal products for human use*, an application has been submitted to the reference and competent authorities of the Member State concerned.
This Decentralised Procedure application (Reference member state, RMS: Hungary, concerned member state, CMS: AT, BE, DE, DK, ES, FI, LU, NL, NO, PT, SE) concerned a generic version of sugammadex (Art 10(1) of Dir. 2001/83/EC), under the trade name **Sugammadex Gebro 100 mg/ml solution for injection.**
The medicinal product Sugammadex Gebro 100 mg/ml solution for injection was developed by S.C. ROMPHARM COMPANY S.R.L. as a generic equivalent to the originator Bridion 100 mg/ml solution for injection. The first marketing authorisation for sugammadex in the European Union was granted on July 25th, 2008 via the centralized procedure for Bridion.

Based on the review of the quality, safety and efficacy data, the Member States have granted marketing authorisation for **Sugammadex Gebro 100 mg/ml solution for injection.**

Sugammadex is indicated for the 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.

A comprehensive description of the indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC, therefore the application contained no new clinical or preclinical data, other than supporting literature where necessary.
The Applicant did not perform any bioequivalence studies, as the conditions for a biowaiver, as outlined in the Guideline of the investigation of Bioavailability and Bioequivalence, have been fulfilled.
The reference medicinal product is Bridion 100 mg/ml solution for injection by Merck Sharp & Dohme Limited. The reference product was first authorised on 25/07/2008 via centralized procedure.

Quality aspects

II. Quality aspects

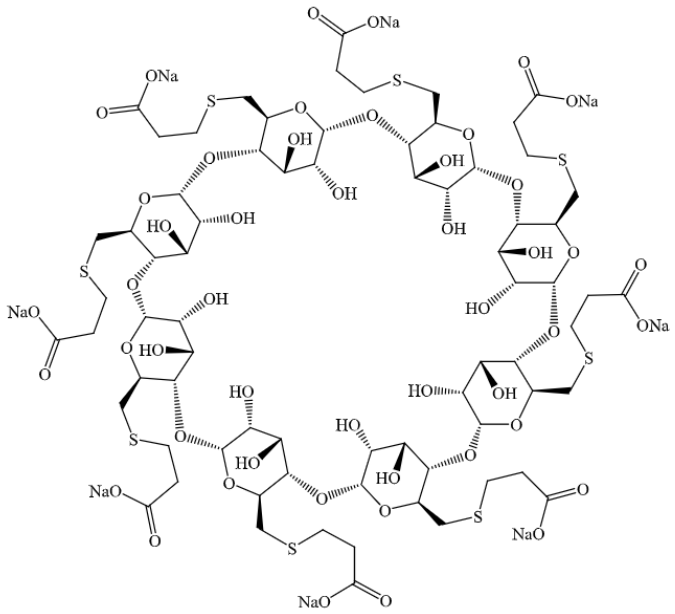
II.1 Introduction

The chemical-pharmaceutical assessment report concerns the application of Sugammadex Gebro 100 mg/ml solution for injection via a decentralized procedure according to Article 10(1) of consolidated Directive 2001/83/EC (i.e. generic application). The product has been developed by S.C. Rompharm Company S.R.L., Romania. The reference medicinal product is Bridion 100 mg/ml solution for injection (Merck Sharp & Dohme B.V.), which has been on the market since 2008.

II.2 Drug Substance

Data on the quality and manufacture of the active substance were provided in the applicant's submission using the Active Substance Master File (ASMF) procedure. The Quality Overall Summary is adequate.

INN name: Sugammadex sodium
Chemical name: 6A,6B,6C,6D,6E,6F,6G,6H-Octakis-S-(2-carboxyethyl)-6A,6B,6C,6D,6E,6F,6G,6H-octathio-γ-Cyclodextrin Octa sodium salt or Octakis-(6-S-(2-carboxyethyl)-6-thio)-cyclomaltooctaose octasodium salt
Structure:



Sugammadex sodium is a modified γ–cyclodextrin, present as a single stereoisomer. The active substance is white to off-white powder to granular powder. It is freely soluble within the pH range of 1.2 and pH 8.0 at room temperature (about 25°C).

The ASMF holder presented complete details of the manufacturing process. Description of the manufacturing process of the active pharmaceutical ingredient (API) is adequate.

Evidence of the structure has been confirmed by analysis of data from IR (Infrared) spectroscopy, NMR (Nuclear Magnetic Resonance) spectroscopy [comprising 1D (^{1}H , ^{13}C and ^{13}C-DEPT135{Distortionless Enhancement by Polarization Transfer using a 135 degree decoupler pulse}) and 2D (COSY {Correlation Spectroscopy}, ROESY {Rotating frame Overhauser Enhancement Spectroscopy}, HMBC {Heteronuclear Multiple Bond Correlation} and HSQC {Heteronuclear Single Quantum Coherence} experiments recorded in D_2O solution], ESI-MS (Electrospray-ionization Mass Spectrometry using negative ionization mode), UV (Ultraviolet) absorption spectroscopy [absorption maximum at 200 nm] and elemental analysis by HRMS (High Resolution Mass Spectrometry). The

presence of sodium as the counter ion is verified through the routine test for sodium content by AAS (Atomic Absorption Spectroscopy). The impurity profile of the API contains detailed information about organic and inorganic impurities, genotoxic impurities and residual solvents.

Sugammadex sodium is not official in the Ph.Eur. Therefore, an in-house specification has been set for the active substance, which includes the following tests: description, pH, water content, identification by IR, HPLC, related substances, assay, residual solvents, sodium content, microbiological purity and bacterial endotoxins. The presented specification is in accordance with the Ph.Eur. general monograph on *Substances for Pharmaceutical Use* and the ICH Q6A guideline. The specifications reflect all relevant quality attributes of the active substance and were found to be adequate to control the quality of the drug substance. The limits set are properly justified.

Testing methods not described in details in the Pharmacopoeia are adequately drawn up and sufficiently validated. Reference materials used by the active substance manufacturer and the drug product manufacturer for the control of the substance are adequately characterised.
The substance complies with the requirements of the EMA guideline on genotoxic impurities.

Batch analysis data justify the limits, indicate the good performance of testing methods and demonstrate the batch to batch consistency of the production.

Stability studies have been performed with the drug substance. According to the presented stability data the proposed re-test period is acceptable if stored in the commercial packaging at 25°C.

Good Manufacturing Practice (GMP) compliance of the API manufacture is demonstrated by the applicant.

II.3 Medicinal Product

The aim of the project was to develop a stable parenteral formulation of Sugammadex, essentially similar to the reference product Bridion 100 mg/ml solution for injection (MAH: Merck Sharp and Dohme).

A satisfactory package of data on development pharmaceutics has been presented. The excipients selected for the drug product are the same as used in the reference product and are well known and widely used pharmaceutical excipients. The pharmaceutical equivalence is justified by comparative impurity analysis. The choice of the packaging material is justified. Interaction study of Sugammadex Gebro 100 mg/ml solution for injection and primary packaging as well as compatibility study with solution for infusions used during the administration of the product have been presented.

As a result of development studies product with the following appearance and composition was obtained:
The drug product is a sterile, clear and colourless to light yellow solution for injection. The pH is between 7.0 and 8.0 and the osmolality is between 300 and 500 mOsm/kg.
The used excipients are Sodium hydroxide, hydrochloride acid, water for injections and nitrogen. The excipients comply with the requirements of their respective Ph. Eur. monographs. Compliance of the product with the general monograph of the European Pharmacopoeia *on the Products with the risk of TSE* has been demonstrated by the Applicant.

A description and flow chart of the manufacturing method has been provided. Appropriate in-process controls are included in the manufacturing process. Satisfactory batch formula were also presented. GMP compliance of the manufacturing site has been demonstrated.

The finished product specification is satisfactory. Acceptance criteria have been justified with respect to conventional pharmaceutical requirements as prescribed in the relevant dosage form monograph of the Ph.Eur. and the ICH Q6A guideline. The test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and complied with the specification.

The packaging material consists of a clear, type I glass vial closed with a grey rubber stopper with aluminium cap and yellow plastic flip-off disc. Specifications and quality certificates for all packaging components are enclosed.

Finished product stability studies have been conducted in accordance with the current guidelines. Based on the results, a shelf-life of 3 years is approved with the following storage restriction: Store below 25°C. Do not freeze. Keep the vials in the outer carton in order to protect from light.

The Summary of Product Characteristics, patient Information Leaflet and label texts are pharmaceutically acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Conclusion: The product has been shown to meet the current regulatory requirements with regards to its quality and content of the active substance as well as dosage-form characteristics until the end of the approved shelf-life consistently. The manufacture and the quality standards applied adequately support the safe use and efficacy of the product.

III. Non-clinical aspects

III.1 Introduction

Pharmacodynamic, pharmacokinetic and toxicological properties of sugammadex are well known. As sugammadex is a widely used, well-known active substance, no further studies are required and the applicant provides none. The non-clinical overview is therefore based on a review of data available in several scientific databases or published in relation to the active ingredient, sugammadex. Overview based on literature review is appropriate.

III.2 Pharmacology

The active substance sugammadex inactivates rocuronium by encapsulating (chelating) the free molecule to form a stable complex. It forms a complex with the neuromuscular blocking agents rocuronium or vecuronium in plasma and thereby reduces the amount of neuromuscular blocking agent available to bind to nicotinic receptors in the neuromuscular junction. This results in the reversal of neuromuscular blockade induced by rocuronium or vecuronium.
The pharmacodynamics of sugammadex have been examined using physicochemical techniques (isothermal titration microcalorimetry), in vitro techniques (tissue bath studies), in vivo methods (muscle contraction in anaesthetized animals) and side effect profile studies. Sugammadex is a potent and effective agent for the reversal of neuromuscular blockade induced by the steroidal neuromuscular blocking agents (NMBA) rocuronium, vecuronium and pipecuronium, but is almost ineffective against non-steroidal neuromuscular blocking agents succinylcholine, atracurium, cis-atracurium and mivacurium.
In a review by Bom et al., 2009 are described the effects of sugammadex in in vitro tissue and in vivo animal experiments. The encapsulation approach allows reversal of any degree of neuromuscular blockade because the dose of sugammadex can be adjusted to encapsulate sufficient neuromuscular blocking molecules to cause effective reversal.

III.3 Pharmacokinetics

No new non-clinical pharmacokinetic studies were conducted by the Applicant. The pharmacokinetics of sugammadex is well known and extensively described in the product information of the originator and published literature.

Most of the non-clinical kinetic data of sugammadex have been collected in conjunction with toxicity or pharmacology studies in the various non-clinical species i.e. rat, guinea pig, rabbit, dog and cat. Upon i.v. administration sugammadex rapidly distributes in the extracellular water compartment.. In all

species studied, the systemic exposure generally increased linearly with dose, and no significant differences between the genders were observed. Clearance is predominantly renal, at a rate approximating the GFR. In the plasma and urine HPLC radiochromatograms no qualitative inter-species differences were observed between rat, dog, and man.

III.4 Toxicology

Published information on toxicological studies with sugammadex were the basis for the evaluation.
No new toxicity studies were submitted by the Applicant for the product, which is acceptable for these type of applications.

The toxicity profiles of cyclodextrins (CDs) depend on the route of administration used.
Sugammadex was of low acute toxicity following single i.v. administration in the mouse and rat with maximum non-lethal doses at or above 2000 mg/kg. At this dose only mild and very transient clinical signs such as staggered gait were observed, which are most likely associated with the injection of a large volume.
Minimal to slight effects on body weight gain, food consumption and RBC parameters indicate (very) slight toxicity at the highest dose level in the repeated dose toxicity studies in rats.
Cardiovascular safety of sugammadex has been sufficiently studied. Sugammadex has a low risk of inducting a disturbance in cardiac conductance and in particular on QT interval duration under the intended conditions of use.
Despite the binding of sugammadex to bone and teeth, in the various non-clinical rat models studied no adverse effect on bone quality, structure and turnover are observed. Moreover, no adverse effects on bone growth, modelling and remodelling have been noted other than those related to the slight non-specific toxicity resulting in a mild degree of growth retardation in juvenile rats upon repeated dosing at the high dose levels. Consequently, a wide safety margin is present for potential effects on bone.
Carcinogenicity studies were not done given the intended use of sugammadex and absence of genotoxic potential. Sugammadex did not induce gene mutations or chromosome aberrations in vivo or in vitro. Sugammadex did not impair male or female fertility in rats at 500 mg/kg/day representing approximately 6- to 50-fold greater exposures as compared to human exposures at recommended dose levels. Further, no morphological alterations of male and female reproductive organs were noted in 4-week toxicity studies in rats and dogs. Sugammadex was not teratogenic in rat and rabbit.

III.5 Ecotoxicity/environmental risk assessment (ERA)

The Applicant provided a rationale for the absence of an ERA and supports the current Marketing Authorization Application (MAA) for the generic product developed for intravenous administration, Sugammadex Gebro 100 mg/ml solution for injection:

Both medicinal products, the reference and the generic, are intended for administration as a solution by intravenous route and contain the same active substance, sugammadex sodium, in the same strength, 100 mg/ml. Also, the generic contains the same excipients, hydrochloric acid, sodium hydroxide and water for injections as the innovator. All excipients are of compendial standard and currently used in parenteral preparations.

Sugammadex Gebro 100 mg/ml is a solution for injection. The primary packaging material is of clear glass vial type I closed with rubber closure, and each vial is labeled and packed into a printed carton box together with a leaflet. The container closure is considered an industry standard and is known to provide adequate protection against moisture ingress.

Regarding the exposure to the environment through the elimination from human bodies, it must be taken into consideration that the overall number of patients who will use the generic similar to that used for others medicinal products that have the same active substance, therapeutic indication and posology. Hence no additional exposure is possible.

Other entry paths into the environment may result from disposal of unused pharmaceuticals, e.g. when shelf life is expired.

According to Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use, chapter 6 Precautionary and Safety Measures to Be Taken For Administration, Disposal And Labelling: "Appropriate disposal of unused pharmaceuticals, e.g., when shelf life has expired, is considered essential to reduce the exposure of the environment. It is therefore recommended that even for medicinal products that do not require special disposal measures, package leaflets (patient information leaflets) should include the following general statement:
"Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment." This indication is mentioned in the patient information leaflet for the medicinal product Sugammadex Gebro.

The Applicant concludes that no potential increase is foreseen of the environmental exposure to the active substance present in Sugammadex Gebro.

The provided justification for the absence of the ERA is acceptable given that the product proposed for marketing is a generic product that will be used interchangeably with other similar products already marketed in Europe. The introduction of these products onto the market is unlikely to result in any significant increase in the combined sales volumes for all sugammadex-containing products, and would thus not be expected to have an adverse effect upon the environment. For this reason a formal environmental risk assessment is not considered to be necessary.

III.6 Discussion on the non-clinical aspects

Pharmacodynamics, pharmacokinetics and toxicology of sugammadex are well-known. As Sugammadex Gebro 100 mg/ml is a generic product, there is no need for further excessive non-clinical studies. The non-clinical part of the application is thus acceptable.

IV. Clinical aspects

IV.1 Introduction

No bioequivalence studies have been performed with the applied product, as the conditions for a biowaiver, as outlined in the Guideline of the investigation of Bioavailability and Bioequivalence, have been fulfilled.
Sugammadex Gebro 100 mg/ml solution for injection is an aqueous solution containing the same concentration of the active substance as the authorised original product. For detailed assessment of the quality aspects and comparison with the reference product, please see the Quality Aspects.

The application contains an adequate review of published clinical data.

IV.2 Pharmacokinetics

The sugammadex pharmacokinetic parameters were calculated from the total sum of non-complex-bound and complex-bound concentrations of sugammadex. Pharmacokinetic parameters as clearance and volume of distribution are assumed to be the same for non-complex-bound and complex-bound sugammadex in anaesthetised subjects.

Distribution
The observed steady-state volume of distribution of sugammadex is approximately 11 to 14 litres in adult patients with normal renal function (based on conventional, non-compartmental pharmacokinetic analysis). Neither sugammadex nor the complex of sugammadex and rocuronium binds to plasma proteins or erythrocytes, as was shown in vitro using male human plasma and whole blood. Sugammadex exhibits linear kinetics in the dosage range of 1 to 16 mg/kg when administered as an IV bolus dose.

Metabolism:
In preclinical and clinical studies no metabolites of sugammadex have been observed and only renal excretion of the unchanged product was observed as the route of elimination.

Elimination
In adult anaesthetized patients with normal renal function the elimination half-life (t1/2) of sugammadex is about 2 hours and the estimated plasma clearance is about 88 ml/min. A mass balance study demonstrated that > 90% of the dose was excreted within 24 hours. 96% of the dose was excreted in urine, of which at least 95% could be attributed to unchanged sugammadex. Excretion via faeces or expired air was less than 0.02% of the dose. Administration of sugammadex to healthy volunteers resulted in increased renal elimination of rocuronium in complex.

Special populations

Renal impairment and age
In a pharmacokinetic study comparing patients with severe renal impairment to patients with normal renal function, sugammadex levels in plasma were similar during the first hour after dosing, and thereafter the levels decreased faster in the control group. Total exposure to sugammadex was prolonged, leading to 17-fold higher exposure in patients with severe renal impairment. Low concentrations of sugammadex are detectable for at least 48 hours post-dose in patients with severe renal insufficiency.
In a second study comparing subjects with moderate or severe renal impairment to subjects with normal renal function, sugammadex clearance progressively decreased and t1/2 was progressively prolonged with declining renal function. Exposure was 2-fold and 5-fold higher in subjects with moderate and severe renal impairment, respectively. Sugammadex concentrations were no longer detectable beyond 7 days post-dose in subjects with severe renal insufficiency.

Table 8: A summary of sugammadex pharmacokinetic (PK) parameters stratified by age and renal function is presented below:

Selected patient characteristics				Mean Predicted PK parameters (CV%)		
Demographics	Renal function Creatinine clearance(ml/min)			Clearance(ml/min)	Volume of distribution at steady state (L)	Elimination half-life (hr)
Adult	Normal		100	88 (22)	12	2 (21)
40 yrs 75 kg	Impaired	Mild Moderate Severe	50 30 10	51 (22) 31 (23) 9 (22)	13 14 14	4 (22) 6 (23) 19 (24)
Elderly	Normal		80	75 (23)	12	2 (21)
75 yrs 75 kg	Impaired	Mild Moderate Severe	50 30 10	51 (24) 31 (23) 9 (22)	13 14 14	3 (22) 6 (23) 19 (23)
Adolescent	Normal		95	77 (23)	9	2 (22)
15 yrs 56 kg	Impaired	Mild Moderate Severe	48 29 10	44 (23) 27 (22) 8 (21)	10 10 11	3 (22) 5 (23) 17 (23)
Child	Normal		51	37 (22)	4	2 (20)
7 yrs 23 kg	Impaired	Mild Moderate Severe	26 15 5	19 (22) 11 (22) 3 (22)	4 4 5	3 (22) 5 (22) 20 (25)

CV=coefficient of variation

Gender:
No gender differences were observed.

Race:
In a study in healthy Japanese and Caucasian subjects no clinically relevant differences in pharmacokinetic parameters were observed. Limited data does not indicate differences in pharmacokinetic parameters in Black or African Americans.

Body weight:
Population pharmacokinetic analysis of adult and elderly patients showed no clinically relevant relationship of clearance and volume of distribution with body weight.

Obesity:
In one clinical study in morbidly obese patients, sugammadex 2 mg/kg and 4 mg/kg was dosed according to actual body weight (n=76) or ideal body weight (n=74). Sugammadex exposure increased in a dose-dependent, linear manner following administration according to actual body weight or ideal body weight. No clinically relevant differences in pharmacokinetic parameters were observed between morbidly obese patients and the general population.

Bioequivalence

No bioequivalence studies have been performed with the applied product. Sugammadex Gebro 100 mg/ml solution for injection is an aqueous solution containing the same concentration of the active substance as the authorised original product.
According to the Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev.1, for parenteral solutions bioequivalence studies are generally not required if the test product is to be administered as an aqueous intravenous solution containing the same active substance as the currently approved product. However, if any excipients interact with the drug substance (e.g. complex formation), or otherwise affect the disposition of the drug substance, a bioequivalence study is required unless both products contain the same excipients in very similar quantity and it can be adequately justified that any difference in quantity does not affect the pharmacokinetics of the active substance.
The Applicant has submitted an application for a Marketing Authorization for Sugammadex Gebro 100 mg/ml solution for injection as a generic version to Bridion® 100mg/ ml solution for injection, marketed by Merck Sharp & Dohme Limited. As stated by the Applicant, Sugammadex solution for injection has a similar qualitative and quantitative composition with the reference drug product Bridion 100mg/mL solution for injection manufactured by MSD. Sugammadex 100mg/mL solution for injection is administered as an aqueous intravenous solution and it contains the same active substance in the same concentration as the reference product Bridion 100mg/mL solution for injection. The qualitative composition of the test product is the same as the reference product.
According to the Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev.1/ Corr** for parenteral solutions bioequivalence studies are generally not required if the test product is to be administered as an aqueous intravenous solution containing the same active substance as the currently approved product. This condition is fulfilled for Sugammadex Gebro. In addition, quantitative composition of Sugammadex Gebro 100 mg/mL solution for injection is entirely the same as the originator with regard to the active substance, the qualitative composition of the test product is the same as the reference product (see M 2.3.P.2), therefore, the conditions for biowaiver are fulfilled for Sugammadex Gebro 100 mg/mL solution for injection.

IV.3 Pharmacodynamics

There were no clinical pharmacology studies performed to evaluate the pharmacodynamics of **Sugammadex Gebro 100 mg/ml solution for injection** and none are required for applications of this type.

Sugammadex is a modified gamma cyclodextrin which is a Selective Relaxant Binding Agent. It forms 1:1 inclusion complexes with the neuromuscular blocking agents rocuronium or vecuronium in plasma and thereby reduces the amount of neuromuscular blocking agent available to bind to nicotinic receptors in the neuromuscular junction. This results in the reversal of neuromuscular blockade induced by rocuronium or vecuronium.
However, sugammadex does not reverse neuromuscular block induced by succinylcholine or benzylisoquinolium compounds.
The mechanism of action of Sugammadex does not result in stimulation of the cholinergic nervous system. There is no need for concomitant administration of antimuscarinic drugs. Furthermore, due to the removal of the muscle relaxant from its site of action, Sugammadex is able to reverse even a very profound neuromuscular block.

IV.4 Clinical efficacy

No new efficacy or safety data have been submitted and none are required. The applicant has provided an adequate review of clinical trials published in the literature, describing the efficacy and safety profile of sugammadex.

IV.5 Clinical safety

No new safety data were submitted and none were required for this application. The applicant has provided an adequate review of clinical trials published in the literature, describing the efficacy and safety profile of sugammadex.

IV.6 Summary of Pharmacovigilance System

The Applicant has submitted three signed Summary of Pharmacovigilance Systems of the proposed MAHs:

For Gebro Pharma GmbH, which is the MAH in AT, BE, DE, DK, LU, NL, NO and in HU signed and dated on 25. April 2016.

For Laboratorios Gebro Pharma S.A., which is the MAH in Spain.

For Jaba Recordati S.A., which is the MAH in Portugal.

Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation 520/2012 and as detailed in the relevant GVP module, the Summary is considered acceptable.

IV.7 Risk Management Plan (version number: 0.3 signed 30.08.2022)

Summary of safety concerns

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

The safety concerns listed by the MAH are appropriate, since it is in line with the latest version reference product's RMP (Bridion, version number: 8.0, dated on 29 Nov 2021).

Pharmacovigilance Plan

Routine pharmacovigilance activities are considered sufficient to manage all of the safety concerns connected to Gebro's product containing sugammadex sodium.

No additional activities are proposed.

Risk Minimisation Measures

Routine risk minimisation measures (i.e. wording in SmPC, PL and classification as a prescription only medicine) are considered sufficient to manage all of the safety concerns connected to Gebro's product containing sugammadex sodium.

No additional activities are proposed. For any further information on risk minimisation, please refer to the product information.

IV.8 PSUR

The requirements for submission of periodic safety update reports for these medicinal products are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

IV.9 Discussion on the clinical aspects

The application concerns the generic product **Sugammadex Gebro 100 mg/ml solution for injection.** **Sugammadex Gebro 100 mg/ml solution for injection** is indicated for the 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.

Since Sugammadex Gebro 100 mg/ml solution for injection is essentially similar to the reference product Bridion 100 mg/ml solution for injection by Merck Sharp & Dohme Limited., no bioequivalence study was deemed necessary.
The application contains an adequate review of published clinical data and no bioequivalence study was required.
There were no objections against granting the marketing authorization from a clinical point of view.

V. Overall conclusion, benefit/risk assessment and recommendation

The risk/benefit ratio is currently estimated as positive.
The application contains an adequate review of published clinical data.
Approval is recommended from the clinical point of view.