Professional Information

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

SUMABID 100 IV

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains sugammadex (as octasodium) equivalent to 100 mg sugammadex.
Each 2mL vial contains sugammadex (as octasodium) equivalent to 200 mg sugammadex
Each mL contains up to 9,7 mg sodium (see section 4.4)
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection.
Clear, colourless to slightly yellow brown solution, practically free from particles in a colourless type I glass (2 mL) vial with a rubber stopper and alu-cap with orange flip top.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

SUMABID is indicated for the routine reversal of neuromuscular blockade induced by rocuronium or vecuronium. **SUMABID** is also indicated for the immediate reversal of neuromuscular blockade at 3 minutes after administration of rocuronium. For the paediatric population, **SUMABID** is only recommended for routine reversal of rocuronium induced blockade in children above 7 years of age.

4.2 Posology and method of administration

Posology

SUMABID injection should be administered under the supervision of an anaesthetist.
SUMABID injection should be administered intravenously as a single bolus injection. The bolus injection may be given rapidly, within 10 seconds, directly into a vein or into an existing IV line.
SUMABID can be injected into the intravenous line of a running infusion with the following

intravenous solutions: Sodium chloride 9 mg/mL (0,9 %), glucose 50 mg/mL (5 %), sodium chloride 4,5 mg/mL (0,45 %) and glucose 25 mg/mL (2,5 %), Ringer's lactate solution, Ringer's solution, glucose 50 mg/mL (5 %) in sodium chloride 9 mg/mL (0,9 %). For paediatric patients **SUMABID** can be diluted using sodium chloride 9 mg/mL (0,9 %) to a concentration of 10 mg/mL.

Sugammadex has only been administered as a single bolus injection in reported clinical studies.

The use of an appropriate neuromuscular monitoring technique is recommended to monitor the recovery of the neuromuscular blockade. When certain medicines that may cause displacement interactions are administered parenterally within 7,5 hours of **SUMABID**, patients should be monitored for signs of recurrence of neuromuscular blockade.

The recommended dose of **SUMABID** depends on the level of neuromuscular blockade to be reversed. The recommended dose does not depend on the anaesthetic regimen. **SUMABID** can be used to reverse different levels of rocuronium or vecuronium induced neuromuscular blockade.

Routine Reversal of Neuromuscular Blockade.

A dose of 4 mg/kg **SUMABID** is recommended if recovery has reached 1 to 2 post-tetanic counts (PTC) [profound blockade] following administration of rocuronium or vecuronium induced blockade (see section 4.4).

A dose of 2 mg/kg **SUMABID** is only recommended if spontaneous recovery has reached the reappearance of second twitch (T_2) [shallow blockade] following rocuronium or vecuronium induced blockade (see section 4.4).

Immediate Reversal

If there is a clinical need for immediate reversal at 3 minutes following administration of rocuronium, a dose of 16 mg/kg **SUMABID** is recommended. There is no data reported to recommend the use of **SUMABID** for immediate reversal following vecuronium induced blockade.

Additional Information on Special Population Groups

Renal Impairment

For mild and moderate renal impairment (creatinine clearance ≥ 30 and < 80 mL/ min): The dose recommendations are the same as for adults without renal impairment. The use of **SUMABID** in patients with severe renal impairment including patients requiring dialysis (CrCl < 30 mL/min) is not recommended (see section 4.4).

Reported studies in patients with severe renal impairment do not provide sufficient safety information to support the use of **SUMABID** in these patients.

Elderly Patients

After administration of **SUMABID** at reappearance of T_2, following a rocuronium induced blockade, the median time to recovery of the T_4/T_1 ratio to 0,9 in adults (18 to 64 years) was 2,2 minutes, in elderly adults (65 to 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, the dose of **SUMABID** should be based on actual body weight. The same dose recommendations as for adults should be followed.

Hepatic Impairment

For mild to moderate hepatic impairment: As **SUMABID** is mainly excreted renally no dose adjustments are required.

Studies in patients with hepatic impairment have not been reported. Caution should be exercised when considering the use of **SUMABID** in patients with severe hepatic impairment or when hepatic impairment is accompanied by coagulopathy (see section 4.4).

Paediatric Population

The data for the paediatric population are limited (one reported study only for reversal of rocuronium induced blockade at reappearance of T_2). There is insufficient information reported on the use of **SUMABID** for children < 7 years of age. There is no information on **SUMABID** use for neonates. Therefore sugammadex is not recommended for use in these populations.

Children and Adolescents

For reversal of rocuronium induced blockade at reappearance of T_2, in children and

adolescents (7 to 17 years) 2 mg/kg **SUMABID** is recommended.
Immediate reversal in children and adolescents has not been reported to be investigated and is therefore not recommended.
SUMABID 100 mg/mL may be diluted to 10 mg/mL to increase the accuracy of dosing in the paediatric population, 7 years and older.

4.3 Contraindications

SUMABID is contra-indicated in patients with known hypersensitivity to sugammadex sodium or to any of the inactive ingredients listed in section 6.1.

4.4 Special warnings and precautions for use

SUMABID is not to be used to reverse depolarising neuromuscular blocking medicines.

As is normal post-anaesthetic practice following neuromuscular blockade, it is recommended to monitor the patient in the immediate post-operative period for untoward events including recurrence of neuromuscular blockade.

Monitoring respiratory function during recovery:

Ventilatory support is mandatory for patients until adequate spontaneous respiration is restored following reversal of neuromuscular blockade. Even if recovery from neuromuscular blockade is complete, other medicinal products used in the peri- and post-operative period could depress respiratory function and therefore ventilatory support might still be required.
Should neuromuscular blockade reoccur following extubation, adequate ventilation should be provided.

Recurrence of neuromuscular blockade:

In reported clinical studies with subjects treated with rocuronium or vecuronium, where sugammadex was administered using a dose labelled for the depth of neuromuscular blockade, an incidence of 0,20 % was reported for recurrence of neuromuscular blockade as based on neuromuscular monitoring or clinical evidence. The use of lower than recommended doses may lead to an increased risk of recurrence of neuromuscular blockade after initial reversal and is not recommended (see section 4.8).

Effect on haemostasis:

In a reported study in volunteers doses of 4 mg/kg and 16 mg/kg of sugammadex resulted

in maximum mean prolongations of the activated partial thromboplastin time (aPTT) by 17 and 22 % respectively and prothrombin time international normalized ratio [PT(INR)] by 11 and 22 % respectively. These limited mean aPTT and PT(INR) prolongations were of short duration (≤ 30 minutes). Based on the reported clinical data-base and on a specific study in patients undergoing hip fracture/major joint replacement surgery there was no clinically relevant effect of sugammadex 4 mg/kg alone or in combination with anticoagulants on the incidence of peri- or post-operative bleeding complications.
In reported *in vitro* experiments a pharmacodynamic interaction (aPTT and PT prolongation) was noted with vitamin K antagonists, unfractionated heparin, low molecular weight heparinoids, rivaroxaban and dabigatran. In patients receiving routine post-operative prophylactic anticoagulation this pharmacodynamic interaction is not clinically relevant. Caution should be exercised when considering the use of sugammadex in patients receiving therapeutic anticoagulation for a pre-existing or co-morbid condition.
An increased risk of bleeding cannot be excluded in patients:

- with hereditary vitamin K dependent clotting factor deficiencies;
- with pre-existing coagulopathies;
- on coumarin derivates and at an INR above 3,5;
- using anticoagulants who receive a dose of 16 mg/kg sugammadex.

If there is a medical need to give sugammadex to these patients the anaesthesiologist needs to decide if the benefits outweigh the possible risk of bleeding complications taking into consideration the patients history of bleeding episodes and type of surgery scheduled. If sugammadex is administered to these patients monitoring of haemostasis and coagulation parameters is recommended.

Waiting times for re-administration with neuromuscular blocking agents after reversal with sugammadex:

Table 1: Re-administration of rocuronium or vecuronium after routine reversal (up to 4 mg/kg sugammadex):

Minimum waiting time	**Neuromuscular blocking agents (NMBA) and dose to be administered**
5 minutes	1,2 mg/kg rocuronium
4 hours	0,6 mg/kg rocuronium or 0,1 mg/kg vecuronium

The onset of neuromuscular blockade may be prolonged up to approximately 4 minutes, and the duration of neuromuscular blockade may be shortened up to approximately 15 minutes after re-administration of rocuronium 1,2 mg/kg within 30 minutes after sugammadex administration.

Based on reported PK modelling the recommended waiting time in patients with mild or moderate renal impairment for re-use of 0,6 mg/kg rocuronium or 0,1 mg/kg vecuronium after routine reversal with sugammadex should be 24 hours. If a shorter waiting time is required, the rocuronium dose for a new neuromuscular blockade should be 1,2 mg/kg.

Re-administration of rocuronium or vecuronium after immediate reversal (16 mg/kg sugammadex):

For the cases where this might be required, a waiting time of 24 hours is suggested.

If neuromuscular blockade is required before the recommended waiting time has passed, a **nonsteroidal neuromuscular blocking agent** should be used. The onset of a depolarizing neuromuscular blocking agent might be slower than expected, because a substantial fraction of postjunctional nicotinic receptors can still be occupied by the neuromuscular blocking agent.

Renal impairment:

SUMABID is not recommended for use in patients with severe renal impairment, creatinine clearance <30 mL/min, including those requiring dialysis.

Because of the estimated prolonged half-life of sugammadex in severe renally impaired patients, a full neuromuscular blockade may not be achieved after re-use of 0,6 mg/kg rocuronium or 0,1 mg/kg vecuronium within 24 hours after sugammadex reversal.

Light anaesthesia:

When neuromuscular blockade was reversed intentionally in the middle of anaesthesia in reported clinical studies, signs of light anaesthesia were noted occasionally (movement, coughing, grimacing and suckling of the tracheal tube).

If neuromuscular blockade is reversed, while anaesthesia is continued, additional doses of anaesthetic and/or opioid should be given as clinically indicated.

Marked bradycardia:

Marked bradycardia has been reported within minutes after the administration of sugammadex for reversal of neuromuscular blockade. Bradycardia may occasionally lead to cardiac arrest (see section 4.8). Patients should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade. Treatment with anti-

cholinergic agents such as atropine should be administered if clinically significant bradycardia is observed.

Hepatic impairment:

SUMABID is not metabolised nor excreted by the liver; therefore dedicated studies in patients with hepatic impairment have not been reported. Patients with severe hepatic impairment should be treated with great caution. In case hepatic impairment is accompanied by coagulopathy see the information on the effect on haemostasis.

Use in Intensive Care Unit (ICU):

Sugammadex has not been reported to be investigated in patients receiving rocuronium or vecuronium in the ICU setting.

Use for reversal of neuromuscular blocking agents other than rocuronium or vecuronium:

SUMABID should not be used to reverse block induced by nonsteroidal neuromuscular blocking agents such as succinylcholine or benzylisoquinolinium compounds.

SUMABID should not be used for reversal of neuromuscular blockade induced by steroidal neuromuscular blocking agents other than rocuronium or vecuronium, since there are no efficacy and safety data reported for these situations. Limited data is reported for reversal of pancuronium induced blockade, but it is advised not to use sugammadex in this situation.

Delayed recovery:

Conditions associated with prolonged circulation time such as cardiovascular disease, old age, or oedematous state (e.g., severe hepatic impairment) may be associated with longer recovery times.

Medicine hypersensitivity reactions:

Medical practitioners should be prepared for the possibility of medicine hypersensitivity reactions (including anaphylactic reactions) and take the necessary precautions (see section 4.8).

Excipient Warning Sodium:

This medicinal product contains up to 9.7 mg sodium per mL, equivalent to 0.5 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

SUMABID contains less than 1 mmol (23 mg) per dose that is essentially ‘sodium free’.

4.5 Interaction with other medicines and other forms of interaction

The information reported in this section is based on binding affinity between **SUMABID** and other medicinal products, non-clinical experiments, reported clinical studies and simulations using a model taking into account the pharmacodynamic effect of neuromuscular blocking agents and the pharmacokinetic interaction between neuromuscular blocking agents and sugammadex. Based on reported data, no clinically significant pharmacodynamic interaction with other medicinal products is expected, with exception of the following:

For toremifene and fusidic acid displacement interactions could not be excluded (no clinically relevant capturing interactions are expected).

For hormonal contraceptives a clinically relevant capturing interaction could not be excluded (no displacement interactions are expected).

Interactions potentially affecting the efficacy of sugammadex (displacement interactions):

Due to the administration of certain medicinal products after sugammadex, theoretically rocuronium or vecuronium could be displaced from sugammadex. As a result recurrence of neuromuscular blockade might be observed. In this situation the patient must be ventilated. Administration of the medicinal product which caused displacement should be stopped in case of an infusion. In situations when potential displacement interactions can be anticipated, patients should be carefully monitored for signs of recurrence of neuromuscular blockade (approximately up to 15 minutes) after parenteral administration of another medicinal product occurring within a period of 7,5 hours after sugammadex administration.

Toremifene:

For toremifene, which has a relatively high binding affinity for sugammadex and for which relatively high plasma concentrations might be present, some displacement of vecuronium or rocuronium from the complex with sugammadex could occur. Medical practitioners should be aware that the recovery of the T_4/T_1 ratio to 0,9 could therefore be delayed in patients who have received toremifene on the same day of the operation.

Intravenous administration of fusidic acid:

The use of fusidic acid in the pre-operative phase may give some delay in the recovery of the T_4/T_1 ratio to 0,9. No recurrence of neuromuscular blockade is reported to be expected in the post-operative phase, since the infusion rate of fusidic acid is over a period of

several hours and the blood levels are cumulative over 2-3 days.

Interactions potentially affecting the efficacy of other medicinal products (capturing interactions):

Due to the administration of sugammadex, certain medicinal products could become less effective due to a lowering of the (free) plasma concentrations. If such a situation is observed, the medical practitioner is advised to consider the re-administration of the medicinal product, the administration of a therapeutically equivalent medicinal product (preferably from a different chemical class) and/or non-pharmacological interventions as appropriate.

Hormonal contraceptives:

The interaction between 4 mg/kg sugammadex and a progestogen was predicted to lead to a decrease in progestogen exposure (34% of AUC) similar to the decrease reported when a daily dose of an oral contraceptive is taken 12 hours too late, which might lead to a reduction in effectiveness. For oestrogens, the effect is expected to be lower. Therefore the administration of a bolus dose of sugammadex is considered to be equivalent to one missed daily dose of oral contraceptive steroids (either combined or progestogen only). If sugammadex is administered at the same day as an oral contraceptive is taken reference is made to missed dose advice in the package leaflet of the oral contraceptive. In the case of non-oral hormonal contraceptives, the patient must use an additional non hormonal contraceptive method for the next 7 days and refer to the advice in the package leaflet of the product.

Interactions due to the lasting effect of rocuronium or vecuronium:

When medicinal products which potentiate neuromuscular blockade are used in the post-operative period special attention should be paid to the possibility of recurrence of neuromuscular blockade. Please refer to the package leaflet of rocuronium or vecuronium for a list of the specific medicinal products which potentiate neuromuscular blockade. In case recurrence of neuromuscular blockade is observed, the patient may require mechanical ventilation and re-administration of sugammadex.

Interference with laboratory tests:

Sugammadex does not interfere with laboratory tests, with the possible exception of the serum progesterone assay. Interference with this test is reported at sugammadex plasma concentrations of 100 microgram/mL (peak plasma level following 8 mg/kg bolus injection).

In a reported study in volunteers doses of 4 mg/kg and 16 mg/kg of sugammadex resulted in maximum mean prolongations of aPTT by 17 and 22 % respectively and of PT(INR) by 11 and 22 % respectively. These limited mean aPTT and PT(INR) prolongations were of short duration (≤ 30 minutes).

In reported *in vitro* experiments a pharmacodynamic interaction (aPTT and PT prolongation) was noted with vitamin K antagonists, unfractionated heparin, low molecular weight heparinoids, rivaroxaban and dabigatran (see section 4.4).

Paediatric population

No formal interaction studies have been reported. The above mentioned interactions for adults and the warnings should also be taken into account for the paediatric population.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety in pregnant women has not been established.

Caution should be exercised when administering **SUMABID** to pregnant women.

Breast-feeding

It is unknown whether sugammadex is excreted in human breast milk. Animal studies have reported excretion of sugammadex in breast milk.

Fertility

The effects with sugammadex on human fertility have not been reported.

4.7 Effects on the ability to drive and use machines

SUMABID has no known influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

SUMABID is administered concomitantly with neuromuscular blocking agents and anaesthetics in surgical patients.

The most commonly reported adverse reactions in surgical patients were cough, airway complication of anaesthesia, anaesthetic complications, procedural hypotension and procedural complication.

Table 2: Tabulated list of adverse reactions

System organ class	Frequencies	Adverse reactions (Preferred terms)
Immune system disorders	Less frequent	Medicine hypersensitivity reactions *(see section 4.4)*
Nervous system disorders	Frequent	Dysgeusia
Respiratory, thoracic and mediastinal disorders	Frequent	Cough
Injury, poisoning and procedural complications	Frequent	Airway complication of anaesthesia Anaesthetic complication *(see section 4.4)* Procedural hypotension Procedural complication Prolonged neuromuscular blockade

Description of selected adverse reactions

Medicine hypersensitivity reactions:

Hypersensitivity reactions, including anaphylaxis, have been reported occurred in some patients and volunteers (for information on volunteers, see "**Information on healthy volunteers**" below). In clinical studies of surgical patients these reactions were reported infrequently and for post-marketing reports the frequency is unknown.

These reactions varied from isolated skin reactions to serious systemic reactions (i.e. anaphylaxis, anaphylactic shock) and have occurred in patients with no prior exposure to sugammadex.

Symptoms associated with these reactions can include: flushing, urticaria, erythematous rash, (severe) hypotension, tachycardia, swelling of tongue, swelling of pharynx, bronchospasm and pulmonary obstructive events. Severe hypersensitivity reactions can be fatal.

Information on Healthy Volunteers

Hypersensitivity reactions, including anaphylaxis, have been observed with sugammadex as in **SUMABID**. In a study in healthy conscious volunteers (placebo, n=150; 4 mg/kg, n=148; and 16 mg/kg, n=150), hypersensitivity reactions were reported frequently with sugammadex 16 mg / kg and infrequent with sugammadex 4 mg/kg or placebo. In this study, dose dependent trends were also observed for dysgeusia, nausea and flushing.

Anaesthetic complication:

Anaesthetic complications, indicative of the restoration of neuromuscular function, include movement of a limb or the body or coughing during the anaesthetic procedure or during surgery, grimacing, or sucking on the endotracheal tube, was judged to be related to treatment in about 1 % of the patients and in none of the placebo group. Most occurrences of anaesthetic complications were mild to moderate.

Marked bradycardia:

In post-marketing, cases of marked bradycardia and bradycardia with cardiac arrest have been reported within minutes after administration of sugammadex (see section 4.4).

Recurrence of neuromuscular blockade:

In reported phase I to III studies with a placebo group, the incidence of recurrence of neuromuscular blockade as measured with neuromuscular monitoring was 2 % after sugammadex and 0 % in the placebo group. Virtually all of these cases were from dose-finding studies in which a sub-optimal dose (< 2 mg/kg) was administered. In cases where recurrence of neuromuscular blockade is observed, the patient must be ventilated.

Additional information on special populations

Pulmonary patients

Bronchospasm was reported as a possibly related adverse event in patients with a history of pulmonary complications. As with all patients with a history of pulmonary complications the physician should be aware of the possible occurrence of bronchospasm.

Paediatric population

A limited database suggests that the safety profile of sugammadex (up to 4 mg/kg) in paediatric patients was reported to be similar to that in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

SUMABID can be removed using haemodialysis with a high flux filter, but not with a low flux filter. Based upon reported clinical studies, sugammadex concentrations in plasma are reduced by up to 70% after a 3 to 6-hour dialysis session.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 34. Other

Pharmacotherapeutic group: all other therapeutic products, antidotes, ATC code:

V03AB35

Mechanism of action

Sugammadex sodium is a modified cyclodextrin. It is a selective relaxant binding agent (SRBA) which forms a complex with the neuromuscular blocking agents rocuronium and vecuronium, and it 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 and vecuronium.

Sugammadex has been administered in doses ranging from 0,5 mg/kg to 16 mg/kg in reported dose response studies of rocuronium induced blockade (0,6, 0,9, 1,0 and 1,2 mg/kg rocuronium bromide with and without maintenance doses) and vecuronium induced blockade (0,1 mg/kg vecuronium bromide with or without maintenance doses) at different time points/depths of blockade. In these reported studies a clear dose-response relationship was observed.

5.2 Pharmacokinetic properties

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 reported steady-state volume of distribution of sugammadex sodium is approximately 11 to 14 litres in adult patients with normal renal function (based on reported conventional, non-compartmental pharmacokinetic analysis). Neither sugammadex nor rocuronium bind to plasma proteins or erythrocytes. Sugammadex sodium exhibits linear kinetics in the dose range of 1 to 16 mg/kg when administered as an IV bolus dose.

Biotransformation

No metabolites of sugammadex have been reported and only renal excretion of the unchanged product was reported as the route of elimination.

Elimination

In adult anaesthetised patients with normal renal function the elimination half-life of sugammadex sodium is reported to be about 2 hours and the estimated plasma clearance is reported to be about 84 mL/min. A mass balance study reported that >90 % of the dose was excreted within 24 hours. Ninety six percent (96%) of the dose was reported to be excreted in urine, of which at least 95% could be attributed to unchanged sugammadex. Excretion via faeces or expired air was < 0,02 % of the dose. Administration of sugammadex sodium to healthy volunteers resulted in increased renal elimination of rocuronium in complex.

Special patient populations

Renal Impairment and Age

In a reported 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 approximately 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. Predicted pharmacokinetic parameters of sugammadex by age group and renal function based on compartmental modelling are reported below:

Selected patient characteristics			**Predicted PK parameters**		
Demographics	Renal function (creatinine clearance in mL/min)		Clearance in mL/min (CV)	Volume of distribution at steady state in litres	Elimination half-life in hours (CV)
Adult 40 years 75 kg	Normal	100	84 (22 %)	11,9	2,0 (19 %)
	Impaired	50	48 (22 %)	13,1	3,6 (20 %)
		30	29 (23 %)	13,7	6,1 (21 %)
		10	9(19 %)	14,2	20,3 (20 %)
Elderly 75 years 75 kg	Normal	80	72 (26 %)	12,4	2,4(23 %)
	Impaired	50	49 (22 %)	13,1	3,5 (19 %)
		30	29 (22 %)	13,7	6,1 (20 %)
		10	8 (19 %)	14,2	21,0 (23 %)
Adolescent 15 years 56 kg	Normal	95	76 (20 %)	9,3	1,7 (17 %)
	Impaired	48	45 (24 %)	10,1	3,0 (21 %)

		29	26 (22 %)	10,5	5,2 (19 %)
		10	7 (18 %)	10,9	17,8 (18 %)
Child	Normal	51	40 (21 %)	4,3	1,5 (16 %)
7 years 23 kg	Impaired	26	20 (20 %)	4,5	2,9 (19 %)
		15	11 (27 %)	4,6	5,2 (24 %)
		5	3 (22 %)	4,7	19,4 (23 %)

Mean and coefficient of variation (CV in %) are reported. For Volume of distribution, no CV could be estimated from the model.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on reported conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity potential, and toxicity to reproduction, local tolerance or compatibility with blood.

Sugammadex is rapidly cleared in preclinical species, although residual sugammadex was reported in bone and teeth of juvenile rats. Preclinical studies in young adult and mature rats reported that sugammadex does not adversely affect tooth colour or bone quality, bone structure, or bone metabolism. Sugammadex has no effects on fracture repair and remodelling of bone.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injection

Hydrogen Chloride or Sodium Hydroxide

Nitrogen

6.2 Incompatibilities

None

6.3 Shelf life

36 Months

After first opening and dilution chemical and physical in-use stability has been demonstrated for 48 hours at 2 °C to 25 °C. From a microbiological point of view, it should be used immediately. If not used immediately, in-use storage times and conditions prior to

use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C unless dilution has taken place under controlled and validated aseptic conditions.

6.4 Special precautions for storage

Solution for injection:

Store at or below 25°C.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Diluted solution for injection:

Store at 2 °C to 8 °C or below 25 °C for maximum of 24 hours).

For storage conditions of the diluted medicinal product, see section 6.3.

6.5 Nature and contents of container

SUMABID is packed in glass type I vials with a bromobutyl rubber stopper. On the vial an aluminium cap with flip top are applied. The aluminium cap is applied to tightly fix the rubber stopper to the glass vial. Pack size: 10 vials of 2 mL packed in a carton box.

6.6 Special precautions for disposal and other handling

None

7. HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD
14 Lautre Road, Stormill, Ext.1,
Roodepoort, 1724
South Africa

8. REGISTRATION NUMBER(S)

56/34/0244

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03 August 2022

10. DATE OF REVISION OF THE TEXT