PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

Sugammadex 100 mg/ml Mylan Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains 100 mg sugammadex (as the sodium salt).

Each 2 mL vial contains 200 mg sugammadex (as the sodium salt).

Each mL contains 9,7 mg sodium.

Sugar free.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear and colourless to slightly yellow solution free from visible particles.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Sugammadex 100 mg/ml Mylan is indicated for the routine reversal of neuromuscular blockade induced by rocuronium or vecuronium. **Sugammadex 100 mg/ml Mylan** is also indicated for the immediate reversal of neuromuscular blockade at 3 minutes after rocuronium administration.

For the paediatric population: **Sugammadex 100 mg/ml Mylan** 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

Sugammadex 100 mg/ml Mylan should be administered under the supervision of an anaesthetist.

Sugammadex 100 mg/ml Mylan 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 **Sugammadex 100 mg/ml Mylan** can be diluted using sodium chloride 9 mg/mL (0,9 %) to a concentration of 10 mg/mL.

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 **Sugammadex 100 mg/ml Mylan**, patients should be monitored for signs of recurrence of neuromuscular blockade.

The recommended dose of **Sugammadex 100 mg/ml Mylan** depends on the level of neuromuscular blockade to be reversed. The recommended dose does not depend on the anaesthetic regimen. **Sugammadex 100 mg/ml Mylan** 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 **Sugammadex 100 mg/ml Mylan** 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 **Sugammadex 100 mg/ml Mylan** is only recommended if spontaneous recovery has reached the reappearance of T2 (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 **Sugammadex 100 mg/ml Mylan** is recommended. There is no data to recommend the use of **Sugammadex 100 mg/ml Mylan** for immediate reversal following vecuronium induced blockade.

Special populations

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 **Sugammadex 100 mg/ml Mylan** in patients with severe renal impairment including patients requiring dialysis (CrCl < 30 mL/min) is not recommended (see section 4.4). Studies done in patients with severe renal impairment do not provide sufficient safety information to support the use of **Sugammadex 100 mg/ml Mylan** in these patients.

Elderly Patients

After administration of **Sugammadex 100 mg/ml Mylan** 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 **Sugammadex 100 mg/ml Mylan** 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 **Sugammadex 100 mg/ml Mylan** is mainly excreted renally no dose adjustments are required.

Studies in patients with hepatic impairment have not been conducted. Caution should be exercised when considering the use of **Sugammadex 100 mg/ml Mylan** 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 study only for reversal of rocuronium induced blockade at reappearance of T_2). There is insufficient information on the use of **Sugammadex 100 mg/ml Mylan** for children < 7 years of age. There is no information on **Sugammadex 100 mg/ml Mylan** use for neonates. Therefore **Sugammadex 100 mg/ml Mylan** 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 **Sugammadex 100 mg/ml Mylan** is recommended. Immediate reversal in children and adolescents has not been investigated and is therefore not recommended. **Sugammadex 100 mg/ml Mylan** may be diluted to 10 mg/mL to increase the accuracy of dosing in the paediatric population, 7 years and older.

Method of administration

Sugammadex 100 mg/ml Mylan 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 (see section 6.6).

4.3 Contraindications

Hypersensitivity to sugammadex sodium or to any of the excipients of **Sugammadex 100 mg/ml Mylan** (see section 6.1).

4.4 Special warnings and precautions for use

Sugammadex 100 mg/ml Mylan is not to be used to reverse depolarising neuromuscular blocking medicines.

With 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 medicines used in the peri- and postoperative 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 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 observed 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 4.2 and section 4.8).

Effect on haemostasis:

In a study done 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) and prothrombin time international normalized ratio [PT(INR)]. These limited mean aPTT and PT(INR) prolongations were of short duration (≤ 30 minutes). Based on the clinical findings and on a specific study done 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 *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 100 mg/ml Mylan** 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 100 mg/ml Mylan** 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 100 mg/ml Mylan** is administered to these patients monitoring of haemostasis and coagulation parameters is recommended.

Waiting times for re-administration with neuromuscular blocking medicines (NMBA) after reversal with Sugammadex 100 mg/ml Mylan:

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

Minimum waiting time	**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 100 mg/ml Mylan** administration.

Based on 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 100 mg/ml Mylan** 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):

A waiting time of 24 hours is recommended.

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

Renal impairment:

Sugammadex 100 mg/ml Mylan is not recommended for use in patients with severe renal impairment, creatinine clearance < 30 mL/min, including those requiring dialysis (see section 5.1).

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 clinical trials, 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 observed within minutes after the administration of **Sugammadex 100 mg/ml Mylan** for reversal of neuromuscular blockade. Cases of bradycardia with cardiac arrest have been reported. (See section 4.8.) Patients

should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade. Treatment with anti-cholinergic medicines such as atropine should be administered if clinically significant bradycardia is observed.

Hepatic impairment:

Sugammadex 100 mg/ml Mylan is not metabolised nor excreted by the liver; therefore dedicated studies in patients with hepatic impairment have not been conducted. 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*** above.

Use in Intensive Care Unit (ICU):

Sugammadex 100 mg/ml Mylan has not been investigated in patients receiving rocuronium or vecuronium in the ICU setting.

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

Sugammadex 100 mg/ml Mylan should not be used to reverse block induced by nonsteroidal neuromuscular blocking medicines such as succinylcholine or benzylisoquinolinium compounds. **Sugammadex 100 mg/ml Mylan** should not be used for reversal of neuromuscular blockade induced by steroidal neuromuscular blocking medicines other than rocuronium or vecuronium, since there are no efficacy and safety data for these situations. Limited data are available for reversal of pancuronium induced blockade, but it is advised not to use **Sugammadex 100 mg/ml Mylan** in this situation.

Delayed recovery:

Conditions associated with prolonged circulation time such as cardiovascular disease, old age (see section 4.2 for the time to recovery in elderly), or oedematous state (e.g., severe hepatic impairment) may be associated with longer recovery times.

Hypersensitivity reactions:

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

Patients on a controlled sodium diet:

Each mL solution contains up to 9,7 mg sodium. A dose of 23 mg sodium is considered essentially 'sodium-free'. If more than 2,4 mL solution needs to be administered, this should be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicines and other forms of interaction

The information in this section is based on binding affinity between **Sugammadex 100 mg/ml Mylan** and other medicines, non-clinical experiments, clinical studies and simulations using a model taking into account the pharmacodynamic effect of neuromuscular blocking medicines and the pharmacokinetic interaction between neuromuscular blocking medicines and sugammadex. Based on these data, no clinically significant pharmacodynamic interaction with other medicines 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 100 mg/ml Mylan (displacement interactions):

Due to the administration of certain medicines after sugammadex, like rocuronium or vecuronium, these could be displaced from **Sugammadex 100 mg/ml Mylan**. As a result recurrence of neuromuscular blockade might be observed. In this situation the patient must be ventilated. Administration of the medicine 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 medicine occurring within a period of 7,5 hours after **Sugammadex 100 mg/ml Mylan** 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 100 mg/ml Mylan** could occur. Medical practitioners attending the patient should be aware that the recovery of the T4/T1 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 cause some delay in the recovery of the T4/T1 ratio to 0,9. No recurrence of neuromuscular blockade is 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. For

re-administration of **Sugammadex 100 mg/ml Mylan** see section 4.2.

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

Administration of **Sugammadex 100 mg/ml Mylan**, could render certain medicines to 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 medicine, the administration of a therapeutically equivalent medicine (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 seen 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 100 mg/ml Mylan** is considered to be equivalent to one missed daily dose of oral contraceptive steroids (either combined or progestogen only). If **Sugammadex 100 mg/ml Mylan** 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:

Special attention should be paid to the possibility of recurrence of neuromuscular blockade when medicines which potentiate neuromuscular blockade are used in the post-operative period [the package leaflet of rocuronium or vecuronium will have a list of the specific medicines which potentiate neuromuscular blockade]. In the case of recurrence of neuromuscular blockade, the patient may require mechanical ventilation and re-administration of **Sugammadex 100 mg/ml Mylan** (see section 4.2).

Interference with laboratory tests:

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

In a 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 *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 performed. The above-mentioned interactions for adults and the warnings in section 4.4 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 **Sugammadex 100 mg/ml Mylan** to pregnant women.

Lactation

It is unknown whether **Sugammadex 100 mg/ml Mylan** is excreted in human breast milk. Animal studies have shown excretion of sugammadex in breast milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from **Sugammadex 100 mg/ml Mylan** therapy.

Fertility

The effects with **Sugammadex 100 mg/ml Mylan** on human fertility have not been investigated. Animal studies to evaluate fertility do not reveal harmful effects.

4.7 Effects on ability to drive and use machines

Sugammadex 100 mg/ml Mylan has no known influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

Sugammadex 100 mg/ml Mylan is administered concomitantly with neuromuscular blocking medicines and anaesthetics in surgical patients. The causality of adverse events is therefore difficult to assess. The most frequently reported adverse reactions in surgical patients were cough, airway complication of anaesthesia, anaesthetic complications, procedural hypotension and procedural complication.

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Adverse reactions**
Immune system disorders	Less frequent	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

c. Description of selected adverse reactions

Hypersensitivity reactions:

Hypersensitivity reactions, including anaphylaxis, have occurred in some patients and volunteers. In clinical trials of surgical patients these reactions were reported uncommonly 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.

Airway Complication of Anaesthesia:

Airway complications of anaesthesia included bucking against the endotracheal tube, coughing, mild bucking, arousal reaction during surgery, coughing during the anaesthetic procedure or during surgery, or anaesthetic procedure-related spontaneous breath of patient.

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 suckling on the endotracheal tube. See section 4.4 light anaesthesia.

Procedural Complication:

Procedural complications included coughing, tachycardia, bradycardia, movement, and increase in heart rate.

Marked bradycardia:

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

Recurrence of neuromuscular blockade:

In clinical studies with subjects treated with rocuronium or vecuronium, where sugammadex was administered using a dose labelled for the depth of

neuromuscular blockade (N=2,022), an incidence of 0,20 % was observed for recurrence of neuromuscular blockade as based on neuromuscular monitoring or clinical evidence (see section 4.4).

Additional information on special populations

Pulmonary patients:

In post-marketing data and in one dedicated clinical trial in patients with a history of pulmonary complications, bronchospasm was reported as a possibly related adverse event. The medical practitioner should be aware of the possible occurrence of bronchospasm in patients with a history of pulmonary complications.

Paediatric population

A limited database suggests that the safety profile of sugammadex (up to 4 mg/kg) in paediatric patients was 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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Based on clinical studies conducted, 1 case of an accidental overdose with 40 mg/kg was reported without any significant adverse reactions. In a human tolerance study conducted, sugammadex was administered in doses up to 96

mg/kg. No dose related adverse events nor serious adverse events were reported. **Sugammadex 100 mg/ml Mylan** can be removed using haemodialysis with a high flux filter, but not with a low flux filter. Based upon 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

Pharmacotherapeutic group: ATC code: V03AB35.

Pharmacological classification: A.34 Other

Sugammadex sodium injection is a modified cyclodextrin. It is a selective relaxant binding medicine (SRBA) which forms a complex with the neuromuscular blocking medicines rocuronium and vecuronium, and it reduces the amount of neuromuscular blocking medicine 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 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 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 observed steady-state volume of distribution of sugammadex sodium is approximately 11 to 14 litres in adult patients with normal renal function (based on 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.

Metabolism

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 anaesthetised patients with normal renal function the elimination half-life of sugammadex sodium is about 2 hours and the estimated plasma clearance is about 84 ml/min. A mass balance study demonstrated that > 90 % of the dose was excreted within 24 hours. Ninety six percent (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 < 0,02 % of the dose. Administration of sugammadex sodium to healthy volunteers resulted in increased renal elimination of rocuronium in complex.

Special population groups

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.

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.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity potential, and toxicity to reproduction, local tolerance or compatibility with blood. Sugammadex has no effects on fracture repair and remodelling of bone.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Sugammadex 100 mg/ml Mylan must not be mixed with other medicines except those mentioned in section 6.6. Physical incompatibility has been reported with verapamil, ondansetron and ranitidine.

6.3 Shelf life

2 years

After first opening and dilution chemical and physical in-use stability has been demonstrated for up to 48 hours at 25 °C. From a microbiological point of view, the diluted product 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 in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store at or below 25 °C.

Do not freeze.

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

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

6.5 Nature and contents of container

Sugammadex 100 mg/ml Mylan is packed in colourless, glass vials, sealed with grey, chlorobutyl rubber stoppers sealed with a flip-off aluminium seal.

Pack size: 10 vials of 2 ml.

6.6 Special precautions for disposal and other handling

Sugammadex 100 mg/ml Mylan 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 %), Ringers lactate solution, Ringers solution, glucose 50 mg/mL (5 %) in sodium chloride 9 mg/mL (0,9 %).

The infusion line should be adequately flushed (e.g., with 0,9 % sodium chloride) between administration of **Sugammadex 100 mg/ml Mylan** and other medicines.

Use in the paediatric population

For paediatric patients **Sugammadex 100 mg/ml Mylan** can be diluted using sodium chloride 9 mg/mL (0,9 %) to a concentration of 10 mg/mL (see section 6.3).

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

MYLAN (PTY) LTD

4 Brewery street

Isando

Gauteng

Republic of South Africa

8 REGISTRATION NUMBER

55/36/0386.385

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22 November 2022

10 DATE OF REVISION OF THE TEXT