ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sugammadex Adroiq 100 mg/mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL contains sugammadex sodium equivalent to 100 mg sugammadex.
Each vial of 2 mL contains sugammadex sodium equivalent to 200 mg sugammadex.
Each vial of 5 mL contains sugammadex sodium equivalent to 500 mg sugammadex.

Excipients with known effect

Contains up to 9.7 mg/mL sodium (see section 4.4).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear and colourless to slightly yellow solution.
The pH is between 7 and 8 and osmolality is between 300 and 500 mOsm/kg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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.

4.2 Posology and method of administration

Sugammadex should only be administered by, or under the supervision of an anaesthetist.
The use of an appropriate neuromuscular monitoring technique is recommended to monitor the recovery of neuromuscular blockade (see section 4.4).

Posology

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

Adults

Routine reversal
A dose of 4 mg/kg sugammadex is recommended if recovery has reached at least 1-2 post-tetanic counts (PTC) following rocuronium or vecuronium induced blockade. Median time to recovery of the T_4/T_1 ratio to 0.9 is around 3 minutes (see section 5.1).
A dose of 2 mg/kg sugammadex is recommended, if spontaneous recovery has occurred up to at least the reappearance of T_2 following rocuronium or vecuronium induced blockade. Median time to recovery of the T_4/T_1 ratio to 0.9 is around 2 minutes (see section 5.1).

Using the recommended doses for routine reversal will result in a slightly faster median time to recovery of the $T_4/T1$ ratio to 0.9 of rocuronium when compared to vecuronium induced neuromuscular blockade (see section 5.1).

Immediate reversal of rocuronium-induced blockade
If there is a clinical need for immediate reversal following administration of rocuronium a dose of 16 mg/kg sugammadex is recommended. When 16 mg/kg sugammadex is administered 3 minutes after a bolus dose of 1.2 mg/kg rocuronium bromide, a median time to recovery of the T_4/T_1 ratio to 0.9 of approximately 1.5 minutes can be expected (see section 5.1).

There is no data to recommend the use of sugammadex for immediate reversal following vecuronium induced blockade.

Re-administration of sugammadex
In the exceptional situation of recurrence of neuromuscular blockade post-operatively (see section 4.4) after an initial dose of 2 mg/kg or 4 mg/kg sugammadex, a repeat dose of 4 mg/kg sugammadex is recommended. Following a second dose of sugammadex, the patient should be closely monitored to ascertain sustained return of neuromuscular function.

Re-administration of rocuronium or vecuronium after sugammadex
For waiting times for re-administration of rocuronium or vecuronium after reversal with sugammadex, see section 4.4.

Special population

Renal impairment
The use of sugammadex in patients with severe renal impairment (including patients requiring dialysis (CrCl < 30 mL/min)) is not recommended (see section 4.4).
Studies in patients with severe renal impairment do not provide sufficient safety information to support the use of sugammadex in these patients (see also section 5.1).
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.

Elderly patients
After administration of sugammadex 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 (18-64 years) was 2.2 minutes, in elderly adults (65-74 years) it was 2.6 minutes and in very elderly adults (75 years or more) it was 3.6 minutes. Even though the recovery times in elderly tend to be slower, the same dose recommendation as for adults should be followed (see section 4.4).

Obese patients
In obese patients, including morbidly obese patients (body mass index ≥ 40 kg/m^2), the dose of sugammadex should be based on actual body weight. The same dose recommendations as for adults should be followed.

Hepatic impairment
Studies in patients with hepatic impairment have not been conducted. Caution should be exercised when considering the use of sugammadex in patients with severe hepatic impairment or when hepatic impairment is accompanied by coagulopathy (see section 4.4).
For mild to moderate hepatic impairment: as sugammadex is mainly excreted renally no dose adjustments are required.

Paediatric population

Children and adolescents (2-17 years)
Sugammadex may be diluted to 10 mg/mL to increase the accuracy of dosing in the paediatric population (see section 6.6).

Routine reversal: A dose of 4 mg/kg sugammadex is recommended for reversal of rocuronium induced blockade if recovery has reached at least 1-2 PTC.
A dose of 2 mg/kg is recommended for reversal of rocuronium induced blockade at reappearance of T_2 (see section 5.1).

Immediate reversal: Immediate reversal in children and adolescents has not been investigated.

Term newborn infants and infants
There is only limited experience with the use of sugammadex in infants (30 days to 2 years), and term newborn infants (less than 30 days) have not been studied. The use of sugammadex in term newborn infants and infants is therefore not recommended until further data become available.

Method of administration

Sugammadex should be administered intravenously as a single bolus injection. The bolus injection should be given rapidly, within 10 seconds, into an existing intravenous line (see section 6.6). Sugammadex has only been administered as a single bolus injection in clinical trials.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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 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 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 clinical data-base (N=3 519) and on a specific study in 1 184 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 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 (NMBA) after reversal with sugammadex:

Table 1: 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 administration.
Based on pharmacokinetic (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 very rare 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

Sugammadex is not recommended for use in patients with severe renal impairment, including those requiring dialysis (see section 5.1).

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

In rare instances, marked bradycardia has been observed 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

Sugammadex 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 (see section 4.2).

Use in intensive care unit (ICU)

Sugammadex has not been investigated in patients receiving rocuronium or vecuronium in the Intensive Care Unit (ICU) setting.

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

Sugammadex should not be used to reverse block induced by nonsteroidal neuromuscular blocking agents such as succinylcholine or benzylisoquinolinium compounds.
Sugammadex 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 for these situations. Limited data are available 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 (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.

Drug hypersensitivity reactions

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

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.

4.5 Interaction with other medicinal products and other forms of interaction

The information in this section is based on binding affinity between sugammadex and other medicinal products, non-clinical experiments, 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 these 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. Clinicians 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 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 see section 4.2.

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 clinician 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 Area Under the Curve (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 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 (see section 4.2).

Interference with laboratory tests

In general sugammadex 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 Activated Partial Thromboplastin Time (aPTT) by 17 and 22% respectively and of PT(INR) by 11 and 22% respectively.
These limited mean Activated Partial Thromboplastin Time(aPTT) and PT(INR) prolongations were of short duration (≤ 30 minutes).
In in vitro experiments a pharmacodynamic interaction (Activated Partial Thromboplastin Time (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

For sugammadex no clinical data on exposed pregnancies are available.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development.
Caution should be exercised when administering sugammadex to pregnant women.

Breast-feeding

It is unknown whether sugammadex is excreted in human breast milk. Animal studies have shown excretion of sugammadex in breast milk. Oral absorption of cyclodextrins in general is low and no effect on the suckling child is anticipated following a single dose to the breast-feeding woman.
A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from sugammadex therapy, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility

The effects with sugammadex 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 Adroiq has no known influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Sugammadex Adroiq is administered concomitantly with neuromuscular blocking agents and anaesthetics in surgical patients. The causality of adverse events is therefore difficult to assess.
The most commonly reported adverse reactions in surgical patients were cough, airway complication of anaesthesia, anaesthetic complications, procedural hypotension and procedural complication (Common (≥ 1/100 to < 1/10)).

The safety of sugammadex has been evaluated in 3 519 unique subjects across a pooled phase I-III safety database. The following adverse reactions were reported in placebo controlled trials where subjects received anaesthesia and/or neuromuscular blocking agents (1 078 subject exposures to sugammadex versus 544 to placebo).

The adverse reactions are listed below by SOC (System Organ Class) and by frequency, most frequent reactions first, with the following guidelines: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 2: Tabulated list of adverse reactions

System organ class	**Frequencies**	**Adverse reactions (Preferred terms)**
Immune system disorders	Uncommon	Drug hypersensitivity reactions (see section 4.4)
Respiratory, thoracic and mediastinal disorders	Common	Cough
Injury, poisoning and procedural complications	Common	Airway complication of anaesthesia Anaesthetic complication (see section 4.4) Procedural hypotension Procedural complication

Description of selected adverse reactions

Drug hypersensitivity reactions

Hypersensitivity reactions, including anaphylaxis, have occurred in some patients and volunteers (for information on volunteers, see Information on healthy volunteers below). 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.
In post-marketing reports, hypersensitivity has been observed for sugammadex as well as for sugammadex-rocuronium complex.

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).

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).

Information on healthy volunteers

A randomised, double-blind study examined the incidence of drug hypersensitivity reactions in healthy volunteers given up to 3 doses of placebo (N=76), sugammadex 4 mg/kg (N=151) or sugammadex 16 mg/kg (N=148). Reports of suspected hypersensitivity were adjudicated by a blinded committee. The incidence of adjudicated hypersensitivity was 1.3%, 6.6% and 9.5% in the placebo, sugammadex 4 mg/kg and sugammadex 16 mg/kg groups, respectively. There were no reports of anaphylaxis after placebo or sugammadex 4 mg/kg. There was a single case of adjudicated anaphylaxis after the first dose of sugammadex 16 mg/kg (incidence 0.7%). There was no evidence of increased frequency or severity of hypersensitivity with repeat dosing of sugammadex. In a previous study of similar design, there were three adjudicated cases of anaphylaxis, all after sugammadex 16 mg/kg (incidence 2.0%). In the Pooled Phase 1 database, Adverse Events (AEs) considered common (≥ 1/100 to < 1/10) or very common (≥ 1/10) and more frequent among subjects treated with sugammadex than in the placebo group, include dysgeusia (10.1%), headache (6.7%), nausea (5.6%), urticaria (1.7%), pruritus (1.7%), dizziness (1.6%), vomiting (1.2%) and abdominal pain (1.0%).

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. As with all patients with a history of pulmonary complications the physician should be aware of the possible occurrence of bronchospasm.

Paediatric population
In studies of paediatric patients 2 to 17 years of age, the safety profile of sugammadex (up to 4 mg/kg) was generally similar to the profile observed in adults.

Morbidly obese patients
In one dedicated clinical trial in morbidly obese patients, the safety profile was generally similar to the profile in adult patients in pooled Phase 1 to 3 studies (see table 2).

Patients with severe systemic disease
In a trial in patients who were assessed as American Society of Anesthesiologists (ASA) Class 3 or 4 (patients with severe systemic disease or patients with severe systemic disease that is a constant threat to life), the adverse reaction profile in these American Society of Anaesthesiologists (ASA) Class 3 and 4 patients was generally similar to that of adult patients in pooled Phase 1 to 3 studies (see table 2 and section 5.1).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare

professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In clinical studies, 1 case of an accidental overdose with 40 mg/kg was reported without any significant adverse reactions. In a human tolerance study sugammadex was administered in doses up to 96 mg/kg. No dose related adverse events nor serious adverse events were reported.

Sugammadex 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: all other therapeutic products, antidotes, ATC code: V03AB35

Mechanism of action

Sugammadex is a modified gamma cyclodextrin which is a selective relaxant binding agent. 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.

Pharmacodynamic effects

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.

Clinical efficacy and safety

Sugammadex can be administered at several time points after administration of rocuronium or vecuronium bromide

Routine reversal – deep neuromuscular blockade

In a pivotal study patients were randomly assigned to the rocuronium or vecuronium group. After the last dose of rocuronium or vecuronium, at 1-2 PTCs, 4 mg/kg sugammadex or 70 mcg/kg neostigmine was administered in a randomised order. The time from start of administration of sugammadex or neostigmine to recovery of the T4/T1 ratio to 0.9 was:

Table 3: Time (minutes) from administration of sugammadex or neostigmine at deep neuromuscular blockade (1-2 Post-tetanic counts (PTCs) after rocuronium or vecuronium to recovery of the T_4/T_1 ratio to 0.9

Neuromuscular blocking agent	Treatment regimen	
	Sugammadex (4 mg/kg)	**Neostigmine (70 mcg/kg)**
Rocuronium		
N	37	37
Median (minutes)	2.7	49.0
Range	1.2-16.1	13.3-145.7
Vecuronium		
N	47	36
Median (minutes)	3.3	49.9
Range	1.4-68.4	46.0-312.7

Routine reversal – moderate neuromuscular blockade

In another pivotal study patients were randomly assigned to the rocuronium or vecuronium group. After the last dose of rocuronium or vecuronium, at the reappearance of T_2, 2 mg/kg sugammadex or 50 mcg/kg neostigmine was administered in a randomised order. The time from start of administration of sugammadex or neostigmine to recovery of the T_4/T_1 ratio to 0.9 was:

Table 4: Time (minutes) from administration of sugammadex or neostigmine at reappearance of T_2 after rocuronium or vecuronium to recovery of the T_4/T_1 ratio to 0.9

Neuromuscular blocking agent	Treatment regimen	
	Sugammadex (2 mg/kg)	**Neostigmine (50 mcg/kg)**
Rocuronium		
N	48	48
Median (minutes)	1.4	17.6
Range	0.9-5.4	3.7-106.9
Vecuronium		
N	48	45
Median (minutes)	2.1	18.9
Range	1.2-64.2	2.9-76.2

Reversal by sugammadex of the neuromuscular blockade induced by rocuronium was compared to the reversal by neostigmine of the neuromuscular blockade induced by *cis*-atracurium. At the reappearance of T_2 a dose of 2 mg/kg sugammadex or 50 mcg/kg neostigmine was administered. Sugammadex provided faster reversal of neuromuscular blockade induced by rocuronium compared to neostigmine reversal of neuromuscular blockade induced by *cis*-atracurium:

Table 5: Time (minutes) from administration of sugammadex or neostigmine at reappearance of T2 after rocuronium or *cis*-atracurium to recovery of the T4/T1 ratio to 0.9

Neuromuscular blocking agent	Treatment regimen	
	Rocuronium and sugammadex (2 mg/kg)	***Cis*-atracurium and neostigmine (50 mcg/kg)**
N	34	39
Median (minutes)	1.9	7.2
Range	0.7-6.4	4.2-28.2

For immediate reversal

The time to recovery from succinylcholine-induced neuromuscular blockade (1 mg/kg) was compared with sugammadex (16 mg/kg, 3 minutes later) – induced recovery from rocuronium-induced neuromuscular blockade (1.2 mg/kg).

Table 6: Time (minutes) from administration of rocuronium and sugammadex or succinylcholine to recovery of the T_1 10%

Neuromuscular blocking agent	Treatment regimen	
	Rocuronium and sugammadex (16 mg/kg)	Succinylcholine (1 mg/kg)
N	55	55
Median (minutes)	4.2	7.1
Range	3.5-7.7	3.7-10.5

In a pooled analysis the following recovery times for 16 mg/kg sugammadex after 1.2 mg/kg rocuronium bromide were reported:

Table 7: Time (minutes) from administration of sugammadex at 3 minutes after rocuronium to recovery of the T_4/T_1 ratio to 0.9, 0.8 or 0.7

	T_4/T_1 to 0.9	T_4/T_1 to 0.8	T_4/T_1 to 0.7
N	65	65	65
Median (minutes)	1.5	1.3	1.1
Range	0.5-14.3	0.5-6.2	0.5-3.3

Renal impairment

Two open label studies compared the efficacy and safety of sugammadex in surgical patients with and without severe renal impairment. In one study, sugammadex was administered following rocuronium induced blockade at 1-2 Post-tetanic counts (PTCs) (4 mg/kg; N=68); in the other study, sugammadex was administered at reappearance of T2 (2 mg/kg; N=30). Recovery from blockade was modestly longer for patients with severe renal impairment relative to patients without renal impairment. No residual neuromuscular blockade or recurrence of neuromuscular blockade was reported for patients with severe renal impairment in these studies.

Morbidly obese patients

A trial of 188 patients who were diagnosed as morbidly obese investigated the time to recovery from moderate or deep neuromuscular blockade induced by rocuronium or vecuronium. Patients received 2 mg/kg or 4 mg/kg sugammadex, as appropriate for level of block, dosed according to either actual body weight or ideal body weight in random, double-blinded fashion. Pooled across depth of block and neuromuscular blocking agent, the median time to recover to a train-of-four (TOF) ratio ≥ 0.9 in patients dosed by actual body weight (1.8 minutes) was statistically significantly faster ($p < 0.0001$) compared to patients dosed by ideal body weight (3.3 minutes).

Paediatric population

A trial of 288 patients aged 2 to < 17 years investigated the safety and efficacy of sugammadex versus neostigmine as a reversal agent for neuromuscular blockade induced by rocuronium or vecuronium. Recovery from moderate block to a train-of-four (TOF) ratio of ≥ 0.9 was significantly faster in the sugammadex 2 mg/kg group compared with the neostigmine group (geometric mean of 1.6 minutes for sugammadex 2 mg/kg and 7.5 minutes for neostigmine, ratio of geometric means 0.22, 95% CI (0.16, 0.32), ($p< 0.0001$)). Sugammadex 4 mg/kg achieved reversal from deep block with a geometric mean of 2.0 minutes, similar to results observed in adults. These effects were consistent for all age cohorts studied (2 to < 6; 6 to < 12; 12 to < 17 years of age) and for both rocuronium and vecuronium (see section 4.2).

Patients with severe systemic disease

A trial of 331 patients who were assessed as American Society of Anaesthesiologists (ASA) Class 3 or

4 investigated the incidence of treatment- emergent arrhythmias (sinus bradycardia, sinus tachycardia, or other cardiac arrhythmias) after administration of sugammadex.
In patients receiving sugammadex (2 mg/kg, 4 mg/kg, or 16 mg/kg), the incidence of treatment-emergent arrhythmias was generally similar to neostigmine (50 µg/kg up to 5 mg maximum dose) + glycopyrrolate (10 µg/kg up to 1 mg maximum dose). The adverse reaction profile in ASA Class 3 and 4 patients was generally similar to that of adult patients in pooled Phase 1 to 3 studies; therefore, no dose adjustment is necessary (see section 4.8).

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 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 dose 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 anaesthetised patients with normal renal function the elimination half-life ($t_{1/2}$) 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 parameters stratified by age and renal function is presented below:

Selected patient characteristics		**Mean predicted PK parameters (CV*%)**		
Demographic	Renal function	Clearance	Volume of	Elimination

Age Body weight	Creatinine clearance (mL/min)			(mL/min)	distribution at steady state (L)	half-life (hr)
Adult	Normal		100	84 (24)	13	2 (22)
40 years 75 kg	Impaired	Mild Moderate Severe	50 30 10	47 (25) 28 (24) 8 (25)	14 14 15	4 (22) 7 (23) 24 (25)
Elderly	Normal		80	70 (24)	13	3 (21)
75 years 75 kg	Impaired	Mild Moderate Severe	50 30 10	46 (25) 28 (25) 8 (25)	14 14 15	4 (23) 7 (23) 24 (24)
Adolescent	Normal		95	72 (25)	10	2 (21)
15 years 56 kg	Impaired	Mild Moderate Severe	48 29 10	40 (24) 24 (24) 7 (25)	11 11 11	4 (23) 6 (24) 22 (25)
Middle childhood	Normal		60	40 (24)	5	2 (22)
9 years 29 kg	Impaired	Mild Moderate Severe	30 18 6	21 (24) 12 (25) 3 (26)	6 6 6	4 (22) 7 (24) 25 (25)
Early childhood	Normal		39	24 (25)	3	2 (22)
4 years 16 kg	Impaired	Mild Moderate Severe	19 12 4	11 (25) 6 (25) 2 (25)	3 3 3	4 (23) 7 (24) 28 (26)

*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.

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 is rapidly cleared in preclinical species, although residual sugammadex was observed in bone and teeth of juvenile rats. Preclinical studies in young adult and mature rats demonstrate 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

Hydrochloric acid (to adjust pH)
Sodium hydroxide (to adjust pH)
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.
Physical incompatibility has been reported with verapamil, ondansetron and ranitidine.

6.3 Shelf life

3 years

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, 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 below 30°C.
Do not freeze.
Keep the vial in the outer carton in order to protect from light.
For storage conditions of the diluted medicinal product, see section 6.3.

6.5 Nature and contents of container

2 mL or 5 mL of solution in type I glass vial closed with chlorobutyl rubber stoppers with red grain aluminium crimp-cap and flip-off cap.
Pack sizes: 10 vials of 2 mL or 10 vials of 5 mL.
Not all pack-sizes may be marketed.

6.6 Special precautions for disposal and other handling

Sugammadex Adroiq 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 Adroiq and other medicinal products.

Use in the paediatric population

For paediatric patients Sugammadex Adroiq can be diluted using sodium chloride 9 mg/mL (0.9%) to a concentration of 10 mg/mL (see section 6.3).

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

7. MARKETING AUTHORISATION HOLDER

Extrovis EU Kft.
Raktarvarosi Ut 9,
Torokbalint, 2045
Hungary

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1733/001
EU/1/23/1733/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 May 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Pharma Pack Hungary Kft
Vasút u. 13, Budaörs
2040 Hungary

Pharma Pack Hungary Kft.
Building B, Raktarvarosi Ut 9,
Torokbalint,
2045 Hungary

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product 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.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON, 10 x 5 mL vials

1. NAME OF THE MEDICINAL PRODUCT

Sugammadex Adroiq100 mg/mL solution for injection
sugammadex

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 mL contains 100 mg sugammadex (as sugammadex sodium).
Each vial of 5 mL contains 500 mg sugammadex (as sugammadex sodium).

3. LIST OF EXCIPIENTS

Other ingredients: hydrochloric acid and/or sodium hydroxide (to adjust pH), water for injections.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
10 vials
500 mg/5 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use
For single use only.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 30°C. Do not freeze. Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Discard any unused solution.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Extrovis EU Kft.
Raktarvarosi Ut 9,
Torokbalint, 2045
Hungary

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1733/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC {number}
SN {number}
NN {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL, 10 x 5 mL vials

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINITRATION

Sugammadex Adroiq100 mg/mL solution for injection
sugammadex
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

500 mg/5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON, 10 x 2 mL vials

1. NAME OF THE MEDICINAL PRODUCT

Sugammadex Adroiq 100 mg/mL solution for injection
sugammadex

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 mL contains 100 mg sugammadex (as sugammadex sodium).
Each vial of 2 mL contains 200 mg sugammadex (as sugammadex sodium).

3. LIST OF EXCIPIENTS

Other ingredients: hydrochloric acid and/or sodium hydroxide (to adjust pH), water for injections.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
10 vials
200 mg/2 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use
For single use only.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 30°C. Do not freeze. Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Discard any unused solution.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Extrovis EU Kft.
Raktarvarosi Ut 9,
Torokbalint, 2045
Hungary

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1733/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC {number}
SN {number}
NN {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL, 10 x 2 mL vials

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINITRATION

Sugammadex Adroiq100 mg/mL solution for injection
sugammadex

IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

200 mg/2 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Sugammadex Adroiq 100 mg/mL solution for injection
sugammadex

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your anaesthetist or doctor.
- If you get any side effects, talk to your anaesthetist or other doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Sugammadex Adroiq is and what it is used for
2. What you need to know before Sugammadex Adroiq is given
3. How Sugammadex Adroiq is given
4. Possible side effects
5. How to store Sugammadex Adroiq
6. Contents of the pack and other information

1. What Sugammadex Adroiq is and what it is used for

What Sugammadex Adroiq is
Sugammadex Adroiq contains the active substance sugammadex. Sugammadex is considered to be a selective relaxant binding agent since it only works with specific muscle relaxants, rocuronium bromide or vecuronium bromide.

What Sugammadex Adroiq is used for
When you have some types of operations, your muscles must be completely relaxed. This makes it easier for the surgeon to do the operation. For this, the general anaesthetic you are given includes medicines to make your muscles relax. These are called muscle relaxants, and examples include rocuronium bromide and vecuronium bromide. Because these medicines also make your breathing muscles relax, you need help to breathe (artificial ventilation) during and after your operation until you can breathe on your own again.
Sugammadex Adroiq is used to speed up the recovery of your muscles after an operation to allow you to breathe on your own again earlier. It does this by combining with the rocuronium bromide or vecuronium bromide in your body. It can be used in adults whenever rocuronium bromide or vecuronium bromide is used and in children and adolescents (aged 2 to 17 years) when rocuronium bromide is used for a moderate level of relaxation.

2. What you need to know before Sugammadex Adroiq is given

You should not be given Sugammadex Adroiq
- if you are allergic to sugammadex or any of the other ingredients of this medicine (listed in section 6).

→ Tell your anaesthetist if this applies to you.

Warnings and precautions
Talk to your anaesthetist before Sugammadex Adroiq is given
- if you have kidney disease or had in the past. This is important as Sugammadex Adroiq is removed from your body by the kidneys.
- if you have liver disease or have had it in the past.

- if you have fluid retention (oedema).
- if you have diseases which are known to give an increased risk of bleeding (disturbances of blood clotting) or anticoagulation medicines.

Children and adolescents
This medicine is not recommended for infants less than 2 years of age.

Other medicines and Sugammadex Adroiq
→ Tell your anaesthetist if you are taking, have recently taken or might take any other medicines. Sugammadex Adroiq may affect other medicines or be affected by them.

Some medicines reduce the effect of Sugammadex Adroiq
→It is especially important that you tell your anaesthetist if you have recently taken:
- toremifene (used to treat breast cancer).
- fusidic acid (an antibiotic).

Sugammadex Adroiq can affect hormonal contraceptives
- Sugammadex Adroiq can make hormonal contraceptives - including the 'Pill', vaginal ring, implants or a hormonal IntraUterine System (IUS) - less effective because it reduces how much you get of the progestogen hormone. The amount of progestogen lost by using Sugammadex Adroiq is about the same as missing one oral contraceptive Pill.
  →If you are taking the Pill on the same day as Sugammadex Adroiq is given to you, follow the instructions for a missed dose in the Pill's package leaflet.
  →If you are using other hormonal contraceptives (for example a vaginal ring, implant or intrauterine system (IUS)) you should use an additional non-hormonal contraceptive method (such as a condom) for the next 7 days and follow the advice in the package leaflet.

Effects on blood tests
In general, Sugammadex Adroiq does not have an effect on laboratory tests. However, it may affect the results of a blood test for a hormone called progesterone. Talk to your doctor if your progesterone levels need to be tested on the same day you receive Sugammadex Adroiq.

Pregnancy and breast-feeding
→ Tell your anaesthetist if you are pregnant or might be pregnant or if you are breast-feeding.
You may still be given Sugammadex Adroiq, but you need to discuss it first.
It is not known whether sugammadex can pass into breast milk. Your anaesthetist will help you decide whether to stop breast-feeding, or whether to abstain from sugammadex therapy, considering the benefit of breast-feeding to the baby and the benefit of Sugammadex Adroiq to the mother.

Driving and using machines
Sugammadex Adroiq has no known influence on your ability to drive and use machines.

Sugammadex Adroiq contains sodium
This medicine contains up to 9.7 mg sodium (main component of cooking / table salt) in each mL. This is equivalent to 0.5% of the recommended maximum daily dietary intake of sodium for an adult.

3. How Sugammadex Adroiq is given

Sugammadex Adroiq will be given to you by your anaesthetist, or under the care of your anaesthetist.

The dose
Your anaesthetist will work out the dose of Sugammadex Adroiq you need based on:
- your weight

- how much the muscle relaxant medicine is still affecting you.

The usual dose is 2-4 mg per kg body weight for adults and for children and adolescents between 2-17 years old. A dose of 16 mg/kg can be used in adults if urgent recovery from muscle relaxation is needed.

How Sugammadex Adroiq is given
Sugammadex Adroiq will be given to you by your anaesthetist. It is given as a single injection through an intravenous line.

If more Sugammadex Adroiq is given to you than recommended
As your anaesthetist will be monitoring your condition carefully, it is unlikely that you will be given too much Sugammadex Adroiq. But even if this happens, it is unlikely to cause any problems.
If you have any further questions on the use of this medicine, ask your anaesthetist or other doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
If these side effects occur while you are under anaesthesia, they will be seen and treated by your anaesthetist.

Common side effects (may affect up to 1 in 10 people)
- Cough
- Airway difficulties that may include coughing or moving as if you are waking or taking a breath
- Light anaesthesia - you may start to come out of deep sleep, so need more anaesthesia. This might cause you to move or cough at the end of the operation
- Complications during your procedure such as changes in heart rate, coughing or moving
- Decreased blood pressure due to the surgical procedure

Uncommon side effects (may affect up to 1 in 100 people)
- Shortness of breath due to muscle cramps of the airways (bronchospasm) occurred in patients with a history of lung problems
- Allergic (drug hypersensitivity) reactions - such as a rash, red skin, swelling of your tongue
- and/or throat, shortness of breath, changes in blood pressure or heart rate, sometimes resulting in a serious decrease of blood pressure. Severe allergic or allergic-like reactions can be life threatening.
- Allergic reactions were reported more commonly in healthy, conscious volunteers
- Return of muscle relaxation after the operation

Frequency not known
- Severe slowing of the heart and slowing of the heart up to cardiac arrest may occur when Sugammadex Adroiq is administered

Reporting of side effects
If you get any side effects, talk to your anaesthetist or other doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side affects you can help provide more information on the safety of this medicine.

5. How to store Sugammadex Adroiq

Storage will be handled by healthcare professionals.

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the carton and on the label after

'EXP'. The expiry date refers to the last day of that month.

Store below 30°C. Do not freeze. Keep the vial in the outer carton in order to protect from light.

After first opening and dilution, store at 2 to 8°C and use within 24 hours.

6. Contents of the pack and other information

What Sugammadex Adroiq contains
- The active substance is sugammadex.
  1 mL solution for injection contains sugammadex sodium equivalent to 100 mg sugammadex.
  Each vial of 2 mL contains sugammadex sodium equivalent to 200 mg sugammadex.
  Each vial of 5 mL contains sugammadex sodium equivalent to 500 mg sugammadex.
- The other ingredients are water for injections, hydrochloric acid and/or sodium hydroxide (for pH adjustment).
- See section 2 "Sugammadex Adroiq contains sodium".

What Sugammadex Adroiq looks like and contents of the pack
Sugammadex Adroiq is a clear and colourless to slightly yellow solution for injection.
It comes in two different pack sizes, containing either 10 vials with 2 mL or 10 vials with 5 mL solution for injection.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Extrovis EU Kft.
Raktarvarosi Ut 9,
Torokbalint, 2045
Hungary

Manufacturer

Pharma Pack Hungary Kft
Vasút u. 13, Budaörs
2040 Hungary

Pharma Pack Hungary Kft.
Building B, Raktarvarosi Ut 9,
Torokbalint,
2045 Hungary

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.