HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use SUGAMMADEX INJECTION safely and effectively. See full prescribing information for SUGAMMADEX INJECTION.

SUGAMMADEX injection, for intravenous use
Initial U.S. Approval: 2015

----------**RECENT MAJOR CHANGES**----------
Indication and Usage (1) 12/2024

----------**INDICATIONS AND USAGE**----------
Sugammadex is indicated for the reversal of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide in adult and pediatric patients aged 2 years and older undergoing surgery. (1)

----------**DOSAGE AND ADMINISTRATION**----------
• Dosing is based on actual body weight (2.1)
• Monitor for twitch responses to determine the timing and dose for sugammadex administration. (2.1)
• Administer as a single bolus injection. (2.1)
For rocuronium and vecuronium:
• 4 mg/kg is recommended if spontaneous recovery of the twitch response has reached 1 to 2 post-tetanic counts (PTC) and there are no twitch responses to train-of-four (TOF) stimulation. (2.2)
• 2 mg/kg is recommended if spontaneous recovery has reached the reappearance of the second twitch in response to TOF stimulation. (2.2)
For rocuronium only:
• 16 mg/kg is recommended if there is a clinical need to reverse neuromuscular blockade soon (approximately 3 minutes) after administration of a single dose of 1.2 mg/kg of rocuronium. Immediate reversal in pediatric patients has not been studied. (2.2)

----------**DOSAGE FORMS AND STRENGTHS**----------
• 200 mg/2 mL (100 mg/mL) in a single-dose vial for bolus injection (3)
• 500 mg/5 mL (100 mg/mL) in a single-dose vial for bolus injection (3)

----------**CONTRAINDICATIONS**----------
Known hypersensitivity to sugammadex or any of its components. (4)

----------**WARNINGS AND PRECAUTIONS**----------
Anaphylaxis: Be prepared for hypersensitivity reactions (including anaphylactic reactions) and take necessary precautions. (5.1)
Marked Bradycardia: Cases of marked bradycardia, some of which have resulted in cardiac arrest, have been observed within minutes after administration. Monitor for hemodynamic changes and administer anticholinergic agents such as atropine if clinically significant bradycardia is observed. (5.2)
Respiratory Function Monitoring: Ventilatory support is mandatory until adequate spontaneous respiration is restored and the ability to maintain a patent airway is assured. Provide adequate ventilation if neuromuscular blockade persists after sugammadex or recurs following extubation. (5.3, 5.4)
Waiting Times for Re-Administration of Neuromuscular Blocking Agents: If re-administration of a neuromuscular blocking agent is required after reversal with sugammadex, waiting times should be based on the dose of sugammadex, and the renal function of the patient. Consider use of a nonsteroidal neuromuscular blocking agent. (5.5)

----------**ADVERSE REACTIONS**----------
• Most common adverse reactions (reported in ≥10% of adult patients at a 2, 4, or 16 mg/kg sugammadex injection dose and higher than the placebo rate): vomiting, pain, nausea, hypotension, and headache. (6.1)
• Most common adverse reactions (reported in ≥10% of pediatric patients 2 to <17 years of age at sugammadex injection doses of 2 or 4 mg/kg) were pain, vomiting, and nausea. (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Accord Healthcare Inc. at 1-866-941-7875 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------**DRUG INTERACTIONS**----------
Toremifene: Concomitant use can delay recovery. (7.2)
Hormonal contraceptives: Patients must use an additional, non-hormonal method of contraception for 7 days following sugammadex injection administration. (5.6, 7.3)

----------**USE IN SPECIFIC POPULATIONS**----------
• Severe Renal Impairment: Not recommended. (8.6)

See 17 for PATIENT COUNSELING INFORMATION.
Additional pediatric use information is approved for Merck Sharp & Dohme LLC's BRIDION® (sugammadex) injection. However, due to Merck Sharp & Dohme LLC's marketing exclusivity rights, this drug product is not labeled with that information.

Revised: 05/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Sugammadex is indicated for the reversal of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide in adult and pediatric patients aged 2 years and older undergoing surgery.

Additional pediatric use information is approved for Merck Sharp & Dohme LLC's BRIDION® (sugammadex) injection. However, due to Merck Sharp & Dohme LLC's marketing exclusivity rights, this drug product is not labeled with that information.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosing and Administration Information

Sugammadex dosing is based on actual body weight.

Sugammadex injection, for intravenous use, should be administered by trained healthcare providers familiar with the use, actions, characteristics, and complications of neuromuscular blocking agents (NMBA) and neuromuscular block reversal agents.

Doses and timing of sugammadex injection administration should be based on monitoring for twitch responses and the extent of spontaneous recovery that has occurred.

Administer sugammadex injection intravenously as a single bolus injection. The bolus injection may be given over 10 seconds, into an existing intravenous line. Sugammadex injection has only been administered as a single bolus injection in clinical trials.

From the time of sugammadex injection administration until complete recovery of neuromuscular function, monitor the patient to assure adequate ventilation and maintenance of a patent airway. Satisfactory recovery should be determined through assessment of skeletal muscle tone and respiratory measurements in addition to the response to peripheral nerve stimulation.

The recommended dose of sugammadex injection does not depend on the anesthetic regimen.

Preparation of dilution for pediatric use:
Sugammadex 100 mg/mL may be diluted to a concentration of 10 mg/mL, using 0.9% sodium chloride injection, USP, to increase the accuracy of dosing in the pediatric population.
• To prepare the required dose, aseptically transfer all the contents of the 2 mL vial of Sugammadex 2mL single-dose vials containing 200 mg sugammadex (100 mg/mL) to a bottle (or intravenous bag) containing 18 mL of 0.9% sodium chloride injection, to achieve a final concentration of 10 mg/mL sugammadex. The diluted solution should be used immediately.
• Sugammadex injection is a single-dose sterile solution without preservatives. Discard any unused portion from the vial.

2.2 Recommended Dosing

Sugammadex injection can be used to reverse different levels of rocuronium- or vecuronium-induced neuromuscular blockade.

For rocuronium and vecuronium:
• A dose of 4 mg/kg sugammadex is recommended if spontaneous recovery of the twitch response has reached 1 to 2 post-tetanic counts (PTC) and there are no twitch responses to train-of-four (TOF) stimulation following rocuronium- or vecuronium-induced neuromuscular blockade *[see Warnings and Precautions (5.8)]*.

• A dose of 2 mg/kg sugammadex is recommended if spontaneous recovery has reached the reappearance of the second twitch (T_2) in response to TOF stimulation following rocuronium- or vecuronium-induced neuromuscular blockade *[see Warnings and Precautions (5.8)]*.

For rocuronium only:
• A dose of 16 mg/kg sugammadex is recommended if there is a clinical need to reverse neuromuscular blockade soon (approximately 3 minutes) after administration of a single dose of 1.2 mg/kg of rocuronium. The efficacy of the 16 mg/kg dose of sugammadex following administration of vecuronium has not been studied. Immediate reversal in pediatric patients has not been studied *[see Clinical Studies (14.1)]*.

2.3 Drug Compatibility

May inject sugammadex injection into the intravenous line of a running infusion with the following intravenous solutions:
• 0.9% sodium chloride
• 5% dextrose
• 0.45% sodium chloride and 2.5% dextrose
• 5% dextrose in 0.9% sodium chloride
• isolyte P with 5% dextrose
• Ringer's lactate solution
• Ringer's solution

Ensure the infusion line is adequately flushed (e.g., with 0.9% sodium chloride) between administration of sugammadex injection and other drugs.

Do not mix sugammadex injection with other products except those listed above.

Sugammadex injection is physically incompatible with verapamil, ondansetron, and ranitidine.

Visually inspect parenteral drug products for particulate matter and discoloration prior to administration, whenever the solution and container permit.

3 DOSAGE FORMS AND STRENGTHS

Sugammadex injection is a sterile, clear, colorless to slightly yellow-brown, non-pyrogenic aqueous solution intended for intravenous infusion. Sugammadex is available as follows:
• 200 mg/2 mL (100 mg/mL) in a single-dose vial for bolus injection
• 500 mg/5 mL (100 mg/mL) in a single-dose vial for bolus injection

4 CONTRAINDICATIONS

Sugammadex is contraindicated in patients with known hypersensitivity to sugammadex or any of its components. Hypersensitivity reactions that occurred 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 *[see Warnings and Precautions (5.1), Adverse Reactions (6)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Anaphylaxis and Hypersensitivity

Clinicians should be prepared for the possibility of drug hypersensitivity reactions (including anaphylactic reactions) and take the necessary precautions *[see Contraindications (4), Adverse Reactions (6.1)]*.

Potentially serious hypersensitivity reactions, including anaphylaxis, have occurred in patients treated with sugammadex. The nature and frequency of anaphylaxis and hypersensitivity associated with sugammadex administration were evaluated in a randomized, double-blind, placebo-controlled, parallel-group, repeat-dose study in which 375 subjects were randomized to receive 3 doses of sugammadex IV with a 5-week washout period: 151 subjects received 4 mg/kg, 148 received 16 mg/kg and 76 received placebo. The frequency of anaphylaxis for the 299 healthy volunteers treated with intravenous sugammadex was 0.3% (n=1 in the sugammadex 16 mg/kg group on the first dose). Signs and symptoms included conjunctival edema, urticaria, erythema, swelling of the uvula and reduction in peak expiratory flow within 5 minutes of dose administration. The most common hypersensitivity adverse reactions reported were nausea, pruritus and urticaria and showed a dose response relationship, occurring more frequently in the 16 mg/kg group compared to the 4 mg/kg and placebo groups.

Anaphylaxis has also been reported in the post-marketing setting, including at doses less than 16 mg/kg. The most commonly described clinical features in reports of anaphylaxis were dermatologic symptoms (including urticaria, rash, erythema, flushing and skin eruption); and clinically important hypotension often requiring the use of vasopressors for circulatory support. In addition, prolonged hospitalization and/or the use of additional respiratory support until full recovery (re-intubation, prolonged intubation, manual or mechanical ventilation) have been noted in a number of the anaphylaxis reports.

5.2 Marked Bradycardia

Cases of marked bradycardia, some of which have resulted in cardiac arrest, have been observed within minutes after the administration of sugammadex *[see Adverse Reactions (6.2)]*. Patients should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade. Treatment with anticholinergic agents, such as atropine, should be administered if clinically significant bradycardia is observed.

5.3 Respiratory Function Monitoring During Recovery

Ventilatory support is mandatory for patients until adequate spontaneous respiration is restored and the ability to maintain a patent airway is assured. Even if recovery from neuromuscular blockade is complete, other drugs used in the peri- and post-operative period could depress respiratory function and therefore ventilatory support might still be required.
Should neuromuscular blockade persist after sugammadex administration or recur following extubation, take appropriate steps to provide adequate ventilation.

5.4 Risk of Prolonged Neuromuscular Blockade

In clinical trials, a small number of patients experienced a delayed or minimal response to the administration of sugammadex *[see Clinical Studies (14.1)]*. Thus, it is important to monitor ventilation until recovery occurs.

5.5 Waiting Times for Re-Administration of Neuromuscular Blocking Agents for Intubation Following Reversal with Sugammadex

A minimum waiting time is necessary before administration of a steroidal neuromuscular blocking agent after administration of sugammadex.

Table 1: Re-administration of Rocuronium or Vecuronium after 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

When rocuronium 1.2 mg/kg is administered within 30 minutes after reversal with sugammadex, the onset of neuromuscular blockade may be delayed up to approximately 4 minutes and the duration of neuromuscular blockade may be shortened up to approximately 15 minutes.

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 reversal with up to 4 mg/kg 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.

For re-administration of rocuronium or administration of vecuronium after reversal of rocuronium with 16 mg/kg sugammadex, a waiting time of 24 hours is suggested.

If neuromuscular blockade is required before the recommended waiting time has elapsed, use a nonsteroidal neuromuscular blocking agent. 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.

5.6 Interactions Potentially Affecting the Efficacy of Other Drugs

Due to the administration of sugammadex, certain drugs, including hormonal contraceptives, could become less effective due to a lowering of the (free) plasma concentrations. In this situation, consider the re-administration of the other drug, the administration of a therapeutically equivalent drug (preferably from a different chemical class), and/or non-pharmacological interventions as appropriate *[see Drug Interactions (7.3)]*.

5.7 Risk of Recurrence of Neuromuscular Blockade Due to Displacement Interactions

Recurrence of neuromuscular blockade may occur due to displacement of rocuronium or vecuronium from sugammadex by other drugs *[see Drug Interactions (7.2)]*. In this situation the patient may require mechanical ventilation. Administration of the drug which caused displacement should be stopped in case of an infusion. The risk of displacement reactions will be the highest in the time period equivalent to 3 times the half-life of sugammadex *[see Clinical Pharmacology (12.3)]*.

5.8 Risk of Recurrence of Neuromuscular Blockade with Lower Than Recommended Dosing

The use of lower than recommended doses of sugammadex may lead to an increased risk of recurrence of neuromuscular blockade after initial reversal and is not recommended *[see Dosage and Administration (2.2), Adverse Reactions (6.1)]*.

5.9 Risk of Recurrence of Neuromuscular Blockade Due to the Administration of Drugs that Potentiate Neuromuscular Blockade

When drugs which potentiate neuromuscular blockade are used in the post-operative phase, special attention should be paid to the possibility of recurrence of neuromuscular blockade. Refer to the package insert for rocuronium or vecuronium for a list of the specific drugs which potentiate neuromuscular blockade. In case recurrence of neuromuscular blockade is observed, the patient may require mechanical ventilation.

5.10 Risk of Coagulopathy and Bleeding

Sugammadex injection doses up to 16 mg/kg were associated with increases in the coagulation parameters activated partial thromboplastin time (aPTT) and prothrombin time/international normalized ratio [PT(INR)] of up to 25% for up to 1 hour in healthy volunteers.

In patients undergoing major orthopedic surgery of the lower extremity who were concomitantly treated with heparin or low molecular weight heparin for thromboprophylaxis, increases in aPTT and PT(INR) of 5.5% and 3.0%, respectively, were observed in the hour following sugammadex 4 mg/kg administration. This clinical trial did not demonstrate an increased blood loss or anemia incidence with sugammadex compared with usual treatment. The rate of adjudicated bleeding events within 24 hours was 2.9% for sugammadex and 4.1% for usual care. The rate of post-operative anemia was 21% for sugammadex and 22% for usual care. The mean 24-hour drainage volume was 0.46 L for sugammadex and 0.48 L for usual care. The need for any post-operative transfusion was 37% for sugammadex and 39% for usual care.

In vitro experiments demonstrated additional aPTT and PT(INR) prolongations for sugammadex in combination with vitamin K antagonists, unfractionated heparin, low molecular weight heparinoids, rivaroxaban, and dabigatran up to ~25% and ~50% at C_{max} levels of sugammadex corresponding to 4 mg/kg and 16 mg/kg doses, respectively.

Since bleeding risk has been studied systematically with only heparin and low molecular weight heparin thromboprophylaxis and 4 mg/kg doses of sugammadex coagulation parameters should be carefully monitored in patients with known coagulopathies, being treated with therapeutic anticoagulation, receiving thromboprophylaxis drugs other than heparin and low molecular weight heparin, or receiving thromboprophylaxis drugs and who then receive a dose of 16 mg/kg sugammadex.

5.11 Renal Impairment

Sugammadex is not recommended for use in patients with severe renal impairment, including those requiring dialysis *[see Use in Specific Populations (8.6)]*. With regard to the recommended waiting time for re-administration in patients with mild or moderate renal impairment, *see Waiting Times for Re-Administration of Neuromuscular Blocking Agents for Intubation Following Reversal with Sugammadex [see Warnings and Precautions (5.5)]*.

5.12 Light Anesthesia

When neuromuscular blockade was reversed intentionally in the middle of anesthesia in clinical trials, e.g., when investigating urgent reversal, signs of light anesthesia were noted occasionally (movement, coughing, grimacing and suckling of the tracheal tube).

5.13 Reversal after Rocuronium or Vecuronium Administration in the ICU

Sugammadex has not been studied for reversal following rocuronium or vecuronium administration in the ICU.

5.14 Reversal of Neuromuscular Blocking Agents Other Than Rocuronium or Vecuronium

Do not use sugammadex to reverse blockade induced by nonsteroidal neuromuscular blocking agents such as succinylcholine or benzylisoquinolinium compounds.

Do not use sugammadex to reverse neuromuscular blockade induced by steroidal neuromuscular blocking agents other than rocuronium or vecuronium.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:
• Anaphylaxis and Hypersensitivity *[see Contraindications (4), Warnings and Precautions (5.1)]*
• Marked Bradycardia *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adult Patients
The data described below reflect 2914 subjects exposed to 2, 4, or 16 mg/kg sugammadex and 544 to placebo in pooled Phase 1-3 studies. The population was 18 to 92 years old, 47% male and 53% female, 34% ASA (American Society of Anesthesiologists) Class 1, 51% ASA Class 2, and 14% ASA Class 3, and 82% Caucasian. Most subjects received a single dose of sugammadex 2 mg/kg or 4 mg/kg.

Adverse reactions reported in ≥10% of patients at a 2, 4, or 16 mg/kg sugammadex dose with a rate higher than the placebo rate are: vomiting, pain, nausea, hypotension, and headache.

All adverse reactions occurring in ≥2% of subjects treated with sugammadex and more often than placebo for adult subjects who received anesthesia and/or neuromuscular blocking agent in pooled Phase 1 to 3 studies are presented in Table 2.

Table 2: Percent of Subject Exposures in Pooled Phase 1 to 3 Studies with Adverse Reactions Incidence ≥ 2%

Body System Preferred Term	Sugammadex 2 mg/kg (N=895) n (%)	Sugammadex 4 mg/kg (N=1921) n (%)	Sugammadex 16 mg/kg (N=98) n (%)	Placebo (N=544) n (%)
Injury, poisoning and procedural complications				
Incision site pain	58 (6)	106 (6)	4 (4)	6 (1)
Procedural complication	13 (1)	27 (1)	8 (8)	3 (1)
Airway complication of anesthesia	11 (1)	13 (1)	9 (9)	0
Anesthetic complication	8 (1)	14 (1)	9 (9)	1 (<1)
Wound hemorrhage	5 (1)	38 (2)	0	8 (1)
Recurrence of neuromuscular blockade	0	1 (<1)	2 (2)	0
Gastrointestinal disorders				
Nausea*	208 (23)	503 (26)	23 (23)	127 (23)
Vomiting*	98 (11)	236 (12)	15 (15)	57 (10)
Abdominal pain*	48 (5)	68 (4)	6 (6)	17 (3)
Flatulence	17 (2)	51 (3)	1 (1)	10 (2)
Dry mouth	9 (1)	5 (<1)	2 (2)	0
General disorders and administration site conditions				
Pain*	434 (48)	993 (52)	35 (36)	207 (38)
Pyrexia	77 (9)	109 (6)	5 (5)	17 (3)
Chills	30 (3)	61 (3)	7 (7)	27 (5)
Nervous system disorders				
Headache	61 (7)	99 (5)	10 (10)	42 (8)
Dizziness	44 (5)	67 (3)	6 (6)	13 (2)
Hypoesthesia	12 (1)	24 (1)	3 (3)	9 (2)
Respiratory, thoracic and mediastinal disorders				
Oropharyngeal pain	42 (5)	66 (3)	5 (5)	27 (5)
Cough	13 (1)	49 (3)	8 (8)	11 (2)
Musculoskeletal and connective tissue disorders				
Pain in extremity	13 (1)	35 (2)	6 (6)	15 (3)
Musculoskeletal pain	16 (2)	33 (2)	1 (1)	6 (1)
Myalgia	5 (1)	17 (1)	2 (2)	3 (1)
Psychiatric disorders				
Insomnia	20 (2)	103 (5)	5 (5)	22 (4)
Anxiety	14 (2)	19 (1)	3 (3)	1 (<1)
Restlessness	3 (<1)	17 (1)	2 (2)	2 (<1)
Depression	2 (<1)	5 (<1)	2 (2)	0
Investigations				
Red blood cell count decreased*	13 (1)	34 (2)	1 (1)	2 (<1)
Electrocardiogram QT interval abnormal*	13 (1)	7 (<1)	6 (6)	4 (1)
Blood creatine phosphokinase increased	9 (1)	14 (1)	2 (2)	1 (<1)
Vascular disorders				
Hypertension*	48 (5)	96 (5)	9 (9)	38 (7)
Hypotension*	33 (4)	102 (5)	13 (13)	20 (4)
Skin and subcutaneous tissue disorders				
Pruritus	17 (2)	50 (3)	2 (2)	9 (2)
Erythema	5 (1)	31 (2)	0	6 (1)
Metabolism and nutrition disorders				
Hypocalcemia	15 (2)	12 (1)	0	4 (1)
Cardiac disorders				
Tachycardia*	17 (2)	29 (2)	5 (5)	4 (1)
Bradycardia*	9 (1)	21 (1)	5 (5)	6 (1)
Surgical and medical procedures				
Hysterectomy	0	0	2 (2)	0

*Combinations of preferred terms are as follows:
Nausea includes preferred terms nausea and procedural nausea
Vomiting includes preferred terms vomiting and procedural vomiting
Abdominal pain includes preferred terms abdominal pain, abdominal pain upper, abdominal discomfort, abdominal pain lower, and epigastric discomfort
Pain includes preferred terms pain and procedural pain
Red blood cell count decreased includes preferred terms red blood cell count decreased, hemoglobin decreased, and hematocrit decreased
Electrocardiogram QT interval abnormal includes preferred terms electrocardiogram QT interval abnormal and electrocardiogram QT interval prolonged
Hypertension includes preferred terms hypertension, procedural hypertension, and blood pressure increased
Hypotension includes preferred terms hypotension, procedural hypotension, and blood pressure decreased
Tachycardia includes preferred terms tachycardia and heart rate increased
Bradycardia includes preferred terms bradycardia and heart rate decreased

Pediatric Patients
2 to <17 years of age
The safety of sugammadex has been assessed in a randomized, active-controlled study of pediatric patients 2 to <17 years of age, with 242 receiving treatment with sugammadex injection. Adverse events occurring in ≥5% of pediatric patients are presented in Table 3. The safety profile was generally consistent with that observed in adults.

Table 3: Pediatric Patients (2 to <17 years of age) with Adverse Events Incidence ≥5% in Done or More Treatment Groups Up to 7 Days Post-Treatment

	Sugammadex 2 mg/kg		Sugammadex 4 mg/kg	
	n	(%)	n	(%)
Subjects in population	51		191	
with one or more specific adverse events	40	(78)	143	(75)
with no specific adverse events	11	(22)	48	(25)
Cardiac disorders	**5**	**(10)**	**16**	**(8)**
Bradycardia*	5	(10)	13	(7)
Eye disorders	**3**	**(6)**	**1**	**(1)**
Gastrointestinal disorders	**8**	**(16)**	**35**	**(18)**
Nausea	1	(2)	12	(6)
Vomiting	4	(8)	20	(10)
Injury, poisoning and procedural complications	**34**	**(67)**	**121**	**(63)**
Incision site pain	3	(6)	6	(3)
Procedural nausea	4	(8)	9	(5)
Procedural pain	30	(59)	111	(58)
Procedural vomiting	3	(6)	5	(3)

*Combines preferred terms of bradycardia and sinus bradycardia
Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears in this table only if its incidence in one or more of the columns meets the incidence criterion in the table title, after rounding.

Anaphylaxis and Hypersensitivity
Hypersensitivity reactions, including anaphylaxis, have occurred in both premarketing clinical trials and in post-marketing spontaneous reports. In a dedicated hypersensitivity study in healthy volunteers, the frequency of anaphylaxis was 0.3% *[see Warnings and Precautions (5.1)]*. 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.

A randomized, 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%, 7% and 9% 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. The frequency of anaphylaxis for the 299 healthy volunteers treated with intravenous sugammadex was 0.3%. There was no evidence of increased frequency or severity of hypersensitivity with repeat dosing.

In a previous study of similar design, there were three adjudicated cases of anaphylaxis, all after sugammadex 16 mg/kg (incidence 1% in the 298 healthy volunteers treated with sugammadex).

Recurrence of Neuromuscular Blockade
In clinical studies with subjects treated with rocuronium or vecuronium, where sugammadex was administered using a dose labeled for the depth of neuromuscular blockade (N=2022), an incidence of <1% was observed for recurrence of neuromuscular blockade as based on neuromuscular monitoring or clinical evidence *[see Warnings and Precautions (5.8)]*.

Bronchospasm
In one dedicated clinical trial and in post-marketing data, in patients with a history of pulmonary complications *[see Use in Specific Populations (8.9)]*, bronchospasm was reported as a possibly related adverse event.

Additional pediatric use information is approved for Merck Sharp & Dohme LLC's BRIDION® (sugammadex) injection. However, due to Merck Sharp & Dohme LLC's marketing exclusivity rights, this drug product is not labeled with that information.

6.2 Post-Marketing Experience

The following adverse reactions have been identified during post-approval use of sugammadex. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac Disorders: Cases of marked bradycardia and bradycardia with cardiac arrest have been observed within minutes after administration of sugammadex *[see Warnings and Precautions (5.2)]*. Other cardiac rhythm abnormalities have included atrial fibrillation, atrioventricular block, cardiac/cardiorespiratory arrest, electrocardiographic [ECG] ST segment changes, supraventricular tachycardia/extrasystoles, tachycardia, ventricular fibrillation, and ventricular tachycardia. Anaphylaxis associated with ECG ST segment changes (elevation or depression) consistent with myocardial ischemia or coronary spasm has also been reported.

General Disorders and Administration Site Conditions: Cases of sugammadex not having the intended effect.

Immune System Disorders: Hypersensitivity events including anaphylactic shock, anaphylactic reaction, anaphylactoid reaction, and Type 1 hypersensitivity have been reported *[see Warnings and Precautions (5.1)]*.

Respiratory, Thoracic, and Mediastinal Disorders: Events of laryngospasm, dyspnea, wheezing, pulmonary edema, and respiratory arrest have been reported.

7 DRUG INTERACTIONS

7.1 Summary

The information reported in sections *7.2 – 7.4* is based on binding affinity between sugammadex and other drugs, preclinical experiments, clinical studies and simulations of a pharmacokinetic-pharmacodynamic (PK-PD) model. Based on these considerations, no clinically significant pharmacodynamic interactions with other drugs are expected, with the exception of toremifene and hormonal contraceptives.

7.2 Interactions Potentially Affecting the Efficacy of Sugammadex

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. The recovery to TOF ratio to 0.9 could therefore be delayed in patients who have received toremifene on the same day of surgery.

7.3 Interaction Potentially Affecting the Efficacy of Hormonal Contraceptives

In vitro binding studies indicate that sugammadex may bind to progestogen, thereby decreasing progestogen exposure. Therefore, the administration of a bolus dose of sugammadex is considered to be equivalent to missing dose(s) of oral contraceptives containing an estrogen or progestogen. If an oral contraceptive is taken on the same day that sugammadex is administered, the patient must use an additional, non-hormonal contraceptive method or back-up method of contraception (such as condoms and spermicides) for the next 7 days.

In the case of non-oral hormonal contraceptives, the patient must use an additional, non-hormonal contraceptive method or back-up method of contraception (such as condoms and spermicides) for the next 7 days.

7.4 Interference with Laboratory Tests

Sugammadex may interfere with the serum progesterone assay. Interference with this test was observed at sugammadex plasma concentrations of 100 mcg/mL, which may be observed for up to 30 minutes after a 16 mg/kg dose.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
There are no clinical trial data on sugammadex use in pregnant women to inform any drug-associated risks. The available data from the pharmacovigilance safety database and published literature on sugammadex injection use in pregnant women are insufficient to identify a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. In animal reproduction studies, there was no evidence of malformations following daily intravenous administration of sugammadex to rats and rabbits during organogenesis at exposures of up to 6 and 8 times, respectively, the maximum recommended human dose (MRHD) of 16 mg/kg. However, there was an increase in the incidence of incomplete ossification of the sternebra and reduced fetal body weights in the rabbit study at 8 times the MRHD, which is a dose level in which maternal toxicity was also observed. In a pre- and postnatal development study, sugammadex treatment resulted in an increase in early postnatal loss, which correlated with maternal behavior (increased incidence of pup cannibalism), at exposures equivalent to the MRHD and higher (*see Data*). The background risk of major birth defects and miscarriage for the indicated population are unknown. However, the background risk in the U.S. general population of major birth defects is 2 to 4% and of miscarriage is 15 to 20% of clinically recognized pregnancies.

Data
Animal Data
In an embryofetal development study in rats, pregnant animals received daily intravenous administration of sugammadex at 0, 20, 100, and 500 mg/kg (0.2, 1, and 6 times the MRHD of 16 mg/kg/day, respectively, based on AUC comparison) during organogenesis (Gestational Days 6 - 17). No treatment-related maternal and embryofetal changes were observed.

In another embryofetal development study, pregnant New Zealand white rabbits received daily intravenous administration of sugammadex at 0, 20, 65, 200 mg/kg (0.6, 2, and 8 times the MRHD, respectively, based on AUC comparison) during organogenesis (Gestational Days 6-18). Fetal body weight decreases (10 and 14%, respectively) were observed in the offspring at maternal doses of 65 mg/kg and 200 mg/kg. In addition, incomplete ossification of sternebra, and unossified 1st metatarsal were noted at a maternal dose of 200 mg/kg/day. Maternal toxicity was also observed at 200 mg/kg. Considering the observed effects of sugammadex on bone *[see Nonclinical Toxicology (13.2)]*, it is possible that these findings may be attributable to drug. There was no evidence of malformations at any dose.

In a prenatal and postnatal development study, pregnant rats were administered sugammadex intravenously at 0, 30, 120, and 500 mg/kg (0.3, 1, and 6 times the MRHD, respectively, based on AUC comparison) from Gestational Day (GD) 6 to Postnatal Day (PND) 21 (corresponding to the beginning of organogenesis through parturition and subsequent pup weaning). Postnatal loss during PND 1 to 4 was noted across control litters and treated litters from dams receiving sugammadex as a result of pup cannibalization by dams. Overall incidence of affected litters was 2, 1, 4, and 3 litters, respectively, at 0, 30, 120, or 500 mg/kg/day. The reason for the increased cannibalism is not known. An effect of sugammadex on steroidal hormones and/or pheromones cannot be ruled out. In addition, there were no drug-related effects on parturition in rats during evaluations for prenatal or postnatal development.

8.2 Lactation

Risk Summary
No data are available regarding the presence of sugammadex in human milk, the effects of sugammadex on the breast fed infant, or the effects of sugammadex on milk production. However, sugammadex is present in rat milk *(see Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for sugammadex and any potential adverse effects on the breastfed infant from sugammadex or from the underlying maternal condition.

Data
In a milk excretion study in rat dams following single intravenous dose of 20