PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

SUBRINEX™, 200 mg/2 mL (100 mg/mL) solution for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL contains 100 mg sugammadex (as sugammadex sodium).

Each vial of 2 mL contains sugammadex sodium equivalent to 200 mg sugammadex.

Excipient(s) with known effect:

Contains up to 9,7 mg/mL sodium (see section 4.4).

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).

Clear and colourless to slightly yellow-brown solution.

The pH is between 7 and 8.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SUBRINEX is indicated for the routine reversal of neuromuscular blockade induced by rocuronium or vecuronium.

SUBRINEX is also indicated for the immediate reversal of neuromuscular blockade at 3 minutes after administration of rocuronium.

For the paediatric population, SUBRINEX is only recommended for routine reversal of rocuronium-induced blockade in children and adolescents above 7 years of age.

4.2 Posology and method of administration

Posology

Sugammadex should only be administered 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). When certain medicines that may cause displacement interactions are administered parenterally within 7,5 hours of SUBRINEX, patients should be monitored for signs of recurrence of neuromuscular blockade.

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.

SUBRINEX can be used to reverse different levels of rocuronium or vecuronium induced neuromuscular blockade.

Adults

Routine reversal of neuromuscular blockade:

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

A dose of 2 mg/kg SUBRINEX is recommended if spontaneous recovery has reached the reappearance of T_2 (shallow blockade) following rocuronium or vecuronium induced blockade (see section 4.4).

Immediate reversal of rocuronium-induced blockade:

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

Special populations

Renal impairment:

For mild and moderate renal impairment (creatinine clearance ≥ 30 and < 80 mL/min): The dose recommendations are the same as for adults without renal impairment. The use of SUBRINEX 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 SUBRINEX in these patients.

Elderly patients:

After administration of SUBRINEX 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, the dose of sugammadex should be based on actual body weight. The same dose recommendations as for adults should be followed.

Hepatic impairment:

For mild to moderate hepatic impairment: As sugammadex is mainly excreted renally no dose adjustments of SUBRINEX are required.

Studies in patients with hepatic impairment have not been conducted. Caution should be exercised when considering the use of SUBRINEX in

patients with severe hepatic impairment, or when hepatic impairment is accompanied by coagulopathy (see section 4.4).

Paediatric population

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

Children and adolescents:

For reversal of rocuronium-induced blockade at reappearance of T_2 in children and adolescents (7 to 17 years) 2 mg/kg SUBRINEX is recommended.

Immediate reversal in children and adolescents has not been investigated and is therefore not recommended.

SUBRINEX 100 mg/mL may be diluted to 10 mg/mL to increase the accuracy of dosing in the paediatric population, 7 years and older.

Method of administration

SUBRINEX should be administered intravenously as a single bolus injection.

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

For instructions for preparation or reconstitution (see section 6.6).

4.3 Contraindications

SUBRINEX is contraindicated in patients with known hypersensitivity to sugammadex or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

SUBRINEX is not to be used to reverse depolarising neuromuscular blocking agents (NMBA).

Waiting times for re-administration with non-depolarising neuromuscular blocking agents (NMBA) after reversal with SUBRINEX:

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

When rocuronium, 1,2 mg/kg is administered within 30 minutes after reversal with SUBRINEX, 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.

Based on PK modelling the recommended waiting time in patients with mild or moderate renal impairment for re-use of 0,6 mg/kg rocuronium or

0,1 mg/kg vecuronium after routine reversal with sugammadex should be 24 hours. If a shorter waiting time is required, the rocuronium dose for a new neuromuscular blockade should be 1,2 mg/kg.

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

A waiting time of 24 hours is recommended.

If neuromuscular blockade is required before the recommended waiting time has passed, a **non-steroidal neuromuscular blocking agent** should be used. The onset of a depolarising neuromuscular blocking agent might be slower than expected because a substantial fraction of post-junctional nicotinic receptors may still be occupied by the neuromuscular blocking agent.

Following neuromuscular blockage, it is recommended to monitor the patient in the immediate post-operative period for untoward events including recurrence of neuromuscular blockade.

Medicine hypersensitivity reactions:

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

Renal impairment:

SUBRINEX is not recommended for use in patients with severe renal impairment, creatinine clearance <30 mL/min, including those requiring dialysis (see section 5.2).

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

Marked bradycardia:

Marked bradycardia has been observed within minutes after the administration of sugammadex for reversal of neuromuscular blockade. Cases of bradycardia with cardiac arrest have been reported (see section 4.8). Patients should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade. Treatment with anti-cholinergic medicines such as atropine should be administered if clinically significant bradycardia is observed.

Monitoring respiratory function during recovery:

Ventilatory support is mandatory for patients until adequate spontaneous respiration is restored following reversal of neuromuscular blockade. Even if recovery from neuromuscular blockade is complete, other medicines used in the peri- and 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.

Effect on haemostasis:

A pharmacodynamic interaction (aPTT and PT prolongation) was noted *in vitro* with vitamin K antagonists, unfractionated heparin, low molecular weight heparinoids, rivaroxaban and dabigatran.

Doses of 4 mg/kg and 16 mg/kg of sugammadex resulted in maximum mean prolongations of the activated partial thromboplastin time (aPTT) and prothrombin (PT) time international normalised ratio (INR). These limited mean aPTT and PT(INR) prolongations were of short duration (≤ 30 minutes).

Published clinical data showed no clinically relevant effect of sugammadex alone or in combination with anticoagulants on the incidence of peri- or post-operative bleeding complications.

Since there is no information on the use of sugammadex at higher doses than 4 mg/kg in patients with known coagulopathies, coagulation parameters should be carefully monitored according to routine clinical practice, including in patients using anticoagulants who receive a dose of 16 mg/kg sugammadex.

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.

The anaesthetist should take into consideration the patient's history of bleeding episodes and type of surgery scheduled. If sugammadex is administered to these patients, monitoring of haemostasis and coagulation parameters is recommended.

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.

Hepatic impairment:

Since sugammadex is not metabolised nor excreted by the liver there are no dedicated studies in patients with hepatic impairment. In case hepatic impairment is accompanied by coagulopathy, see the information on the **Effect on haemostasis** above.

Light anaesthesia:

When neuromuscular blockade was reversed intentionally in the middle of anaesthesia, 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.

Use in intensive care unit (ICU):

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

Use for reversal of neuromuscular blockers other than rocuronium or vecuronium:

SUBRINEX should not be used to reverse block induced by non-steroidal neuromuscular blockers such as succinylcholine or benzylisoquinolinium compounds.

SUBRINEX should not be used for reversal of neuromuscular blockade induced by steroidal neuromuscular blockers 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 SUBRINEX in this situation.

Recurrence of neuromuscular blockade:

Recurrence of neuromuscular blockade based on neuromuscular monitoring or clinical evidence has been reported in patients treated with rocuronium or vecuronium, where sugammadex was administered using a dose labelled for the depth of neuromuscular blockade. 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).

Sodium:

SUBRINEX 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 medicines and other forms of interaction

The information in this section is based on binding affinity between sugammadex and other medicines, available data on non-clinical experiments, data on clinical studies and simulations using a model considering the pharmacodynamic effect of neuromuscular blockers and the pharmacokinetic interaction between neuromuscular blockers and sugammadex.

Based on these data, clinically significant pharmacodynamic interaction with other medicines is not expected, with exception of toremifene, fusidic acid and hormonal contraceptives. For these medicines a clinically relevant capturing interaction could not be excluded.

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

Due to the administration of certain medicines 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 should be ventilated.

Administration of the medicine which caused displacement should be stopped in case of an infusion. In situations when potential displacement interactions can be anticipated, patients should be carefully monitored for signs of recurrence of neuromuscular blockade (approximately up to 15 minutes), after parenteral administration of another medicine occurring within a period of 7,5 hours after SUBRINEX administration.

SUBRINEX should be used cautiously when co-administered with:

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 of the train of four ratio, 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 to 3 days.

For re-administration of sugammadex see section 4.2.

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

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

Hormonal contraceptives:

The interaction between 4 mg/kg sugammadex and a progestogen was predicted to lead to a decrease in progestogen exposure 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 SUBRINEX is considered to be equivalent to one missed daily dose of oral contraceptive steroids (either combined or progestogen only). If SUBRINEX is administered at the same day as an

oral contraceptive is taken reference is made to missed dose advice in the patient information leaflet of the oral contraceptive.

In the case of non-oral hormonal contraceptives, the patient should use an additional non-hormonal contraceptive method for the next 7 days and refer to the advice in the patient information leaflet of the product.

Interactions due to the lasting effect of rocuronium or vecuronium:

When medicines 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 medicines 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:

SUBRINEX has been shown to interfere with the serum progesterone assay.

This interference was observed in plasma samples spiked with a concentration of SUBRINEX in the same range as obtained for C_{max} after a dose of 16 mg/kg.

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 considered for the paediatric population.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety in pregnant women has not been established.

Breastfeeding

Excretion of sugammadex in human milk has not been studied but can be expected based on the pre-clinical data. Animal studies have shown excretion of sugammadex in breast milk. Caution should be exercised when administering sugammadex to breastfeeding women.

Fertility

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

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

a. Summary of the safety profile

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

b. Tabulated summary of adverse reactions

Immune system disorders	
Less frequent:	Medicine hypersensitivity reactions (see section 4.4)
Frequency unknown:	Anaphylaxis, anaphylactic shock
Nervous system disorders	
Frequent:	Dysgeusia, headache
Frequency unknown:	Dizziness
Cardiac disorders	
Frequency unknown:	Marked bradycardia, bradycardia with cardiac arrest.
Respiratory, thoracic and mediastinal disorders	
Frequent:	Cough
Frequency unknown:	Bronchospasm
Gastro-intestinal disorders	
Frequency unknown:	Nausea, vomiting, abdominal pain

Skin and subcutaneous tissue disorders	
Frequency unknown:	Pruritus, urticaria
Injury, poisoning and procedural complications	
Frequent:	Airway complication of anaesthesia, anaesthetic complication (see ***Anaesthetic complication*** below), procedural hypotension, procedural complication (see ***Procedural complication*** below), prolonged neuromuscular blockade (with sub-optimal doses)

c. Description of selected adverse reactions

Hypersensitivity reactions:

Hypersensitivity reactions, including anaphylaxis, have occurred in some patients and volunteers; for post-marketing reports the frequency is unknown. There was no evidence of increased frequency of severity of hypersensitivity with repeat dosing of sugammadex.

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

Symptoms associated with these reactions can include flushing, urticaria, erythematous rash, (severe) hypotension, tachycardia, swelling of tongue,

swelling of pharynx, bronchospasm and pulmonary obstructive events. Severe hypersensitivity reactions can be fatal.

Airway complication of anaesthesia

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

Anaesthetic complication:

Anaesthetic complications, indicative of the restoration of neuromuscular function, include movement of a limb or the body or coughing during the anaesthetic procedure or during surgery, grimacing, or sucking on the endotracheal tube. See section 4.4 Light anaesthesia.

Procedural complication:

Procedural complication included coughing, tachycardia, bradycardia, movement, and increase in heartrate.

Recurrence of neuromuscular blockade:

Recurrence of neuromuscular blockade as measured with neuromuscular monitoring occurred less frequently. In cases where recurrence of neuromuscular blockade is observed, the patient should be ventilated (see section 4.4).

Marked bradycardia:

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

Additional information on special populations

Pulmonary patients:

Bronchospasm was reported as a possibly related adverse event in patients with a history of pulmonary complications.

Paediatric population:

Some data suggests that the safety profile of sugammadex (up to 4 mg/kg) in paediatric patients above 7 years old was similar to that in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "*6.04 Adverse Drug Reactions & Quality Problem Reporting Form*", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

SUBRINEX can be removed using haemodialysis with a high-flux filter, but not with a low flux filter. Reportedly, 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

Category and class: A32.16: Other

Mechanism of action

Sugammadex is a modified cyclodextrin, which is a selective relaxant binding agent (SRBA). It forms a complex with the neuromuscular blockers rocuronium and vecuronium and it reduces the amount of neuromuscular blocking agent available to bind to nicotinic receptors in the neuromuscular junction. This results in the reversal of neuromuscular blockade induced by rocuronium or vecuronium.

Pharmacodynamic effects

Sugammadex has reportedly been administered in doses ranging from 0,5 mg/kg to 16 mg/kg in dose-response studies of rocuronium-induced blockade (0,6; 0,9; 1,0 and 1,2 mg/kg rocuronium bromide with and without

maintenance doses) and vecuronium induced blockade (0,1 mg/kg vecuronium bromide with or without maintenance doses) at different time points/depths of blockade. In these studies, a clear dose-response relationship was observed.

5.2 Pharmacokinetic properties

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

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 rocuronium binds to plasma proteins or erythrocytes. Sugammadex exhibits linear kinetics in the dosage range of 1 mg/kg to 16 mg/kg when administered as an IV bolus dose.

Biotransformation:

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 (t½) of sugammadex is about 2 hours and the estimated plasma clearance is about 88 mL/min, with > 90 % of the dose excreted within 24 hours. Ninety six percent (96 %) of the dose was excreted in urine, of which at least 95 % could be attributed to unchanged sugammadex. Excretion via faeces or expired air was 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 published 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 another study comparing subjects with moderate or severe renal impairment to subjects with normal renal function, sugammadex clearance progressively decreased and t½ 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.

Predicted pharmacokinetic parameters of sugammadex by age group and renal function based on compartmental modelling are presented below:

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

*CV=coefficient of variation

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (to adjust pH)

Sodium hydroxide (to adjust pH)

Water for injection

6.2 Incompatibilities

SUBRINEX must not be mixed with other medicines except those mentioned in section 6.6.

Physical incompatibility has been reported with verapamil, ondansetron and ranitidine.

6.3 Shelf life

48 months

After first opening and dilution chemical and physical in-use stability has been demonstrated for 48 hours at 2 °C to 25 °C. From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store at or below 25 °C.

Do not freeze.

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

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

6.5 Nature and contents of container

2 mL of solution in 5 mL clear, colourless, type I glass vial closed with bromobutyl rubber stoppers with aluminium crimp-cap and a plastic flip-off seal.

Pack sizes: 1 or 10 vials of 2 mL.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

SUBRINEX 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 SUBRINEX and other medicines.

Use in the paediatric population:

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

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

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Abex Pharmaceutica (Pty) Ltd

Suite C, Rubenstein Ridge

617 Rubenstein Drive

Moreleta Park, 0181

8. REGISTRATION NUMBER

56/32.16/1040.039

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 18 June 2024

Date of latest renewal: *Not applicable.*

10. DATE OF REVISION OF THE TEXT

Not applicable.