SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cisatracurium 2mg/ml solution for injection/infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of cisatracurium besilate contains 2.68 mg corresponding to 2 mg as cisatracurium besilate base

One ampoule of 2.5 ml contains 5 mg of cisatracurium

One ampoule of 5 ml contains 10 mg of cisatracurium

One ampoule of 10 ml contains 20 mg of cisatracurium

3 PHARMACEUTICAL FORM

Solution for injection/infusion.

Colourless to pale yellow or greenish yellow solution. Practically free from visible particulate matter.

4 CLINICAL PARTICULARS

Cisatracurium is an intermediate-duration, non-depolarising neuromuscular blocking agent for intravenous administration.

4.1 Therapeutic indications

Cisatracurium is indicated for use during surgical and other procedures in adults and children aged 1 month and over. Cisatracurium is also indicated for the use in adults requiring intensive care. Cisatracurium can be used as an adjunct to general anaesthesia, or sedation in the Intensive Care Unit (ICU) to relax skeletal muscles, and to facilitate tracheal intubation and mechanical ventilation.

4.2 Posology and method of administration

Cisatracurium should only be administered by or under the supervision of anaesthetists or other clinicians who are familiar with the use and action of neuromuscular blocking agents. Facilities for tracheal intubation, and maintenance of pulmonary ventilation and adequate arterial oxygenation have to be available.

Please note that Cisatracurium should not be mixed in the same syringe or administered simultaneously through the same needle as propofol injectable emulsion or with alkaline solutions such as sodium thiopentone. (see section 6.2).

Cisatracurium contains no antimicrobial preservative and is intended for single patient use.

Monitoring advice

As with other neuromuscular blocking agents, monitoring of neuromuscular function is recommended during the use of Cisatracurium in order to individualise dosage requirements.

Use by intravenous bolus injection

Dosage in adults

Tracheal Intubation.

The recommended intubation dose of Cisatracurium for adults is 0.15 mg/kg (body weight). This dose produced good to excellent conditions for tracheal intubation 120 seconds after administration of Cisatracurium, following induction of anaesthesia with propofol.

Higher doses will shorten the time to onset of neuromuscular block.

The following table summarises mean pharmacodynamic data when Cisatracurium was administered at doses of 0.1 to 0.4 mg/kg (body weight) to healthy adult patients during opioid (thiopentone/fentanyl/midazolam) or propofol anaesthesia.

Cisatracurium Dose mg/kg (body weight)	**Anaesthetic Background**	**Time to 90% T1* Suppression (min)**	**Time to Maximum T1* Suppression (min)**	**Time to 25% Spontaneous T1*Recovery (min)**
0.1	Opioid	3.4	4.8	45
0.15	Propofol	2.6	3.5	55
0.2	Opioid	2.4	2.9	65
0.4	Opioid	1.5	1.9	91

* T1 Single twitch response as well as the first component of the Train-of-four response of the adductor pollicis muscle following supramaximal electrical stimulation of the ulnar nerve.

Enflurane or isoflurane anaesthesia may extend the clinically effective duration of an initial dose of Cisatracurium by as much as 15%.

Maintenance. Neuromuscular block can be extended with maintenance doses of Cisatracurium. A dose of 0.03 mg/kg (body weight) provides approximately 20 minutes of additional clinically effective neuromuscular block during opioid or propofol anaesthesia.

Consecutive maintenance doses do not result in progressive prolongation of effect.

Spontaneous Recovery. Once spontaneous recovery from neuromuscular block is underway, the rate is independent of the Cisatracurium dose administered. During opioid or propofol anaesthesia, the median times from 25 to 75% and from 5 to 95% recovery are approximately 13 and 30 minutes, respectively.

Reversal. Neuromuscular block following Cisatracurium administration is readily reversible with standard doses of anticholinesterase agents. The mean times from 25 to 75% recovery and to full clinical recovery (T4:T1 ratio ≥ 0.7) are approximately 4 and 9 minutes respectively, following administration of the reversal agent at an average of 10% T1 recovery.

Dosage in paediatric patients

Tracheal Intubation (paediatric patients aged 1 month to 12 years): As in adults, the recommended intubation dose of Cisatracurium is 0.15 mg/kg (body weight) administered rapidly over 5 to 10 seconds. This dose produces good to excellent conditions for tracheal intubation 120 seconds following injection of Cisatracurium. Pharmacodynamic data for this dose are presented in the tables below.

Cisatracurium has not been studied for intubation in ASA Class III-IV paediatric patients. There are limited data on the use of Cisatracurium in paediatric patients under 2 years of age undergoing prolonged or major surgery.

In paediatric patients aged 1 month to 12 years, Cisatracurium has a shorter clinically effective duration and a faster spontaneous recovery profile than those observed in adults under similar anaesthetic conditions. Small differences in the pharmacodynamic profile were observed between the age ranges 1 to 11 months and 1 to 12 years which are summarised in the tables below:

Paediatric Patients aged 1 to 11 months

Cisatracurium Dose mg/kg (body weight)	**Anaesthetic Background**	**Time to 90% Suppression (min)**	**Time to Maximum Suppression (min)**	**Time to 25% Spontaneous T1 Recovery (min)**
0.15	Halothane	1.4	2.0	52
0.15	Opioid	1.4	1.9	47

Paediatric Patients aged 1 to 12 years

Cisatracurium Dose	**Anaesthetic Background**	**Time to 90% Suppression (min)**	**Time to Maximum Suppression**	**Time to 25% Spontaneous T1 Recovery**

mg/kg (body weight)			(min)	(min)
0.15	Halothane	2.3	3.0	43
0.15	Opioid	2.6	3.6	38

When Cisatracurium is not required for intubation: A dose of less than 0.15 mg/kg can be used. Pharmacodynamic data for doses of 0.08 and 0.1 mg/kg for paediatric patients aged 2 to 12 years are presented in the table below:

Cisatracurium Dose mg/kg (body weight)	Anaesthetic Background	Time to 90% Suppression (min)	Time to Maximum Suppression (min)	Time to 25% Spontaneous T1 Recovery (min)
0.08	Halothane	1.7	2.5	31
0.1	Opioid	1.7	2.8	28

Administration of Cisatracurium following suxamethonium has not been studied in paediatric patients (see section 4.5).

Halothane may be expected to extend the clinically effective duration of a dose of Cisatracurium by up to 20%. No information is available on the use of Cisatracurium in children during anaesthesia with other halogenated fluorocarbon anaesthetic agents, but these agents may also be expected to extend the clinically effective duration of a dose of Cisatracurium.

Maintenance (paediatric patients aged 2-12 years). Neuromuscular block can be extended with maintenance doses of Cisatracurium. In paediatric patients aged 2 to 12 years, a dose of 0.02 mg/kg (body weight) provides approximately 9 minutes of additional clinically effective neuromuscular block during halothane anaesthesia.

Consecutive maintenance doses do not result in progressive prolongation of effect.

There are insufficient data to make a specific recommendation for maintenance dosing in paediatric patients under 2 years of age. However, very limited data from clinical studies in paediatric patients under 2 years of age suggest that a maintenance dose of 0.03 mg/kg may extend clinically effective neuromuscular block for a period of up to 25 minutes during opioid anaesthesia.

Spontaneous Recovery. Once recovery from neuromuscular block is underway, the rate is independent of the Cisatracurium dose administered. During opioid or halothane anaesthesia, the median times from 25 to 75% and from 5 to 95% recovery are approximately 11 and 28 minutes, respectively.

Reversal. Neuromuscular block following Cisatracurium administration is readily reversible with standard doses of anticholinesterase agents. The mean times from 25 to 75% recovery and to full clinical recovery (T4:T1 ratio $\geq$ 0.7) are approximately 2

and 5 minutes respectively, following administration of the reversal agent at an average of 13% T1 recovery.

Use by intravenous infusion

Dosage in adults and children aged 2 to 12 years

Maintenance of neuromuscular block may be achieved by infusion of Cisatracurium. An initial infusion rate of 3 μg/kg (body weight)/min (0.18 mg/kg/hr) is recommended to restore 89 to 99% T1 suppression following evidence of spontaneous recovery. After an initial period of stabilisation of neuromuscular block, a rate of 1 to 2 μg/kg (body weight)/min (0.06 to 0.12 mg/kg/hr) should be adequate to maintain block in this range in most patients.

Reduction of the infusion rate by up to 40% may be required when Cisatracurium is administered during isoflurane or enflurane anaesthesia. (see section 4.5).

The infusion rate will depend upon the concentration of cisatracurium in the infusion solution, the desired degree of neuromuscular block, and the patient's weight. The following table provides guidelines for delivery of undiluted Cisatracurium.

Infusion Delivery Rate of Cisatracurium injection 2 mg/ml

Patient (body weight) (Kg)	**Dose (μg/kg/min)**				**Infusion Rate**
	1.0	**1.5**	**2.0**	**3.0**	
20	0.6	0.9	1.2	1.8	mL/hr
70	2.1	3.2	4.2	6.3	mL/hr
100	3.0	4.5	6.0	9.0	mL/hr

Steady rate continuous infusion of Cisatracurium is not associated with a progressive increase or decrease in neuromuscular blocking effect.

Following discontinuation of infusion of Cisatracurium, spontaneous recovery from neuromuscular block proceeds at a rate comparable to that following administration of a single bolus.

Dosage in neonates (aged less than 1 month)
The use of Cisatracurium in neonates is not recommended as it has not been studied in this patient population.

Dosage in elderly patients
No dosing alterations are required in elderly patients. In these patients Cisatracurium has a similar pharmacodynamics profile to that observed in young adult patients but, as with other neuromuscular blocking agents, it may have a slightly slower onset.

Dosage in patients with renal impairment
No dosing alterations are required in patients with renal failure.

In these patients Cisatracurium has a similar pharmacodynamic profile to that observed in patients with normal renal function but it may have a slightly slower onset.

Dosage in patients with hepatic impairment
No dosing alterations are required in patients with end-stage liver disease. In these patients

Cisatracurium has a similar pharmacodynamic profile to that observed in patients with normal hepatic function but it may have a slightly faster onset.

Dosage in patients with cardiovascular disease
When administered by rapid bolus injection (over 5 to 10 seconds) to adult patients with serious cardiovascular disease (New York Heart Association Class I-III) undergoing coronary artery bypass graft (CABG) surgery, Cisatracurium has not been associated with clinically significant cardiovascular effects at any dose studied (up to and including 0.4 mg/kg (8x ED_{95}). However, there are limited data for doses above 0.3 mg/kg in this patient population).

Cisatracurium has not been studied in children undergoing cardiac surgery.

Dosage in Intensive Care Unit (ICU) patients
Cisatracurium may be administered by bolus dose and/or infusion to adult patients in the ICU.

An initial infusion rate of Cisatracurium of 3 μg/kg (body weight)/min (0.18 mg/kg/hr) is recommended for adult ICU patients. There may be wide interpatient variation in dosage requirements and these may increase or decrease with time. In clinical studies the average infusion rate was 3 μg/kg/min [range 0.5 to 10.2 μg/kg (body weight)/min (0.03 to 0.6 mg/kg/hr)]

The median time to full spontaneous recovery following long-term (up to 6 days) infusion of Cisatracurium in ICU patients was approximately 50 minutes.

The recovery profile after infusions of Cisatracurium to ICU patients is independent of duration of infusion.

4.3 Contraindications

Cisatracurium is contra-indicated in patients known to be hypersensitive to cisatracurium, atracurium, or benzenesulfonic acid.

4.4 Special warnings and precautions for use

Product specific topics

Cisatracurium paralyses the respiratory muscles as well as other skeletal muscles but has no known effect on consciousness or pain threshold. Cisatracurium should be only administered by or under the supervision of anaesthetists or other clinicians who

are familiar with the use and action of neuromuscular blocking agents. Facilities for tracheal intubation, and maintenance of pulmonary ventilation and adequate arterial oxygenation have to be available.

Caution should be exercised when administering Cisatracurium to patients who have shown hypersensitivity to other neuromuscular blocking agents since a high rate of cross-sensitivity (greater than 50%) between neuromuscular blocking agents has been reported (see section 4.3).

Cisatracurium does not have significant vagolytic or ganglion- blocking properties. Consequently, Cisatracurium has no clinically significant effect on heart rate and will not counteract the bradycardia produced by many anaesthetic agents or by vagal stimulation during surgery.

Patients with myasthenia gravis and other forms of neuromuscular disease have shown greatly increased sensitivity to non-depolarising blocking agents. An initial dose of not more than 0.02 mg/kg Cisatracurium is recommended in these patients.

Severe acid-base and/or serum electrolyte abnormalities may increase or decrease the sensitivity of patients to neuromuscular blocking agents.

There is no information on the use of Cisatracurium in neonates aged less than one month since it has not been studied in this patient population.

Cisatracurium has not been studied in patients with a history of malignant hyperthermia. Studies in malignant hyperthermia- susceptible pigs indicated that cisatracurium does not trigger this syndrome.

There have been no studies of cisatracurium in patients undergoing surgery with induced hypothermia (25 to 28°C).

As with other neuromuscular blocking agents the rate of infusion required to maintain adequate surgical relaxation under these conditions may be expected to be significantly reduced.

Cisatracurium has not been studied in patients with burns; however, as with other non-depolarising neuromuscular blocking agents, the possibility of increased dosing requirements and shortened duration of action must be considered if Cisatracurium injection is administered to these patients.

Cisatracurium is hypotonic and must not be applied into the infusion line of a blood transfusion.

Intensive Care Unit (ICU) Patients:

When administered to laboratory animals in high doses, laudanosine, a metabolite of cisatracurium and atracurium, has been associated with transient hypotension and in some species, cerebral excitatory effects. In the most sensitive animal species, these effects occurred at laudanosine plasma concentrations similar to those that have been observed in some ICU patients following prolonged infusion of atracurium.

Consistent with the decreased infusion rate requirements of cisatracurium, plasma laudanosine concentrations are approximately one third those following atracurium infusion.

There have been rare reports of seizures in ICU patients who have received atracurium and other agents. These patients usually had one or more medical conditions predisposing to seizures (eg. cranial trauma, hypoxic encephalopathy, cerebral oedema, viral encephalitis, uraemia). A causal relationship to laudanosine has not been established.

4.5 Interaction with other medicinal products and other forms of interaction

Many drugs have been shown to influence the magnitude and/or duration of action of non-depolarising neuromuscular blocking agents, including the following:

Increased Effect:

By anaesthetic agents such as enflurane, isoflurane, halothane (see section 4.2) and ketamine, by other nondepolarising neuromuscular blocking agents or by other drugs such as antibiotics (including the aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin and clindamycin), anti- arrhythmic drugs (including propranolol, calcium channel blockers, lignocaine, procainamide and quinidine), diuretics, (including frusemide and possibly thiazides, mannitol and acetazolamide), magnesium and lithium salts and ganglion blocking drugs (trimetaphan, hexamethonium).

Rarely, certain drugs may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome; increased sensitivity to non-depolarising neuromuscular blocking agents might result. Such drugs include various antibiotics, β-blockers (propranolol, oxprenolol), anti-arrhythmic drugs (procainamide, quinidine), anti-rheumatic drugs (chloroquine, D penicillamine), trimetaphan, chlorpromazine, steroids, phenytoin and lithium.

Administration of suxamethonium to prolong the effects of non- depolarising neuromuscular blocking agents may result in a prolonged and complex block which can be difficult to reverse with anticholinesterases.

Decreased effect:

A decreased effect is seen after prior chronic administration of phenytoin or carbamazepine.

Treatment with anticholinesterases, commonly used in the treatment of Alzheimer's disease e.g. donepezil, may shorten the duration and diminish the magnitude of neuromuscular blockade with cisatracurium.

No effect:

Prior administration of suxamethonium has no effect on the duration of neuromuscular block following bolus doses of Cisatracurium or on infusion rate requirements.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of Cisatracurium in pregnant women. Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition and postnatal development (see section 5.3). The potential risk for humans is unknown.

Cisatracurium should not be used during pregnancy.

Breast-feeding

It is not known whether cisatracurium or its metabolites are excreted in human milk.

A risk to the breastfed infant cannot be excluded. However, due to the short half-life, an influence on the breastfed infant is not to be expected if the mother restarts breast-feeding after the effects of the substance have worn off. As a precaution breast-feeding should be discontinued during treatment at least for five elimination half-lives of cisatracurium, i.e. for about 3 hours after the last dose or the end of infusion of cisatracurium.

Fertility

Fertility studies have not been performed.

4.7 Effects on ability to drive and use machines

This precaution is not relevant to the use of Cisatracurium. Cisatracurium will always be used in combination with a general anaesthetic and therefore the usual precautions relating to performance of tasks following general anaesthesia apply

4.8 Undesirable effects

Data from pooled internal clinical trials were used to determine the frequency of very common to uncommon adverse reactions.

The following convention has been used for the classification of frequency:- very common ≥ 1/10, common ≥ 1/100 and <1/10, uncommon ≥ 1/1000 and <1/100, rare ≥ 1/10,000 and <1/1000, very rare < 1/10,000.

Clinical Trial Data

Cardiac disorders

Common: Bradycardia

Vascular disorders

Common: Hypotension

Uncommon: Cutaneous flushing

Respiratory, thoracic and mediastinal disorders

Uncommon: Bronchospasm

Skin and subcutaneous tissue disorders

Uncommon: Rash

Postmarketing Data

Immune system disorders

Very rare: Anaphylactic reaction, anaphylactic shock

Anaphylactic reactions of varying degrees of severity have been observed after the administration of neuromuscular blocking agents, including anaphylactic shock. Very rarely, severe anaphylactic reactions have been reported in patients receiving Cisatracurium in conjunction with one or more anaesthetic agents.

Musculoskeletal and connective tissue disorders

Very rare: Myopathy, muscle weakness

There have been some reports of muscle/weakness and/or myopathy following prolonged use of muscle relaxants in severely ill patients in the ICU. Most patients were receiving concomitant corticosteroids. These events have been reported infrequently in association with Cisatracurium and a causal relationship has not been established.

Reporting of suspected adverse reactions

If you get any side effects, talk to your doctor, this includes any possible side effects not listed in this leaflet you can also report side effects directly via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

4.9 Overdose

Symptoms and signs

Prolonged muscle paralysis and its consequences are expected to be the main signs of overdosage with Cisatracurium.

Management

It is essential to maintain pulmonary ventilation and arterial oxygenation until adequate spontaneous respiration returns. Full sedation will be required since consciousness is not impaired by Cisatracurium. Recovery may be accelerated by the administration of anti- cholinesterase agents once evidence of spontaneous recovery is present.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Cisatracurium is a neuromuscular blocking agent, ATC code: M03A C11.

Cisatracurium is an intermediate-duration, non-depolarising benzylisoquinolinium skeletal muscle relaxant.

Pharmacodynamic effects

Clinical studies in man indicated that Cisatracurium is not associated with dose dependent histamine release even at doses up to and including 8 x ED95.

Cisatracurium binds to cholinergic receptors on the motor end-plate to antagonise the action of acetylcholine, resulting in a competitive block of neuromuscular transmission. This action is readily reversed by anticholinesterase agents such as neostigmine or edrophonium.

The ED95 (dose required to produce 95% depression of the twitch response of the adductor pollicis muscle to stimulation of the ulnar nerve) of cisatracurium is estimated to be 0.05 mg/kg bodyweight during opioid anaesthesia (thiopentone/fentanyl/midazolam).

The ED95 of cisatracurium in children during halothane anaesthesia is 0.04 mg/kg.

5.2 Pharmacokinetic properties

Biotransformation/Elimination

Cisatracurium undergoes degradation in the body at physiological pH and temperature by Hofmann elimination (a chemical process) to form laudanosine and the monoquaternary acrylate metabolite. The monoquaternary acrylate undergoes hydrolysis by non-specific plasma esterases to form the monoquaternary alcohol metabolite. Elimination of cisatracurium is largely organ independent but the liver and kidneys are primary pathways for the clearance of its metabolites.

These metabolites do not possess neuromuscular blocking activity.

Pharmacokinetics in adult patients

Non-compartmental pharmacokinetics of cisatracurium are independent of dose in the range studied (0.1 to 0.2 mg/kg, i.e. 2 to 4 x ED95).

Population pharmacokinetic modelling confirms and extends these findings up to 0.4 mg/kg (8 x ED95).

Pharmacokinetic parameters after doses of 0.1 and 0.2 mg/kg Cisatracurium administered to healthy adult surgical patients are summarised in the table below:

Parameter	**Range of Mean Values**
Clearance	4.7 to 5.7 mL/min/kg
Volume of distribution at steady state	121 to 161 mL/kg
Elimination half-life	22 to 29 min

Pharmacokinetics in elderly patients

There are no clinically important differences in the pharmacokinetics of cisatracurium in elderly and young adult patients. The recovery profile is also unchanged.

Pharmacokinetics in patients with renal/hepatic impairment

There are no clinically important differences in the pharmacokinetics of cisatracurium in patients with end-stage renal failure or end stage liver disease and in healthy adult patients. Their recovery profiles are also unchanged.

Pharmacokinetics during infusions

The pharmacokinetics of cisatracurium after infusions of Cisatracurium are similar to those after single bolus injection. The recovery profile after infusion of Cisatracurium is independent of duration of infusion and is similar to that after single bolus injection.

Pharmacokinetics in Intensive Care Unit (ICU) patients

The pharmacokinetics of cisatracurium in ICU patients receiving prolonged infusions are similar to those in healthy surgical adults receiving infusions or single bolus injections. The recovery profile after infusions of Cisatracurium in ICU patients is independent of duration of infusion.

Concentrations of metabolites are higher in ICU patients with abnormal renal and/or hepatic function (see section 4.4). These metabolites do not contribute to neuromuscular block.

5.3 Preclinical safety data

Acute toxicity

Meaningful acute studies with cisatracurium could not be performed.

For symptoms of toxicity see “Overdosage”

Subacute Toxicity:

Studies with repeated administration for three weeks in dogs and monkeys showed no compound specific toxic signs.

Mutagenicity

Cisatracurium was not mutagenic in an in vitro microbial mutagenicity test at concentrations up to 5000μg/plate.

In an in vivo cytogenetic study in rats, no significant chromosomal abnormalities were seen at s.c doses up to 4 mg/kg.

Cisatracurium was mutagenic in an in vitro mouse lymphoma cell mutagenicity assay, at concentrations of 40μg/ml and higher.

A single positive mutagenic response for a drug used infrequently and/or briefly is of questionable clinical relevance.

Carcinogenicity

Carcinogenicity studies have not been performed.

Reproductive toxicology

Fertility studies have not been performed. Reproductive studies in rats have not revealed any adverse effects of cisatracurium on foetal development.

Local tolerance

The result of an intra-arterial study in rabbits showed that Cisatracurium injection is well tolerated and no drug related changes were seen.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzene sulfonic acid solution 32% w/v, water for injections.

6.2 Incompatibilities

Degradation of cisatracurium besilate has been demonstrated to occur more rapidly in lactated Ringer's Injection and 5% Dextrose and lactated Ringer's Injection than in the infusion fluids listed under Section 6.6.

Therefore it is recommended that lactated Ringer's Injection and 5% Dextrose and lactated Ringer's Injection are not used as the diluent in preparing solutions of Cisatracurium for infusion.

Since Cisatracurium is stable only in acidic solutions it should not be mixed in the same syringe or administered simultaneously through the same needle with alkaline solutions, e.g., sodium thiopentone. It is not compatible with ketorolac trometamol or propofol injectable emulsion.

6.3 Shelf life

Shelf-life before dilution: 18 months

From a microbiological point of view, the product should be used immediately. If not used immediately, according chemical and physical in-use stability has been demonstrated to be up to 24 hours at 2 to 8°C and 25°C 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 to 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions (see section 6.6).

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C). Do not freeze.

Store in the original package 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

Cisatracurium 2 mg/ml solution for injection/infusion

2.5ml in ampoule (glass): box of 5 and 10

5ml in ampoule (glass): box of 5 and 10

10ml in ampoule (glass): box of 5 and 10

Type I, clear, neutral glass ampoules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

This product is for single use only. Use only clear and almost colourless up to slightly yellow/greenish yellow coloured solutions. The product should be visually inspected before use, and if the visual appearance has changed or if the container is damaged, the product must be discarded.

Diluted Cisatracurium is physically and chemically stable to be up to 24 hours at 2 - 8°C and 25°C at concentrations between 0.1 and 2 mg/mL in the following infusion fluids, in either polyvinyl chloride or polypropylene containers.

Sodium Chloride (0.9% w/v) Intravenous Infusion.

Glucose (5% w/v) Intravenous Infusion.

Sodium Chloride (0.18% w/v) and Glucose (0.45% w/v) Intravenous Infusion.

Sodium Chloride (0.45% w/v) and Glucose (5% w/v) Intravenous Infusion.

However, since the product contains no antimicrobial preservative, dilution should be carried out immediately prior to use, or failing this be stored as directed under section 6.3.

Cisatracurium has been shown to be compatible with the following commonly used peri-operative drugs, when mixed in conditions simulating administration into a running intravenous infusion via a Y-site injection port: alfentanil hydrochloride, droperidol, fentanyl citrate, midazolam, hydrochloride and sufentanil citrate. Where other drugs are administered through the same indwelling needle or cannula as Cisatracurium, it is recommended that each drug be flushed through with an adequate volume of a suitable intravenous fluid, e.g., Sodium Chloride Intravenous Infusion (0.9% w/v).

As with other drugs administered intravenously, when a small vein is selected as the injection site, Cisatracurium should be flushed through the vein with a suitable intravenous fluid, e.g., sodium chloride intravenous infusion (0.9% w/v).

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

7 MARKETING AUTHORISATION HOLDER

Hikma Farmacêutica (Portugal), S.A.

Estrada do Rio da Mó, 8, 8A e 8B - Fervença

2705-906 Terrugem SNT

Portugal

Tel.:+ 351 219 608 410

portugalgeral@hikma.com

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