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SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

CISTRAX 5 mg/2,5 ml (Solution for injection or infusion)

CISTRAX 10 mg/5 ml (Solution for injection or infusion)

CISTRAX 150 mg/30 ml (Solution for injection or infusion)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CISTRAX 5 mg/2,5 ml: Each 2,5 ml vial contains cisatracurium besylate equivalent to 2 mg/ml cisatracurium.

CISTRAX 10 mg/5 ml: Each 5 ml vial contains cisatracurium besylate equivalent to 2 mg/ml cisatracurium.

CISTRAX 150 mg/30 ml: Each 30 ml vial contains cisatracurium besylate equivalent to 5 mg/ml cisatracurium.

Contains no preservative.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection or infusion.

A clear colourless to slightly yellow or greenish yellow solution, free from visible particles.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

CISTRAX is used during surgical procedures to relax skeletal muscles and to facilitate controlled ventilation.

CISTRAX is suitable for endotracheal intubation especially where subsequent muscle relaxation is required.

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4.2 POSOLOGY AND METHOD OF ADMINISTRATION

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

Administration by intravenous bolus injection:

Dosage in adults:

Tracheal intubation:

The recommended intubation dose of CISTRAX for adults is 0,15 mg/kg. This dose produces good to excellent conditions for tracheal intubation 120 seconds after the injection. Higher doses will shorten the time to onset of the neuromuscular block.

CISTRAX administered at doses of 0,1 to 0,4 mg/kg to healthy adult patients during opioid (thiopentone/fentanyl/midazolam) or propofol anaesthesia, is summarised in the following table according to its mean pharmacodynamic data:

Initial CISTRAX dose (mg/kg)	Anaesthetic background	Time to 90 % T_1[a] suppression (min)	Time to maximum T_1[a] suppression (min)	Time to 25 % spontaneous T_1[a] 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

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[a] 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.

Maintenance:

The neuromuscular block can be extended with maintenance doses of CISTRAX. A dose of 0,03 mg/kg 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 CISTRAX dose. During opioid or propofol anaesthesia, the ~~mean~~ median times, from 25 % to 75 % and from 5 % to 95 % recovery, are approximately 13 and 30 minutes respectively.

Reversal:

The neuromuscular block following CISTRAX administration is reversible with standard doses of anticholinesterase medicines. Following administration of the reversal medicine at an average of 10 % T1 recovery, 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.

Dosage in paediatric patients aged 1 month to 12 years:

Tracheal intubation:

The recommended intubation dose of CISTRAX is 0,15 mg/kg administered rapidly over 5 to 10 seconds. This dose produces good to excellent conditions for tracheal intubation 120 seconds following the injection of CISTRAX. If a shorter clinical duration is required, pharmacodynamic data suggest that a dose of 0,1 mg/kg may produce similar intubation conditions at 120 to 150 seconds.

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In paediatric patients aged 1 month to 12 years of age, CISTRAX has a shorter clinically effective duration and a faster spontaneous recovery profile than those observed in adults under similar anaesthetic conditions. Pharmacodynamic data for the recommended CISTRAX dose are presented in the tables below and small differences, which are summarised below, were observed between the age ranges 1 to 11 months and 1 to 12 years.

Paediatric patients aged 1 to 11 months

Initial CISTRAX dose (mg/kg)	Anaesthetic background	Time to 90 % suppression (min)	Time to maximum suppression (min)	Time to 25 % spontaneous T_1 recovery (min)
0,15	Halothane	1,4	2,0	52
0,15	Opioid	1,4	2,0	47

Paediatric patients aged 1 to 12 years

Initial CISTRAX dose (mg/kg)	Anaesthetic background	Time to 90 % suppression (min)	Time to maximum suppression (min)	Time to 25 % spontaneous T_1 recovery (min)
0,08	Halothane	1,7	2,5	31
0,1	Opioid	1,7	2,8	28
0,15	Halothane	2,3	3,0	43
0,15	Opioid	2,6	3,6	38

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The clinically effective duration of a CISTRAX dose may be expected to extend up to 20 % with halothane. No information is available on the use of CISTRAX in children during isoflurane anaesthesia, but these medicines may also be expected to extend the clinically effective duration of a CISTRAX dose by up to 20 %.

Maintenance

The neuromuscular block can be extended with maintenance doses of CISTRAX.

During halothane anaesthesia, a dose of 0,02 mg/kg provides approximately 9 minutes of additional clinically effective neuromuscular block. Consecutive maintenance doses do not result in progressive prolongation of effect.

Spontaneous recovery:

Once recovery from neuromuscular block is underway, the rate is independent of the CISTRAX 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:

The neuromuscular block following CISTRAX administration is reversible with standard doses of anticholinesterase medicines. Following the administration of the reversal medicine at an average of 13 % T_1 recovery, the mean times from 25 % to 75 % recovery and to full clinical recovery (T4:T1 ratio ≥0,7), are approximately 2 and 5 minutes respectively.

Administration by intravenous infusion:

Dosage in adults and children aged 2 to 12 years:

The maintenance of a neuromuscular block may be achieved by the infusion of CISTRAX. An initial infusion rate of 3 µg/kg/min (0,18 mg/kg/h) is recommended to restore 89 % to 99 % T_1 suppression following evidence of spontaneous recovery. A rate of 1 to 2 µg/kg/min (0,06 to 0,12 mg/kg/h) should be adequate to maintain the

neuromuscular block in this range in most patients after an initial period of stabilisation of the neuromuscular block in this range in most patients.

During isoflurane or enflurane anaesthesia, a reduction of the infusion rate by up to 40 % may be required when CISTRAX is administered (see section 4.5). The infusion rate will depend upon the concentration of cisatracurium in the infusion solution, the desired degree of the neuromuscular block and the weight of the patient.

The following table provides guidelines for delivery of undiluted CISTRAX:

Infusion delivery rate of CISTRAX 2 mg/ml:

Patient weight	Dose (µg/kg/min)				Infusion rate
	1,0	1,5	2,0	3,0	
20	0,6	0,9	1,2	1,8	ml/h
70	2,1	3,2	4,2	6,3	ml/h
100	3,0	4,5	6,0	9,0	ml/h

A progressive increase or decrease in the neuromuscular blocking effect is not associated with a steady rate continuous infusion of CISTRAX.

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

Dosage in neonates aged less than 1 month:

No dosage recommendation for neonates can be made until further information is available (see section 4.3).

Special populations

Dosage in elderly patients:

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In elderly patients, CISTRAX has a similar pharmacodynamic profile to that observed in young adult patients, but it may have a slightly slower onset. No dose alterations are required in elderly patients.

Dosage in patients with renal impairment:

In patients with renal impairment, CISTRAX has a similar pharmacodynamic profile to that observed in patients with normal renal function, but it may have a slightly slower onset. No dose alterations are required in patients with renal impairment.

Dosage in patients with hepatic impairment:

In patients with hepatic impairment, CISTRAX has a similar pharmacodynamic profile to that observed in patients with normal hepatic function, but it may have a slightly faster onset. No dosing alterations are required in patients with end-stage liver disease.

Dosage in patients with cardiovascular disease

CISTRAX has been used to provide neuromuscular block in patients undergoing cardiac surgery. CISTRAX has not been associated with clinically significant cardiovascular effects in any dose studied [up to and including 0,4 mg/kg (8x ED95)], when administered by rapid bolus injection (over 5 to 10 seconds) to patients with serious cardiovascular disease.

Dosage in intensive care unit (ICU) patients:

CISTRAX may be administered by bolus dose and/or infusion to adult patients in the ICU. An initial infusion rate of 3 µg/kg/min (0,18 mg/kg/h) CISTRAX is recommended for adult ICU patients. Dosage requirements may vary widely between patients and these variations 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/min (0,03 to 0,6 mg/kg/h)]. The mean time to full spontaneous recovery following long-term infusion (up to 6 days) of CISTRAX in ICU patients was approximately 50 minutes.

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Infusion delivery rate of CISTRAX 5 mg/ml

Patient weight	Dose (µg/kg/min)				Infusion rate
	1,0	1,5	2,0	3,0	
70	0,8	1,2	1,7	2,5	ml/h
100	1,2	1,8	2,4	3,6	ml/h

The recovery profile after CISTRAX infusions to ICU patients, is independent of the duration of infusion.

Dosage in patients undergoing hypothermic cardiac surgery:

The rate of infusion required to maintain adequate surgical relaxation under these conditions may be expected to be significantly reduced.

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

Method of administration

CISTRAX is used by intravenous bolus injection and intravenous infusion.

For single use only.

For further instructions on dilution, refer to section 6.6.

4.3 CONTRA-INDICATIONS

- CISTRAX is contra-indicated in patients with a known hypersensitivity to cisatracurium, atracurium, benzene sulphonic acid or to any of the ingredients of CISTRAX (see section 6.1).
- Pregnancy and lactation, as the use and safety of CISTRAX has not been established in women who are pregnant and breastfeeding (see section 4.6).

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- CISTRAX has not been studied in neonates, and is therefore contrainidicated.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

CISTRAX paralyses the respiratory muscles and other skeletal muscles but has no effect on consciousness or pain threshold.
CISTRAX should only be administered by or under the supervision of an anaesthetist or other clinicians who are familiar with the use and action of neuromuscular blocking medicines. Facilities for tracheal intubation, maintenance of pulmonary ventilation and adequate arterial oxygenation must be available. Monitoring of neuromuscular function is recommended during the use of CISTRAX in order to individualise dosage requirements.

- CISTRAX must not be administered into the infusion line of a blood transfusion, as it is hypotonic.
- Patients who have received CISTRAX should have their respiration assisted or controlled until CISTRAX has been inactivated or antagonised.
- Great caution should be exercised when administering CISTRAX to patients with a history of allergic hypersensitivity to any other neuromuscular blocking medicines, since high rates of cross-reactivity (greater than 50 %) between neuromuscular blocking medicines have been reported (see section 4.3).
- CISTRAX does not have significant vagolytic or ganglion-blocking properties at recommended doses and does not induce histamine release. CISTRAX is therefore associated with greater cardiovascular stability. CISTRAX has no clinically significant effect on the heart rate and will not counteract the bradycardia produced by many anaesthetic medicines or by vagal stimulation during surgery.
- The response to CISTRAX is often unpredictable in patients with neuromuscular disorders and great care should be taken in these patients. Patients with myasthenia gravis and other forms of neuromuscular

disease have shown increased sensitivity to non-depolarising blocking medicines. CISTRAX is recommended at an initial dose of not more than 0,02 mg/kg in these patients.

- Persistent muscle weakness and/or myopathy have been reported following prolonged use of CISTRAX in ICU patients. Most reports were associated with concomitant corticosteroid administration.
- Severe acid-base and/or serum electrolyte abnormalities may increase or decrease the sensitivity of patients to CISTRAX.
- A reduction in body temperature may necessitate a reduction in the CISTRAX dose since cooling reduces the rate of inactivation of CISTRAX.
- There have been no studies of cisatracurium in patients undergoing surgery with induced hypothermia (25 to 28 °C). The rate of infusion required to maintain adequate surgical relaxation under these conditions may be expected to be significantly reduced.
- CISTRAX 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.
- CISTRAX has not been studied in patients with burn wounds. Resistance to the effects of CISTRAX may occur in patients with burn wounds, the possibility of increased dosing requirements and shortened duration of action must be considered if CISTRAX is administered to these patients

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 of those following atracurium infusion.

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

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

CISTRAX may influence neuromuscular transmission and interfere with the action of both competitive and depolarising neuromuscular blockers, resulting in the potentiation or antagonism of a neuromuscular block. In general adverse interactions are potentially more serious in patients with impaired neuromuscular function.

Increased effect by:

- *Anaesthetics:* Medicines such as halogenated anaesthetics (enflurane, isoflurane, halothane) and ketamine can increase the potentiation effect of CISTRAX. Neuromuscular blockers are potentiated in a dose-dependent manner by inhalation anaesthetics and the dose of CISTRAX may need to be reduced depending on the anaesthetic used.
- Other non-depolarising neuromuscular blocking medicines.
- *Antibiotics:* Including the aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin and clindamycin. High concentrations of certain antibiotics may produce a muscle paralysis that may be additive when used concurrently with CISTRAX.
- *Antidysrhythmic medicine:* Propranolol, lidocaine, procainamide and quinidine have some neuromuscular blocking activity and may enhance the block produced by CISTRAX.
- *Calcium-channel blockers:* Calcium-channel blockers such as diltiazem, nicardipine, nifedipine and verapamil enhance the effect of CISTRAX. Verapamil may interfere with the release of acetylcholine and prolonged use may lead to a reduction in intracellular calcium concentrations. Potentiation of the

neuromuscular block may occur and the block may be resistant to reversal with neostigmine and edrophonium may be required.

- *Diuretics:* Furosemide and possibly thiazides, mannitol and acetazolamide may enhance the effects of CISTRAX due to the potassium-depleting effects of diuretics.
- *Magnesium salts:* Magnesium salts reduce the release of and the sensitivity to acetylcholine, thus contributing to the neuromuscular blockade. It may potentiate the effect of CISTRAX, and the neuromuscular block is deepened and prolonged. A reduction in the CISTRAX dose may be required. Magnesium salts must be used with caution in the post-operative period, as the use shortly after recovery from CISTRAX may lead to recurarisation.
- *Lithium salts:* Lithium may prolong the neuromuscular block produced by CISTRAX.
- *Ganglion blocking medicines:* Trimetaphan and hexamethonium may prolong the neuromuscular block when used concurrently with CISTRAX and may have direct neuroblocking activity and some activity against plasma cholinesterase.

Decreased effect by:

- *Anti-epileptic medication:* Patients receiving chronic carbamazepine or phenytoin have been reported to be resistant to CISTRAX and rapid recovery from the neuromuscular block may occur.
- *Anticholinesterases:* Anticholinesterases, including ecothiopate, edrophonium, galantamine, neostigmine, pyridostigmine, rivastigmine and possibly donepezil may antagonise the effect of CISTRAX, thereby shortening the duration and diminishing the magnitude of neuromuscular blockade.
- *Immunosuppressants:* Antagonism of the neuromuscular blocking effects of competitive neuromuscular blockers have been reported with azathioprine, although the effects may not be of clinical significance.

Other effects:

- *Aprotinin:* Caution is advised when aprotinin is used with CISTRAX, as apnoea has been reported.

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- *Benzodiazepines:* Potentiation, antagonism and no interactions have been reported when diazepam and CISTRAX were used concurrently.
- *Botulinum A toxin:* The neuromuscular block induced by botulinum toxins may be enhanced by CISTRAX.
- *Neuromuscular blockers:* Prior administration of suxamethonium has no effect on the duration of neuromuscular block following bolus doses of CISTRAX injections or on infusion rate requirements. Administration of suxamethonium to prolong the effects of non-depolarising neuromuscular blocking medicines may result in a prolonged and complex block which can be difficult to reverse with anticholinesterases.

The combination of competitive blockers may have additive or synergistic effects and the interaction may differ depending on which blocker was administered first. Caution is needed if a small dose of a short-acting blocker is given near the end of an operation in which a long- acting blocker has been given previously, since the resulting block may be greater and longer than desired.

Certain medicines may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome. Increased sensitivity to CISTRAX may result. Such medicines include various antibiotics, beta-blockers (propranolol, oxprenolol), antidysrhythmic medicines (procainamide, quinidine), anti-rheumatic medicines (chloroquine, D-penicillamine), trimetaphan, chlorpromazine, steroids, phenytoin and lithium (see section 4.4).

4.6 PREGNANCY AND LACTATION

CISTRAX should not be used in pregnancy and lactation (see section 4.3).

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. The potential risk for humans is unknown. CISTRAX should not be used during pregnancy (see section 4.3).

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Breastfeeding

It is not known whether cisatracurium, as in CISTRAX, or its metabolites are excreted in human milk. A risk to the breastfed infant cannot be excluded. As a precaution breastfeeding should be discontinued during treatment with CISTRAX.

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 CISTRAX.

CISTRAX will always be used in combination with a general anaesthetic and therefore the usual precautions relating to performance of tasks following general anaesthesia apply.
CISTRAX has minor influence on the ability to drive or operate machinery.

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that CISTRAX does not adversely affect their ability to do so safely (see section 4.8).

4.8 UNDESIRABLE EFFECTS

System organ class	Frequency	Adverse reaction
Immune system disorders	Less frequent	Anaphylactic reaction, anaphylactic shock
Cardiac disorders	Frequent	Bradycardia
Vascular disorders	Frequent	Hypotension

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	Less frequent	Cutaneous flushing
Respiratory, thoracic and mediastinal disorders	Less frequent	Bronchospasm
Gastro-intestinal disorders	Less frequent	Reduced gastrointestinal motility
Skin and subcutaneous tissue disorders	Less frequent	Rash
Musculoskeletal, connective tissue and bone disorders	Less frequent	Muscle weakness, myopathy
General disorders and administration site conditions	Less frequent	Hypothermia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the “Adverse drug reaction and quality problem reporting form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.

4.9 OVERDOSE

Symptoms:

Prolonged muscle paralysis and its consequences, such as prolonged apnoea and cardiovascular collapse, are expected to be the main signs of an overdose with CISTRAX.

Treatment

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It is essential to maintain pulmonary ventilation and arterial oxygenation until adequate spontaneous respiration returns. CISTRAX does not impair consciousness and full sedation is required. Recovery may be accelerated by the administration of anticholinesterase medicines once evidence of spontaneous recovery is present.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Category and class: A 17.1 Peripherally-acting muscle relaxants

Pharmacotherapeutic group: Neuromuscular blocking agent, ATC code: M03AC11

Mechanism of action

Cisatracurium is an intermediate-duration, non-depolarising benzylisoquinolinium skeletal muscle relaxant. It blocks neural transmission at the myoneural junction by binding with cholinergic receptor sites, antagonising the action of acetylcholine. This action is readily reversed by anticholinesterase medicines such as neostigmine or edrophonium.

5.2 PHARMACOKINETIC PROPERTIES

The onset of action of cisatracurium is between 2-8 minutes after intravenous administration.

Cisatracurium undergoes rapid nonenzymatic degradation in the bloodstream by Hofmann elimination, at physiological pH and temperature, to form laudanosine and the monoquaternary acrylate metabolite. Laudanosine may cause CNS stimulation. Monoquaternary alcohol metabolite is formed by the hydrolysis of the monoquaternary acrylate by non-specific plasma esterases.

Pharmacokinetics in Adult patients:

The ED_{95} (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 ED_{95} of cisatracurium besylate in children during halothane anaesthesia is 0,04 mg/kg. 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 ED_{95}). 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

Special populations:

Elderly patients:

There are no clinically significant differences in the pharmacokinetics of cisatracurium in elderly patients and adult patients.

Patients with renal impairment:

There are no clinically significant differences in the pharmacokinetics of patients with end- stage renal failure and healthy adult patients.

The recovery profile of cisatracurium is unchanged in the presence of renal failure.

Patients with hepatic impairment:

There are no clinically significant differences in the pharmacokinetics of patients with end- stage liver disease and healthy adult patients. The recovery profile is unchanged in the presence of liver disease.

Pharmacokinetics during infusion:

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

Intensive care unit (ICU) patients:

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

When laudanosine was administered to experimental animals, high concentrations were associated with hypotension and, in some species, cerebral excitation. However, there is

no evidence that laudanosine has caused such effects in man even after prolonged infusions of cisatracurium to ICU patients with impaired renal and/or hepatic function.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Benzene sulphonic acid (pH adjustment)

Water for injection

6.2 INCOMPATIBILITIES

Since CISTRAX is stable 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. CISTRAX is chemically incompatible with lactated Ringer’s injection and 5 % dextrose and lactated Ringer’s injection.

6.3 SHELF-LIFE

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Unopened vial: 18 months

After dilution:

From a microbiological point of view, CISTRAX 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 – 8 °C or at or below 25 °C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store between 2 – 8 °C. Do not freeze.

Keep vials in 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

CISTRAX 5 mg/2,5 ml is filled into a 2 ml USP type I clear glass vial closed with a 13 mm grey, bromobutyl RTS rubber stopper and sealed with a red 13 mm aluminium flip-off seal, packed in an outer carton containing 5 vials.

CISTRAX 10 mg/5 ml is filled into a 6 ml USP type I clear glass vial closed with a 20 mm grey, bromobutyl RTS rubber stopper and sealed with a green 20 mm aluminium flip-off seal, packed in an outer carton containing 5 vials.

CISTRAX 150 mg/30 ml is filled into a 30 ml USP type I clear glass vial closed with a 20 mm grey, bromobutyl RTS rubber stopper and sealed with a green 20 mm aluminium flip-off seal, packed in an outer carton containing a single vial.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Dilution:

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CISTRAX is to be used after dilution with an infusion fluid for administration to patients. CISTRAX is compatible with 0,9 % sodium chloride injection, 5 % dextrose injection and combinations of 5 % dextrose and 0,9 % sodium chloride injection.

Discard any unused solution.

CISTRAX has been shown to be compatible with the following commonly used peri-operative medicines, 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 medicines are administered through the same indwelling needle or cannula as CISTRAX, it is recommended that each medicine be flushed through with an adequate volume of a suitable intravenous fluid, e.g. Sodium Chloride Intravenous Infusion (0,9 % w/v).

When a small vein is selected as the injection site, CISTRAX should be flushed through the vein with a suitable intravenous fluid, e.g. Sodium Chloride Intravenous Infusion (0,9% w/v).

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBERS

CISTRAX 5 mg/2,5 ml: 50/17.1/0131

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CISTRAX 10 mg/5 ml: 50/17.1/0132

CISTRAX 150 mg/30 ml: 50/17.1/0133

9. DATE OF FIRST AUTHORISATION

30 September 2016

10. DATE OF REVISION OF TEXT

01 November 2024