NIMBEX™ INJECTION 2 MG/ML

NIMBEX™ FORTE INJECTION 150 MG/30 ML

Cisatracurium

QUALITATIVE AND QUANTITATIVE COMPOSITION

Ampoules:

A sterile solution containing cisatracurium (bis-cation) (as besylate) 2.68 mg per mL equivalent to 2 mg cisatracurium per ml, without an antimicrobial preservative, supplied in an ampoule.

Vials:

A sterile solution containing cisatracurium (bis-cation) (as besylate) 201.0 mg per 30 mL equivalent to 150 mg cisatracurium per 30 ml, without an antimicrobial preservative, supplied in a vial.

PHARMACEUTICAL FORM

Solution for injection or infusion.

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

CLINICAL PARTICULARS

Indications

NIMBEX is an intermediate-duration, non-depolarising neuromuscular blocking agent for intravenous (i.v.) administration. *NIMBEX* is indicated for use during surgical and other procedures and in intensive care. It is 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.

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

Dosage and Administration

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

- **Use by I.V. bolus injection in adults**

Tracheal intubation: The recommended intubation dose of *NIMBEX* for adults 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 injection.

Higher doses will shorten the time to onset of neuromuscular block. Table 1 summarises mean pharmacodynamic data when *NIMBEX* injection was administered at doses of 0.1 to 0.4 mg/kg to healthy adult patients during opioid (thiopentone/fentanyl/midazolam) or propofol anaesthesia.

Table 1: Mean Pharmacodynamic Data Following a Range of *NIMBEX* Doses

Initial *NIMBEX* injection dose (mg/kg)	Anaesthetic background	Time to 90% T_1[a] suppression (minutes)	Time to maximum T_1[a] suppression (minutes)	Time to 25% spontaneous T_1[a] recovery (minutes)
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

[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.

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

Maintenance: Neuromuscular block can be extended with maintenance doses of *NIMBEX* . 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 *NIMBEX* 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 *NIMBEX* administration is readily reversible with standard doses of anticholinesterase agents. The mean times from 25 to 75% recovery and to full clinical recovery (T_4:T_1 ratio more than or equal to 0.7) are approximately 2 and 5 minutes, respectively, following administration of the reversal agent at an average of 13% T_1 recovery.

- **Use by I.V. bolus injection in children (1 month to 12 years of age)**

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

Tracheal intubation: As in adults, the recommended initial intubation dose of *NIMBEX* 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 injection of *NIMBEX*. Pharmacodynamic data for this dose are presented in the tables 2 and 3. 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.

In paediatric patients aged 1 month to 12 years, *NIMBEX* 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 Tables 2 and 3 below.

Table 2: Paediatric Patients aged 1 to 11 months

Initial *NIMBEX* injection dose (mg/kg)	Anaesthetic background	Time to 90% suppression (minutes)	Time to maximum suppression (minutes)	Time to 25% spontaneous T_1 recovery (minutes)
0.15	Halothane	1.4	2.0	52
0.15	Opioid	1.4	1.9	47

Table 3: Paediatric Patients aged 1 to 12 years

Initial *NIMBEX* injection Dose (mg/kg)	Anaesthetic background	Time to 90% suppression (minutes)	Time to maximum suppression (minutes)	Time to 25% spontaneous T_1 recovery (minutes)
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

Halothane may be expected to extend the clinically effective duration of *NIMBEX* by up to 20%. No information is available on the use of *NIMBEX* in children during isoflurane or enflurane anaesthesia but these agents may also be expected to extend the clinically effective duration of a dose of *NIMBEX* by up to 20%.

Maintenance (paediatric patients aged 2-12 years): Neuromuscular block can be extended with maintenance doses of *NIMBEX* injection. A dose of 0.02 mg/kg 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 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 *NIMBEX* 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 *NIMBEX* administration is readily reversible with standard doses of anticholinesterase agents. The mean times from 25 to 75% recovery and to full clinical recovery (T_4:T_1 ratio more than or equal to 0.7) are approximately 2 and 5 minutes, respectively, following administration of the reversal agent at an average of 13% T_1 recovery.

- **Use by I.V. infusion in adults and children (2 to 12 years of age)**

Maintenance of neuromuscular block may be achieved by infusion of *NIMBEX* . An initial infusion rate of 3 micrograms/kg/min (0.18 mg/kg/h) is recommended to restore 89 to 99% T_1 suppression following evidence of spontaneous recovery. After an initial period of stabilisation of neuromuscular block, a rate of 1 to 2 micrograms/kg/min (0.06 to 0.12 mg/kg/h) 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 *NIMBEX* is administered during isoflurane or enflurane anaesthesia. (*see Interactions*).

The infusion rate will depend upon the concentration of *NIMBEX* in the infusion solution, the desired degree of neuromuscular block, and the patient's weight. Table 4 provides guidelines for delivery of undiluted *NIMBEX*.

Table 4: Infusion Delivery Rate of *NIMBEX* 2 mg/mL

Patient weight (kg)	Dose (micrograms/kg/min) 1.0	1.5	2.0	3.0	Infusion rate
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

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

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

- **Neonates aged less than 1 month**

No dosage recommendation for neonates can be made as administration of *NIMBEX* has not been studied in this patient population.

- **Elderly**

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

- **Patients with renal impairment**

No dosing alterations are required in patients with renal failure. In these patients *NIMBEX* has a similar pharmacodynamic profile to that observed in patients with normal renal function but it may have a slightly slower onset.

- **Patients with hepatic impairment**

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

- **Patients with cardiovascular disease**

When administered by rapid bolus injection (over 5 to 10 seconds) to patients with serious cardiovascular disease *NIMBEX* has not been associated with clinically significant

cardiovascular effects at any dose studied (up to and including 0.4 mg/kg (8 x ED_{95})). However, there are limited data for doses above 0.3 mg/kg in this patient population. *NIMBEX* has not been studied in children undergoing cardiac surgery.

- **ICU patients**

NIMBEX may be administered by bolus dose and/or infusion to adult patients in the ICU.

An initial infusion rate of *NIMBEX* of 3 micrograms/kg/min (0.18 mg/kg/h) is recommended for adult ICU patients. There may be wide inter-patient variation in dosage requirements and these may increase or decrease with time. In clinical studies the average infusion rate was 3 micrograms/kg/min [range 0.5 to 10.2 micrograms/kg/min (0.03 to 0.6 mg/kg/h)]. Table 5 provides guidelines for delivery of undiluted *NIMBEX*.

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

Table 5: Infusion Delivery Rate of *NIMBEX* Injection 5 mg/mL

Patient weight (kg)	Dose (micrograms/kg/min) 1.0	1.5	2.0	3.0	Infusion rate
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 infusions of *NIMBEX* to ICU patients is independent of duration of infusion.

- **Patients undergoing hypothermic cardiac surgery**

There have been no studies of *NIMBEX* in patients undergoing surgery with induced hypothermia (25°C 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.

Contraindications

NIMBEX is contraindicated in patients known to be hypersensitive to cisatracurium, atracurium, or benzenesulfonic acid.

Warnings and Precautions

NIMBEX paralyses the respiratory muscles as well as other skeletal muscles but has no known effect on consciousness or pain threshold. *NIMBEX* 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 should 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 Contraindications).*

NIMBEX does not have significant vagolytic or ganglion-blocking properties. Consequently, *NIMBEX* 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 *NIMBEX* 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.

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

NIMBEX 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 *NIMBEX* is administered to these patients.

NIMBEX is hypotonic and must not be administered into the infusion line of a blood transfusion.

- **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.

Consistent with the decreased infusion rate requirements of *NIMBEX*, 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 (e.g. cranial trauma, hypoxic encephalopathy, cerebral oedema, viral encephalitis, uremia).

A causal relationship to laudanosine has not been established.

Interactions

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

Anaesthetics:

- volatile agents such as enflurane, isoflurane and halothane
- ketamine
- other non-depolarising neuromuscular blocking agents.

Other drugs:

- antibiotics: including the aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin and clindamycin
- anti-arrhythmic drugs: including propranolol, calcium channel blockers, lidocaine, procainamide and quinidine
- diuretics: including furosemide and possibly thiazides, mannitol and acetazolamide
- magnesium salts
- lithium salts
- 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, beta-blockers (propanolol, 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 anticholinsterases.

Decreased effect

- 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 *NIMBEX* or on infusion rate requirements.

Pregnancy and Lactation

Fertility

Fertility studies have not been performed.

Pregnancy

There are no adequate and well-controlled studies of *NIMBEX* in pregnant women. Because animal studies are not always predictive of human response, *NIMBEX* should be used during pregnancy only if the expected benefit to the mother outweighs any potential risk to the foetus.

Teratogenicity

Teratology testing in rats revealed no maternal or foetal toxicity or teratogenic effect.

Lactation

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

Effects on Ability to Drive and Use Machines

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

Adverse Reactions

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 to <1/10, uncommon ≥ 1/1000 to <1/100, rare ≥ 1/10,000 to <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

Post Marketing Data

Immune system disorders

Very rare	Anaphylactic reaction

Anaphylactic reactions of varying degrees of severity have been observed after the administration of neuromuscular blocking agents. Very rarely, severe anaphylactic reactions have been reported in patients receiving *NIMBEX* 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 *NIMBEX* and a causal relationship has not been established.

Overdose

Symptoms and Signs

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

Treatment

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 *NIMBEX*. Recovery may be accelerated by the administration of anticholinesterase agents once evidence of spontaneous recovery is present.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

ATC Code

Pharmacotherapeutic group: Peripherally acting muscle relaxants: Other quaternary ammonium compounds, ATC code: M03AC11.

Mechanism of Action

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

Pharmacodynamic Effects

Clinical studies in man indicated that *NIMBEX* is not associated with dose-dependent histamine release even at doses up to and including 8 x ED_{95}.

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 ED_{95} of *NIMBEX* in children during halothane anaesthesia is 0.04 mg/kg.

Pharmacokinetics

Non-compartmental pharmacokinetics of *NIMBEX* are independent of dose in the range studied (0.1 to 0.2 mg/kg, i.e. 2 to 4 x ED_{95}).

Population pharmacokinetic modelling confirms and extends these findings up to 0.4 mg/kg (8 x ED_{95})

Distribution

After doses of 0.1 and 0.2 mg/kg *NIMBEX* administered to healthy adult surgical patients volume of distribution at steady-state is 121 to 161 ml/kg.

Metabolism

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.

These metabolites do not possess neuromuscular blocking activity.

Elimination

Elimination of cisatracurium is largely organ-independent but the liver and kidneys are primary pathways for the clearance of its metabolites.

I.V. bolus injection

Pharmacokinetic parameters after doses of 0.1 and 0.2 mg/kg *NIMBEX* administered to healthy adult surgical patients are summarised in Table 6 below.

Table 6: Mean Pharmacokinetic Data Following a range of *NIMBEX* Doses

Parameter	Range of mean values
Clearance	4.7 to 5.7 mL/min/kg
Elimination half-life	22 to 29 minutes

I.V. infusion

The pharmacokinetics of cisatracurium after infusion are similar to those after single bolus injection. Pharmacokinetics were studied in healthy adult surgical patients who received an initial 0.1 mg/kg bolus dose of cisatracurium followed by a maintenance infusion of *NIMBEX* to maintain 89 to 99% T_1 suppression. Mean clearance of cisatracurium was 6.9 ml/kg/min and elimination half-life was 28 minutes. The recovery profile after infusion of *NIMBEX* is independent of duration of infusion and is similar to that after single bolus injections.

Special Patient Populations

- **Elderly**

There are no clinically important differences in the pharmacokinetics of cisatracurium in elderly and young adult patients. In a comparative study, plasma clearance was not affected by age. Minor differences in volume of distribution (+17%) and half-life (+4 minutes) did not affect the recovery profile (*see Dosage and Administration*).

- **Patients with renal impairment**

There are no clinically important differences in the pharmacokinetics of cisatracurium in patients with end-stage renal failure and in healthy adult patients. In a comparative study, there were no statistically significant or clinically important differences in

pharmacokinetic parameters of *NIMBEX*. The recovery profile of *NIMBEX* is unchanged in the presence of renal failure (*see Dosage and Administration*).

- **Patients with hepatic impairment**

There are no clinically important differences in the pharmacokinetics of cisatracurium in patients with end-stage liver disease and in healthy adult patients. In a comparative study of patients undergoing liver transplantation and healthy adults, there were small differences in volume of distribution (+21%) and clearance (+16%), but no difference in elimination half-life of cisatracurium. The recovery profile was unchanged (*see Dosage and Administration*).

- **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. Mean clearance of cisatracurium was 7.5 mL/kg/min and elimination half-life was 27 minutes. The recovery profile after infusions of *NIMBEX* 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 Warnings and Precautions*). These metabolites do not contribute to neuromuscular block.

Pre-Clinical Safety Data

Mutagenicity

The mutagenic risk to patients undergoing muscle relaxation with *NIMBEX* is considered negligible.

Carcinogenicity

Carcinogenicity studies have not been performed.

PHARMACEUTICAL PARTICULARS

List of Excipients

Benzenesulphonic acid solution 32% w/v, Water for injections.

Incompatibilities

Degradation of cisatracurium besylate 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 Instructions for Use/Handling.

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 *NIMBEX* for infusion.

Since *NIMBEX* 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, eg, sodium thiopentone. It is not compatible with ketorolac, trometamol or propofol injectable emulsion.

Shelf Life

Shelf life before dilution: 2 years

Chemical and physical in-use stability has been demonstrated for at least 24 hours at 5˚C and 25˚C (*see Instructions for Use/Handling*).

From a microbiological point of view, the 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 to 8˚C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Special Precautions for Storage

Store between 2°C and 8°C.
Protect from light.
Do not freeze.

NIMBEX contains no antimicrobial preservative therefore dilution should be carried out immediately prior to use and administration should commence as soon as possible thereafter. Any unused solution diluted in an infusion fluid, or remaining in a used vial or open ampoule, should be discarded.

Nature and Contents of Container

Nimbex Injection 2 mg/mL, 2.5mL and 5mL presentations: box of 5 ampoules. Clear Type I glass ampoules with a nominal capacity of 3 mL and 5mL respectively.

Nimbex Forte Injection 150 mg/30 mL: box of 1. Clear type I glass vial, nominal size 30 ml closed with a bromobutyl rubber stopper and sealed with an aluminium collar with a plastic flip-off top.

Not all presentations will be marketed locally.

Instructions for Use/Handling

Diluted *NIMBEX* is physically and chemically stable for at least 24 hours between 5°C and 25°C at concentrations between 0.1 and 2.0 mg/mL in the following infusion fluids, in either polyvinyl chloride (PVC) or polypropylene:

sodium chloride (0.9% w/v) i.v. infusion
dextrose (5% w/v) i.v. infusion
sodium chloride (0.18% w/v) and dextrose (4% w/v) i.v. infusion
sodium chloride (0.45% w/v) and dextrose (2.5% w/v) i.v. infusion.

However, since the product contains no antimicrobial preservative dilution should be carried out immediately prior to use, administration should commence as soon as possible thereafter and any remaining solution should be discarded.

NIMBEX has been shown to be compatible with the following commonly used peri-operative drugs, when mixed in conditions simulating administration into a running i.v. 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 *NIMBEX*, it is recommended that each drug be flushed through with an adequate volume of a suitable i.v. fluid, e.g. sodium chloride i.v. infusion 0.9% (w/v).

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

Not all presentations are available in every country.

Manufactured by:
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Parma,
Italy.

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