SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Mivacron 2mg/ml Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 2mg mivacurium (As mivacurium chloride)

Each 5ml ampoule contains 10mg mivacurium. (As mivacurium chloride)
Each 10ml ampoule contains 20mg mivacurium. (As mivacurium chloride)

For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection. (Short term: Injection)
A clear, pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Mivacron is a highly selective, short-acting, non-depolarising neuromuscular blocking agent with a fast recovery profile.

Mivacron is indicated as an adjunct to general anaesthesia to relax skeletal muscles and to facilitate tracheal intubation and mechanical ventilation in adults, children and infants 2 months and over.

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

4.2 Posology and method of administration

Use by injection in adults:
Mivacron is administered by intravenous injection. The mean dose required to produce 95% suppression of the adductor pollicis single twitch response to ulnar nerve stimulations (ED_{95}) is 0.07 mg/kg (range 0.06 to 0.09) in adults receiving narcotic anaesthesia.

The following dose regimens are recommended for tracheal intubation:-

i. A dose of 0.2 mg/kg, administered over 30 seconds, produces good to excellent conditions for tracheal intubation within 2 to 2.5 minutes.

ii. A dose of 0.25 mg/kg administered as a divided dose (0.15 mg/kg followed 30 seconds later by 0.1 mg/kg), produces good to excellent conditions for tracheal intubation within 1.5 to 2.0 minutes of completion of administration of the first dose portion.

The recommended bolus dose range for healthy adults is 0.07 to 0.25 mg/kg. The duration of neuromuscular blockade is related to the dose. Doses of 0.07, 0.15, 0.20

and 0.25 mg/kg produce clinically effective block for approximately 13, 16, 20 and 23 minutes, respectively.

Doses of up to 0.15 mg/kg may be administered over 5 to 15 seconds. Higher doses should be administered over 30 seconds or as a divided dose in order to minimise the possibility of occurrence of cardiovascular effects.

Full block can be prolonged with maintenance doses of Mivacron. Doses of 0.1 mg/kg administered during narcotic anaesthesia each provide approximately 15 minutes of additional clinically effective block.

Successive supplementary doses do not give rise to accumulation of neuromuscular blocking effect.

The neuromuscular blocking action of mivacurium is potentiated by isoflurane or enflurane anaesthesia. If steady-state anaesthesia with isoflurane or enflurane has been established, the recommended initial Mivacron dose should be reduced by up to 25%. Halothane appears to have only a minimal potentiating effect on Mivacron and dose reduction of Mivacron is probably not necessary.

Once spontaneous recovery is underway it is complete in approximately 15 minutes and is independent of the dose of Mivacron administered.

The neuromuscular block produced by Mivacron can be reversed with standard doses of anti-cholinesterase agents. However, because spontaneous recovery after mivacurium is rapid, reversal may not be routinely required since it shortens recovery time by only 5 to 6 minutes.

Use as an infusion in adults:
Continuous infusion of Mivacron may be used to maintain neuromuscular block. Upon early evidence of spontaneous recovery from an initial Mivacron dose, an infusion rate of 8 to 10 micrograms/kg/min (0.5 to 0.6 mg/kg/hr) is recommended.

The initial infusion rate should be adjusted according to the patient's response to peripheral nerve stimulation and clinical criteria.

Adjustments of the infusion rate should be made in increments of approximately 1 microgram/kg/min (0.06 mg/kg/hr). In general a given rate should be maintained for at least 3 minutes before a rate change is made.

On average, an infusion rate of 6 to 7 micrograms/kg/min will maintain neuromuscular block within the range of 89% to 99% for extended periods in adults receiving narcotic anaesthesia. During steady-state isoflurane or enflurane anaesthesia, reduction in the infusion rate by up to 40% should be considered. A study has shown that the mivacurium infusion rate requirement should be reduced by up to 50% with sevoflurane. With halothane, smaller reductions in infusion rate may be required.

Spontaneous recovery after Mivacron infusion is independent of the duration of infusion and comparable to recovery reported for single doses.

Continuous infusion of Mivacron has not been associated with the development of tachyphylaxis or cumulative neuromuscular blockade.

Mivacron (2 mg/ml) may be used undiluted for infusion.

Mivacron is compatible with the following infusion fluids:

- sodium chloride intravenous infusion (0.9% w/v)
- glucose intravenous infusion (5% w/v)
- sodium chloride (0.18% w/v) and glucose (4% w/v) intravenous infusion
- Lactated Ringer's Injection United States Pharmacopoeia (USP)

When diluted with the listed infusion solutions in the proportion of 1 plus 3 (i.e. to give 0.5 mg/ml) Mivacron injection has been shown to be chemically and physically stable for at least 48 hours at 30°C. 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.

Dose in infants and children aged 7 months to 12 years:
Mivacron has a higher ED_{95} (approximately 0.1 mg/kg), faster onset, shorter clinically effective duration of action and more rapid spontaneous recovery in infants and children aged 7 months to 12 years, than in adults.

The recommended bolus dose range for infants and children aged 7 months to 12 years is 0.1 to 0.2 mg/kg administered over 5 to 15 seconds. When administered during stable narcotic or halothane anaesthesia a dose of 0.2 mg/kg produces clinically effective block for an average of 9 minutes.

A Mivacron dose of 0.2 mg/kg is recommended for tracheal intubation in infants and children aged 7 months to 12 years. Maximum block is usually achieved within 2 minutes following administration of this dose and intubation should be possible within this time.

Maintenance doses are generally required more frequently in infants and children than in adults. Available data suggest that a maintenance dose of 0.1 mg/kg will give approximately 6 to 9 minutes of additional clinically effective block during narcotic or halothane anaesthesia.

Infants and children generally require higher infusion rates than adults.

During halothane anaesthesia the mean infusion rate required to maintain 89% to 99% neuromuscular block in patients aged 7 to 23 months is approximately 11 micrograms/kg/min (approximately 0.7 mg/kg/hr) [range: 3 to 26 micrograms/kg/min (approximately 0.2 to 1.6 mg/kg/hr)].

For children aged 2 to 12 years the equivalent mean infusion rate is approximately 13 to 14 micrograms/kg/min (approximately 0.8 mg/kg/hr) [range: 5 to 31 micrograms/kg/min (approximately 0.3 to 1.9 mg/kg/hr)] during halothane or narcotic anaesthesia.

The neuromuscular blocking action of mivacurium is potentiated by inhalational agents. A study has shown that the mivacurium infusion rate requirement should be reduced by up to 70% with sevoflurane in children aged 2 to 12 years.

Once spontaneous recovery is underway, it is complete in approximately 10 minutes.

Dose in infants aged 2 to 6 months:

Mivacron has a similar ED_{95} to that in adults (0.07 mg/kg), but a faster onset, shorter clinically effective duration of action and more rapid spontaneous recovery in infants aged 2 to 6 months than in adults.

The recommended bolus dose range for infants aged 2 to 6 months is 0.1 to 0.15 mg/kg administered over 5 to 15 seconds. When administered during stable halothane anaesthesia a dose of 0.15 mg/kg produces clinically effective block for an average of 9 minutes.

A Mivacron dose of 0.15 mg/kg is recommended for tracheal intubation in infants aged 2 to 6 months. Maximum block is achieved approximately 1.4 minutes following administration of this dose and intubation should be possible within this time.

Maintenance doses are generally required more frequently in infants aged 2 to 6 months than in adults. Available data suggest that a maintenance dose of 0.1 mg/kg will give approximately 7 minutes of additional clinically effective block during halothane anaesthesia.

Infants aged 2 to 6 months generally require higher infusion rates than adults. During halothane anaesthesia the mean infusion rate required to maintain 89 to 99% neuromuscular block is approximately 11 micrograms/kg/min (approximately 0.7 mg/kg/hr) [range: 4 to 24 micrograms/kg/min (approximately 0.2 to 1.5 mg/kg/hr)].

Once spontaneous recovery is underway, it is complete in approximately 10 minutes.

Dose in neonates and infants under 2 months of age:
The safety and efficacy of Mivacurium chloride in neonates and infants less than 2 months has not yet been established. No recommendation on posology can be made.

Dose in the elderly:
In elderly patients receiving single bolus doses of Mivacron, the onset time, duration of action and recovery rate may be extended relative to younger patients by 20 to 30%. Elderly patients may also require decreased infusion rates or smaller or less frequent maintenance bolus doses.

Dose in patients with cardiovascular disease:
In patients with clinically significant cardiovascular disease, the initial dose of Mivacron should be administered over 60 seconds. Mivacron has been administered in this way with minimal haemodynamic effects to patients undergoing cardiac surgery.

Dose in patients with reduced renal function:
In patients with end-stage renal disease the clinically effective duration of block produced by 0.15 mg/kg is approximately 1.5 times longer than in patients with normal renal function. Subsequently, dosage should be adjusted according to individual clinical response.

Prolonged and intensified neuromuscular blockade may also occur in patients with acute or chronic renal failure as a result of reduced levels of plasma cholinesterase (see section 4.4 Special warnings and precautions for use***)***.

Dose in patients with reduced hepatic function:
In patients with end-stage liver disease the clinically effective duration of block produced by 0.15 mg/kg is approximately three times longer than in patients with normal hepatic function. This prolongation is related to the markedly reduced plasma

cholinesterase activity seen in these patients. Subsequently, dosage should be adjusted according to individual clinical response.

Dose in patients with reduced plasma cholinesterase activity:
Mivacurium is metabolised by plasma cholinesterase. Plasma cholinesterase activity may be diminished in the presence of genetic abnormalities of plasma cholinesterase (e.g. patients heterozygous or homozygous for the atypical plasma cholinesterase gene), in various pathological conditions (see section 4.4 Special warnings and precautions for use). The possibility of prolonged neuromuscular block following administration of Mivacron must be considered in patients with reduced plasma cholinesterase activity. Mild reductions (i.e. within 20% of the lower limit of the normal range) are not associated with clinically significant effects on duration (see section 4.3 Contraindications and section 4.4 Special warnings and precautions for use for information about homozygous and heterozygous patients).

Dose in obese patients:
In obese patients (those weighing 30% or more above their ideal bodyweight for height), the initial dose of Mivacron should be based upon ideal bodyweight and not actual bodyweight.

Monitoring:
In common with all neuromuscular blocking agents, monitoring of neuromuscular function is recommended during the use of Mivacron in order to individualise dosage requirements.

With Mivacron, significant train-of-four fade is not seen during onset. It is often possible to intubate the trachea before complete abolition of the train-of-four response of the adductor pollicis muscle has occurred.

4.3 Contraindications

Hypersensitivity to mivacurium or to any of the excipients listed in section 6.1.

Mivacron is contraindicated in patients known to be homozygous for the atypical plasma cholinesterase gene (see section 4.4 Special warnings and precautions for use).

4.4 Special warnings and precautions for use

In common with all the other neuromuscular blocking agents, Mivacron paralyses the respiratory muscles as well as other skeletal muscles but has no effect on consciousness. Mivacron should be administered only by or under the close supervision of an experienced anaethestist with adequate facilities for endotrachael intubation and artificial ventilation.

Prolonged and intensified neuromuscular blockade following mivacurium may occur secondary to reduced plasma cholinesterase activity in the following states or pathological conditions:

- physiological variation as in pregnancy and the puerperium (see section 4.6 Fertility, pregnancy and lactation)
- genetically determined abnormalities of plasma cholinesterase (see below and section 4.3 Contraindications)
- severe generalised tetanus, tuberculosis and other severe or chronic infections
- chronic debilitating disease, malignancy, chronic anaemia and malnutrition

- myxoedema and collagen diseases
- decompensated heart disease
- peptic ulcer
- burns (see below)
- end-stage hepatic failure, (see section 4.2 Posology and method of administration)
- acute, chronic or end-stage renal failure (see section 4.2 Posology and method of administration)
- iatrogenic: following plasma exchange, plasmapheresis, cardiopulmonary bypass, and as a result of concomitant drug therapy (see section 4.5 Interaction with other medicinal products and other forms of interaction).

In common with suxamethonium/succinylcholine, patients homozygous for the atypical plasma cholinesterase gene (1 in 2500 patients) are extremely sensitive to the neuromuscular blocking effect of mivacurium. In three such adult patients, a small dose of 0.03 mg/kg (approximately the ED_{10-20} in genotypically normal patients), produced complete neuromuscular block for 26 to 128 minutes.

In patients heterozygous for the atypical plasma cholinesterase gene, the clinically effective duration of block of mivacurium 0.15 mg/kg is approximately 10 minutes longer than in control patients.

Once spontaneous recovery had begun, neuromuscular block in these patients was antagonised with conventional doses of neostigmine.

Patients with burns may develop resistance to non-depolarising neuromuscular blocking agents and require increased doses. However, such patients may also have reduced plasma cholinesterase activity, requiring dose reduction. Consequently, burn patients should be given a test dose of 0.015 to 0.020 mg/kg mivacurium followed by appropriate dosing guided by monitoring of block with a nerve stimulator.

Caution should be exercised in administering Mivacron to patients with a history suggestive of an increased sensitivity to the effects of histamine e.g. asthma. If Mivacron is used in this group of patients it should be administered over 60 seconds.

Caution should also be exercised when administering Mivacron 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.

Mivacron should be administered over a period of 60 seconds to patients who may be unusually sensitive to decreases in arterial blood pressure, for example those who are hypovolaemic.

In adults doses of Mivacron of greater than or equal to 0.2 mg/kg (greater than or equal to 3 x ED_{95}) have been associated with histamine release when administered by rapid bolus injection. However, the slower administration of the 0.2 mg/kg Mivacron dose and the divided administration of the 0.25 mg/kg Mivacron dose (see section 4.2 Posology and method of administration) minimise the cardiovascular effects of these doses. Cardiovascular safety did not appear to be compromised in children given a rapid bolus dose of 0.2 mg/kg in clinical studies.

Mivacron does not have significant vagal or ganglion blocking properties in the recommended dosage range. Recommended doses of Mivacron consequently have no clinically significant effects on heart rate and will not counteract the bradycardia produced by many anaesthetic agents or by vagal stimulation during surgery.

In common with other non-depolarising neuromuscular blocking agents, increased sensitivity to mivacurium can be expected in patients with myasthenia gravis, other forms of neuromuscular disease and cachectic patients. Severe acid base or electrolyte abnormalities may increase or reduce sensitivity to mivacurium.

Mivacron solution is acidic (approximately pH 4.5) and should not be mixed in the same syringe or administered simultaneously through the same needle with highly alkaline solutions (e.g. barbiturate solutions). It has been shown to be compatible with some commonly used peri-operative drugs supplied as acidic solutions, e.g. fentanyl, alfentanil, sufentanil, droperidol and midazolam. Where other anaesthetic agents are administered through the same indwelling needle or cannula as used for Mivacron, and compatibility has not been demonstrated, it is recommended that each drug is flushed through with physiological saline.

Studies in malignant hyperthermia-susceptible pigs indicated that Mivacron does not trigger this syndrome. Mivacron has not been studied in malignant hyperthermia-susceptible patients.

Reversal of neuromuscular block: As with other neuromuscular blocking agents, evidence of spontaneous recovery should be observed prior to administration of reversal agent (e.g. neostigmine). The use of a peripheral nerve stimulator to evaluate recovery prior to and following reversal of neuromuscular block is strongly recommended.

No data are available on the long-term use of Mivacron in patients undergoing mechanical ventilation in the intensive care unit.

The use in neonates and infants less than two months is not recommended due to limited data (see also section 4.2 and 5.1).

4.5 Interaction with other medicinal products and other forms of interaction

The neuromuscular block produced by mivacurium may be potentiated by the concomitant use of inhalational anaesthetics such as enflurane, isoflurane, sevoflurane and halothane.

Mivacron has been safely administered following suxamethonium-facilitated tracheal intubation. Evidence of spontaneous recovery from suxamethonium should be observed prior to administration of Mivacron.

In common with all non-depolarising neuromuscular blocking agents, the magnitude and/or duration of non-depolarising neuromuscular block may be increased and infusion requirements may be reduced as a result of interaction with:

- antibiotics, including the aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin and clindamycin
- anti-arrhythmic drugs: propranolol, calcium channel blockers, lidocaine, procainamide and quinidine
- diuretics: furosemide and possibly thiazides, mannitol and acetazolamide
- magnesium salts
- ketamine
- lithium salts
- ganglion blocking drugs: trimetaphan, hexamethonium

Drugs that may reduce plasma cholinesterase activity may also prolong the neuromuscular blocking action of Mivacron. These include anti-mitotic drugs, monoamine oxidase inhibitors, ecothiophate iodide, pancuronium, organophosphates, anti-cholinesterases, certain hormones, bambuterol and selective serotonin reuptake inhibitors.

Rarely, certain drugs may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome: increased sensitivity to Mivacron would be consequent on such a development. Such drugs include various antibiotics, beta-blockers (propranolol, oxprenolol), antiarrhythmic drugs (procainamide, quinidine), anti-rheumatic drugs (chloroquine, D-pencillamine), trimetaphan, chlorpromazine, steroids, phenytoin and lithium.

The administration of combinations of non-depolarising neuromuscular blocking agents in conjunction with Mivacron may produce a degree of neuromuscular blockade in excess of that which might be expected from an equipotent total dose of Mivacron. Any synergistic effect may vary between drug combinations.

A depolarising muscle relaxant such as suxamethonium chloride should not be administered to prolong the neuromuscular blocking effects of non-depolarising agents, as this may result in a prolonged and complex block which can be difficult to reverse with anti-cholinesterase drugs.

4.6 Fertility, pregnancy and lactation

Fertility
Fertility studies have not been performed.

Pregnancy
Animal studies have indicated that mivacurium has no adverse effect on foetal development.

Mivacron should not be used during pregnancy unless the expected clinical benefit to the mother outweighs any potential risk to the foetus.

Plasma cholinesterase levels decrease during pregnancy. Mivacurium has been used to maintain neuromuscular block during Caesarean section, but due to the reduced levels of plasma cholinesterase, dosage adjustments to the infusion rate were necessary. A further reduction in the infusion rate may also be required during Caesarean section in patients pre-treated with magnesium sulfate, due to the potentiating effects of magnesium.

Breast-feeding
It is not known whether mivacurium is excreted in human milk.

4.7 Effects on ability to drive and use machines

This precaution is not relevant to the use of mivacurium. Mivacurium 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

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common ($\geq$1/10), common ($\geq$1/100 to <1/10), uncommon

(≥1/1000 to <1/100), rare (≥1/10000 to <1/1000) and very rare (<1/10,000) including isolated reports.

Immune disorders

Very rare:	Severe anaphylactic or anaphylactoid reaction. Severe anaphylactic or anaphylactoid reactions have been reported in patients receiving mivacurium chloride in conjunction with one or more anaesthetic agents.

Cardiac disorders

Uncommon	Transient tachycardia†

Vascular disorders

Very common	Flushing†
Uncommon:	Hypotension†

Respiratory, thoracic and mediastinal disorders

Uncommon:	Bronchospasm†

Skin and subcutaneous tissue disorders

Uncommon:	Erythema†, urticaria†

†Associated with the use of mivacurium there have been reports of skin flushing, erythema, urticaria, hypotension, transient tachycardia or bronchospasm which have been attributed to histamine release. These effects are dose-related and more common following initial doses of 0.2 mg/kg or more when given rapidly and are reduced if mivacurium chloride is injected over 30 to 60 seconds or in divided doses over 30 seconds.

The safety profile in children is similar to that in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdosage

Symptoms and Signs:

Prolonged muscle paralysis and its consequences are the main signs of overdosage with neuromuscular blocking agents. However, the risk of haemodynamic side effects especially decreases in blood pressure may be increased.

Management:

It is essential to maintain a patent airway together with assisted positive pressure ventilation until spontaneous respiration is adequate.

Full sedation will be required since consciousness is not impaired.

Recovery may be hastened by the administration of anti-cholinesterase agents accompanied by atropine or glycopyrrolate, once evidence of spontaneous recovery is present. Cardiovascular support may be provided by proper positioning of the patient and administration of fluids or vasopressor agents as required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Peripherally acting muscle relaxants, other quaternary ammonium compounds
ATC code: M03AC10

Mivacurium is a short-acting, non-depolarising skeletal muscle relaxant which is hydrolysed by plasma cholinesterase. Mivacurium binds competitively with cholinergic receptors on the motor end-plate to prevent the action of acetylcholine, resulting in a blockade of neuromuscular transmission. This is readily reversed by the administration of the cholinesterase inhibitors, neostigmine and edrophonium.

5.2 Pharmacokinetic properties

Mivacurium chloride is a mixture of three stereoisomers. The trans-trans and cis-trans stereoisomers comprise 92% to 96% of mivacurium chloride and when studied in cats their neuromuscular blocking potencies are not significantly different from each other or from mivacurium chloride. The cis-cis isomer has been estimated from studies in cats to have one-tenth of the neuromuscular blocking potency of the other two stereoisomers.

Enzymatic hydrolysis by plasma cholinesterase is the primary mechanism for inactivation of mivacurium and yields a quaternary alcohol and a quaternary monoester metabolite. Pharmacological studies in cats and dogs have shown that the metabolites possess insignificant neuromuscular, autonomic or cardiovascular activity at concentrations higher than seen in man.

5.3 Preclinical safety data

Mutagenicity
Mivacurium has been evaluated in four short-term mutagenicity tests. Mivacurium was non-mutagenic in the Ames Salmonella assay, the mouse lymphoma assay, the human lymphocyte assay and the *in vivo* rat bone marrow cytogenetic assay.

Carcinogenicity
There is no information available on whether mivacurium has carcinogenic potential.

Teratogenicity
Animal studies have indicated that mivacurium has no adverse effect on foetal development.

Fertility
Fertility studies have not been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (for pH adjustment)
Water for injections

6.2 Incompatibilities

Mivacron injection is acidic (approximately pH 4.5) and should not be mixed with highly alkaline solutions e.g. barbiturates.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6 Special precautions for disposal and other handling.

6.3 Shelf life

Unopened: 18 months
Once opened, use immediately and discard any unused contents.

When diluted with the listed infusion solutions in Section 6.6, in the proportion of 1 plus 3 (i.e. to give 0.5 mg/ml), Mivacron injection has been shown to be chemically and physically stable for at least 48 hours at 30°C. However, since the product contains no antimicrobial preservative, dilution should be carried out under full aseptic conditions immediately prior to use, administration should commence as soon as possible thereafter, and any remaining solution should be discarded.

6.4 Special precautions for storage

Store below 25°C. Do not freeze. Keep the ampoules in the outer carton in order to protect from light.

6.5 Nature and contents of container

5 x 5ml glass ampoules (Type I) in an outer cardboard carton
5 x 10ml glass ampoules (Type I) in an outer cardboard carton

6.6 Special precautions for disposal and other handling

For single use only.

Since no antimicrobial preservative is included, Mivacron Injection must be used under full aseptic conditions and any dilution carried out immediately before use. Any unused solution in open ampoules should be discarded.

No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Mivacron Injection has been shown to be compatible with some commonly used peri-operative drugs supplied as acidic solutions. Where such agents are administered through the same indwelling needle or cannula as used for Mivacron Injection and compatibility has not been demonstrated, it is recommended that each drug is flushed through with physiological saline.

Mivacron is compatible with the following infusion fluids:

- sodium chloride intravenous infusion (0.9% w/v)
- glucose intravenous infusion (5% w/v)
- sodium chloride (0.18% w/v) and glucose (4% w/v) intravenous infusion
- Lactated Ringer's Injection United States Pharmacopoeia (USP)

<u>Instructions to open the ampoule:</u>

Ampoules are equipped with the OPC (One Point Cut) opening system and must be opened following the below instructions:

- Hold with the hand the bottom part of the ampoule
- Put the other hand on the top of the ampoule positioning the thumb above the coloured point and press

7. MARKETING AUTHORISATION HOLDER

Aspen Pharma Trading Limited,
3016 Lake Drive,
Citywest Business Campus,
Dublin 24,
Ireland

8. MARKETING AUTHORISATION NUMBER

PA 1691/031/001

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