SUMMARY OF PRODUCT CHARACTERISTICS

1  NAME OF THE MEDICINAL PRODUCT

Suxamethonium Chloride 100mg/2ml Solution for Injection

2  QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2ml of solution contains 100mg (50mg in 1ml) of suxamethonium Chloride.

For the full list of excipients, see section 6.1.

3  PHARMACEUTICAL FORM

Solution for Injection.
Clear, colourless, sterile solution.

4  CLINICAL PARTICULARS

4.1  Therapeutic indications

Suxamethonium is a short acting depolarising neuromuscular blocking agent for producing muscular relaxation during anaesthesia. It is used in anaesthesia as a muscle relaxant to facilitate endotracheal intubation, mechanical ventilation and a wide range of surgical and obstetric procedures.

It is also used to reduce the intensity of muscle contractions associated with Pharmacologically or electrically-induced convulsions.

4.2  Posology and method of administration

Posology

The dosage for adults and children is dependent on body weight and the degree of muscular relaxation required. The usual single dose for an adult is in the range of 20 to 100mg intravenously, depending on the patient's body
weight and the degree of muscular relaxation required. Infants and young children are relatively resistant to suxamethonium.

Paediatric population: A suggested dose for children is in the range of 1 to 2mg/kg body weight, intravenously.

If necessary, the intramuscular route may be used and a dose up to 2.5mg/kg body weight may be given intramuscularly to adults or children to a maximum total of 150mg. For administration by continuous intravenous infusion, a 0.1 to 0.2% Solution may be used and the adult dose ranges from 2 to 5mg per minute.

Older people: Dosage requirements of suxamethonium in older patients are comparable to those for younger adults.

The elderly may be more susceptible to cardiac arrhythmias, especially if digitalis-like drugs are also being taken. See also 'Special warnings and precautions for use.

Method of Administration
Suxamethonium Chloride is usually administered by the intravenous route. It is given intravenously after anaesthesia has been induced and should not be administered to the conscious patient. Assisted respiration is necessary.

4.3 Contraindications

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

Suxamethonium should not be administered to a patient who is not fully anaesthetised. Neuromuscular function should be monitored when suxamethonium is being used over a prolonged period.

Suxamethonium causes a significant transient rise in intra-ocular pressure and therefore it should not be used in the presence of glaucoma, detached retina or open eye injury unless the potential benefit of its use outweighs the potential risk to the eye.

Suxamethonium is contra-indicated in patients with a personal or family history of malignant hyperthermia. Suxamethonium can trigger sustained myofibrillar contractions in susceptible individuals. If this occurs, all anaesthetic agents known to be associated with it (including suxamethonium) must be stopped and full supportive measures implemented immediately. Intravenous dantrolene sodium is the primary specific therapeutic drug and should be given as soon as possible after the diagnosis is made.

Suxamethonium is contra-indicated in patients with inherited atypical or low serum level of pseudocholinesterase.
An acute transient rise in serum potassium often occurs following the administration of suxamethonium in normal individuals; the magnitude of this rise is of the order of 0.5 mmol/litre. In certain pathological states or conditions this increase in serum potassium following suxamethonium administration may be excessive and cause serious cardiac arrhythmias and cardiac arrest.

For this reason the use of suxamethonium is contra-indicated in:

- Patients recovering from major trauma or severe burns; the period of greatest risk of hyperkalaemia is from about 5 to 70 days after the injury and may be further prolonged if there is delayed healing due to persistent infection.

- Patients with neurological deficits involving acute major muscle wasting (upper and/or lower motor neurone lesions); the potential for potassium release occurs within the first 6 months after the acute onset of the neurological deficit and correlates with the degree and extent of muscle paralysis. Patients who have been immobilised for prolonged periods of time may be at similar risk.

- Suxamethonium is also contra-indicated in patients with pre-existing hyperkalaemia. In the absence of hyperkalaemia and neuropathy, renal failure is not a contra-indication to the use of a normal single dose of suxamethonium, although multiple or large doses may cause clinically significant rises in serum potassium and should not be used.

- Patients with skeletal muscle myopathies e.g. Duchenne muscular dystrophy (increased risk of malignant hyperthermia, ventricular dysrhythmias and cardiac arrest secondary to acute rhabdomyolysis with hyperkalaemia - see above).

- Suxamethonium is contra-indicated in patients with cerebral palsy.

- Patients with a personal or family history of congenital myotonic diseases such as myotonia congenita and dystrophia myotonica (risk of severe myotonic spasms and rigidity).

### 4.4. Special Warnings and Precautions for Use

Suxamethonium paralyses the respiratory muscles as well as other skeletal muscles but has no effect on consciousness.

Suxamethonium should be administered only by or under close supervision of an anaesthetist who is familiar with its actions, characteristics and hazards, who is skilled in the management of artificial respiration and only where there are adequate facilities for immediate endotracheal intubation with the administration of oxygen by intermittent positive pressure ventilation.

Cross-sensitivity
High rates of cross-sensitivity (greater than 50%) between neuromuscular blocking agents have been reported. Therefore, where possible, before administering suxamethonium, hypersensitivity to other neuromuscular blocking agents should be excluded. Suxamethonium, should only be used when absolutely essential in susceptible patients. Patients who experience a hypersensitivity reaction under general anaesthesia should be tested subsequently for hypersensitivity to other neuromuscular blockers.

Suxamethonium should not be mixed in the same syringe with any other agent, especially thiopental.

Cholinesterase deficiency

In patients with low levels of plasma cholinesterase or with an abnormal pseudocholinesterase, suxamethonium should be used only with extreme caution and where the benefits of the drug are considered to outweigh the risks.

Suxamethonium is rapidly hydrolysed by plasma cholinesterase. Deficiencies of this enzyme result in prolonged and intensified neuromuscular block. Deficiency may be

- congenital (1/3,000 of the population)
- physiological (during pregnancy and purpurium)
- acquired (in conjunction with liver disease, malnutrition, carcinomatosis, pregnancy, uraemia/renal disease, connective tissue disorders, thyroid disorders, severe burns, severe generalised tetanus, tuberculosis and other severe or chronic infections). Recovery from suxamethonium may be delayed in liver disease due to low serum pseudocholinesterase levels, caution is advised.
- iatrogenic (during cardiopulmonary bypass, following plasma exchange/plasmapheresis, and with other drugs - see section 4.5).

With prolonged use of suxamethonium, the characteristic depolarising blockade (Phase I block) may change to one with characteristics of a non-depolarising blockade (Phase II block), leading to prolonged respiratory depression or apnoea. Although the characteristics of a developing Phase II block resemble those of a true non-depolarising block, the former cannot always be fully or permanently reversed by anticholinesterase agents. When a Phase II block is fully established, its effects will then usually be fully reversible with standard doses of neostigmine accompanied by an anticholinergic agent.

Tachyphylaxis occurs after repeated administration of suxamethonium.

It is inadvisable to use suxamethonium in patients with advanced myasthenia gravis, neurological disorders, myotonia or muscular disease.

Although patients with advanced myasthenia gravis are resistant to suxamethonium they develop a state of Phase II block which can result in delayed recovery.

Patients with myasthenic (Eaton-Lambert) syndrome are more sensitive than normal to suxamethonium and the dose should be reduced.
Caution should be exercised when using suxamethonium in children, since paediatric patients are more likely to have an undiagnosed myopathy or an unknown predisposition to malignant hyperthermia and rhabdomyolysis, which places them at increased risk of serious adverse events following suxamethonium (see section 4.3 Contraindications and section 4.8 Adverse Reactions).

Bradycardia and other cardiac dysrhythmias

In healthy adults, suxamethonium occasionally causes a mild transient slowing of the heart rate on initial administration. Bradycardias are more commonly observed in children and on repeated administration of suxamethonium in both children and adults. Pre-treatment with intravenous atropine or glycopyrrolate significantly reduces the incidence and severity of suxamethonium-related bradycardia.

In the absence of pre-existing or evoked hyperkalaemia, ventricular arrhythmias are rarely seen following suxamethonium administration. Cardiac arrhythmias can develop in patients receiving digitalis glycosides who are given suxamethonium. Patients taking digitalis-like drugs are however more susceptible to such arrhythmias. The action of suxamethonium on the heart may cause changes in cardiac rhythm including cardiac arrest.

Raised intra-ocular pressure (IOP)
Suxamethonium causes a transient increase in intraocular pressure and should not be used in the presence of penetrating eye injury except where the potential benefits outweigh the injury to the eye.

Suxamethonium should be used with caution in patients who have shown hypersensitivity to any neuromuscular blocking drug.

Hypothermia may prolong neuromuscular blocking action.

4.5. Interactions with other medicinal products and other forms of Interaction

Certain drugs or chemicals are known to reduce normal plasma cholinesterase activity and may therefore prolong the neuromuscular blocking effects of suxamethonium. These include:

Antibacterials
Enhanced effects of suxamethonium with
- Aminoglycosides
- Clindamycin, polymyxins and vancomycin
- Piperacillin

Antimalarials
- Quinine - effects of suxamethonium possibly enhanced

Antipsychotics
Enhanced effects of suxamethonium with
- Promazine
- Promethazine
- Chlorpromazine
- Phenelzine
- Lithium carbonate

General anaesthetic agents
- Propofol – increased risk of myocardial depression and bradycardia
- Volatile liquid GAs – enhanced effects of suxamethonium
- Ketamine and propanidid – possible prolonged block

Analgesics
Enhanced effects of suxamethonium with
- Morphine, morphine antagonists, pethidine, pancuronium,

Anti-arrhythmics
- Lidocaine (lignocaine) – enhanced and prolonged neuromuscular blockade
- Quinidine, procainamide and verapamil
- Beta-blockers

Local anaesthetics
Enhanced effects of suxamethonium with
- Procaine
- Cocaine
- Chloroprocaine
- Lidocaine (see above)

Cardiac glycosides
- Possible increased risk of bradycardia and other dysrhythmias, including ventricular dysrhythmias and cardiac arrest (also see sections 4.4 and 4.8).
- More susceptible to the effects of suxamethonium exacerbated by hyperkalaemia

Cytotoxics
Enhanced effects of suxamethonium with
- Cyclophosphamide
- Thiotepa
- Other alkylating agents (chlorethamine: tretamine)

Immunomodulators
- Azathioprine – prolonged neuromuscular blockade

Magnesium
- Parenteral magnesium – enhanced neuromuscular blockade

Metoclopramide
• Enhanced effects of suxamethonium

Parasympathetics
Enhanced effects of suxamethonium with
• Donepezil, edrophonium, galantamine, neostigmine, physostigmine, pyridostigmine and rivastigmine
• Tacrine hydrochloride

Sympathomimetics (beta agonists)
• Bambuterol and terbutaline – enhanced effects of suxamethonium

Anti-histamines
• Diphenhydramine – enhanced effects of suxamethonium

Volatile inhalational anaesthetic agents
• Halothane, enfurane, desflurane, isoflurane, diethylether and methoxyflurane have little effect on the Phase I block of Suxamethonium Chloride injection but will accelerate the onset and enhance the intensity of a Phase II suxamethonium-induced block.

Drugs known to reduce normal plasma cholinesterase
In addition to the drugs listed above, certain other drugs and chemicals are known to reduce normal plasma cholinesterase activity and therefore may prolong the neuromuscular effect of suxamethonium. These include
• Organophosphorous insecticides and metriphonate
• Ecothiopate eye drops (prolonged apnoea after suxamethonium has occurred)
• Trimetaphan
• Selective serotonin reuptake inhibitors (SSRI).

The following have potentially adverse effects on plasma cholinesterase activity
• Aprotinin
• Oestrogens and oral contraceptives
• Oxytocin
• High-dose steroids

Liver disease, cancer, pregnancy, dehydration, electrolyte imbalances and overdosage (due to excessive production of succinylmonocholine) may also prolong the action of suxamethonium.

4.6. Fertility, pregnancy and Lactation

Fertility and Pregnancy
No studies of the effect of suxamethonium on female fertility or pregnancy have been performed.
Suxamethonium has no direct action on the uterus or other smooth muscle structures. In normal therapeutic doses it does not cross the placental barrier in sufficient amounts to affect the respiration of the infant.

The benefits of the use of suxamethonium as part of a rapid sequence induction for general anaesthesia normally outweigh the possible risk to the foetus.

Plasma cholinesterase levels fall during the first trimester of pregnancy to about 70 to 80% of their pre-pregnancy values; a further fall to about 60 to 70% of the pre-pregnancy levels occurs within 2 to 4 days after delivery. Plasma cholinesterase levels then increase to reach normal over the next 6 weeks. Consequently, a high proportion of pregnant and puerperal patients may exhibit mildly prolonged neuromuscular blockade following Suxamethonium Injection.

Suxamethonium Chloride Injection should not be used unless clearly necessary.

Breast-Feeding
It is not known whether suxamethonium is excreted in breast milk, therefore, caution should be exercised following administration of suxamethonium to nursing mothers.

**4.7. Effects on Ability to Drive and Use Machines**

Suxamethonium chloride has a major influence on the ability of an individual to drive or operate machinery.

**4.8 Undesirable effects**

Adverse reactions are listed below by system organ class and frequency. Estimated frequencies were determined from published data. Frequencies are defined as follows:

- very common (≥1/10);
- common (≥1/100 and <1/10),
- uncommon (≥1/1,000 and <1/100);
- rare (≥1/10,000 and <1/1,000);
- very rare (<1/10,000).

**Immune system disorders**

- Very rare Anaphylactic reactions.

**Eye disorders**
### Common
- Increased intraocular pressure.

### Cardiac disorders
**Common**
- Bradycardia, tachycardia.
- Arrhythmias (including ventricular arrhythmias), cardiac arrest.

**Rare**

There are case reports of hyperkalaemia-related cardiac arrests following the administration of suxamethonium to patients with congenital cerebral palsy, tetanus, Duchenne muscular dystrophy, and closed head injury. Such events have also been reported rarely in children with hitherto undiagnosed muscular disorders.

### Vascular disorders
**Common**
- Skin flushing.

### Hypertension and hypotension have also been reported.

### Respiratory, thoracic and mediastinal disorders
**Rare**
- Bronchospasm, prolonged respiratory depression†, apnoea.

† Individuals with decreased plasma cholinesterase activity exhibit a prolonged response to suxamethonium. Approximately 0.05% of the population has an inherited cause of reduced cholinesterase activity.

Please refer to section 4.4 Special Warnings and Precautions for Use.

### Gastrointestinal disorders
**Very common**
- Increased intragastric pressure.
- Excessive salivation has also been reported

### Skin and subcutaneous tissue disorders
**Common**
- Rash.
- Muscle fasciculation, post-operative muscle pains (Please refer to section 4.4 Special Warnings and Precautions for Use).

**Very common**
- Myoglobinuria#

**Common**
- Myoglobinemia#

**Rare**
- Trismus

# Rhabdomyolysis has also been reported (see section 4.3 Contraindications and section 4.4 Special Warnings and Precautions
General disorders and administration site conditions

Malignant hyperthermia (Please refer to section 4.4 Special Warnings and Precautions for Use).

Investigations

Transient blood potassium increase.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9. Overdose

Apnoea and prolonged muscle paralysis are the main and serious effects of overdosage. It is essential to maintain the airway and to ensure adequate ventilation until spontaneous respiration occurs.

Neostigmine and other anticholinesterase drugs are not antidotes to suxamethonium but would normally intensify the depolarisation effect. However, in some cases when the action of suxamethonium is prolonged, the characteristic depolarising (Phase I) block may change to one with characteristics of a non-depolarising (Phase II) block.

The decision to use neostigmine to reverse a Phase II suxamethonium-induced block depends on the judgement of the clinician in the individual case. Valuable information in regard to this decision will be gained by monitoring neuromuscular function.

To investigate this possibility, the short-acting anticholinesterase drug, edrophonium, may be given intravenously. If an obvious improvement is maintained for several minutes, neostigmine may be given with atropine. Subsequently, the patient should be observed carefully and if apnoea recurs, a further dose of neostigmine is indicated.

Transfusion of fresh whole blood, frozen plasma, or other source of pseudocholinesterase will help the destruction of suxamethonium.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Peripherally acting muscle relaxants, choline derivatives, ATC code: M03AB01.

Short-acting depolarising neuromuscular blocking agent.

A cholinester of succinic acid, the cation formed by the succinic acid radical with the quaternary ammonium group at each end of the molecule is the active part. Deteriorates in hot climates.

A depolarising neuromuscular blocking drug of brief duration, its action being prolonged by repeated doses. Its action can be prolonged by various drugs or by a deficiency of cholinesterase due to liver disease or an inherited enzyme deficiency.

5.2. Pharmacokinetic Properties

Following intravenous administration, there is rapid hydrolysis by pseudocholinesterase with the initial metabolite being succinylmonocholine a weak neuro-muscular drug. This is metabolised to succinic acid with only a small amount excreted in the urine.

Only a small fraction of suxamethonium reaches the neuromuscular junction. Its action is terminated by diffusion away from the end plate. Succinylcholine does not readily cross the placenta.

5.3. Preclinical Safety Data

Genotoxicity:
No bacterial mutation assays have been conducted.
There are some data to suggest a weak clastogenic effect in mice, but not in patients who had received suxamethonium chloride.

Carcinogenicity:
Carcinogenicity studies have not been performed.

Embryo-foetal Development:
Animal reproduction studies have not been conducted with suxamethonium. It is also not known whether suxamethonium can affect reproductive capacity or cause foetal harm when administered to a pregnant woman.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients

Sodium Acetate
Water for Injections

6.2 Incompatibilities

This medicinal product must not be mixed in the same syringe with any other agent especially thiopentone.

6.3 Shelf Life

18 months

6.4 Special precautions for storage

Store in a refrigerator (2°-8°C).
Do not freeze.
Keep the ampoule in the outer carton in order to protect from light.

6.5 Nature and Contents of Container

2m1, clear glass ampoules, glass type I Ph.Eur. borosilicate glass, packed in cardboard cartons to contain 10 x 2ml ampoules.

6.6 Special precautions for disposal and other handling

For IM and IV injection.
If only part used, discard the remaining solution immediately after first use.

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

7 MARKETING AUTHORISATION HOLDER

MercuryPharm Ltd
4045, Kingswood Road,
City West Business Park,
Co Dublin, Ireland
8 MARKETING AUTHORISATION NUMBER(S)

PL 15372/0007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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