SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Suxamethonium Chloride Injection BP 50mg/ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Suxamethonium Chloride Injection BP 100mg in 2ml.
For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection.
Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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 muscular contractions associated with
pharmacologically or electrically-induced convulsions.

4.2 Posology and method of administration

Usually by bolus intravenous injection.

*Adults:* The dose is dependent on body weight, the degree of muscular relaxation
required, the route of administration, and the response of individual patients.
To achieve endotracheal intubation Suxamethonium Chloride is usually administered
intravenously in a dose of 1 mg/kg. This dose will usually produce muscular relaxation in
about 30 to 60 seconds and has a duration of action of about 2 to 6 minutes. Larger doses
will produce more prolonged muscular relaxation, but doubling the dose does not
necessarily double the duration of relaxation.
Supplementary doses of Suxamethonium Chloride of 50% to 100% of the initial dose administered at 5 to 10 minute intervals will maintain muscle relaxation during short surgical procedures performed under general anaesthesia.

For prolonged surgical procedures Suxamethonium Chloride may be given by intravenous infusion as a 0.1% to 0.2% solution, diluted in 5% glucose solution or sterile isotonic saline solution, at a rate of 2.5 to 4 mg per minute. The infusion rate should be adjusted according to the response of individual patients.

The total dose of Suxamethonium Chloride given by repeated intravenous injection or continuous infusion should not exceed 500 mg per hour.

**Children:** Infants and young children are more resistant to Suxamethonium Chloride compared with adults.

The recommended intravenous dose of Suxamethonium Chloride for neonates and infants is 2 mg/kg. A dose of 1 mg/kg in older children is recommended. When Suxamethonium Chloride is given as intravenous infusion in children, the dosage is as for adults with a proportionately lower initial infusion rate based on body weight. Suxamethonium Chloride may be given intramuscularly to infants at doses up to 4 to 5 mg/kg and in older children up to 4 mg/kg. These doses produce muscular relaxation within about 3 minutes. A total dose of 150 mg should not be exceeded.

**Use in the elderly:** Dosage requirements of Suxamethonium Chloride in the elderly 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’.

### 4.3 Contraindications

Suxamethonium Chloride has no effect on the level of consciousness and should not be administered to a patient who is not fully anaesthetised.

Hypersensitivity to suxamethonium may exist in rare instances, and Suxamethonium Chloride should not be administered to patients known to be hypersensitive to the drug.

As suxamethonium can act as a trigger of sustained myofibrillar contraction in susceptible individuals, Suxamethonium Chloride is contra-indicated in patients with a personal or family history of malignant hyperthermia. If this condition occurs unexpectedly, all anaesthetic agents known to be associated with its development (including Suxamethonium Chloride) must be immediately discontinued, and full supportive measures must be immediately instituted. Intravenous dantrolene sodium is the primary specific therapeutic drug and is recommended as soon as possible after the diagnosis is made.

Suxamethonium Chloride is contra-indicated in patients known to have an inherited atypical plasma cholinesterase activity.

An acute transient rise in serum potassium often occurs following the administration of Suxamethonium Chloride 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 Chloride administration may be excessive and cause serious cardiac arrhythmias and cardiac arrest. For this reason the use of Suxamethonium Chloride 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.

- Patients with pre-existing hyperkalaemia. In the absence of hyperkalaemia and neuropathy, renal failure is not a contraindication to the administration of a normal single dose of Suxamethonium Chloride Injection, but multiple or large doses may cause clinically significant rises in serum potassium and should not be used.

- Suxamethonium Chloride should be avoided in patients with a personal or family history of congenital myotonic diseases such as myotonia congenita and dystrophia myotonica since its administration may on occasion be associated with severe myotonic spasms and rigidity.

- Suxamethonium Chloride should not be used in patients with skeletal muscle myopathies e.g. Duchenne muscular dystrophy since its administration may be associated with malignant hyperthermia, ventricular dysrhythmias and cardiac arrest secondary to acute rhabdomyolysis with hyperkalaemia.

Suxamethonium causes a significant transient rise in intra-ocular pressure, and should therefore not be used in the presence of open eye injuries or where an increase in intra-ocular pressure is undesirable unless the potential benefit of its use outweighs the potential risk to the eye.

### 4.4 Special warnings and precautions for use

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

High rates of cross-sensitivity 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 Chloride should not be mixed in the same syringe with any other agent, especially thiopental.

During prolonged administration of Suxamethonium Chloride, it is recommended that the patient is fully monitored with a peripheral nerve stimulator in order to avoid overdosage.

Suxamethonium Chloride is rapidly hydrolysed by plasma cholinesterase which thereby limits the intensity and duration of the neuromuscular blockade.

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. Prolonged and intensified neuromuscular blockade following Suxamethonium Chloride Injection may occur secondary to reduced plasma cholinesterase activity in the following states or pathological conditions: physiological variation as in pregnancy and the puerperium; genetically determined abnormal plasma cholinesterase; severe generalised tetanus, tuberculosis, other severe or chronic infections; following severe burns; chronic debilitating disease, malignancy, chronic anaemia and malnutrition; end-stage hepatic failure, acute or chronic renal failure; autoimmune diseases: myxoedema, collagen diseases; iatrogenic: following plasma exchange, plasmapheresis, cardiopulmonary bypass, and as a result of concomitant drug therapy (see Interactions).

If Suxamethonium Chloride is given over a prolonged period, the characteristic depolarising neuromuscular (or Phase I) block may change to one with characteristics of a non-depolarising (or Phase II) block. 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 Chloride.

Muscle pains are frequently experienced after administration of suxamethonium and most commonly occur in ambulatory patients undergoing short surgical procedures under general anaesthesia. There appears to be no direct connection between the degree of visible muscle fasciculation after Suxamethonium Chloride administration and the incidence or severity of pain. The use of small doses of nondepolarising muscle relaxants given minutes before suxamethonium administration has been advocated for the reduction of incidence and severity of suxamethonium-associated muscle pains. This technique may require the use of doses of suxamethonium in excess of 1mg/kg to achieve satisfactory conditions for endotracheal intubation.

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).
In patients with severe sepsis, the potential for hyperkalaemia seems to be related to the severity and duration of infection.

It is inadvisable to administer Suxamethonium Chloride to patients with advanced myasthenia gravis. Although these patients 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 Chloride, necessitating dosage reduction.

In healthy adults, Suxamethonium Chloride 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. 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.

4.5 Interaction 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 Chloride. These include: organophosphorous insecticides and metriphonate; ecothiopate eye drops; trimetaphan; specific anticholinesterase agents: neostigmine, pyridostigmine, physostigmine, edrophonium; tacrine hydrochloride; cytotoxic compounds: cyclophosphamide, mechlorethamine, triethylene-melamine, and thiopeta; psychiatric drugs: phenelzine, promazine and chlorpromazine; anaesthetic agents and drugs: ketamine, morphine and morphine antagonists, pethidine, pancuronium, propanidid.

Other drugs with potentially deleterious effects on plasma cholinesterase activity include aprotinin, diphenhydramine, promethazine, oestrogens, oxytocin, high-dose steroids, and oral contraceptives, terbutaline and metoclopramide.

Certain drugs or substances may enhance or prolong the neuromuscular effects of Suxamethonium Chloride by mechanisms unrelated to plasma cholinesterase activity. These include: magnesium salts; lithium carbonate; quinine and chloroquine; antibiotics such as the aminoglycosides, clindamycin and polymyxins; antiarrhythmic drugs: quinidine, procainamide, verapamil, beta-blockers, lidocaine and procaine; volatile inhalational anaesthetic agents: halothane, enflurane, 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.

Patients receiving digitalis-like drugs are more susceptible to the effects of suxamethonium-exacerbated hyperkalaemia.
4.6 Pregnancy and lactation

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 Chloride injection.

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

4.7 Effects on ability to drive and use machines

Not applicable.

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.

Rare: Arrhythmias (including ventricular arrhythmias), cardiac arrest.

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.

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.

Musculoskeletal and connective tissue disorders

Very common: Muscle fasciculation, post-operative muscle pains (Please refer to section 4.4 Special Warnings and Precautions for Use).

Common: Myoglobininaemia*, myoglobinuria*.

Rare: Trismus

* Rhabdomyolysis has also been reported (see section 4.3 Contraindications and section 4.4 Special Warnings and Precautions for Use)

General disorders and administration site conditions

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

Common: Transient blood potassium increase.

4.9 Overdose

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

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.

If neostigmine is used its administration should be accompanied by appropriate doses of an anticholinergic agent such as atropine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Suxamethonium is closely related in structure to acetylcholine. Suxamethonium is quickly hydrolysed by plasma cholinesterase. Suxamethonium acts on the skeletal muscle motor endplate just like acetylcholine as an agonist, to cause flaccid paralysis of muscle (phase 1 block). Suxamethonium diffuses slowly to the endplate and the concentration at the endplate persists for long enough to cause loss of electrical excitability. The depolarisation of the muscle endplate establishes a voltage gradient and this causes opening of voltage-dependent ion channels of the muscle leading to transient contraction of the muscle. Although the end-plate stays depolarised, the muscle membrane accounts for this depolarisation and remains flaccid. If suxamethonium is kept continuously present during infusion, the junctional membrane slowly regains its resting potential with the return of neuromuscular transmission; to maintain the effect, a higher infusion rate is required (tachyphylaxis). With continued infusion, neuromuscular transmission will fail again (phase 2 block) even though the membrane potential of the end-plate stays unchanged and normal or near normal. A phase 2 block has clinical characteristics of a non-depolarising block. A phase 2 block may be associated with prolonged neuromuscular blockade and apnoea. The mechanism of this block is not known but channel blocking by penetration of suxamethonium into the sub-end plate cytoplasm, intracellular accumulation of calcium and
sodium, the loss of intracellular potassium, and activation of Na,K-ATPase all contribute.

5.2. Pharmacokinetic Properties

Neuromuscular-blocking drugs are used mainly in anaesthesia to produce muscle relaxation. Although complete relaxation can be produced by anaesthetic drugs alone, the concentrations needed to obliterate spinal reflexes are high and it is much more satisfactory to produce paralysis by blocking neuromuscular transmission. The drugs are given intravenously, and act within about 30 to 60 seconds. Suxamethonium acts for about 2 to 6 minutes, being hydrolysed by plasma cholinesterase (pseudocholinesterase). One molecule of choline is split off rapidly to form succinylmonocholine (a weak muscle relaxant), which is then slowly hydrolysed to succinic acid and choline. Only a small proportion of suxamethonium is excreted unchanged in the urine.

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

Hydrochloric Acid
6.2. Incompatibilities

Suxamethonium Chloride is rapidly destroyed by alkalis and should not be mixed with alkaline injections such as thiopentone sodium. In combination with barbiturates, either free barbituric acid will precipitate or the Suxamethonium Chloride will be hydrolysed depending on the final pH of the admixture. Suxamethonium should not be mixed with barbiturates in the same syringe or given simultaneously through the same needle. A haze forms in 30 minutes when Suxamethonium Chloride 0.5 or 1mg in 4ml is mixed with methohexital sodium 100mg in 10ml.

Due to the potentially large number of incompatibilities, other drugs should not be mixed in the syringe.

6.3 Shelf life

18 months. Suxamethonium Chloride 50 mg/ml BP may be stored for short periods at temperatures not exceeding 25°C, but should be returned to the fridge, whenever possible. Once initially removed from refrigerated storage the product should be discarded after 28 days. Storage up to 25°C should only occur in exceptional circumstances.

6.4 Special precautions for storage

Store between 2 – 8 °C. Do not freeze. Keep in the outer carton.

6.5. Nature and Contents of Container

Prefilled syringe of clear Type 1 glass (2ml).

6.6 Special precautions for disposal

For intravenous injection under medical direction.

Use once and discard any remaining solution.
No needle is provided with this syringe

7. MARKETING AUTHORISATION HOLDER

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