

Summary of Product Characteristics

1. **NAME OF THE MEDICINAL PRODUCT**

Suxamethonium Chloride Injection BP 100mg/2ml.

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each 2ml of solution contains Suxamethonium Chloride 100mg (50mg/ml)

For a full list of excipients, see section 6.1

3. **PHARMACEUTICAL FORM**

Solution for injection or infusion.

Clear colourless sterile solution.

4. **CLINICAL PARTICULARS**

4.1 Therapeutic indications

As a short-acting neuromuscular blocking agent for muscle relaxation during anaesthesia, including that for electroconvulsive therapy.

4.2 Posology and method of administration

Method administration: Intravenous or Intramuscular.

Intravenous:

Adults: The usual dose is 20 to 100mg, which may be repeated if necessary. For electroconvulsive therapy, the usual dose is 0.5 to 0.75mg/kg body weight.

Children: 1 to 2mg/kg body weight.

Neonates: 1 to 2mg, followed by 0.25 to 0.5mg/kg supplements to a maximal dose of 50mg.

Continuous Intravenous Infusion:

500mg Suxamethonium Chloride Injection B.P. in 500ml sterile isotonic saline solution, giving a dilution of 0.1%, may be administered at a rate of 2.5 - 5.0mg per minute in an adult, and at a proportionately lower rate in children, depending on bodyweight.

Intramuscular:

Infants and children: 2mg/kg bodyweight to a maximum total dose of 150mg.

Use in the elderly:

Dosage requirements of Suxamethonium Chloride Injection BP in the elderly are comparable to those of younger adults.

4.3 Contraindications

Use in patients with a history of previous prolonged apnoea after suxamethonium or in those with atypical 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 0.5mmol/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 contraindicated in the following patients:

- Patients recovering from major trauma or severe burns; the period of the greatest risk of hyperkalaemia is from 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 six 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 also 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 single dose of suxamethonium, but multiple or large doses may cause clinically significant rises in serum potassium and should not be used.

Use in patients with Duchenne muscular dystrophy, congenital cerebral palsy, ventricular dysrhythmias, secondary to acute rhabdomyolysis with hyperkalaemia, motor neurone lesions, tetanus and uremia.

Hypersensitivity to the active ingredient.

Penetrating wounds of the eye.

Use in any patient who is not fully anaesthetised.

Personal or family history of malignant hyperthermia.

4.4 Special warnings and precautions for use

This product must be administered only by anaesthetists familiar with its use, and where facilities for controlled respiration and insufflation with oxygen are available for immediate use.

While a single dose of this drug normally causes a depolarising block, repeated doses may cause a non-depolarizing block.

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 administration and the incidence or severity of pain.

This agent may cause a bradycardia and may potentiate the bradycardia due to halothane or other agents. This should be borne in mind when such agents are used during anaesthetic procedures and use should be preceded by atropine. Continuous infusion may give rise to tachycardia and rise in blood pressure.

This product may cause cardiac arrhythmias and ventricular fibrillation in states of hyperkalaemia. Appropriate resuscitative equipment should be to hand in such cases where use of suxamethonium is unavoidable.

Approximately one person in three thousand is unable to hydrolyze suxamethonium, due to presence of abnormal serum cholinesterase (atypical pseudocholinesterase). When administering suxamethonium for the first time, it is recommended that the dose does not exceed 30 to 50mg in order to avoid prolonged apnoea.

This agent should be used with caution in ill and cachectic patients, in patients with malignant hyperthermia and rhabdomyolysis acid-base disturbances or electrolyte imbalance, parenchymatous liver disease, obstructive jaundice, carcinomatosis, in those in contact with certain insecticides, e.g. organophosphorous compounds and in those receiving therapeutic radiation.

Caution should be exercised when this drug is used in neonates, since they are relatively resistant to its action and may develop a phase 2 (non depolarizing) block rapidly.

This agent causes a temporary rise in intraocular pressure.

This agent should be administered with particular caution to patients with myasthenia gravis, as administration may lead to a dual block, from which recovery is neither as rapid nor complete as in normal patients.

This agent may give rise to allergic reactions including bronchospasm.

Muscarinic effects of this compound e.g. increased bronchial and salivary secretions may be prevented by atropine.

When this agent is given as an infusion, this should be monitored with care to avoid overdose.

Suxamethonium administration has been associated with the onset of malignant hyperthermia. This risk appears to increase with concomitant administration of volatile anaesthesia. If the condition occurs unexpectedly, all anaesthetic agents known to be associated with its development must be immediately discontinued and full supportive measures must be immediately instituted. Intravenous dantrolene sodium is recommended as an adjunct to supportive measures in the management of this problem.

This agent should not be mixed with other compounds.

A single intravenous dose of 50mg of this agent paralyzes from 2 to 4 minutes. Apnoea lasting longer than 15 minutes after such a dose in an adequately oxygenated patient is evidence of abnormal response.

Certain individuals may express a variant cholinesterase that hydrolyses suxamethonium more rapidly than is normally observed, which may manifest as resistance to suxamethonium or as shortening of the duration of neuromuscular blockade. Its elevation may not be detected by routine laboratory assessments of cholinesterase activity. The incidence of expression of one cholinesterase variant has been reported as 9% in Europe.

4.5 Interactions with other medicinal products and other forms of interaction

Neostigmine and related compounds potentiate the action of suxamethonium as does propanidid and tacrine. Ecothiopate eye drops should be discontinued prior to general anaesthesia.

The effects of this agent may be potentiated by antibiotics of the aminoglycoside and polypeptide groups and also by a low body temperature.

Suxamethonium may potentiate bradycardia due to halothane or other drugs used concomitantly.

Antineoplastic drugs, such as cyclophosphamide and thiotepa, may prolong the neuromuscular block of suxamethonium.

4.6 Pregnancy and lactation

At normal therapeutic doses, suxamethonium does not cross the placental barrier in sufficient amounts to affect the respiration of the infant. However, the drug should be used during pregnancy only if the potential benefit outweighs any possible risks to the foetus.

Plasma cholinesterase levels fall during pregnancy and may not return to normal levels until several weeks postpartum. Therefore, a high proportion of pregnant and puerperal patients may have some prolongation of neuromuscular blockade following suxamethonium injection.

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 ($\geq 1/10$); common ($\geq 1/100$ and $<1/10$), uncommon ($\geq 1/1,000$ and $<1/100$); rare ($\geq 1/10,000$ 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's 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 and circulatory collapse (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: Myoglobinaemia, myoglobinuria

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

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

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

If a phase II block develops, the decision to use an anticholinesterase will depend on the judgement of the clinician in the individual case. If neostigmine is used, it should be accompanied by appropriate dose of an anticholinergic drug such as atropine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Suxamethonium is a depolarising muscle relaxant. It acts as an acetylcholine agonist by combining with cholinergic receptors of the motor end-plate to produce depolarisation. The depolarisation, which is prolonged, may produce transient muscle fasciculation.

Suxamethonium is resistant to breakdown by acetylcholinesterase.

5.2 Pharmacokinetic properties

Following intravenous injection, suxamethonium acts in about 30 to 60 seconds and has a duration of action of about 2 to 6 minutes. After intramuscular injection, it acts in 2 to 3 minutes and has a duration of action of about 10 to 30 minutes.

After injection, suxamethonium is rapidly hydrolysed by pseudocholinesterase (plasma cholinesterase) to succinylmonocholine, which has weak muscle-relaxant properties. Further metabolism yields succinic acid and choline. Only a small proportion of suxamethonium is excreted unchanged in the urine. The gene controlling production of pseudocholinesterase exhibits polymorphism and enzyme activity varies between individuals.

5.3 Preclinical safety data

No further information other than that which is included in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium acetate
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

18 months.

For single use only, any unused solution should be discarded.

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C)
Do not freeze.
Keep ampoules in the outer carton.

6.5 Nature and contents of container

2ml, clear glass ampoules, type 1 Ph.Eur. borosilicate glass packed in cardboard cartons to contain 10 x 2ml ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7. **MARKETING AUTHORIZATION HOLDER**

Antigen Pharmaceuticals Ltd.
Chandler House
Castle Street
Roscrea
Co Tipperary
Ireland

8. **MARKETING AUTHORIZATION NUMBER**

PA 73/110/1

9. **DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION**

Date of first authorisation: 20 December 1988
Date of last renewal: 20 December 2008

10. **DATE OF REVISION OF THE TEXT**

25 March 2010