SUXAMETHONIUM CHLORIDE FRESENIUS 100 mg/2 ml

Description
Clear, colourless sterile solution in 2 ml amber glass ampoules.

Composition
Each 2 ml ampoule contains 100 mg of suxamethonium chloride.

Mode of Action
Suxamethonium chloride is a depolarizing, neuromuscular blocking agent. The initial effect is to depolarize the membrane in the same manner as acetylcholine, but more persistently, which results in a brief period of firing manifested by transient muscular fasciculation. This phase is succeeded shortly by neuromuscular paralysis, the mechanism and even the primary site of which are still uncertain and controversial.

Summary of Pharmacodynamics and Pharmacokinetics
After injection, suxamethonium is rapidly hydrolysed by pseudocholinesterase (plasma cholinesterase) in plasma. One molecule of choline is split off rapidly to form succinylmonocholine which is then slowly hydrolysed to succinic acid and choline. Only a small proportion of suxamethonium is excreted unchanged in the urine.

Following intravenous injection suxamethonium chloride acts in about 30 to 60 seconds and has a duration of action of about 2 to 6 minutes. Following intramuscular injection it acts in 2 to 3 minutes and has a duration of action of about 10 to 30 minutes. It is used in surgical and other procedures in which a rapid onset and brief duration of muscle relaxation is needed, as in intubation endoscopies and electroconvulsive therapy.

Indications
Suxamethonium 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 muscular contractions associated with pharmacologically or electrically-induced convulsions.

Side Effects/Adverse Reaction
Prolonged neuromuscular blockade and apnoea may occur in patients with low serum concentrations of pseudocholinesterase and in those with an atypical pseudocholinesterase. The same conditions could result when excessive amounts of suxamethonium accumulate at the neuromuscular junction, for example following high or repeated doses. Tachyphylaxis may occur with repeated doses. The nature of the block may change to one with characteristics similar to competitive block. This is known as phase II block.

The administration of suxamethonium results in transient fasciculations during the onset of depolarizing block. Rhabdomyolysis, myoglobinuria have been reported and may be associated with muscle damage following fasciculations.

Malignant hyperpyrexia is a less frequent complication in patients anaesthetized with halothane and nitrous oxide or other general anaesthetic agents and has been increasingly associated with concomitant administration of Suxamethonium; it occurs in subjects with musculoskeletal disorders and also in apparently healthy individuals who, it has been suggested, might be genetically predisposed to this syndrome. The symptoms are increasing hyperthermia with or without muscular hypertonicity, often fatal cardiovascular complications, severe acidosis, hyperkalaemia, and haemoglobinuria or myoglobinuria.

Hypersensitivity reactions to suxamethonium have been reported and bronchospasm has occasionally occurred. Muscular pain similar to that following strenuous exercise may occur in the immediate postoperative period, particularly in patients who are ambulant but it is not related to dosage or the degree of fasciculation. A transient rise in intra-gastric pressure may occur secondary to abdominal muscle fasciculation.

Suxamethonium also causes a transient rise in intra-ocular pressure, and salivary gland enlargement. There may be some increase in bowel movements and in gastric, bronchial and salivary secretion due to the muscarinic action of suxamethonium. It is not generally recommended in uraemic patients especially those with high serum-potassium concentrations.

Depolarisation of skeletal muscle produces an immediate increase in plasma-potassium concentration and this can have serious consequences in some patients.

Stimulation of the vagus nerve and parasympathetic ganglia by suxamethonium chloride may be followed by bradycardia, other arrhythmias, and hypotension. This may be exacerbated by the raised plasma-potassium concentration. Cardiac arrest has been reported. Tachycardia and an increase in blood pressure due to stimulation of sympathetic ganglia has also been reported.

Direct release of histamine from mast cells occurs. Flushing, skin rash, bronchospasm and shock have been reported.

Warning/Precautions
Prolonged apnoea occurs in patients with low serum concentrations of pseudocholinesterase and in those with an atypical pseudocholinesterase. Hypothermia may enhance the neuromuscular blocking effects of suxamethonium chloride and an increase in body temperature may reduce them. Many drugs may interact with suxamethonium. The mechanism of action may be due to a direct effect on neuromuscular transmission and alteration of enzyme activity.

Suxamethonium may interact with the following substances to produce prolonged paralysis; some aminoglycoside or polypeptide antibiotics administered by intraperitoneal injection, magnesium sulphate, narcotic analgesics, propanidid, quinidine, cyclophosphamide, cimetidine, metoclopramide, phenelzine, oestrogens, bambuterol. Tachyphylaxis and phase II block develop earlier and after smaller total doses of suxamethonium when inhalation anaesthetics are used. Bradycardia due to suxamethonium may be enhanced by halothane or cyclopropane but diminished or prevented by thiopentone. Administration of suxamethonium before or after the use of non-polarising relaxants such as tubocurarine may cause a mixed block. Procaine, cocaine and chloroprocaine may competitively enhance the neuromuscular blocking activity of suxamethonium. The depolarizing effects of suxamethonium may also be enhanced by neostigmine and other anticholinesterases; it has been recommended that eye-drops containing a long-acting anticholinesterase such as ecothiopate should be discontinued at least 2 weeks before the administration of suxamethonium.

The effects of digitalis may be enhanced by suxamethonium, leading to cardiac arrhythmias.

Contraindication
Suxamethonium chloride is contra-indicated in patients who have suffered burns, exhibit myotonia and muscular denervation and muscular dystrophies or are known to have atypical pseudocholinesterase. A family history of malignant hyperthermia is also a contra-indication.
It is also contra-indicated in patients with bone fractures, renal impairment with a raised plasma-potassium concentration, severe long-lasting sepsis, and severe hyperkalaemia.
Suxamethonium chloride is contra-indicated in patients with glaucoma, penetrating wounds of eye or while the eyeball is open, or after initial surgers in massively traumatised patients. Its use is also inadvisable in patients with advanced myasthenia gravis, neurological defects or phaeochromocytoma.
The safety of suxamethonium chloride has not been established in pregnancy and lactation.

Recommended Dose and Directions for Use
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 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 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 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 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 compared with adults. The recommended intravenous dose of suxamethonium for neonates and infants is 2 mg/kg. A dose of 1 mg/kg in older children is recommended.
When suxamethonium 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 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 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.

Use in Pregnancy and Lactation:
The safety of suxamethonium chloride has not been established in pregnancy and lactation.
Pregnancy:
Mildly prolonged maternal paralysis may occur.
Lactation:
No information available.

Interaction With Other Medicaments/Drug Interactions
- ACE inhibitors and angiotensin-II antagonists: enhanced hypotensive effects with baclofen and tizanidine.
- Alcohol: enhanced sedative effect with baclofen, methocarbamol and tizanidine.
- Anaesthetics General: effects of non-depolarizing muscle relaxants enhanced by enflurane and other inhalation anaesthetics.
- Analgesics: ibuprofen and possibly other NSAIDs reduce excretion of baclofen (increased risk of toxicity)
- Anti-arrhythmics: procainamide and quinidine enhance muscle relaxant effect; lidocaine prolongs action of suxamethonium
- Antibacterials: effects of non-depolarizing muscle relaxants enhanced by aminoglycosides, clindamycin, colistin and piperacillin.
- Antidepressants: effect of non-depolarizing muscle relaxants antagonized by carbamazepine and phenytoin (recovery from neuromuscular blockade accelerated).
- Antihypertensives: enhanced hypotensive effect with baclofen and tizanidine.
- Anxiolytics and Hypnotics: enhanced sedative effects with baclofen and tizanidine.
- Beta-blockers: propranolol enhances muscle relaxant effect; possible enhanced hypotensive effect and bradycardia with tizanidine.
- Botulinum Toxin: neuromuscular block enhanced by non-depolarizing muscle relaxants (risk of toxicity).
- Calcium-channel blockers: nifedipine and verapamil enhance effect of non-depolarizing muscle relaxants; hypotension, myocardial depression, and hyperkalaemia reported with intravenous dantrolene and verapamil; risk of arrhythmias with diltiazem and intravenous dantrolene.
- Cardiac glycosides: arrhythmias if suxamethonium given with digoxin; possible bradycardia if tizanidine given with digoxin.
- Cytotoxics: cyclophosphamide and thiotepa enhance effects of suxamethonium.
- Diuretics: enhanced hypotensive effect with baclofen and tizanidine.
- Dopaminergics: agitation, confusion and hallucinations possible with baclofen and levodopa.
- Lithium: lithium enhances muscle relaxant effect; baclofen possible aggravates hyperkinesis.
- Magnesium salts: parenteral magnesium enhances effect of non-depolarizing muscle relaxants.
- Memantine: effect of baclofen and dantrolene possibly modified by memantine.
- Parasympathomimetics: ecothiopate eye-drops, edrophonium, galantamine, neostigmine, pyridostigmine, rivastigmine and possibly donepezil enhance effect of suxamethonium but antagonize effects of non-depolarizing muscle relaxants.
- Sympathomimetics: bambuterol enhances effect of suxamethonium.

Incompatibilities
Suxamethonium should not be combined with other aqueous solutions of medicaments except with intravenous solution of 5% sodium chloride.

Symptoms and Treatment of Overdose
See side effects and special precautions. Prolonged apnoea should be treated by assisted respiration with nitrous oxide and oxygen until spontaneous respiration is fully restored. Transfusion of fresh whole blood, frozen plasma, or other source of pseudocholinesterase will help the destruction of the suxamethonium. Neostigmine should not be used.
Sometimes, though not always, when the action of suxamethonium is prolonged, the myoneural block ceases. Assisted respiration should be continued until spontaneous respiration begins to return. A short acting anticholinesterase such as edrophonium 10 mg may then be given intravenously. If an obvious improvement is maintained for several minutes, neostigmine, 1 to 2 mg, may be given. The immediate use of neostigmine is not advisable owing to the difficulty of determining the nature of the block.

Presentation
This injection is available in 2 ml.
10 ampoules are packed into one polystyrene box or printed outer carton box.

Storage Condition
Protect from light and store in a refrigerator 2 to 8 °C. Keep out of reach of children.

Shelf Life
The injections can be used up to 18 months from the date of manufacture if kept as recommended.

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Date of revision of package insert
March 2019

12-1303/03-19
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