

PRESCRIBING INFORMATION

 Succinylcholine Chloride Injection
20 mg/mL
USP
Sterile Solution

Neuromuscular Blocking Agent

Alveda Pharmaceuticals Inc.
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Control no. 165084

Date of Preparation:

August 29, 2014

PRESCRIBING INFORMATION

NAME OF DRUG

Succinylcholine Chloride Injection

THERAPEUTIC CLASSIFICATION

Neuromuscular Blocking Agent

ACTION AND CLINICAL PHARMACOLOGY

Succinylcholine is an ultra short-acting, depolarizing-type, skeletal muscle relaxant. As does acetylcholine, it combines with the cholinergic receptors of the motor end plate to produce depolarization. This depolarization may be observed as fasciculations. Subsequent neuromuscular transmission is inhibited so long as adequate concentration of succinylcholine remains at the receptor site. Onset of flaccid paralysis is rapid (less than one minute after i.v. administration), and with single administration lasts approximately 4 to 6 minutes.

Succinylcholine is rapidly hydrolysed by plasma cholinesterase to succinylmonocholine (which possesses clinically insignificant depolarizing muscle relaxant properties) and then more slowly to succinic acid and choline (see **PRECAUTIONS**). About 10% of the drug is excreted unchanged in the urine. The paralysis following administration of succinylcholine chloride is progressive, initially involving consecutively the levator muscles of the face, muscles of the glottis and finally the intercostals and the diaphragm and all other skeletal muscles.

Succinylcholine has no direct action on the uterus or other smooth muscle structures. Because it is highly ionized and has low fat solubility, it does not readily cross the placenta.

Tachyphylaxis occurs with repeated administration (see **PRECAUTIONS**).

Depending on the dose and duration of succinylcholine administration, the characteristic depolarizing neuromuscular block (Phase I block) may change to a block with characteristics superficially resembling a nondepolarizing block (Phase II block). This may be associated with prolonged respiratory muscle paralysis or weakness in patients who manifest the transition to Phase II block. When this diagnosis is confirmed by peripheral nerve stimulation, it may sometimes be reversed with anticholinesterase drugs such as neostigmine (see **PRECAUTIONS**). Anticholinesterase drugs may not always be effective. If given before succinylcholine is metabolized by cholinesterase, anticholinesterase drugs may prolong rather than shorten paralysis.

Succinylcholine has no direct effect on the myocardium. Succinylcholine stimulates both autonomic ganglia and muscarinic receptors which may cause changes in cardiac rhythm, predominantly bradycardia and occasional asystoles. Changes in rhythm including cardiac arrest, may also result from vagal stimulation, which may occur during surgical procedures, or from hyperkalemia, particularly in children (see **PRECAUTIONS-Pediatric Use**). These effects are enhanced by halogenated anesthetics.

Succinylcholine causes an increase in intraocular pressure immediately after its injection and during the fasciculation phase, and causes slight increases which may persist after onset of complete paralysis (see **WARNINGS**).

Succinylcholine may cause slight increases in intracranial pressure immediately after its injection and during the fasciculation phase (see **PRECAUTIONS**).

As with other neuromuscular blocking agents, the potential for releasing histamine is present following succinylcholine administration. Signs and symptoms of histamine-mediated release such as flushing, hypotension and bronchoconstriction are, however, uncommon in normal clinical usage.

Succinylcholine has no effect on consciousness, pain threshold or cerebation. It should be used only with adequate anesthesia (see **WARNINGS**).

The onset and duration of action of succinylcholine may be altered by dehydration and electrolyte imbalance, and by the use of other medications such as depolarizing or non-depolarizing muscle relaxants.

INDICATIONS AND CLINICAL USE

Succinylcholine chloride is indicated as an adjunct to general anesthesia, to facilitate tracheal intubation, and to provide skeletal muscle relaxation during surgery or mechanical ventilation.

CONTRAINDICATIONS

Succinylcholine is contraindicated in persons with personal or familial history of malignant hyperthermia, skeletal muscle myopathies, and known hypersensitivity to the drug.

It is also contraindicated in patients after the acute phase of injury following major burns, multiple trauma, extensive denervation of skeletal muscle, or upper motor neuron injury, unless clinical circumstances require immediate securing of the airway, because succinylcholine administered to such individuals may result in severe hyperkalemia which may result in cardiac arrest (see **WARNINGS**). The risk of hyperkalemia in these patients increases over time and usually peaks at 7 to 10 days after the injury. The risk is dependent on the extent and location of the injury. The precise time of onset and the duration of the risk period are not known.

Acute rhabdomyolysis with hyperkalemia can occur when used in individuals with a skeletal muscle myopathy such as Duchenne's muscular dystrophy (see **PRECAUTIONS – Pediatric Use**).

WARNINGS

In infants and children, especially in boys under eight years of age, the rare possibility of inducing life-threatening hyperkalemia in undiagnosed myopathies by the use of succinylcholine must be balanced against the risk of alternative means of securing the airway.

Succinylcholine should be used only by those skilled in the management of artificial respiration and only when facilities are instantly available for tracheal intubation and for providing adequate ventilation of the patient, including the administration of oxygen under positive pressure and the elimination of carbon dioxide. The clinician must be prepared to assist or control respiration.

To avoid distress to the patient, succinylcholine should not be administered before unconsciousness has been induced. In emergency situations, however it may be necessary to administer succinylcholine before unconsciousness is induced.

Succinylcholine is metabolized by plasma cholinesterase and should be used with caution, if at all, in patients known to be or suspected of being homozygous for the atypical plasma cholinesterase gene.

Hyperkalemia

Succinylcholine should be administered with **GREAT CAUTION** to patients suffering from hyperkalemia because in these circumstances succinylcholine may induce serious cardiac arrhythmias or cardiac arrest due to hyperkalemia.

GREAT CAUTION should be observed if succinylcholine is administered to patients during the acute phase of injury following major burns, multiple trauma, extensive denervation of skeletal muscle, or upper motor neuron injury (see **CONTRAINDICATIONS**). The risk of hyperkalemia in these patients increases over time and usually peaks at 7 to 10 days after the injury. The risk is dependent on the extent and location of the injury. The precise time of onset and the duration of the risk period are undetermined. Patients with chronic abdominal infection, subarachnoid hemorrhage, or conditions causing degeneration of central and peripheral nervous systems should receive succinylcholine with **GREAT CAUTION** because of the potential for developing severe hyperkalemia.

Immediate treatment of hyperkalemia should include hyperventilation, i.v. calcium, i.v. sodium bicarbonate and I.V. glucose (with or without insulin).

Malignant Hyperthermia

Succinylcholine administration has been associated with acute onset of malignant hyperthermia, a potentially fatal hypermetabolic state of skeletal muscle. The risk of developing malignant hyperthermia following succinylcholine administration increases with the concomitant administration of volatile anesthetics. Malignant hyperthermia frequently presents as intractable spasm of the jaw muscles (masseter spasm) which may progress to generalized rigidity, increased oxygen demand, tachycardia, tachypnea and profound hyperpyrexia.

Successful outcome depends on recognition of early signs, such as jaw muscle spasm, increase of end-tidal carbon dioxide concentrations, or generalized rigidity to initial administration of succinylcholine for tracheal intubation, or failure of tachycardia to respond to deepening anesthesia. Skin mottling, rising temperature and coagulopathies may occur later in the course of the hypermetabolic process. In short procedures, these symptoms and signs may not appear until the patient is in the recovery room. Recognition of the syndrome is a signal for discontinuance of anesthesia, attention to increased oxygen consumption, requirement for a marked increase in

minute ventilation to correct respiratory acidosis, supplementary i.v. bicarbonate to control metabolic acidosis, support of circulation, assurance of adequate urinary output and institution of measures to control rising temperature. Dantrolene sodium, intravenously, is recommended as an adjunct to supportive measures in the management of this problem. Consult literature references and the dantrolene prescribing information for additional information about the management of malignant hyperthermic crisis. Continuous monitoring of temperature and expired CO₂ is recommended as an aid to early recognition of malignant hyperthermia.

Other

In adults the incidence of bradycardia, which may progress to asystole, is greater after a second dose of succinylcholine. In infants and young children, bradycardia and transient asystole may occur after one dose of succinylcholine. The incidence and severity of bradycardia is greater in infants and children than in adults. Pretreatment with anticholinergic agents (e.g. atropine), in most cases, will reduce the occurrence of bradyarrhythmias.

Succinylcholine causes an increase in intraocular pressure. It should not be used in instances in which an increase in intraocular pressure is undesirable (e.g. narrow angle glaucoma, penetrating eye injury) unless the potential benefit of this use outweighs the potential risk.

Succinylcholine is acidic (pH = 3.5) and should not be mixed with alkaline solutions having a pH greater than 8.5 (e.g. barbiturate solutions) (see **PHARMACEUTICALS INFORMATION, Stability - Compatibility**).

PRECAUTIONS

General

When succinylcholine is given over a prolonged period of time, the characteristic depolarization block of the myoneural junction (Phase I block) may change to a block with characteristics superficially resembling a nondepolarizing block (Phase II block). Prolonged respiratory muscle paralysis or weakness may be observed in patients manifesting this transition to Phase II block.

The transition from Phase I to Phase II block has been reported in 7 of 7 patients studied under halothane anesthesia after an accumulated dose of 2 to 4 mg/kg succinylcholine (administered in repeated, divided doses). The onset of Phase II block coincided with the onset of tachyphylaxis and prolongation of spontaneous recovery. In another study, using balanced anesthesia (N₂O/O₂/narcotic-thiopental) and succinylcholine infusion, the transition was less abrupt, with great individual variability in the dose of succinylcholine required to produce Phase II block. Of 32 patients studied, 24 developed Phase II block. Tachyphylaxis was not associated with the transition to Phase II block, and 50% of the patients who developed Phase II block experienced prolonged recovery.

When Phase II block is suspected in cases of prolonged neuromuscular blockade, positive diagnosis should be made by peripheral nerve stimulation, prior to administration of any anticholinesterase drug. Reversal of Phase II block is a medical decision which must be made upon the basis of the individual clinical pharmacology and the experience and judgment of the physician. The presence of Phase II block is indicated by fade of responses to successive stimuli (preferably "train of four"). The use of an anticholinesterase drug to reverse Phase II block should be accompanied by appropriate doses of an anticholinergic drug to prevent disturbances of cardiac rhythm. After adequate reversal of Phase II block with an anticholinesterase agent, the patient

should be continually observed for at least 1 hour for signs of return of muscle relaxation. Reversal should not be attempted unless: (1) a peripheral nerve stimulator is used to determine the presence of Phase II block (since anticholinesterase agents will potentiate succinylcholine-induced Phase I block), and (2) spontaneous recovery of muscle twitch has been observed for at least 20 minutes and has reached a plateau with further recovery proceeding slowly; this delay is to ensure complete hydrolysis of succinylcholine by plasma cholinesterase prior to administration of the anticholinesterase agent. Should the type of block be misdiagnosed, depolarization of the type initially induced by succinylcholine (i.e. Phase I block), will be prolonged by an anticholinesterase agent.

Succinylcholine should be employed with caution in patients with fractures or muscle spasm because the initial muscle fasciculations may cause additional trauma.

Succinylcholine may cause a transient increase in intracranial pressure; however, adequate anesthetic induction prior to administration of succinylcholine will minimize this effect.

Succinylcholine may increase intragastric pressure, which could result in regurgitation and possible aspiration of stomach contents.

Neuromuscular blockade may be prolonged in patients with hypokalemia or hypocalcemia.

Reduced Plasma Cholinesterase Activity

Succinylcholine should be used carefully in patients with reduced plasma cholinesterase (pseudocholinesterase) activity. The likelihood of prolonged neuromuscular block following administration of succinylcholine must be considered in such patients (**see DOSAGE AND ADMINISTRATION**).

Plasma cholinesterase activity may be diminished in the presence of genetic abnormalities of plasma cholinesterase (e.g. patients heterozygous or homozygous for atypical plasma cholinesterase gene), pregnancy, severe liver or kidney disease, malignant tumors, infections, burns, anemia, decompensated heart disease, peptic ulcer, or myxedema. Plasma cholinesterase activity may also be diminished by chronic administration of oral contraceptives, glucocorticoids, or certain monoamine oxidase inhibitors and by irreversible inhibitors of plasma cholinesterase, (e.g. organophosphate insecticides, echothiophate, and certain antineoplastic drugs).

Patients homozygous for atypical plasma cholinesterase gene (1 in 2500 patients) are extremely sensitive to the neuromuscular blocking effect of succinylcholine. In these patients, a 5 to 10 mg test dose of succinylcholine may be administered, or neuromuscular blockade may be produced by the cautious administration of a 1 mg/mL solution of succinylcholine by intravenous drip. Apnea or prolonged muscle paralysis should be treated with controlled respiration.

Drug Interactions

Drugs which may enhance the neuromuscular blocking action of succinylcholine include: promazine, oxytocin, aprotinin, certain non-penicillin antibiotics, quinidine, β -adrenergic blockers, procainamide, lidocaine, trimethaphan, lithium carbonate, magnesium salts, quinine, chloroquine, diethylether, isoflurane, desflurane, metoclopramide and terbutaline. The presence of an inhalational anesthetic may exacerbate the side effects of succinylcholine in infants and children (see **ADVERSE REACTIONS**).

The neuromuscular blocking effect of succinylcholine may be enhanced by drugs that reduce plasma cholinesterase activity (e.g. chronically administered oral contraceptives, glucocorticoids, or certain monoamine oxidase inhibitors) or by drugs that irreversibly inhibit plasma cholinesterase (see **PRECAUTIONS**).

If other neuromuscular blocking agents are to be used during the same procedure, the possibility of a synergistic or antagonistic effect should be considered.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There have been no long-term studies performed in animals to evaluate carcinogenic potential.

Pregnancy

Teratogenic Effects

Animal reproduction studies have not been conducted with succinylcholine chloride. It is also not known whether succinylcholine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Succinylcholine should be given to a pregnant woman only if clearly needed.

Nonteratogenic Effects

Plasma cholinesterase levels are decreased by approximately 24% during pregnancy and for several days postpartum. Therefore, a higher proportion of patients may be expected to show increased sensitivity (prolonged apnea) to succinylcholine when pregnant than when nonpregnant.

Labor and Delivery

Succinylcholine is commonly used to provide muscle relaxation during delivery by cesarean section. While small amounts of succinylcholine are known to cross the placental barrier, under normal conditions the quantity of drug that enters fetal circulation after a single dose of 1 mg/kg to the mother should not endanger the fetus. However, since the amount of drug that crosses the placental barrier is dependent on the concentration gradient between the maternal and fetal circulations, residual neuromuscular blockade (apnea and flaccidity) may occur in the newborn after repeated high doses to, or in the presence of atypical plasma cholinesterase in, the mother.

Nursing Mothers

It is not known whether succinylcholine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised following succinylcholine administration to a nursing woman.

Pediatric Use

There are rare reports of ventricular dysrhythmias, cardiac arrest and death secondary to acute rhabdomyolysis with hyperkalemia in apparently healthy infants and children who receive succinylcholine (see WARNINGS). Several of these individuals were subsequently

found to be suffering from a myopathy such as Duchenne's muscular dystrophy whose clinical signs were not obvious. When a healthy appearing infant or child suddenly develops cardiac arrest soon after administration of succinylcholine, immediate treatment of hyperkalemia should include hyperventilation, i.v. calcium, i.v. sodium bicarbonate and i.v. glucose (with or without insulin). Treatment for acute rhabdomyolysis, including a single dose of dantrolene, should also be considered.

Unlike in adults, the incidence of bradycardia in infants and young children is common after one dose of succinylcholine. The incidence and severity of bradycardia is greater in infants and children than in adults. Pre-treatment with anticholinergic agents (e.g. atropine), in most cases, will reduce the occurrence of bradyarrhythmias.

ADVERSE REACTIONS

Adverse reactions to succinylcholine consist primarily of an extension of its pharmacological actions. Succinylcholine causes profound muscle relaxation resulting in respiratory depression to the point of apnea; this effect may be prolonged. Hypersensitivity reactions, including anaphylaxis may occur in rare instances. The following additional adverse reactions have been reported: cardiac arrest, malignant hyperthermia, arrhythmias, bradycardia, tachycardia, hypertension, hypotension, hyperkalemia, prolonged respiratory depression or apnea, increased intraocular pressure, muscle fasciculation, jaw rigidity, postoperative muscle pain, rhabdomyolysis with possible myoglobinuric acute renal failure, excessive salivation, and rash.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, ON K1A0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of the side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms

Overdosage with succinylcholine may result in neuromuscular block beyond the time needed for surgery and anesthesia. This may be manifested by skeletal muscle weakness, decreased respiratory reserve, low tidal volume, prolonged respiratory depression or apnea.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Treatment

The primary treatment is maintenance of a patent airway and respiratory support until recovery of normal respiration is assured. Depending on the dose and duration of succinylcholine administration, the characteristic depolarizing neuromuscular block (Phase I) may change to a block with characteristics superficially resembling a nondepolarizing block (Phase II) (see **PRECAUTIONS**).

The decision to use neostigmine to reverse a Phase II succinylcholine-induced block depends on the judgment 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.

DOSAGE AND ADMINISTRATION

The dosage of succinylcholine should be individualized and should always be determined by the clinician after careful assessment of the patient (see **WARNINGS**).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Solutions which are not clear and colourless should not be used.

Adults

For Short Surgical Procedures

The average dose required to produce neuromuscular blockade and to facilitate tracheal intubation is 0.6 mg/kg Succinylcholine Chloride Injection given intravenously. The optimum dose will vary among individuals and may be from 0.3 to 1.1 mg/kg for adults.

Following administration of doses in this range, neuromuscular blockade develops in about 1 minute; maximum blockade may persist for about 2 minutes, after which recovery takes place within 4 to 6 minutes. However, very large doses may result in more prolonged blockade. A 5 to 10 mg test dose may be used to determine the sensitivity of the patient and the individual recovery time (see **PRECAUTIONS**).

For Long Surgical Procedures

The dose of succinylcholine administered by infusion depends upon the duration of the surgical procedure and the need for muscle relaxation. The average rate for an adult ranges between 2.5 and 4.3 mg per minute.

Solutions containing from 1 to 2 mg per mL succinylcholine have commonly been used for continuous infusion (see **PHARMACEUTICAL INFORMATION, Stability-Compatibility**). The more dilute solution (1 mg per mL) is probably preferable from the standpoint of ease of control of the rate of administration of the drug and, hence, of relaxation. This intravenous solution containing 1 mg per mL may be administered at a rate of 0.5 mg (0.5 mL) to 10 mg (10 mL) per minute to obtain the required amount of relaxation. The amount required per minute will depend upon the individual response as well as the degree of relaxation required. Avoid overburdening the circulation with a large volume of fluid. It is recommended that neuromuscular function be carefully monitored with a peripheral nerve stimulator when using succinylcholine by infusion in order to avoid overdose, detect development of Phase II block, follow its rate of recovery, and assess the effects of reversing agents (see **PRECAUTIONS**).

Children

The intravenous dose of succinylcholine is 2 mg/kg for infants and small children; for older children and adolescents the dose is 1 mg/kg (see **WARNINGS** and **PRECAUTIONS-Pediatric Use**).

Rarely, I.V. bolus administration of succinylcholine in infants and children may result in malignant ventricular arrhythmias and cardiac arrest secondary to acute rhabdomyolysis with hyperkalemia. In such situations, an underlying myopathy should be suspected.

Intravenous bolus administration of succinylcholine in infants and young children may result in profound bradycardia or, rarely, asystole. Unlike in adults, the incidence of bradycardia in infants and children is greater after a single dose of succinylcholine. The occurrence of bradyarrhythmias, in most cases, will be reduced by pretreatment with an anticholinergic drug (e.g. atropine) (see **PRECAUTIONS – Pediatric Use**).

Intramuscular Use

If necessary, succinylcholine may be given intramuscularly to infants, older children or adults when a suitable vein is inaccessible. A dose of up to 3 or 4 mg/kg may be given, but not more than 150 mg total dose should be administered by this route. The onset of effect of succinylcholine given intramuscularly is usually observed in about 2 to 3 minutes.

PHARMACEUTICAL INFORMATION

Drug Substance

Trade Name

Succinylcholine Chloride Injection

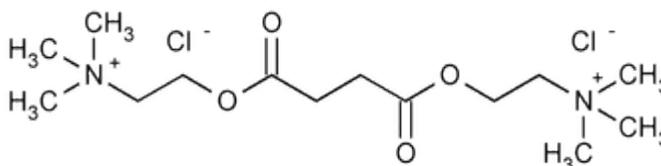
Proper Name

Succinylcholine chloride

Chemical Name

2,2'-[1,4-dioxo-1,4-butanediyl]bis(oxy)]bis[N,N,N,-trimethylethanaminium]dichloride

Structural Formula



Molecular Formula

C₁₄H₃₀Cl₂N₂O₄

Molecular Weight

361.31

Description

Succinylcholine chloride is a white, odorless, slightly bitter powder, that is very soluble in water. It is unstable in alkaline solutions, but relatively stable in acid solutions, depending upon the concentration of the solution and the storage temperature.

Stability - Compatibility

Succinylcholine is acidic (pH=3.5) and should not be mixed with alkaline solutions having a pH greater than 8.5 (e.g., barbiturate solutions).

Succinylcholine is rapidly hydrolyzed, quickly loses potency, and may cause a precipitate to form when mixed with alkaline solutions of other drugs. Preferably, succinylcholine should be separately injected and should not be mixed in the same syringe nor administered simultaneously through the same needle with solutions of short-acting barbiturates, such as Pentothal (sodium thiopental) or other drugs which have an alkaline pH.

Admixtures containing 1 to 2 mg per mL of succinylcholine may be prepared by diluting succinylcholine with a sterile solution, such as 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP. **Such admixtures should be used within 24 hours after preparation.** Aseptic techniques should be used to prepare the diluted product. Admixtures of succinylcholine should be prepared for single patient use only. The unused portion of the diluted succinylcholine should be discarded.

Storage Recommendations

Succinylcholine Chloride Injection in multidose vials must be kept refrigerated (2 to 8°C) to prevent loss of potency. These products are stable for up to 28 days after first puncture without significant loss of potency, if stored at 2 – 8°C.

Availability

Succinylcholine Chloride Injection is supplied as a sterile solution in 10mL and 20mL multidose vials with rubber stopper.

Each mL of sterile solution contains: succinylcholine chloride (anhydrous base) 20 mg equivalent to 22 mg dihydrate, sodium chloride (for isotonicity), and hydrochloric acid (pH adjustment). Also contains methylparaben (1.8 mg/mL) and propylparaben (0.2 mg/mL) as preservatives.

MORE INFORMATION

For more information, please contact the sponsor at:

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