

Hikma launches Succinylcholine Chloride Injection, USP

London, 13 July, 2021 – Hikma Pharmaceuticals PLC (Hikma), the multinational pharmaceutical company, has launched Succinylcholine Chloride Injection, USP 20mg/mL in the US, through its US affiliate, Hikma Pharmaceuticals USA Inc. Succinylcholine Chloride Injection, USP is an important medicine used in the treatment of COVID-19 patients. It is indicated, in addition to general anesthesia, to facilitate tracheal intubation, and to provide skeletal muscle relaxation during surgery or mechanical ventilation.

Riad Mishlawi, President of Injectables said, “We are very pleased to launch Succinylcholine Chloride Injection in the US, a neuromuscular blocking agent and an important drug used in the treatment of COVID-19. Hikma is committed to making affordable medicines accessible to those in need and is proud to be supplying the US market with a wide portfolio of injectable medicines used to treat COVID-19 patients in intensive care.”

According to IQVIA, US sales of Succinylcholine Chloride Injection, USP 20mg/mL were approximately \$43 million in the 12 months ending May 2021.

Hikma is the third largest US supplier of generic injectable medicines by volume, with a growing portfolio of over 100 products. Today one in every six injectable generic medicines used in US hospitals is a Hikma product.

- ENDS -

Enquiries

Hikma Pharmaceuticals PLC

Susan Ringdal
EVP, Strategic Planning and Global Affairs

+44 (0)20 7399 2760/ +44 7776 477050
uk-investors@hikma.uk.com

Steve Weiss
David Belian
US Communications and Public Affairs

+1 732 720 2830/ +1 732 788 8279
+1 732 720 2814/+1 848 254 4875
uscommunications@hikma.com

About Hikma

(LSE: HIK) (NASDAQ Dubai: HIK) (OTC: HKMPY) (rated BBB-/stable S&P and BBB-/stable Fitch)

Hikma helps put better health within reach every day for millions of people around the world. For more than 40 years, we've been creating high-quality medicines and making them accessible to the people who need them. Headquartered in the UK, we are a global company with a local presence across the United States (US), the Middle East and North Africa (MENA) and Europe, and we use our unique insight and expertise to transform cutting-edge science into innovative solutions that transform people's lives. We're committed to our customers, and the people they care for, and by thinking creatively and acting practically, we provide them with a broad range of branded and non-branded generic medicines. Together, our 8,600 colleagues are helping to shape a healthier world that enriches all our communities. We are a leading licensing partner, and through our venture capital arm, are helping bring innovative health technologies to people around the world. For more information, please visit: www.hikma.com

Important Safety Information for Succinylcholine Chloride Injection, USP 20mg/mL:

BOXED WARNING

WARNING

RISK OF CARDIAC ARREST FROM HYPERKALEMIC RHABDOMYOLYSIS

There have been rare reports of acute rhabdomyolysis with hyperkalemia followed by ventricular dysrhythmias, cardiac arrest and death after the administration of succinylcholine to apparently healthy pediatric patients who were subsequently found to have undiagnosed skeletal muscle myopathy, most frequently Duchenne's muscular dystrophy.

This syndrome often presents as peaked T-waves and sudden cardiac arrest within minutes after the administration of the drug in healthy appearing pediatric patients (usually, but not exclusively, males, and most frequently 8 years of age or younger). There have also been reports in adolescents.

Therefore, when a healthy appearing infant or child develops cardiac arrest soon after administration of succinylcholine, not felt to be due to inadequate ventilation, oxygenation or anesthetic overdose, immediate treatment for hyperkalemia should be instituted. This should include administration of intravenous calcium, bicarbonate, and glucose with insulin, with hyperventilation. Due to the abrupt onset of this syndrome, routine resuscitative measures are likely to be unsuccessful. However, extraordinary and prolonged resuscitative efforts have resulted in successful resuscitation in some reported cases. In addition, in the presence of signs of malignant hyperthermia, appropriate treatment should be instituted concurrently.

Since there may be no signs or symptoms to alert the practitioner to which patients are at risk, it is recommended that the use of succinylcholine in pediatric patients should be reserved for emergency intubation or instances where immediate securing of the airway is necessary, e.g., laryngospasm, difficult airway, full stomach, or for intramuscular use when a suitable vein is inaccessible (see **PRECAUTIONS: Pediatric Use** and **DOSAGE AND ADMINISTRATION**).

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, 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.

WARNINGS & PRECAUTIONS

- 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.
- Severe anaphylactic reactions to neuromuscular blocking agents, including succinylcholine, have been reported. These reactions have, in some cases, been life-threatening and fatal. Since allergic cross-reactivity has been reported in this class, request information from your patients about previous anaphylactic reactions to other neuromuscular blocking agents.
- Administration of succinylcholine chloride results in paralysis, which may lead to respiratory arrest and death; this progression may be more likely to occur in a patient for whom it is not intended. Confirm proper selection of intended product and avoid confusion with other injectable solutions that are present in critical care and other clinical settings.
- Succinylcholine should be administered with **GREAT CAUTION** to patients suffering from electrolyte abnormalities and those who may have massive digitalis toxicity, 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. The risk of hyperkalemia in these patients increases over time and usually peaks at 7 to 10 days after the injury.
- 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.
- 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.
- In both adults and pediatric patients the incidence of bradycardia, which may progress to asystole, is higher following a second dose of succinylcholine. The incidence and severity of bradycardia is higher in pediatric patients than adults.
- 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 its 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).
- 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 non-depolarizing block (Phase II block).
- 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.
- 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.

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.

There have been post-marketing reports of severe allergic reactions (anaphylactic and anaphylactoid reactions) associated with use of neuromuscular blocking agents, including succinylcholine. These reactions, in some cases, have been life threatening and fatal. Because these reactions were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency.

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 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.

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

USE IN SPECIFIC POPULATIONS

Carcinogenesis, Mutagenesis, Impairment of Fertility

There have been no long-term studies performed in animals to evaluate carcinogenic potential of succinylcholine. Genetic toxicology studies have not been completed to evaluate the genotoxic potential of succinylcholine. There are no studies to evaluate the potential impact of succinylcholine on fertility.

Pregnancy

Risk Summary

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

Clinical Considerations

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 caesarean 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

Safety and effectiveness of succinylcholine chloride have been established in pediatric patient age groups, neonate to adolescent. There are rare reports of ventricular dysrhythmias and cardiac arrest secondary to acute rhabdomyolysis with hyperkalemia in apparently healthy pediatric patients who receive succinylcholine. Many of these pediatric patients were subsequently found to have a skeletal muscle myopathy such as Duchenne's muscular dystrophy whose clinical signs were not obvious.

Since it is difficult to identify which patients are at risk, it is recommended that the use of succinylcholine in pediatric patients should be reserved for emergency intubation or instances where immediate securing of the airway is necessary, e.g., laryngospasm, difficult airway, full stomach, or for intramuscular use when a suitable vein is inaccessible. As in adults, the incidence of bradycardia in pediatric patients is higher following the second dose of succinylcholine. The incidence and severity of bradycardia is higher in pediatric patients than adults. Pre-treatment with anticholinergic agents, e.g., atropine, may reduce the occurrence of bradyarrhythmias.

Geriatric Use

Clinical studies of succinylcholine chloride did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

DOSAGE AND ADMINISTRATION

The dosage of succinylcholine should be individualized and should always be determined by the clinician after careful assessment of the patient.

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 colorless should not be used.



Accidental administration of neuromuscular blocking agents may be fatal. Store succinylcholine chloride injection with the cap and ferrule intact and in a manner that minimizes the possibility of selecting the wrong product.

Refer to package insert for dosage recommendations for Short Surgical Procedures, Long Surgical Procedures, Pediatrics, and Intramuscular Use.

Overdosage

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, or apnea. 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 non-depolarizing block (Phase II).

ENDING INFORMATION

For additional information, please refer to the [Package Insert](#) for full prescribing information, available on www.hikma.com.

To report SUSPECTED ADVERSE REACTIONS, contact Hikma Pharmaceuticals USA Inc. at 1-877-845-0689, or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Manufactured by:

HIKMA FARMACÊUTICA (PORTUGAL), S.A.

Estrada do Rio da Mó, 8, 8A e 8B – Fervença – 2705-906 Terrugem SNT, PORTUGAL

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Berkeley Heights, NJ 07922

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