**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

**Suxamethonium chlorid VUAB 100 mg**
Powder for solution for injection/ infusion

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One injection vial contains 100 mg of suxamethonium chloride (as suxamethonium chloride dihydrate 110 mg).

## 3. PHARMACEUTICAL FORM

Powder for solution for injection/ infusion.
White to almost white powder.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

Suxamethonium chlorid VUAB is used as a muscle relaxant during general anesthesia. It is used as a muscle relaxant to facilitate endotracheal intubation, particularly rapid intubation, for mechanical ventilation and for a wide range of surgical and obstetric procedures. It is also used in severe laryngospasm and to reduce the intensity of muscular contractions associated with pharmacologically or electrically induced convulsions.

### 4.2. Posology and method of administration

Method of administration
The product is usually administered intravenously in the form injection or infusion, intramuscular administration is also possible. In case of severe laryngospasm it is possible to administer product intralingual or intraosseous.

Posology in adults: The dose is dependent on body weight, the degree of muscular relaxation required, the route of administration, and the response of individual patients. Intravenous single dose of suxamethonium-chloride is for all age groups 1.0 to 1.5 mg/kg of total body weight.
Posology in paediatric population:
The recommended intravenous dose for neonates and infants is 2 mg/kg of total body weight. A dose of 1.5-2 mg/ kg total body weight is recommended in young children, and 1 mg/kg of total body weight in older children and adolescents is recommended. Product can be administered intramuscular in dose 2 – 4 mg/kg of total body weight (up to 4 ml of solution in injectiom site).

Posology in elderly: The recommended dosage in elderly is identical to that of adult patients of younger age. The elderly may be more susceptible to cardiac arrhythmias, especially if digitalis-like drugs are also being taken. For more information, see section 4.4.

In case of prolong administration (intermittent or continuous) the intensity and nature of neuromuscular blockage should be controlled with help of aneurostimulator, because there is a risk of Phase II blockage.

Method of administration:
For intravenous administration, the content of the vial should be diluted with 10 ml of water for injection or isotonic saline solution, resultant concentration is 1% for a 100 mg vial. For infusion administration, it should further be diluted to concentration 0.1% - 0.2% with sterile isotonic saline solution. The infusion rate should be adjusted according to the response of individual patients. Recomended infusion rate should be 2.5 – 4 mg/min.

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

### 4.3. Contraindications

Product has no effect on the level of consciousness and it should *not* be administered to a patient who is not fully anaesthetized.

Hypersensitivity to active substance or any excipient listed in section 6.1.

As suxamethonium-chloride can act as a trigger of sustained myofibrillar contraction in susceptible individuals, product 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 chlorid VUAB) 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.

Product 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 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 product administration may be excessive and cause serious cardiac arrhythmias and cardiac arrest. For these reasons the use of product 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, which include 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 immobilized 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 contra-indication to the administration of a normal single dose of product, but multiple or large doses may cause clinically significant rises in serum potassium and should not be used.

Suxamethonium-chloride causes a significant transient rise in intra-ocular pressure, and should therefore not be used in the presence of decompensated glaucoma, 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.

Product should be avoided in patients with a personal or family history of congenital myotonic diseases such as myotonia congenita and myotonic dystrophysince its administration may on occasion be associated with severe myotonic spasms and rigidity.

Product 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, and secondary, to acute rhabdomyolysis with hyperkalaemia.

Product should not be used in patients with intracranial arterial aneurysma, severe intracranial hypertension, severe bradycardia, compressive fracture of spinal cord, injury of spinal cord and vertebral dislocation, paraplegia, dehydratation with electrolyte disturbances and with functional pulmonary disorders.

### 4.4. Special warnings and precautions for use

Product should be administered only under close supervision of an anaesthesiologist familiar with its actions, characteristics and hazards, who is skilled in providing mechanical ventilation, 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 (greater than 50%) between neuromuscular blocking agents have been reported. Therefore, where possible, before administering suxamethonium-chloride, hypersensitivity to other neuromuscular blocking agents should be excluded. Suxamethonium-chloride should be used in susceptible patients only when absolutely essential. Patients who experience a hypersensitivity reaction under general anaesthesia should be tested subsequently for hypersensitivity to other neuromuscular blockers.

Product should not be mixed in the same syringe with any other agent, especially thiopental.

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

Product 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-chloride. Approximately 0.05% of the population has an inherited cause of reduced cholinesterase activity. Prolonged and intensified neuromuscular blockade following product administration may occur secondary to reduced plasma cholinesterase activity in the following states or pathological conditions: physiological anomalies 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; malignant tumour; chronic anaemia and malnutrition; end-stage hepatic failure; acute or chronic renal failure; auto-immune diseases: myxoedema; collagen diseases; iatrogenic disorders: conditions following plasma exchange, plasmapheresis, cardiopulmonary bypass, and as a result of concomitant drug therapy (see 4.5).

If product is given over a prolonged period, the characteristic depolarizing 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 may occur after repeated administration of product.

Muscle pains are frequently experienced after administration of suxamethonium-chloride, most commonly 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 product administration and the incidence or severity of pain. The use of small doses of non-depolarising muscle relaxants given several minutes before suxamethonium-chloride administration has been advocated for the reduction of incidence and severity of suxamethonium-chloride-associated muscle pains. This technique may require the use of doses of suxamethonium-chloride in excess of 1 mg/kg to achieve satisfactory conditions for endotracheal intubation.

Caution should be exercised when using suxamethonium-chloride in children, since pediatric patients are more likely to have an undiagnosed myopathy or may have unknown predisposition to malignant hyperthermia and rhabdomyolysis, which places them at increased risk of severe adverse events following suxamethonium-chloride (see section 4.3 and 4.8).

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 product to patients with advanced myasthenia gravis. Although these patients are resistant to suxamethonium-chloride they develop a state of Phase II block which can result in delayed recovery. Patients with myasthenic Eaton-Lambert syndrome are more sensitive to product than normal patients, and they require decreased doses.

In healthy adults, product 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-chloride-related bradycardia.

In the absence of pre-existing or evoked hyperkalaemia, ventricular arrhythmias are rarely seen following suxamethonium-chloride administration. Patients taking digitalis-like drugs are however more susceptible to such arrhythmias. The action of suxamethonium-chloride 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 product. 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 thiotepa; 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 product by mechanisms unrelated to plasma cholinesterase activity. These include: magnesium salts; lithium carbonate; azathioprine; 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. These substances have little effect on the Phase I block after product 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-chloride-exacerbated hyperkalaemia.

Plasma cholinesterase concentration can be influenced by haemodilution, malnutrition, uremia, carcinoma and burns.

### 4.6. Fertility, pregnancy and lactation

Fertility
No studies of the effect of suxamethonium-chloride on female fertility have been performed.

Pregnancy
No studies of the effect of suxamethonium-chloride on pregnancy have been performed. Suxamethonium-chloride 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.

Administration of suxamethonium-chloride can be considered, if it is essentially necessary.

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 product injection.

Lactation
No information of the effect of suxamethonium-chloride during lactation are known.

### 4.7. Effects on ability to drive and use machines

Irrelevant.
Suxamethonium-chloride will always be used in combination with a general anesthetic and therefore the usual precautions relating to performance of tasks following general anesthesia apply.

### 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 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to <1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Investigations
Common Transient blood potassium increase.

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-chloride to patients with congenital cerebral palsy, tetanus, Duchenne muscular dystrophy, and closed head injury. Such events have also been reported rarely in children with undiagnosed muscular disorders.

Eye disorders
Common Increased intraocular pressure.

Respiratory, thoracic and mediastinal disorders
Rare
Bronchospasm, prolonged respiratory depression (see 4.4), apnoea.

Gastrointestinal disorders
Very common
Increased intragastric pressure.
Excessive salivation.

Skin and subcutaneous tissue disorders
Common Rash.
Not known
Systemic contact dermatitis.

Musculoskeletal and connective tissue disorders
Very common
Muscle fasciculation, post-operative muscle pains (see 4.4).
Common Myoglobinaemia, myoglobinuria. (Rhabdomyolysis has also been reported (see section 4.3 and 4.4)
Rare
Trismus.

Vascular disorders
Common
Skin flushing.
Hypertension and hypotension.

Immune system disorders
Very rare
Anaphylactic reactions.

General disorders and administration site conditions
Very rare
Malignant hyperthermia (see 4.4).

Nervous system disorders
Not known
Increased intracranial pressure.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important.
It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

### 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-chloride-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.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: muscle relaxants, peripherally acting agents, cholin derivatives
ATC code: M03AB01

Suxamethonium-chloride is short-acting depolarizing muscular relaxant. It displaces acetylcholine on cholinergic receptors of motor endplate and initialy disturbes excitation of muscular fiber by depolarization. State of depolarization is also directly maintained by preventing of repolarisation, subsequnently, released acetylcholine binds to depolarized motor endplate and remains ineffective.

### 5.2. Pharmacokinetic properties

Only limited amount of dates about character of suxamethonium-chloride is known, particularly because of extremely rapid metabolism. In normal individuals, suxamethonium-chloride is metabolized quickly and in large extent by plasmatic cholinesterase, primarily to monosuccinylcholine, which has mild relaxant effect. In the following phase it lyses to the body's own substances-the succinic acidand cholin, which are separated renaly. 80% of administered active substance is hydrolyzed prior to reaching the nerve junctions. About 10% of suxamethonium-chloride is excreted unchanged in urine. Muscle relaxation begins usually in 60 seconds. The effect subsides in 3 - 6 minutes.

### 5.3. Preclinical safety data

Suxamethonium-chloride has been used over 50 years. Long-term experiences with this product compensated lack of results of preclinical studies. Long-term studies investigating mutagenic potential, carcinogenic potential and reproduction toxicity are not available.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

None.

### 6.2. Incompatibilities

In alkaline medium the product becomes inactivated quickly and may precipitate, therefore product should not be mixed with solutions of barbiturates with short effect (thiopental) and in infusion administration should not be mixed with alkaline solutions as Ringer-lactate and Hartmann solution.

### 6.3. Shelf life

Before first opening: The expiry date of the product is indicated on the packaging materials
After first opening: Product must be used immediately after opening of the vial.
After reconstitution: Chemical and physical in-use stability of the drug product after reconstitution before administration has been demonstrated for 24 hours at 2 to 8°C.
From a microbiological point of view, the medicinal product should be used immediately.
If not used immediately, in-use storage times and conditions after reconstitution before administration are the responsibility of the user and normally the period should not be longer than 24 hours at 2 to 8°C, unless the reconstitution took place under controlled and validated aseptic conditions.

### 6.4. Special precautions for storage

Store below $25^0$c.
Store in the original package in order to protect from light.
Storage conditions of this medicinal product after reconstitution are presented in section 6.3.

### 6.5. Nature and contents of container

Suxamethonium chlorid VUAB 100 mg:
Colorless glass vial (class I or II), rubber stopper, aluminium cap or aluminium flip-off cap, box.

Content of the pack:
Suxamethonium chlorid 100 mg, inj.+inf.plv.sol.: 1 vial with 110 mg of product.

### 6.6. Special precautions for disposal

Instructions for reconstitution (and further dilution)
This product should be diluted only with water for injection or sterile isotonic saline solution.

For intravenous administration the content of the vial is diluted with 10 ml of water for injection or sterile isotonic saline solution, resultant concentration is 1% in 100 mg vial. For infusion administration solution is further diluted to concentration 0.1% - 0.2% with sterile isotonic saline solution.

Parenteral products must be visually checked before use to ensure they do not contain any particles and that they are not discolored. If they are, solutions must not be used.

Any unused product or waste material should be disposed of in accordance with local requirements.

## 7. MANUFACTURER

**VUAB PHARMA A.S.**
**VLTAVSKÁ 53**
**25263 ROZTOKY**
**CZECH REPUBLIC**

## 8. REGISTRATION HOLDER:

**DAVID MARGALIT & CO. LTD.**
**P.O.BOX 16666 TEL AVIV**

## 9. PRODUCT REGISTRATION NO.:

**166-27-35120**

Approved on December 2020