# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Murexal 10 mg/mL solution for injection in pre-filled syringe

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution for injection contains 10 mg of suxamethonium chloride anhydrous (as 11 mg of suxamethonium chloride dihydrate).
Each 10 ml pre-filled syringe contains 100 mg of suxamethonium chloride anhydrous (as 110 mg of suxamethonium chloride dihydrate).

Excipient with known effect:
Each ml of solution for injection contains 2.79 mg equivalent to 0.12 mmol of sodium.
Each 10 ml pre-filled syringe contains 27.9 mg equivalent to 1.2 mmol of sodium.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Solution for injection (injection).
Clear and colourless solution.
pH: 3.0 – 4.5
Osmolality: 250-350 mOsm/Kg

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Murexal is indicated as a muscle relaxant to facilitate endotracheal intubation during induction of general anaesthesia or emergency situations, in adults and paediatric population above 12 years of age.

### 4.2 Posology and method of administration

Suxamethonium should be administered only by or under close supervision of an experienced clinician (anaesthesist, intensivist, emergency physician) familiar with its action, characteristics and hazards, who is skilled in the management of intubation and artificial respiration and only where there are adequate facilities for immediate endotracheal intubation with administration of oxygen by intermittent positive pressure ventilation. It is given intravenously after anaesthesia has been induced and should not be administered to the conscious patient.

Posology

*Adults*

To achieve endotracheal intubation, suxamethonium chloride is usually administered by bolus intravenous injection in a dose of 1 mg/kg body weight. 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.

Murexal is limited to a single administration.

The use of small doses of non-depolarising muscle relaxants given minutes before suxamethonium administration has been advocated for the reduction of incidence and severity of suxamethonium-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 (see section 4.4).

*Special populations*

*Elderly*
Dose requirements of suxamethonium in elderly are comparable to those for adults.

*Renal impairment*
A single dose of suxamethonium may be administered to patients with renal insufficiency in the absence of hyperkalaemia. Multiple or larger doses may cause clinically significant rises in serum potassium and should not be used.

*Hepatic impairment*
No dose adjustment is required in patients with hepatic impairment. Termination of the action of suxamethonium is dependent on plasma cholinesterase, which is synthetised in the liver. Although plasma cholinesterase levels often fall in patients with liver disease, levels are seldom low enough to significantly prolong suxamethonium-induced apnoea (see section 4.4).

*Paediatric population*

Adolescents over 12 years: the posology is similar to that of the adults.

Murexal should not be given to children under 12 years of age because the sub-graduation of the pre-filled syringe does not allow an accurate administration of the product in this population.

Method of administration

Murexal is for intravenous use. The pre-filled syringe is not suitable for use in a syringe driver.

**4.3 Contraindications**

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Suxamethonium has no effect on the level of consciousness and should not be administered in patients who are not under general anaesthesia (see section 4.2).
- Personal or family history of malignant hyperthermia. Suxamethonium can trigger sustained myofibrillar contractions in susceptible individuals (see section 4.4).
- Patients known to have an inherited atypical plasma cholinesterase (butyrylcholinesterase) activity (history of previous prolonged and/or intensified response - see section 4.4)
- Patients with or who are susceptible to hyperkalaemia (see section 4.4). Suxamethonium is contra-indicated in patients:
    - with pre-existing hyperkalaemia. In the absence of hyperkalaemia and neuropathy, renal failure is not a contraindication to the administration of a normal single dose of suxamethonium injection, but multiple or large doses may cause clinically significant rises in serum potassium and should not be used.
    - recovering from major trauma or severe burns. The period of the greatest risk of hyperkalaemia may be further prolonged if there is persistent infection with delayed healing
    - with neurological deficits and acute major muscle wasting (e.g. 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 immobilised for prolonged periods of time may be at similar risk.

- Patient with skeletal muscle myopathies (e.g. Duchenne muscular dystrophy) as administration of suxamethonium may be associated with malignant hyperthermia, ventricular dysrhythmias and cardiac arrest secondary to acute rhabdomyolysis with hyperkalaemia.
- Personal or family history of congenital myotonic diseases such as myotonia congenita and dystrophia myotonica (risk of severe myotonic spasms and rigidity).
- Suxamethonium causes a significant transient rise in intra-ocular pressure, and should therefore not be used in the presence of 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.

**4.4 Special warnings and precautions for use**

**Suxamethonium paralyses the respiratory muscles as well as other skeletal muscles but has no effect on consciousness.**

The use of an appropriate neuromuscular monitoring technique is recommended for the evaluation of neuromuscular block and recovery.

*Anaphylactic reaction*
Allergical or non-allergical anaphylactic reaction are reported during anaesthetic induction, sometimes in patients who were never exposed to curare. Most common manifestations are skin eruption (erythema-like) or rash, generalised or limited to injection site, which may potentially develop into anaphylactic shock and/or bronchospasm. In certain case, bronchospasm and/or anaphylactic shock are not associated with cutaneous manifestations. Quincke's oedema have also been reported.
Occurrence of first sign enforces definitive withdrawal of Murexal, if the administration was not totally performed, and administration of symptomatic treatment.

In case of allergic reaction, symptomatic treatment should be administered. Allergology tests should also be performed (immediate sample, then skin test) (see section 4.8).

*Cross-sensitivity*
High rates of cross-sensitivity (greater than 50 %) between neuromuscular blocking medicinal products have been reported. Therefore, where possible, before administering suxamethonium, hypersensitivity to other neuromuscular blocking medicinal products should be excluded. Suxamethonium should only be used when absolutely essential in susceptible patients. Patients who experience a hypersensitivity reaction under general anaesthesia should be tested subsequently for hypersensitivity to other neuromuscular blockers.

*Reduced activity or deficiency of plasma cholinesterase*
Suxamethonium 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. Approximately 0.05% of the population has an inherited cause of reduced cholinesterase activity resulting in a prolonged duration of action of suxamethonium by more than 1 hour. In case of prolonged curarisation, controlled ventilation needs to be continued until spontaneous breathing occurs and muscular function normalises.
Prolonged and intensified neuromuscular blockade following suxamethonium injection may occur secondary to reduced plasma cholinesterase activity in the following states or pathological conditions:
- physiological variation as in pregnancy and the puerperium (see section 4.6);
- genetically determined abnormal plasma cholinesterase (see section 4.3);
- severe generalised tetanus, tuberculosis, other severe or chronic infections;
- severe burns (see section 4.3);
- chronic debilitating disease, malignancy, chronic anaemia and malnutrition;
- end-stage hepatic failure, acute or chronic renal failure (see section 4.2);
- auto-immune diseases: myxoedema;
- collagen diseases;
- iatrogenic: following plasma exchange, plasmapheresis, cardiopulmonary bypass, and as a result of concomitant drug therapy (see section 4.5).

*Malignant hyperthermia*
As suxamethonium could be used concomitantly with other anesthetic medicinal products (halogenated) and as malignant hyperthermia during anaesthesia could occur even in absence of known trigger factor, physicians should be familiar with early signs, diagnosis and treatment of malignant hyperthermia. Isolated masseter spasm could occur and prevent intubation while other muscles are relaxed, but it could also be a early sign of malignant hyperthermia so other signs of malignant hyperthermia crisis should be sought.
If malignant hyperthermia occurs, all anaesthetic medicinal products known to be associated with it (including suxamethonium) must be discontinued and full supportive measures implemented immediately. Intravenous dantrolene sodium is the primary specific therapeutic medicinal products and should be given as soon as possible after the diagnosis is made.

*Muscle pains*
Muscle pains are frequently experienced after administration of suxamethonium and most commonly occur in ambulatory patients undergoing short surgical procedures under general anaesthesia (see section 4.8). There appears to be no direct connection between the degree of visible muscle fasciculation after suxamethonium administration and the incidence or

severity of pain. Suxamethonium should be used with caution in patients with fractures or muscle spasms because the initial muscle fasciculations may cause additional trauma.

*Hyperkalaemia*
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 suxamethonium administration may be excessive and cause serious cardiac arrhythmias and cardiac arrest. In patients with severe sepsis, the potential for hyperkalaemia seems to be related to the severity and duration of infection.

*Myasthenia gravis and other myasthenic syndromes*
It is inadvisable to administer suxamethonium to patients with advanced myasthenia gravis. Although these patients are resistant to suxamethonium they develop a state of Phase II block which can result in delayed recovery. Patients with myasthenic Eaton-Lambert syndrome are more sensitive than normal to suxamethonium, necessitating dosage reduction.

*Bradycardia and other cardiac dysrhythmias*
Suxamethonium has no direct effect on the myocardium, but by stimulation of both autonomic ganglia and muscarinic receptors suxamethonium may cause changes in cardiac rhythm, including cardiac arrest.
In healthy adults, suxamethonium 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. Suxamethonium may also potentiate the bradycardia due to halothane or other medicinal products. This should be borne in mind when both medicinal products are used during anaesthetic procedures. Pre-treatment with intravenous atropine or glycopyrrolate significantly reduces the incidence and severity of suxamethonium-related bradycardia.
In the absence of pre-existing or evoked hyperkalaemia, ventricular arrhythmias are rarely seen following suxamethonium administration. Patients taking digitalis-like medicinal products are however more susceptible to such arrhythmias.

*Muscarinic effects*
The muscarinic effects of suxamethonium, e.g. increased bronchial and salivary secretions, may be prevented by the prophylactic administration of atropine.

*Increase in intraocular pressure*
Administration of suxamethonium is not recommended in patient undergoing open eyeball surgery.

*Sodium content*
This medicinal product contains 27.9 mg sodium per 10 mL, equivalent to 1.4 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

*Paediatric population*
This medicinal product is not recommended for children under 12 years of age because the sub-graduation of the pre-filled syringe does not allow an accurate administration of the product in this population. In case of use in the population above 12 years of age, caution should be exercised since younger patients are more likely to have an undiagnosed myopathy or an unknown predisposition to malignant hyperthermia and rhabdomyolysis, which places them at increased risk of serious adverse effects following suxamethonium (see sections 4.3 and 4.8).

**4.5 Interaction with other medicinal products and other forms of interactions**

Certain medicinal products or chemicals **are known** to **reduce normal plasma cholinesterase activity** and may therefore **prolong the neuromuscular blocking effects** of suxamethonium:

- *Antipsychotics:* phenelzine, promazine

- *Cytotoxics:* cyclophosphamide, thiotepa, irinotecan

- *General anaesthetic medicinal products:* ketamine

- *Histamine antagonists:* high concentrations of cimetidine may inhibit pseudocholinesterase

- *Local anaesthetics and/or antiarrhytmics:* procaine, chloroprocaine, lidocaine and procainamide

- *Metoclopramide*

- *Parasympathetics:* donepezil, galantamine, neostigmine, pyridostigmine, rivastigmine, edrophonium, tacrine hydrochloride

- *Sympathamomimetics (beta agonists):* bambuterol and terbutaline

- *Organophosphorous substances*: diazinon, malathion, chlorpyrifos, dichlorvos, propetamphos, dimpylate

- *Ecothiopate eye drops*

- *Selective serotonin reuptake inhibitors (SSRI)*

- *Other medicinal products with* ***potentially*** *deleterious effect* ***on plasma cholinesterase activity****:* aprotinin, chlorpromazin, oestrogens and oestrogen-containing oral contraceptives, oxytocin, high-dose steroids.

Certain medicinal products or substances **mayenhance** or **prolong** the neuromuscular blocking effects of suxamethonium by mechanisms **unrelated to plasma cholinesterase activity**:

- *Antiarrhytmics:* quinidine, verapamil

- *Antibacterials* (enhanced effects of suxamethonium): aminoglycosides, lincosamides (such as clindamycin and lincomycin), polymyxins (such colistin and polymyxin B) and vancomycin

- *Anticonvulsants:* carbamazepine, phenytoin

- *Beta-blockers* (Enhanced/prolonged neuromuscular blockade)*:* esmolol

- *Immunomodulators* (prolonged neuromuscular blockade): azathioprine

- *Lithium carbonate*

- *Quinine and Chloroquine*

- *Magnesium:* parenteral magnesium (enhanced neuromuscular blockade)

- *Volatile inhalational medicinal products*: halothane, enflurane, desflurane, isoflurane, diethylether and methoxyflurane have little effect on the Phase I block of suxamethonium injection but will accelerate the onset and enhance the intensity of a Phase II suxamethonium-induced block

Certain medicinal products or substances **mayexacerbate some adverse effects** of suxamethonium:

- *Cardiac glycosides:* Patients receiving digitalis-like medicinal products are more susceptible to the effects of suxamethonium-exacerbated by hyperkalaemia.

- *General anaesthetic medicinal products:* propofol (increased risk of myocardial depression and bradycardia)

**Other interactions**

- *Competitive neuromuscular blockers*: combination of competitive neuromuscular blockers may have additive or synergistic effects. However, the sequence of administration may also affect the interaction. The previous use of a small dose of a competitive neuromuscular blocker (e.g vecuronium) generally reduces the effects of suxamethonium, but if suxamethonium is given during recovery from a competitive neuromuscular blocker, antagonism, enhancement or a combinaton of the two may occur. The effects of a competitive blocker may be increased if it is given after suxamethonium.

**4.6 Fertility, pregnancy and lactation**

Pregnancy

Suxamethonium 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 fetal breathing movements.

The benefits of the use of suxamethonium as part of a rapid sequence induction for general anaesthesia normally outweigh the possible risk to the foetus.
Plasma cholinesterase levels fall during the first trimester of pregnancy to about 70 to 80% of their pre-pregnancy levels; 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 suxamethonium injection (see section 4.4). Suxamethonium is not embryotoxic or teratogenic in two animal species. The use of suxamethonium may be considered during pregnancy, if necessary. However, caution should be exercised following administration of suxamethonium to pregnant and puerperal patients.

Breastfeeding
It is not known whether suxamethonium or its metabolites are excreted in human milk. However, because suxamthonium is rapidly hydrolysed by plasma cholinesterase (pseudocholinesterase) to an inactive metabolite, no effects on the breastfed newborns/infants are anticipated.

Fertility
There is no data from the use of suxamethonium on fertility. However, because suxamthonium is rapidly hydrolysed by plasma cholinesterase (pseudocholinesterase) to an inactive metabolite, no effects on fertility are anticipated once the pharmacological effect is over.

**4.7 Effects on ability to drive and use machines**

Murexal has a major influence on the ability to drive and use machines.
Suxamethonium will always be used in combination with a general anaesthetic and therefore the usual precautions relating to performance of tasks following general anaesthesia 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 and <1/10), uncommon (≥1/1,000 and <1/100); rare (≥1/10,000 and <1/1,000); very rare (<1/10,000).

| | | |
|---|---|---|
| ***Immune system disorders*** | | |
| Common | Anaphylactic reactions either allergic or non-allergic (non-specific histamine release), pruritus, cardiovascular disorders, bronchospasm, serious anaphylactic shock (could be fatal) (see section 4.4). | |
| Not known | Quincke's oedema | |
| ***Nervous system disorders*** | | |
| Common | Transient increase of intracranial pressure* | |
| ***Eye disorders*** | | |
| Common | Increased intraocular pressure* | |
| ***Cardiac disorders*** | | |
| Common | Arrhythmias (including ventricular arrhythmias), bradycardia, tachycardia. | |
| Not known | Cardiac arrest. | |
| ***Vascular disorders*** | | |
| Common | Skin flushing, hypotension | |
| Not known | Hypertension | |
| ***Respiratory, thoracic and mediastinal disorders*** | | |
| Rare | Bronchospasm, prolonged respiratory depression | |
| Not known | Excessive bronchial secretion, apnoea | |
| ***Gastrointestinal disorders*** | | |
| Common<br><br>Not known | Increased intragastric pressure*<br><br>Excessive gastric secretion<br>Salivary gland enlargement | |
| 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 (see section 4.4) | |
| Common | Myoglobinaemia, myoglobinuria | |
| Rare | Trismus | |
| Not known | Rhabdomyolysis (see sections 4.3 and 4.4) | |
| ***General disorders and administration site conditions*** | | |
| Common | Injection site erythema | |
| Rare | Malignant hyperthermia (see section 4.4) | |
| ***Investigations*** | | |
| Common | Transient blood potassium increase | |

*Initial increase of intracranial, intraocular and intragastric pressure is normalised in few minutes.

Description of selected adverse reactions
There are case reports of hyperkalaemia-related cardiac arrests following the administration of suxamethonium to patients with congenital cerebral palsy, tetanus, spinal cord injury muscular dystrophy, and closed head injury. Such events have also been reported rarely in children with previously undiagnosed muscular disorders.

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. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

**4.9 Overdose**

Apnoea and prolonged muscle paralysis are the main serious effects of overdose. It is essential, therefore, to maintain the airway and adequate ventilation until spontaneous respiration occurs.
Neostigmine and other anticholinesterase medicinal products are not antidotes to suxamethonium but would normally intensify the depolarisation effect. However, in some cases when the action of suxamethonium is prolonged, the characteristic depolarising (Phase I) block may change to one with characteristics of a non-depolarising (Phase II) block. The decision to use neostigmine to reverse a Phase II suxamethonium-induced block depends on the judgement 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 medicinal product such as atropine.

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: musculo-skeletal system; muscle relaxants, peripherally acting agents; choline derivatives, ATC code: M03AB01

Mechanism of action
Suxamethonium is an ultra-short acting depolarising, neuromuscular blocking substance.

Pharmacodynamic effects
Suxamethonium is closely related in structure to acetylcholine. Similar to acetylcholine, suxamethonium acts on the skeletal muscle motor endplate, to cause flaccid paralysis (Phase I block). Suxamethonium diffuses slowly to the endplate and the concentration at the endplate persists for long enough to cause loss of electrical excitability. The depolarisation of the muscle endplate establishes a voltage gradient and this causes opening of voltage-dependent ion channels of the muscle leading to transient contraction of the muscle. Although the end-plate stays depolarised, the muscle membrane accounts for this depolarization and remains flaccid.
If suxamethonium is continuously infused, the junctional membrane slowly regains its resting potential with the return of neuromuscular transmission(tachyphylaxis); hence to maintain the effect, a higher infusion rate is required. With continued infusion, neuromuscular transmission will fail again (Phase II block) even though the membrane potential of the end-plate stays relatively unchanged. A Phase II block has the clinical characteristics of a non-depolarising block. A Phase II block may be associated with prolonged neuromuscular blockade and apnoea. The mechanism of this block is not known but channel

blocking by penetration of suxamethonium into the sub-end plate cytoplasm, intracellular accumulation of calcium and sodium, the loss of intracellular potassium, and activation of Na,K-ATPase all contribute.
The short duration of action of suxamethonium is considered to be due to its rapid metabolism in the blood. Suxamethonium is rapidly hydrolysed by plasma cholinesterase to succinylmonocholine which possesses clinically insignificant depolarising muscle relaxant properties.

**5.2 Pharmacokinetic properties**

Following intravenous injection, suxamethonium acts within about 30 to 60 seconds and has a duration of action of 2 to 6 minutes, being hydrolysed by plasma cholinesterase (pseudocholinesterase). One molecule of choline is split off rapidly to form succinylmonocholine (a weak muscle relaxant), which is then slowly hydrolysed to succinic acid and choline. Only a small proportion of suxamethonium is excreted unchanged in the urine.
The gene controlling the expression of plasma cholinesterase exhibits polymorphism and enzyme activity varies between individuals. Occasional patients have been reported to exhibit prolonged apnea after administration of suxamethonium. Most of these patients presented atypical plasma cholinesterase or cholinesterase deficiency due to allelic variations, hepatic or renal disease, or nutritional disorders affecting clearance of the active substance. Some medicinal products can inhibit the enzyme synthesis or alter its activity (see section 4.5).

**5.3 Preclinical safety data**

There is no pre-clinical data of relevance to the prescriber which is additional to that already included in other sections of the Summary of Products Characteristics.

**6 PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Sodium chloride,
Succinic acid,
Sodium hydroxide or hydrochloric acid (for pH adjustment),
Water for injection.

**6.2 Incompatibilities**

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

**6.3 Shelf life**

2 years.
After opening, the medicinal product must be used immediately.

This medicinal product may be stored for a short period at temperatures not exceeding 25 °C. In all cases, once initially removed from refrigerated storage, the medicinal product should be discarded after 30 days.

**6.4 Special precautions for storage**

Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the pre-filled syringe in its unopened blister until use.
For storage conditions after first opening of the medicinal product, see section 6.3.

**6.5 Nature and contents of container**

10 ml solution for injection in a pre-filled syringe (polypropylene), with plunger stopper (chlorobutyl), without a needle, with a graduated self- adhesive transparent label (sub - graduations of 0.5 ml from 0 until 10 ml). An end-cap (polypropylene) protects the syringe tip.
The pre-filled syringe is individually packed in a transparent blister.
Available in cardboard boxes of 1 or 10 pre-filled syringes.

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal and other handling**

**Instructions for use:**

***Please prepare the syringe carefully as follows***

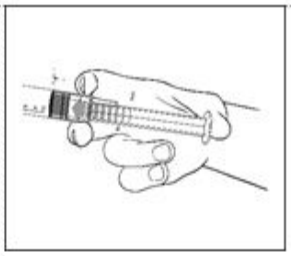
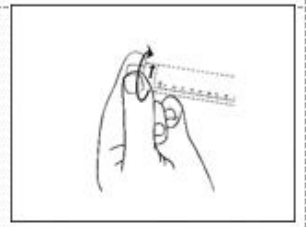
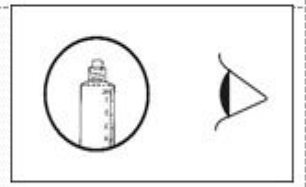
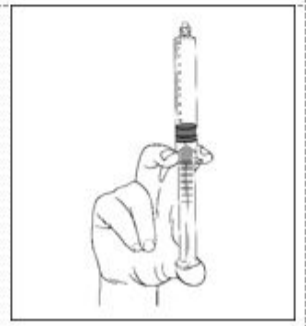
The pre-filled syringe is for single patient only. Discard syringe after use. Do not reuse.

The medicinal product should be inspected visually for particles and discoloration prior to administration. Only clear colourless solution free from particles or precipitates should be used.
The medicinal product should not be used if the tamper evident seal on the syringe is broken.

The external surface of the syringe is sterile until the blister is opened. The blister must not be opened until use.

When handled using an aseptic method, this medicinal product can be placed on a sterile field once it has been removed from the blister.

1) Withdraw the sterile pre-filled syringe from the blister.

| | |
|---|---|
|  | 2) Push on the plunger to free the bung. The sterilisation process may have caused adhesion of the bung to the body of the syringe. |
|  | 3) Twist off the end cap to break the seal. In order to avoid contamination, do not touch the exposed luer connection. |
|  | 4) Check the syringe seal tip has been completely removed. If not, replace the cap and twist again |
|  | 5) Expel the air by gently pushing the plunger. |

6) Connect the syringe to an access device or a needle. Push the plunger slowly to inject the required volume.

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

**7 MARKETING AUTHORISATION HOLDER**

Laboratoire Aguettant
1 Rue Alexander Fleming
69007 LYON
France

**8 MARKETING AUTHORISATION NUMBER**

PA1968/010/001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 24th April 2020

**10 DATE OF REVISION OF THE TEXT**