| Product name: ESMERON 10mg/ mL Solution for Injection<br>Proprietary<br>Rocuronium Bromide | 1.5.5.2 PROPOSED AMENDED PROFESSIONAL INFORMATION<br><br>CLEAN COPY |
|---|---|
| MSD(Pty)Ltd | |
| Mydriasis-Fixed pupils Safety Label Update | |

**SCHEDULING STATUS**

| S4 |
|---|

## 1. NAME OF THE MEDICINE

ESMERON®

50 mg = 5 ml

100 mg = 10 ml

ROCURONIUM BROMIDE

Solution for intravenous injection in vials

## 2. QUALITATIVE AND QUANTITAVIE COMPOSITION

ESMERON 50 mg = 5 ml

Each 5 ml vial contains 50 mg rocuronium bromide.

ESMERON 100 mg = 10 ml

Each 10 ml vial contains 100 mg rocuronium bromide.

For a full list of excipients, see section 6.1

## 3. PHARMACEUTICAL FORM

ESMERON 50 mg = 5 ml: 5 ml vial containing a clear, colourless to faintly yellow, aqueous solution.

ESMERON 100 mg = 10 ml: 10 ml vial containing a clear, colourless to faintly yellow, aqueous solution.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

ESMERON is indicated as an adjunct to general anaesthesia to facilitate tracheal intubation during routine and rapid sequence induction, and to provide skeletal muscle relaxation during surgery. ESMERON is also indicated as an adjunct in the Intensive Care Unit to facilitate intubation and mechanical ventilation for up to 3 days in adults 18 to 65 years.

### 4.2 Posology and method of administration

**Dosage**

ESMERON should only be administered by, or under supervision of, experienced doctors who are familiar with the action and use of these medicines.

The dosage of ESMERON should be individualised in each patient. The method of anaesthesia and the expected duration of surgery, the method of sedation and the expected

duration of mechanical ventilation, the possible interaction with other medication that is administered concomitantly, and the condition of the patient should be taken into account when determining the dose.

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

Inhalational anaesthetics potentiate the neuromuscular blocking effects of ESMERON. Potentiation however, becomes clinically relevant in the course of anaesthesia, when the volatile agents have reached the tissue concentrations required for this interaction. Consequently, adjustments with ESMERON should be made by administering smaller maintenance doses at less frequent intervals or by using lower infusion rates of ESMERON during long lasting procedures (longer than 1 hour) under inhalational anaesthesia (see **section 4.5**).

**Risk of Medication Errors:** Accidental administration of neuromuscular blocking agents may result in serious adverse events, including fatal outcomes. Store ESMERON with the cap and ferrule intact and in a manner that minimizes the possibility of selecting the wrong product (see **section 4.4** ).

In adult patients the following dosage recommendations serve as a general guideline for tracheal intubation and muscle relaxation for short to long lasting surgical procedures and for use in the Intensive Care Unit.

**Surgical Procedures**

**Tracheal intubation**

The standard intubating dose during routine anaesthesia is 0,6 mg/kg ESMERON, after which adequate intubation conditions are established within 90 seconds.

A dose of 1 mg/kg ESMERON is recommended for facilitating tracheal intubation conditions during rapid sequence induction of anaesthesia. At this dose adequate intubation conditions are established within 60 seconds in nearly all patients.

**Higher doses**

Should there be reason for selection of larger doses in individual patients, initial doses up to 2 mg/kg ESMERON have been administered during surgery without adverse cardiovascular effects being noted. The use of these high dosages of ESMERON decreases the onset time and increases the duration of action (see section 5, 5.1 **Pharmacodynamic properties**).

**Maintenance dosing**

The recommended maintenance dose is 0,15 mg/kg ESMERON. In the case of long-term inhalational anaesthesia, this should be reduced to 0,075 to 0,1 mg/kg ESMERON. The maintenance doses should best be given as a bolus when twitch height has recovered to 25 % of control twitch height, or when 2 to 3 responses to train of four stimulation are present (see section 5, 5.1 **Pharmacodynamic properties**).

No cumulation of effect (progressive increase in duration of action) with repetitive maintenance dosing at the recommended level has been observed.

**Continuous infusion**

If ESMERON is administered by continuous infusion it is recommended to give a loading dose of 0,6 mg/kg ESMERON and, when neuromuscular block starts to recover, to start administration by infusion. The infusion rate should be adjusted to maintain twitch response at 10 % of control twitch height or to maintain 1 to 2 responses to train of four stimulation. In adults under intravenous anaesthesia, the infusion rate required to maintain neuromuscular block at this level ranges from 0,3 to 0,6 mg/kg/h and under inhalational anaesthesia the infusion rate ranges from 0,3 to 0,4 mg/kg/h. Continuous monitoring of neuromuscular block is recommended since infusion rate requirements vary from patient to patient and with the anaesthetic method used.

**Paediatric patients**

For infants (28 days to 23 months), children (2 to 11 years) and adolescents (12 to 18 years) the recommended intubation dose during routine anaesthesia and maintenance dose are similar to those in adults.

For continuous infusion in paediatrics the infusion rates, with exception of children, are the same as for adults. For children higher infusion rates might be necessary. For children the same initial infusion rates as for adults are recommended, and this should be adjusted to maintain twitch response at 10 % of control twitch height, or to maintain 1 or 2 responses to train of four stimulation during the procedure.

The experience with ESMERON in rapid sequence induction in paediatric patients is limited. ESMERON is therefore not recommended, for facilitating tracheal intubation conditions during rapid sequence induction in paediatric patients.

**Special populations**

**Geriatric patients and patients with hepatic and/or biliary tract disease and/or renal failure**

The standard intubation dose for geriatric patients and patients with hepatic and/or biliary tract disease and/or renal failure during routine anaesthesia is 0,6 mg/kg ESMERON.

Regardless of the anaesthetic technique used, the recommended maintenance dose for these patients is 0,075 to 0,1 mg/kg ESMERON, and the recommended infusion rate is 0,3 to 0,4 mg/kg/h (see **Continuous infusion**). See **section 4.4**.

**Overweight and obese patients**

When used in overweight or obese patients (defined as patients with a body mass of 30 % or more above ideal body mass) doses should be reduced taking into account an ideal body weight.

**Intensive Care Procedures**

**Tracheal intubation**

For tracheal intubation, the same doses should be used as described above under surgical procedures.

**Maintenance dosing**

The use of an initial loading dose of 0,6 mg/kg ESMERON is recommended, followed by a continuous infusion as soon as twitch height recovers to 10 % or upon reappearance of 1 to 2 twitches to train of four stimulation. Dosage should always be titrated to effect in the individual patient. The recommended initial infusion rate for the maintenance of a neuromuscular block of 80 to 90 % (1 to 2 twitches to train of four stimulation) in adult patients is 0,3 to 0,6 mg/kg/h during the first hour of administration, which will need to be decreased during the following 6 to 12 hours, according to individual response. Thereafter, individual dose requirements remain relatively constant.

A large between patient variability in hourly infusion rates has been found, with mean hourly infusion rates ranging from 0,2 to 0,5 mg/kg/h depending on nature and extent of organ failure(s), concomitant medication and individual patient characteristics. To provide optimal individual patient control, monitoring of neuromuscular transmission is strongly recommended. Safety and efficacy beyond 3 days has not been established.

Following continuous infusion in the Intensive Care Unit, the time to recovery of the train of four ratio to 0,7 depends on the level of block at the end of the infusion. After a continuous infusion for 20 hours or more the median (range) time between return of $T_2$ to train of four stimulation and recovery of the train of four ratio to 0,7 approximates 1,5 (1 to 5) hours in patients without multiple organ failure and 4 (1 to 25) hours in patients with multiple organ failure.

**Administration**

ESMERON is administered intravenously either as a bolus injection or as a continuous infusion.

**4.3 Contraindications**

Hypersensitivity to rocuronium or to the bromide ion or to any of the excipients.

There is insufficient data to support recommendations for the use of ESMERON in neonates (0 to 1 month).

ESMERON is not recommended for the facilitation of mechanical ventilation in the intensive care in paediatric and geriatric patients due to a lack of data on safety and efficacy.

Safety in pregnancy and lactation has not been demonstrated (see **section 4.6** ).

**4.4 Special warnings and precautions for use**

**Anaphylaxis**

Anaphylactic and anaphylactoid reactions may occur. Precautions for treating such reactions should always be taken, particularly in the case of previous anaphylactic reactions to neuromuscular blocking agents, since allergic cross-reactivity to neuromuscular blocking agents has been reported.

**Histamine Release and Histaminoid Reactions**

Since neuromuscular blocking agents are known to be capable of inducing histamine release both locally at the site of injection and systemically, the possible occurrence of itching and erythematous reactions at the site of injection and/or generalised histaminoid (anaphylactoid) reactions should always be taken into consideration when administering these medicines.

In clinical studies only a slight increase in mean plasma histamine levels has been observed following rapid bolus administration of 0,3 to 0,9 mg/kg ESMERON.

It is not recommended to use potentially dangerous machinery or drive a car within 24 hours after the full recovery from the neuromuscular blocking action of ESMERON.

**Appropriate Administration and Monitoring**

Since ESMERON causes paralysis of the respiratory muscles, ventilatory support is mandatory for patients treated with this medicine until adequate spontaneous respiration is restored. It is important to anticipate intubation difficulties, particularly when used as part of a rapid sequence induction technique.

**Residual Curarisation**

Residual curarisation has been reported for ESMERON. In order to prevent complications resulting from residual curarisation, it is recommended to extubate only after the patient has recovered sufficiently from neuromuscular block. Geriatric patients (65 years or older) may be at increased risk for residual neuromuscular block. Other factors which could cause residual curarisation after extubation in the post-operative phase (such as medicine interactions or patient condition) should also be considered. If not used as part of standard clinical practice, the use of a reversal agent should be considered, especially in those cases where residual curarisation is more likely to occur.

**Long-Term Use in an Intensive Care Unit**

Following long term use of ESMERON in the Intensive Care Unit, prolonged paralysis and/or skeletal muscle weakness has been noted. In order to help preclude possible prolongation of neuromuscular block and/or overdosage it is strongly recommended that neuromuscular transmission is monitored throughout the use of ESMERON.

Patients should receive adequate analgesia and sedation. Furthermore, ESMERON should be titrated to effect in the individual patients by, or under supervision of, experienced doctors who are familiar with its actions and with appropriate neuromuscular monitoring techniques.

Myopathy after long-term administration of ESMERON in the Intensive Care Unit, in combination with corticosteroid therapy, has been reported. Therefore, for patients receiving both ESMERON and corticosteroids, the period of use of ESMERON should be limited as much as possible.

**Use with Suxamethonium**

If suxamethonium is used for intubation, the administration of ESMERON should be delayed until the patient has clinically recovered from the neuromuscular block induced by suxamethonium.

**Risk of Death due to Medication Errors**

Administration of ESMERON results in paralysis, which may lead to respiratory arrest and death, a progression that 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. If another healthcare

provider is administering the product, ensure that the intended dose is clearly labelled and communicated.

**The following conditions may influence the pharmacokinetics and/or pharmacodynamics of ESMERON:**

**Hepatic and/or biliary tract disease and renal failure**

Because rocuronium is excreted in urine and bile, ESMERON should be used with caution in patients with clinically significant hepatic and/or biliary diseases and/or renal failure. In these patient groups prolongation of action has been observed with doses of 0,6 mg/kg ESMERON.

**Prolonged circulation time**

Conditions associated with prolonged circulation time such as cardiovascular disease, old age and oedematous states resulting in an increased volume of distribution, may contribute to a slower onset of action. The duration of action may also be prolonged due to reduced plasma clearance.

**Neuromuscular disease**

ESMERON should be used with extreme caution in patients with neuromuscular disease or after poliomyelitis, since the response to neuromuscular blocking agents may be considerably altered in these cases. The magnitude and direction of this alteration may vary widely. In patients with *myasthenia gravis* or with the myasthenic (Eaton-Lambert) syndrome, small doses of ESMERON may have profound effects and ESMERON should be titrated to the response.

**Hypothermia**

In surgery under hypothermic conditions, the neuromuscular blocking effect of ESMERON is increased and the duration prolonged.

**Obesity**

ESMERON may exhibit a prolonged duration and a prolonged spontaneous recovery in obese patients, when the administered doses are calculated on actual body weight.

**Burns**

Patients with burns are known to develop resistance to non-depolarising neuromuscular blocking agents. It is recommended that the dose is titrated to response.

**Conditions which may increase the effects of ESMERON:**

Hypokalaemia (e.g. after severe vomiting, diarrhoea and diuretic therapy), hypermagnesaemia, hypocalcaemia (after massive transfusions), hypoproteinaemia, dehydration, acidosis, hypercapnoea, cachexia.

Severe electrolyte disturbances, altered blood pH or dehydration should therefore be corrected when possible.

**4.5 Interaction with other medicines and other forms of interaction**

The following medicines have been shown to influence the magnitude and/or duration of action of non-depolarising neuromuscular blocking agents:

**Effect of other medicines on ESMERON**

**Increased effect**

- Halogenated volatile anaesthetics potentiate the neuromuscular block of ESMERON. The effect only becomes apparent with maintenance dosing (see “section 4.2**, Surgical Procedures, Maintenance dosing”**). Reversal of the block with acetylcholinesterase inhibitors could also be inhibited.
- After intubation with suxamethonium (see **“section 4.2”** ).

- Long-term concomitant use of corticosteroids and ESMERON in the Intensive Care Unit may result in prolonged duration of neuromuscular block or myopathy (see "**section 4.4**" ).

**Other medicines**

- **Antibiotics:** Aminoglycoside, lincosamide and polypeptide antibiotics, acylaminopenicillin antibiotics.
- Diuretics, quinidine and its isomer quinine, magnesium salts, calcium channel blocking agents, lithium salts, local anaesthetics (lidocaine iv bupivacaine epidural) and acute administration of phenytoin or ß-blocking agents.

Recurarisation has been reported after post-operative administration of: aminoglycoside, lincosamide, polypeptide and acylamino-penicillin antibiotics, quinidine, quinine and magnesium salts (see "**section 4.4**" ).

**Decreased effect**

- Prior chronic administration of phenytoin or carbamazepine.
- Protease inhibitor homologues (such as gabexate and ulinastatin).

**Variable effect**

- Administration of other non-depolarising neuromuscular blocking agents in combination with ESMERON may produce attenuation or potentiation of the neuromuscular block, depending on the order of administration and the neuromuscular blocking agent used.
- Suxamethonium given after the administration of ESMERON, may produce potentiation or attenuation of the neuromuscular blocking effect of ESMERON.

**Effect of ESMERON on other medicines**

ESMERON combined with lidocaine (lignocaine) may result in a quicker onset of action of lidocaine.

**4.6 Fertility, pregnancy and lactation**

Safety in pregnancy and lactation has not been demonstrated.

**Caesarean Section**

In patients undergoing Caesarean section, ESMERON can be used as part of a rapid sequence induction technique, provided no intubation difficulties are anticipated and a sufficient dose of anaesthetic agent is administered or following suxamethonium facilitated

intubation. However ESMERON, administered in doses of 0,6 mg/kg may not produce adequate conditions for intubation until 90 seconds after administration. This dose has been shown to be safe in patients undergoing Caesarean section. ESMERON does not affect Apgar score, foetal muscle tone or cardiorespiratory adaptation.

From umbilical cord blood sampling it is apparent that only limited placental transfer of rocuronium bromide occurs, which does not lead to the observation of clinical adverse effects in the newborn.

Doses of 1,0 mg/kg have been investigated during rapid sequence induction of anaesthesia, but not in Caesarean section patients. Therefore, only a dose of 0,6 mg/kg is recommended in this patient group.

Reversal of neuromuscular block, induced by neuromuscular blocking agents may be inhibited or unsatisfactory in patients receiving magnesium salts for toxaemia of pregnancy, because magnesium salts enhance neuromuscular blockade. Therefore, in these patients the dosage of ESMERON should be reduced and be titrated to twitch response.

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

Since Esmeron is used as an adjunct to general anesthesia, the usual precautionary measures after a general anesthesia should be taken for ambulatory patients.

**4.8 Undesirable effects**

The most commonly occurring adverse drug reactions include injection site pain/reaction, changes in vital signs and prolonged neuromuscular block. The most frequently reported serious adverse drug reactions during post-marketing surveillance is 'anaphylactic and anaphylactoid reactions' and associated symptoms. See also further explanations below.

The following side effects have been reported and the frequencies indicators are as follows: Uncommon/Rare (< 1/100, > 1/10 000); Very rare (< 1/10 000)

| | Uncommon/Rare (< 1/100, > 1/10 000); | Very rare (< 1/10 000) |
| --- | --- | --- |
| **Immune system disorders** | | hypersensitivity, anaphylactic reaction, anaphylactoid reaction, anaphylactic shock, anaphylactoid shock (see **section 4.4**) |

| | | |
| --- | --- | --- |
| **Eye disorders** | | Mydriasis<br>Fixed pupils |
| **Nervous system disorders** | | flaccid paralysis |
| **Cardiac disorders** | tachycardia | |
| **Vascular disorders** | hypotension | circulatory collapse and shock, flushing |
| **Respiratory, thoracic and mediastinal disorders** | | bronchospasm |
| **Skin and subcutaneous tissue disorders** | | angioneurotic oedema, urticaria, rash, erythematous rash |
| **Musculoskeletal and connective tissue disorders** | | after long-term use in the Intensive Care Unit muscular weakness and a few cases of steroid myopathy have been reported (see **section 4.4**) |

| | | |
|---|---|---|
| **General disorders and administration site conditions** | medicine ineffective, decreased medicine effect/therapeutic response, increased medicine effect/therapeutic response, injection site pain, injection site reaction | facial oedema, malignant hyperthermia |
| **Injury, poisoning and procedural complications** | prolonged neuromuscular block, delayed recovery from anaesthesia | airway complication of anaesthesia. |

**Anaphylaxis**

Although very rare, severe anaphylactic reactions to ESMERON have been reported. Anaphylactic/anaphylactoid reactions are bronchospasm, cardiovascular changes (e.g. hypotension, tachycardia, circulatory collapse-shock), and cutaneous changes (e.g. angioedema, urticaria). These reactions have, in some cases, been fatal. Due to the possible severity of these reactions, the necessary precautions should always be taken in anticipation thereof.

**Histamine release**

See "**section 4.4**".

**Prolonged neuromuscular block**

The most frequent adverse reaction to ESMERON consists of an extension of the medicine's pharmacological action beyond the time period required. This may vary from skeletal muscle weakness to profound and prolonged skeletal muscle paralysis resulting in respiratory insufficiency or apnoea.

**Myopathy**

Myopathy has been reported in the Intensive Care Unit after the use of ESMERON in combination with corticosteroids (see section 4.4).

**Local injection site reactions**

Pain on injection has been noted in patients who underwent rapid sequence induction of anaesthesia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

**4.9 Overdose**

In the event of overdosage and prolonged neuromuscular block, the patient should continue to receive ventilatory support and sedation. At the start of spontaneous recovery an acetylcholinesterase inhibitor (e.g. neostigmine, edrophonium, pyridostigmine) should be administered in adequate doses. When administration of an acetylcholinesterase inhibiting agent fails to reverse the neuromuscular effects of ESMERON, ventilation must be continued until spontaneous breathing is restored. Repeated dosage of an acetylcholinesterase inhibitor can be dangerous.

In animal studies, severe depression of cardiovascular function, ultimately leading to cardiac collapse did not occur until a cumulative dose of 750 x $ED_{90}$ 135 mg/kg was administered.

Further treatment is symptomatic and supportive.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

A.17.1 Peripherally acting muscle relaxants

Rocuronium bromide is a non-depolarising neuromuscular blocking agent. It acts by competing for nicotinic cholinoceptors at the motor end-plate. This action is antagonised by acetylcholinesterase inhibitors such as neostigmine, edrophonium and pyridostigmine.

The $ED_{90}$ (dose required to produce 90 % depression of the twitch response of the thumb to stimulation of the ulnar nerve) during balanced anaesthesia is approximately 0,3 mg/kg rocuronium bromide. The $ED_{90}$ in infants is lower than in adults and children (0,25, 0,35 and 0,40 respectively).

The clinical duration (the duration until spontaneous recovery to 25 % of control twitch height) with 0,6 mg/kg rocuronium bromide is 30 to 40 minutes. The total duration (time until spontaneous recovery to 90 % of control twitch height) is 50 minutes. The mean time of

spontaneous recovery of twitch response from 25 to 75 % (recovery index) after a bolus dose of 0,6 mg/kg rocuronium bromide is 14 minutes.

With lower dosages of 0,3 to 0,45 mg/kg rocuronium bromide (1 to 1,5 x $ED_{90}$), onset of action is slower and duration of action is shorter (13 to 26 minutes). With high doses of 2 mg/kg the clinical duration is 110 minutes.

**Cardiovascular surgery**

In patients scheduled for cardiovascular surgery, the most common cardiovascular changes during the onset of maximum block following 0,6 to 0,9 mg/kg rocuronium bromide are an increase in heart rate up to 9 %, and an increase in mean arterial blood pressure up to 16 % from the control values.

**Special populations**

Mean onset time in infants and children at an intubation dose of 0,6 mg/kg is slightly shorter than in adults. The duration of relaxation and the time to recovery tend to be shorter in children compared to infants and adults.

**Reversal of muscle relaxation**

Administration of acetylcholinesterase inhibitors, (neostigmine, pyridostigmine or edrophonium) at reappearance of $T_2$ or at the first signs of clinical recovery, antagonises the action of rocuronium bromide.

**5.2 Pharmacokinetic properties**

After intravenous administration of a single bolus dose of rocuronium bromide the plasma concentration time course runs in three exponential phases. In normal adults, the mean (95 % CI) elimination half-life is 73 (66 to 80) minutes, the (apparent) volume of distribution at steady state conditions is 203 (193 to 214) ml/kg and plasma clearance is 3,7 (3,5 to 3,9) ml/kg/min.

The plasma clearance in geriatric patients and in patients with renal dysfunction was reduced, in most studies however without reaching the level of statistical significance. In patients with hepatic disease, the mean elimination half-life is prolonged by 30 minutes and the mean plasma clearance is reduced by 1 ml/kg/min.

In infants (3 months to 1 year), the apparent volume of distribution at steady state conditions is increased compared to adults and children (1 to 8 years). In older children (3 to 8 years), a trend is seen towards higher clearance and shorter elimination half-life (approximately 20 minutes) compared to adults, younger children and infants.

When administered as a continuous infusion to facilitate mechanical ventilation for 20 hours or more, the mean elimination half-life and the mean (apparent) volume of distribution at steady state are increased. A large between patient variability is found in controlled clinical studies, related to nature and extent of (multiple) organ failure and individual patient characteristics. In patients with multiple organ failure a mean (± SD) elimination half-life of 21,5 (± 3,3) hours, a (apparent) volume of distribution at steady state of 1,5 (± 0,8) l/kg and a plasma clearance of 2,1 (± 0,8) ml/kg/min were found.

Rocuronium is excreted in urine and bile. Excretion in urine approaches 40 % within 12 to 24 hours. After injection of a radio-labelled dose of rocuronium bromide, excretion of the radio-label is on average 47 % in urine and 43 % in faeces after 9 days. Approximately 50 % is recovered as the parent compound.

## 6. PHARAMCEUTICAL PARTICULARS

### 6.1 List of excipients

Sodium acetate,

sodium chloride,

glacial acetic acid and

water for injection.

**6.2 Incompatibilities**

Physical incompatibility has been documented for ESMERON when added to solutions containing the following medicines: amphotericin, amoxicillin, azathioprine, cefazolin, cloxacillin, dexamethasone, diazepam, enoximone, erythromycin, famotidine, frusemide, hydrocortisone sodium succinate, insulin, methohexital, methylprednisolone, prednisolone sodium succinate, thiopental, trimethoprim and vancomycin. ESMERON is also incompatible with Intralipid.

ESMERON must not be mixed with other medicinal products except those mentioned above.

If ESMERON is administered via the same infusion line that is also used for other medicines, it is important that this infusion line is adequately flushed (e.g. with 0,9 % NaCl) between administration of ESMERON and medicines, for which incompatibility with ESMERON has been demonstrated, or for which compatibility with ESMERON has not been established.

**6.3 Shelf Life**

Unopened: 3 years.

After opening the vial: Use immediately and discard any unused contents.

After dilution: diluted product (see section 6.6 for possible infusion fluids) should be used immediately and any unused contents should be discarded.

### 6.4 Special precautions for storage

Store at 2 to 8 °C.

ESMERON may be stored at a temperature not exceeding 30 °C, for a maximum period of 12 weeks. After first removal from the refrigerator, the 12 week shelf life applies.

After opening of the container the solution is chemically stable for 24 hours at room temperature. Since ESMERON does not contain a preservative, any unused solution should be discarded.

Keep out of reach of children.

### 6.5 Nature and contents of container

ESMERON 50 mg = 5 ml: Cartons containing 10 x 5 ml clear, glass vials each of which contains 50 mg rocuronium bromide in aqueous solution.

ESMERON 100 mg = 10 ml: Cartons containing 10 x 10 ml clear, glass vials each of which contains 100 mg rocuronium bromide in aqueous solution.

Not all strengths are marketed.

**6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

**Compatibilities**

Compatibility studies with the following infusion fluids have been performed. In nominal concentrations of 0,5 mg/ml and 2 mg/ml ESMERON has been shown to be compatible with: 0,9 % NaCl, 5 % Dextrose, 5 % Dextrose in saline, Sterile water for injection, Lactated Ringer's and Haemaccel.

Administration should begin immediately after mixing, and should be completed within 24 hours. Unused solutions should be discarded.

**7. HOLDER OF CERTIFICATE OF REGISTRATION**

MSD (Pty) Ltd

117 16th Road

Halfway House

1685

South Africa

**8. REGISTRATION NUMBERS**

ESMERON 50 mg = 5 ml: 30/17.1/0192

ESMERON 100 mg = 10 ml: 30/17.1/0193

**9. DATE OF FIRST AUTHORISATION**

Date of registration: 23 February 1996

**10. DATE OF REVISION OF THE TEXT**

Date of most recent approval: 30 August 2017 (SR-PIN: 03 March 2019)

| Namibia Only | |
|---|---|
| Registration Number | 05/17.1/0015 |
| Scheduling Status | NS2 |

CCDS-MK8085-SOi-072018

CCDS-MK8085-SOi-022022