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**MSD ARTWORK**

Item No.: XXXXXX  
Revision Date & No.: XXXXXX-X  
Pharma Code: XXX  
Schawk Job No.: 372067A01

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Technical Info Profile

**SCHAWKI!**

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**Pr** Proprietary

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For Position Only

**Norcuron® 10mg**  
Powder for solution for injection  
VECURIONIUM BROMIDE

**INFORMATION FOR THE DOCTOR**

**1. TRADE NAME OF THE MEDICINAL PRODUCT**  
Norcuron 10 mg, powder for solution for injection.

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**  
1 vial contains 10mg Vecuronium bromide which corresponds to 2mg vecuronium bromide per ml.  
Excipient: Each vial contains 4.2mg (0.18mmol) sodium. For full list of excipients, see section 6.1.

**3. PHARMACEUTICAL FORM**  
Powder for solution for injection.  
A white to off-white sterile powder.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic Indications**  
Norcuron is indicated as an adjunct to general anaesthesia to facilitate tracheal intubation and to provide skeletal muscle relaxation during surgery in adults, neonates, infants, children and adolescents

**4.2 Posology and Method of Administration**

**Dosage**  
Like other neuromuscular blocking agents, Norcuron should only be administered by, or under the supervision of, experienced clinicians who are familiar with the action and use of these drugs. Like with all other neuromuscular blocking agents, the dosage of Norcuron should be individualised in each patient. The anaesthetic method used, the expected duration of surgery, the possible interaction with other drugs that are administered before or during anaesthesia and the condition of the patient should be taken into account when determining the dose.

The use of an appropriate neuromuscular monitoring is recommended to monitor neuromuscular blockade and recovery. Inhalational anaesthetics do potentiate the neuromuscular blocking effects of Norcuron. This 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 Norcuron should be made by administering smaller maintenance doses at less frequent intervals or by using lower infusion rates of Norcuron during long lasting procedures (longer than 1 hour) under inhalational anaesthesia (see section 4.5).

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

**Tracheal intubation:**  
The standard intubation dose during routine anaesthesia is 0.08 to 0.1 mg vecuronium bromide per kg body weight, after which adequate intubation conditions are established within 90 to 120 seconds in nearly all patients.

**Dosages of Norcuron for surgical procedures after intubation with suxamethonium:**  
Recommended doses: 0.03 to 0.05 mg vecuronium bromide per kg body weight.

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

**Maintenance dosing:**  
The recommended maintenance dose is 0.02 to 0.03 mg vecuronium bromide per kg body weight. These maintenance doses should be given when twitch height has recovered to 25% of control twitch height.

**Dosing in elderly patients:**  
The same intubation and maintenance doses as for younger adults (0.08-0.1mg/kg and 0.02-0.03mg/kg, respectively) can be used. However, the duration of action is prolonged in elderly compared to younger subjects due to changes in pharmacokinetic mechanisms. The onset time in elderly is similar to younger adults.

**Paediatric Population:**  
**Adolescents (12-17 years)**  
Although there is very little information on dosage in adolescents, it is advised to use the same dose as in adults, based on the physiological development at this age.  
**Children (2-11 years)**  
Dose requirements in children are higher than for adults and neonates (see 'Paediatric patients' in section 5.1). However, the same intubation and maintenance doses as for adults (0.08-0.1mg/kg and 0.02-0.03 mg/kg, respectively) are usually sufficient. Since the duration of action is shorter in children, maintenance doses are required more frequently.  
**Neonates (0-27 days) and Infants (28 days-23 months)**  
Because of possible variations in the sensitivity of the neuromuscular junction, especially in neonates (up to 4 weeks) and probably in infants up to 4 months of age, an initial test dose of 0.01 to 0.02 mg vecuronium bromide per kg body weight followed by incremental doses until 90 to 95% depression of twitch response is achieved is recommended. In neonatal surgery the dose should not exceed 0.1 mg/kg.  
Dose requirements in older infants (5-23 months) are the same as in adults. However, since the onset time of Norcuron in these patients is considerably shorter than in adults and children, the use of high intubating doses in general is not required for early development of good intubating conditions.

Since the duration of action and recovery time with Norcuron is longer in neonates and infants than in children and adults, maintenance doses are required less frequently. (See 'Paediatric patients' in section 5.1.)

**Preterm newborn infants**  
There are insufficient data to support dose recommendations for the use of vecuronium bromide in preterm newborn infants

**Dose requirements for administration of Norcuron by continuous infusion:**  
If Norcuron is administered by continuous infusion, it is recommended to give a loading dose first (See 'Tracheal intubation') and, when neuromuscular block starts to recover, to start administration of Norcuron 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, the infusion rate required to maintain neuromuscular block at this level, ranges from 0.3 to 1.4 micrograms vecuronium bromide/kg/min. For neonates and infants see above. Repeat monitoring of neuromuscular block is recommended since infusion rate requirements vary from patient to patient and with the anaesthetic method used.

**Continuous infusion in paediatric patients**  
There are insufficient data concerning continuous infusion of Vecuronium in paediatric patients, therefore no dose recommendations can be made.

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

**Higher doses.**  
Should there be reason for selection of larger doses in individual patients; initial doses ranging from 0.15 mg up to 0.3 mg vecuronium bromide per kg body weight have been administered during surgery both under halothane and neurolept anaesthesia without adverse cardiovascular effects being noted as long as ventilation is properly maintained. The use of these high dosages of Norcuron pharmacodynamically decreases the onset time and increases the duration of action.

**Administration**  
Norcuron should be administered following reconstitution. Norcuron is administered intravenously either as a bolus injection or as a continuous infusion (see also section 6.8).

**4.3 Contraindications**  
Hypersensitivity to vecuronium or the bromide ion or to any of the excipients of Norcuron.

**4.4 Special Warnings and Precautions for Use**  
Since Norcuron causes paralysis of the respiratory muscles, ventilatory support is mandatory for patients treated with this drug until adequate spontaneous respiration is restored.

As with other neuromuscular blocking agents, residual curarization has been reported for Norcuron. In order to prevent complications resulting from residual curarization, it is recommended to extubate only after the patient has recovered sufficiently from neuromuscular block. Other factors which could cause residual curarization after extubation in the post-operative phase (such as drug 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 curarization is more likely to occur.

Anaphylactic reactions can occur following the administration of neuromuscular blocking agents. Precautions for treating such reactions should always be taken. Particularly in the case of previous anaphylactic reactions to neuromuscular blocking agents, special precautions should be taken since allergic cross-reactivity between neuromuscular blocking agents has been reported.

Since Norcuron has no cardiovascular effects within the clinical dosage range, it does not attenuate bradycardia that may occur due to the use of some types of anaesthetics and opiates or due to vagal reflexes during surgery. Therefore, reassessment of the use and/or dosage of vagolytic drugs such as atropine for premedication or at induction of anaesthesia, may be of value for surgical procedures during which vagal reactions are more likely to occur (e.g. surgical procedures where anaesthetic drugs with known vagal stimulatory effects are used e.g. ophthalmic, abdominal or anorectal surgery etc).

In general, following long term use of neuromuscular blocking agents in the ICU, prolonged paralysis and/or skeletal muscle weakness has been noted. In order to help preclude possible prolongation of neuromuscular block and/or overdose it is strongly recommended that neuromuscular transmission is monitored throughout the use of neuromuscular blocking agents. In addition, patients should receive adequate analgesia and sedation. Furthermore, neuromuscular blocking agents should be titrated to effect in the individual patients by or under supervision of experienced clinicians who are familiar with their actions and with appropriate neuromuscular monitoring techniques.

Myopathy after long term administration of non-depolarising neuromuscular blocking agents in the ICU in combination with corticosteroid therapy has been reported frequently. Therefore, for patients receiving both neuromuscular blocking agents and corticosteroids, the period of use of the neuromuscular blocking agent should be limited as much as possible.

**The following conditions may influence the pharmacokinetics and/or pharmacodynamics of Norcuron:**  
Hepatic and/or biliary tract disease and renal failure  
Because vecuronium is excreted in bile and in urine, Norcuron 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, especially when high doses of vecuronium (0.15-0.2mg/kg bodyweight) were administered in patients with hepatic disease.

**Prolonged circulation time**  
Conditions associated with prolonged circulation time such as cardiovascular disease, old age, oedematous state resulting in an increased volume of distribution, may contribute to an increase in the onset time of neuromuscular block. The duration of action may also be prolonged due to a reduced plasma clearance.

**Neuromuscular disease**  
As with other neuromuscular blocking agents, Norcuron 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 the myasthenia (Eaton Lamber) syndrome, small doses of Norcuron may have profound effects and Norcuron should be titrated to the response.

**Hypothermia**  
In operations under hypothermia, the neuromuscular blocking effect of Norcuron is increased and the duration is prolonged.

**Obesity**  
Like other neuromuscular blocking agents, Norcuron 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-depolarizing agents. It is recommended that the dose is titrated to response.

**Conditions which may increase the effects of Norcuron are:**  
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.**

**Patients on a controlled sodium diet:**  
Each ml solution contains 2 mg sodium. A dose of 23 mg sodium is considered essentially 'sodium-free'. If more than 11.5 ml solution needs to be administered, this should be taken into consideration by patients on a controlled sodium diet.

**4.5 Interaction with other medicinal products and other forms of interaction**  
The following drugs have been shown to influence the magnitude and/or duration of action of non-depolarizing neuromuscular blocking agents:

**Effect of other drugs on Norcuron**  
**Increased effect:**  
Halogenated volatile anaesthetics potentiate the neuromuscular block of Norcuron. The effect only becomes apparent with maintenance dosing (see also section 4.2). Reversal of the block with anticholinesterase inhibitors could also be inhibited. After intubation with suxamethonium (see section 4.2).  
Long-term concomitant use of corticosteroids and Norcuron in the ICU may result in prolonged duration of neuromuscular block or myopathy (see also section 4.4 and 4.8)

**Other drugs:**

- antibiotics: aminoglycoside, lincosamide and polypeptide antibiotics, acylamino-penicillin antibiotics
- diuretics, thiamine, quinidine, magnesium salts, calcium channel blocking agents, lithium salts, cimetidine, lidocaine and acute administration of phenytoin or  $\beta$ -blocking agents.

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

**Decreased effect:**

- neostigmine, edrophonium, pyridostigmine, aminopyridine derivatives
- prior chronic administration of phenytoin or carbamazepine

**Variable effect:**  
Administration of other non-depolarizing neuromuscular blocking agents in combination with Norcuron may produce attenuation of potentiation of the neuromuscular block, depending on the order of administration and the neuromuscular blocking agent used.

Suxamethonium given after the administration of Norcuron may produce potentiation or attenuation of the neuromuscular blocking effect of Norcuron.

**Effect of Norcuron on other drugs**  
**Effect of Norcuron on lidocaine**  
Norcuron combined with lidocaine may result in a quicker onset of action of lidocaine.

**4.6 Pregnancy and Lactation**  
Animal studies do not indicate an effect on fertility. There are insufficient data on the use of Norcuron during animal or human pregnancy to assess potential harm to the foetus. Norcuron should be given to a pregnant woman only when the attending physician decides that the benefits outweigh the risks.

**Caesarean section**  
Studies with Norcuron, administered in doses up to 0.1mg/kg, have shown its safety for use in Caesarean section. In caesarean section the dose should not exceed 0.1mg/kg.

In several clinical studies Norcuron did not affect Apgar score, foetal muscle tonus or cardiorespiratory adaptation. From umbilical cord blood sampling it is apparent that only very little placental transfer of Norcuron occurs which did not lead to the observation of any clinical adverse effect in the newborn.

**Note:**  
Reversal of Norcuron-induced neuromuscular block may be inhibited or unsatisfactory in patients receiving magnesium sulphate for toxoemia of pregnancy because magnesium salts enhance neuromuscular block. Therefore, in patients receiving magnesium sulphate the dosage of Norcuron should be reduced and be carefully titrated to twitch response.

**Lactation**  
There are no human data on the use of Norcuron during lactation. Norcuron should be given to lactating women only when the attending physician decides that the benefits outweigh the risks.

- medicines for manic depressive illness (bipolar disorder)  
- magnesium salts  
- the medicine called cimetidine, used to treat stomach ulcers, heartburn or acid reflux.

- certain medicines used to make you sleep during surgery (anaesthetics)  
- medicines which cause increased volume of urine (diuretics)  
- certain local anaesthetics (lidocaine)  
- certain medicines for epilepsy during an operation (phenytoin)

**Medicines which decrease the effect of Norcuron**

- certain medicines for epilepsy (phenytoin or carbamazepine)
- acetylcholinesterase inhibitors, medicines for the treatment of myasthenia gravis (e.g. neostigmine, edrophonium, pyridostigmine, aminopyridine derivatives)

In addition, you may be given other medicines before or during surgery which can alter the effects of Norcuron. These include certain anaesthetics, other muscle relaxants, medicines such as phenytoin and medicines which reverse the effects of Norcuron. Norcuron may make certain anaesthetics work more quickly. Your anaesthetist will take this into account when deciding the correct dose of Norcuron for you.

**Pregnancy and Breast feeding**

— Tell your anaesthetist if you are pregnant or might be pregnant, or if you are breast feeding.  
Your anaesthetist may still give you Norcuron, but you may need to discuss it first. Norcuron may be given to you if you are having a Caesarean section.

**MSD PROFILE**

Profile: BS 12\_335  
Profile Revision: 01  
Profile Revision Date: 250512  
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Pharma Code Braille Grid Tamper Evident

Profile Perforation Fold

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For Position Only

**Norcuron® 10mg**  
Powder for solution for injection  
VECURIONIUM BROMIDE

**INFORMATION FOR THE PATIENT**

Norcuron is one of a group of drugs called *muscle relaxants*.

Muscle relaxants are used during an operation as part of a general anaesthetic. When you have an operation your muscles must be completely relaxed. This makes it easier for the surgeon to perform the operation.

Normally, your nerves send messages called *impulses* to your muscles. Norcuron acts by blocking these impulses so that your muscles relax. Because your breathing muscles also relax, you will need help to breathe (*artificial ventilation*) during and after your operation until you can breathe on your own again.

During the operation your anaesthetist will keep check on the effect of the muscle relaxant, and if necessary will give you some more. At the end of surgery, the effects of the drug are allowed to wear off and you will start breathing on your own. Sometimes the anaesthetist will give you another drug to help speed this up.

**You should not receive Norcuron**

- if you are allergic (*hypersensitive*) to vecuronium, the bromide ion or any of the other ingredients in Norcuron.

— Tell your anaesthetist if this applies to you.

**Take special care with Norcuron**  
Your anaesthetist needs to know before you receive this medicine:

- If you are allergic to **muscle relaxants**
- if you have had **kidney, heart, liver or gall bladder** disease
- if you have had diseases affecting **nerves and muscles** (e.g. poliomyelitis, myasthenia gravis)

**1. WHAT NORCURON IS AND WHAT IT IS USED FOR**  
— Tell your anaesthetist if any of these applies to you.  
**Some conditions may influence the effects of Norcuron - for example:**

- low calcium levels in the blood
- low potassium levels in the blood
- high magnesium levels in the blood
- low levels of protein in the blood
- too much carbon dioxide in the blood
- loss of too much water from the body, for example by being sick, diarrhoea or sweating
- too much acid in the blood
- general ill-health
- burns
- being very overweight (*obesity*)
- very low body temperature (*hypothermia*)

If you have any of these conditions, your anaesthetist will take it into account when deciding the correct dose of Norcuron for you.

**Other medicines and Norcuron**  
— Tell your anaesthetist if you are taking other medicines or have recently taken them. This includes medicines or herbal products that you have bought without a prescription. Norcuron may affect other medicines or be affected by them.

**Medicines which increase the effect of Norcuron**

- certain **antibiotics**
- certain medicines for **heart disease or high blood pressure** (*water tablets, calcium channel blockers, beta-blockers and quinidine*)
- certain **anti-inflammatory medicines** (*corticosteroids*)

**Medicines which decrease the effect of Norcuron**

- medicines for **manic depressive illness (bipolar disorder)**
- **magnesium salts**
- the medicine called **cimetidine**, used to treat stomach ulcers, heartburn or acid reflux.
- certain medicines **used to make you sleep** during surgery (*anaesthetics*)
- medicines which cause **increased volume of urine** (*diuretics*)
- certain **local anaesthetics (lidocaine)**
- certain medicines for **epilepsy** during an operation (*phenytoin*)

**Medicines which decrease the effect of Norcuron**


- certain medicines for **epilepsy (phenytoin or carbamazepine)**
- **acetylcholinesterase inhibitors, medicines for the treatment of myasthenia gravis** (e.g. neostigmine, edrophonium, pyridostigmine, aminopyridine derivatives)

In addition, you may be given other medicines before or during surgery which can alter the effects of Norcuron. These include certain anaesthetics, other muscle relaxants, medicines such as phenytoin and medicines which reverse the effects of Norcuron. Norcuron may make certain anaesthetics work more quickly. Your anaesthetist will take this into account when deciding the correct dose of Norcuron for you.

**Pregnancy and Breast feeding**

— Tell your anaesthetist if you are pregnant or might be pregnant, or if you are breast feeding.  
Your anaesthetist may still give you Norcuron, but you may need to discuss it first. Norcuron may be given to you if you are having a Caesarean section.


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**4.7 Effects on ability to Drive and Use Machines**  
Since Norcuron 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**  
Adverse Drug Reactions (ADRs) are rare (<1/1000). The most commonly occurring ADRs include changes in vital signs and prolonged neuromuscular block. The most frequently reported ADR during post-marketing surveillance is 'anaphylactic and anaphylactoid reactions' and associated symptoms (reporting frequency < 1/100 000). See also the explanations below the table.

MedDRA SOC	Preferred Term <sup>1</sup>	
	Uncommon/rare (<1/100,>1/10 000)	Very rare (<1/10 000)
Immune system disorders	Hypersensitivity	Anaphylactic reaction Anaphylactoid reaction Anaphylactic shock Anaphylactoid shock
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 edema Urticaria Erythematous rash
Musculoskeletal and connective tissue disorders		Muscular weakness <sup>†</sup> Steroid myopathy <sup>‡</sup>
General disorders and administration site conditions	Drug ineffective Decreased drug effect/therapeutic response	Face oedema Injection site pain
	Increased drug effect/therapeutic response	Injection site reaction
Injury, poisoning and procedural complications	Prolonged neuromuscular block Delayed recovery from anesthesia	Airway complication of anesthesia

MedDRA version 8.0

<sup>1</sup> Frequencies are estimates derived from post-marketing surveillance reports and data from the general literature.

<sup>2</sup> After long-term use in the ICU

**Prolonged Neuromuscular block**  
The most frequent adverse reaction to nondepolarizing blocking agents as a class consists of an extension of the drug's pharmacological action beyond the time period needed. This may vary from skeletal muscle weakness to profound and prolonged skeletal muscle paralysis resulting in respiratory insufficiency or apnea. A few cases of myopathy have been reported after Norcuron was used in the ICU in combination with corticosteroids (see section 4.4).

**Anaphylactic reactions**  
Although very rare, severe anaphylactic reaction to neuromuscular blocking agents, including Norcuron, have been reported. Anaphylactic/anaphylactoid reactions usually comprise of several signs or symptoms, e.g.: 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, one should always assume they may occur and take the necessary precautions.

**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 (see also under anaphylactic reactions above) should always be taken into consideration when administering these drugs.

Experimental studies with intradermal injection of Norcuron have demonstrated that this drug has only a weak capacity for inducing local histamine release. Controlled studies in man failed to demonstrate any significant rise in plasma histamine levels after intravenous administration of Norcuron. Nevertheless, such cases have rarely been reported during large scale use of Norcuron.

**4.9 Overdose**  
In the event of overdose and prolonged neuromuscular block, the patient should continue to receive ventilatory support and sedation. In this situation there are two options for the reversal of neuromuscular block: (1) Sugammadex can be used for reversal of intense (profound) and deep block. The dose of Sugammadex to be administered depends on the level of neuromuscular block. The use of Sugammadex for the purposes of reversal of vecuronium-induced blockade is recommended for use only in the adult population. There are specific circumstances for which Sugammadex may be useful (refer to section 5.1 Reversal of neuromuscular block). (2) An acetylcholinesterase inhibitor (e.g. neostigmine, edrophonium, pyridostigmine) can be used once spontaneous recovery starts and should be administered in adequate doses. When administration of a cholinesterase inhibiting agent fails to reverse the neuromuscular effects of Norcuron, ventilation must be continued until spontaneous breathing is restored. Repeated dosage of a cholinesterase inhibitor can be dangerous.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic Properties**  
Pharmacotherapeutic group: muscle relaxants, peripherally acting agents, ATC code: M03A C03

Norcuron (vecuronium bromide) is a non-depolarising neuromuscular blocking agent, chemically designated as the aminosteroid 1-(3alpha,17beta-diacetoxy-2beta piperidino-5alpha-androstan-16beta-yl)-methylpiperidinium bromide.

Norcuron blocks transmission process between the motor nerve-ending and striated muscle by binding competitively with acetylcholine to the nicotinic receptors located in the motor end-plate region of striated muscle.

Unlike depolarising neuromuscular blocking agents, such as suxamethonium, Norcuron does not cause muscle fasciculations.

Within the clinical dosage range, Norcuron exerts no vagolytic nor ganglion blocking activity.

**Tracheal intubation**  
Within 90 to 120 seconds following intravenous administration of a dose of 0.08 to 0.1 mg vecuronium bromide per kg body weight, good to excellent conditions for tracheal intubation occur and within 3 to 4 minutes following administration of these dosages, general muscle paralysis adequate for any type of surgery is established. The duration of action to 25% recovery of control twitch height (clinical duration) with this dose is 24 to 60 minutes. The time to 95% recovery of control twitch height following this dose is approximately 60 to 80 minutes.

With higher dosages of Norcuron, onset time to maximal block is shortened and duration of action is prolonged.

Continuous intravenous infusion  
In case Norcuron is administered by continuous intravenous infusion, a steady state neuromuscular blockade of 90% can be maintained at a constant rate of drug delivery and without clinically significant prolongation of the recovery time from neuromuscular block at termination of the infusion.

Norcuron has no cumulative effects if maintenance doses are administered at 25% recovery of control twitch height. Several maintenance doses can therefore be given in succession. The above-mentioned properties make that Norcuron can be used as well in short, as in long lasting surgical procedures.

**Reversal of neuromuscular block**  
The action of vecuronium can be antagonised either by Sugammadex or by acetylcholinesterase inhibitors, such as neostigmine, pyridostigmine or edrophonium. Sugammadex can be given for routine reversal at 1-2 post-tetanic counts to reappearance of T<sub>1</sub>. Acetylcholinesterase inhibitors can be administered at reappearance of T<sub>1</sub> or at the first signs of clinical recovery. The use of Sugammadex for the purposes of reversal of vecuronium-induced blockade is recommended for use only in the adult population.

**Paediatric population**  
Neonates and infants:  
In neonates and infants the ED<sub>50</sub> dose of vecuronium bromide under nitrous oxide in oxygen anaesthesia was found to be approximately the same (approx. 47 µg/kg body weight) as in adults.

The onset time of Norcuron in neonates and infants is considerably shorter as compared to children and adults, probably due to the shorter circulation time and larger cardiac output. Also, a greater sensitivity of the neuromuscular junction to the action of neuromuscular blocking agents in these patients may account for a more rapid onset of action.

The duration of action and recovery time with Norcuron is longer in neonates and infants than in adults. Maintenance doses of Norcuron should therefore be less frequently administered.

Children:  
In children the ED<sub>50</sub> dose of vecuronium bromide under nitrous oxide in oxygen anaesthesia was found to be higher than in adults (0.081 vs. 0.043 mg/kg bodyweight, respectively). In comparison to adults, the duration of action and recovery time with Norcuron in children are in general approximately 30% and 20-30% shorter respectively.

Similar to adults, cumulative effects with repeat maintenance doses of approximately one quarter of the initial dose are administered at 25% recovery of control twitch height are not observed in paediatric patients.

**5.2 Pharmacokinetic Properties**  
After intravenous administration of 0.1-0.15mg/kg vecuronium, the distribution half-life of vecuronium amounts to 1.2-1.4 minutes.

Vecuronium is mainly distributed in the extracellular fluid compartment. At steady state, the volume of distribution is 0.19-0.51 l kg<sup>-1</sup> in adult patients.

The plasma clearance of vecuronium amounts to 3.0-6.4 ml kg<sup>-1</sup> min<sup>-1</sup> and its plasma elimination half-life is 26-117 minutes.

The extent of metabolism of vecuronium is relatively low. In humans, a 3-hydroxy derivative having approximately 50% less neuromuscular blocking potency than vecuronium is formed in the liver. In patients not suffering from renal nor hepatic failure, the plasma concentration of this derivative is below detection limit, and does not contribute to the neuromuscular block occurring after administration of Norcuron.

Biliary excretion is the main elimination route. It is estimated that within 24 hours after intravenous administration of Norcuron, 40 to 60% of the dose administered is excreted into the bile as monoquaternary compounds. Approximately 95% of these monoquaternary compounds is unchanged vecuronium and less than 5% is 3-hydroxy vecuronium. Prolonged duration of action has been observed in patients with liver disease and/or biliary tract disease, probably as a result of decreased clearance leading to an increased elimination half-life.

Renal elimination is relatively low. The amount of monoquaternary compounds excreted in the urine collected by intravesical catheter for 24 hours following Norcuron administration 20-30% of the dose administered. In patients with renal failure, the duration of action may be prolonged. This is probably the result of an increased sensitivity to vecuronium, but it could also be the result of a reduced plasma clearance.

**Paediatric population**  
There are limited pharmacokinetic data for vecuronium in the paediatric population. After intravenous administration, vecuronium plasma clearance is similar across neonates, infants and children (2.8-9.0 ml kg<sup>-1</sup> min<sup>-1</sup>) and not different from the clearance in adults. Volume of distribution at steady state (V<sub>ss</sub>), in infants is similar to the one in adult patients (0.29-0.43 l/kg), whereas it is slightly smaller in children (0.13 – 0.32 l/kg).

**5.3 Preclinical Safety Data**  
Vecuronium bromide showed no genotoxic embryonic or teratogenic potential. Single and repeated dose toxicity studies in rats, dogs and cats revealed no special hazard for humans.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of Excipients**

- Citric acid monohydrate
- Disodium hydrogen phosphate dihydrate
- Mannitol (E421)
- Sodium hydroxide (for pH adjustment)
- Phosphoric acid (for pH adjustment)

**6.2 Compatibility**  
As is the case for many other drugs, incompatibility has been documented for Norcuron when added to thiopental.

Except for those solutions with which Norcuron has been shown to be compatible, it is not recommended that Norcuron should be mixed with other solutions, or drugs in the same syringe or bag (see Section 6.5 - Compatibility).

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If Norcuron is administered via the same infusion line that is also used for other drugs, it is important that this infusion line is adequately flushed (e.g. with 0.9% NaCl) between administration of Norcuron and drugs for which incompatibility with Norcuron has been demonstrated or for which compatibility with Norcuron has not been established.

**6.3 Shelf Life**  
Unopened: 2 years

The reconstituted product should be used immediately

**6.4 Special Precautions for Storage**  
Do not store above 25°C. Keep the container in the outer carton. For storage conditions of the reconstituted solution, see section 6.3.

Do not use Norcuron when the solution, after reconstitution, contains particles or is not clear.

**6.5 Nature and contents of container**  
Norcuron 10 mg  
Packaging of 10 vials each containing 10 mg vecuronium bromide. All vials are made of type 1 glass. Not all pack sizes may be marketed. In correspondence please quote packaging number.

**6.6 Instructions for use/handling**  
Norcuron 10mg  
Addition of 5 ml of water for injections results in an isotonic solution of pH 4 containing 2 mg vecuronium bromide per ml (2 mg/ml)

Alternatively, in order to obtain a solution with a lower concentration, Norcuron 10 mg may be reconstituted with a volume up to 10 ml of the following infusion fluids:

- 5% glucose injection fluid
  - 0.9% sodium chloride injection fluid
  - Lactated Ringer's solution
  - Lactated Ringer's injection and 5 % glucose
  - Glucose 5 % and 0.9 % sodium chloride injection
- Compatibility:**  
When Norcuron is reconstituted with water for injections, the resultant solution can be mixed with the following infusion fluids, packed in PVC or glass, to a dilution up to 40mg/litre:
- 0.9% NaCl solution
  - 5% glucose solution
  - Ringer's solution
  - Ringer's glucose

The above-mentioned reconstituted solution can also be injected into the line of a running infusion of the following fluids:

- Lactated Ringer's solution
- Lactated Ringer's solution and 5% glucose
- Glucose 5% and 0.9% NaCl solution
- Normsol M with glucose 5%
- Haemacel
- Dextran-40 5% in 0.9% NaCl solution

Compatibility studies with other infusion fluids have not been performed.

Any unused solution should be discarded.

For single use only.

**7. NAME AND ADDRESS OF MARKETING AUTHORISATION HOLDER**  
NV Organon  
Kloosterstraat 6  
5349 AB Oss  
The Netherlands

**8. MARKETING AUTHORISATION NUMBER**  
PA 964/22

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION**  
13 March 1987/13 March 2007

**10. DATE OF REVISION OF THE TEXT**  
June 2012

**Driving and using machines**  
Do not drive or use machines until advised it is safe to do so. Because Norcuron is given as part of a general anaesthetic, you may feel tired, weak or dizzy for some time afterwards. Your anaesthetist will be able to advise you on how long the effects are likely to last.

**Important information about some of the ingredients of Norcuron**  
**Patients on a controlled sodium diet:**  
In most cases you will get less than 1 mmol sodium (23 mg) per daily dose, i.e. essentially 'sodium-free', but sometimes you will get more than 1 mmol sodium per day. Inform your doctor if you are on a controlled sodium diet before the medical operation.

**3. HOW NORCURON IS GIVEN**  
**How much and when to use Norcuron**  
Norcuron can be used in adults and children of all ages

The dose will be determined by the doctor. You will be given Norcuron before or during a surgical procedure. The usual dose is 0.08 to 0.1 mg vecuronium bromide per kg body weight and the effect is 24 to 60 minutes. During the procedure it will be checked whether Norcuron is still working. You may be given additional doses if they are needed. The dose that you receive will depend on various factors. These include possible interactions with any other drugs you may have been given, the expected duration of the procedure, your age and the state of your health.

**Overdose**  
As your anaesthetist will be monitoring your condition carefully so it is unlikely that you will be given too much Norcuron. However if this happens, your anaesthetist will keep you breathing artificially (on a ventilator) until you can breathe on your own. You will be kept asleep while this takes place.

**If you forgot to take Norcuron:**  
This is not applicable for Norcuron.

**4. POSSIBLE SIDE EFFECTS**  
Like all medicines, Norcuron can have side effects, but not everyone gets them. If these side effects occur while you are under anaesthetic, they will be seen and treated by your anaesthetist.

**Uncommon side effects** (up to 1 in 100 people given Norcuron are affected)

- the drug is too effective, or not effective enough
- the drug works for longer than expected
- lowering of blood pressure
- increased heart rate

**Very rare side effects** (less than 1 in 10,000 people given Norcuron are affected)

- allergic /hypersensitivity/ reactions, (such as difficulty in breathing, collapse of the circulation and shock), which can be fatal in some cases
- tightness of the chest by muscle cramps of the airways (bronchospasm) and temporary absence or stopping of breathing (apnoea)
- muscle weakness

- swelling, rash or redness of the skin (such as face oedema, flushing or wheals)
- pain near the site of injection
- long term muscle dysfunction usually observed after concurrent use of Norcuron and corticosteroids (anti-inflammatory medicines) in critically ill patients (steroid myopathy)

**If any of the side effects gets serious**  
Or if you notice any side effects not listed in this leaflet:  
→ Tell your anaesthetist or other doctor.

**5. HOW NORCURON IS STORED**  
Keep Norcuron out of reach and sight of children. Norcuron is stored in the hospital. Do not store above 25°C. Keep the container in the outer carton. For single use only.

Do not use Norcuron after the expiry date stated on the label and carton after "Use by". The expiry date refers to the last day of the month.

Do not use Norcuron when you notice that the solution after reconstitution contains particles or is not clear. The reconstituted product should be used immediately.

**6. FURTHER INFORMATION**  
**What Norcuron contains**  
The active substance of Norcuron is vecuronium bromide 10 mg per vial. It is dissolved before use to make a solution.


The other ingredients are citric acid monohydrate, disodium hydrogen phosphate dihydrate, mannitol (E421), sodium hydroxide and phosphoric acid.

**What Norcuron looks like and contents of the pack**  
Norcuron is a white to off-white sterile powder for solution for injection. There are 10 vials of Norcuron per pack.

**Marketing Authorisation Holder and Manufacturer**  
**Marketing Authorisation Holder:**  
NV Organon, Kloosterstraat 6, 5349 AB, Oss, The Netherlands

**Manufacturer:**  
NV Organon, Kloosterstraat 6, 5349 AB, Oss, The Netherlands or Schering-Plough, Saint Charles, 60590 Eragny sur Epte, France

This patient leaflet was last updated March 2013



Profile: BS 12\_335  
Profile Revision: 01  
Profile Revision Date: 250512  
Dimensions (mm): 361 x 435.5

Over Sticker

Varnish Free

Text Free

Pharma Code

Braille Grid

Tamper Evident

Profile

Perforation

Fold

