PACKAGE LEAFLET

Package leaflet: Information for the user

Rocuronium bromide 10 mg / mL Solution for injection / infusion

Rocuronium bromide

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Rocuronium bromide is and what it is used for

Rocuronium bromide is a muscle relaxant. Muscle relaxants are used during a surgical procedure to assist in general anaesthesia. During a surgical procedure, your muscles must be completely relaxed. This makes it easier for the surgeon to perform the surgical procedure. Normally, the nerves send signals to your muscles. Rocuronium bromide can temporarily block these signals, thereby causing your muscles to relax. Because the muscles needed for breathing also relax, you will be given artificial respiration until you can breathe on your own again. During the surgical procedure, the effect of the muscle relaxant will be constantly monitored and, if necessary, you will be given some more Rocuronium bromide. At the end of surgery, the effects of Rocuronium bromide are allowed to wear off and you can start breathing on your own. Sometimes, another medicine will be given to speed up this recovery. Rocuronium bromide can also be used in intensive care.

2. What you need to know before you use Rocuronium bromide

You must not be given Rocuronium bromide
- if you are allergic to rocuronium or any of the other ingredients of this medicine (listed in section 6).

Tell your doctor if this applies to you.

Warnings and precautions
- Your medical history can affect the way in which you are given Rocuronium bromide. Tell your doctor if you have, or have ever had, the following:
- an allergy to muscle relaxants
- poor kidney function (renal impairment) or kidney disease
- a cardiovascular disease
- oedema formation (fluid accumulation, e.g. on your ankles)
- liver disease, gallbladder or bile duct disease or poor liver function
- diseases affecting the nerves and muscles
- history of malignant hyperthermia (sudden fever with rapid heartbeat, rapid breathing and stiffness, pain and/or weakness in your muscles).

• Some medical conditions may affect the way Rocuronium bromide works.
For example:
- low potassium levels in the blood (hypokalaemia)
- high magnesium levels in the blood (hypermagnesaemia), e.g. when treating toxaemia of pregnancy with magnesium salts
- low calcium levels in the blood (hypocalcaemia)
- low protein levels in the blood (hypoproteinaemia)
- lack of fluids (dehydration)
- too much acid in the blood (acidosis)
- too much carbon dioxide in the blood (hypercapnia)
- general weak condition
- being overweight
- burns.
If any of these conditions apply to you, your doctor will take this into account when deciding on the right dose of Rocuronium bromide for you.

Children/Elderly
Rocuronium bromide can be used in children (from newborn babies up to puberty) and the elderly.

Other medicines and Rocuronium bromide
Tell your doctor if you are using, have recently used or might use any other medicines. This will help your doctor determine the right dose of Rocuronium bromide for you.

The following medicines may influence the effect of Rocuronium bromide:
• Medicines which increase the effect of Rocuronium bromide:
- certain anaesthetics
- long-term use of corticosteroids (anti-inflammatory medicines) together with Rocuronium bromide in intensive care
- certain medicines used to treat bacterial infections (antibiotics)
- certain medicines used for manic depressive illness (lithium)
- certain medicines for heart disease or high blood pressure (quinidine, calcium channel blockers, beta-blockers)
- certain medicines used to treat malaria (quinine)
- water tablets (diuretics)
- magnesium salts
- local anaesthetics (lidocaine and bupivacaine)
- short-term use of medicines for epilepsy (phenytoin), e.g. during surgery.

• Medicines which decrease the effect of Rocuronium bromide:
- long-term use of corticosteroids (anti-inflammatory medicines) or medicines for epilepsy (phenytoin and carbamazepine)
- medicines for pancreatitis, problems with blood clotting and acute blood loss (protease inhibitors: gabexate, ulinastatin).

• Medicines with a variable effect on Rocuronium bromide:
- other muscle relaxants.

Rocuronium bromide may influence the effect of the following medicines:
• The effect of local anaesthetics (lidocaine) may be increased.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this medicine.

<u>Pregnancy</u>
No harmful effects have been seen in animal studies, but there are no data from clinical studies of rocuronium bromide in pregnant women. Therefore, rocuronium bromide should be used with caution

in pregnant women.

Caesarian section
A doctor will decide whether rocuronium bromide can be used for a caesarean section. It has been shown that a dose of 0.6 mg rocuronium bromide per kilogram of body weight can be safely used during caesarean section and has no harmful effect on the baby.

Breast-feeding
Breast-feeding should be delayed for 6 hours after using this medicine.

Driving and using machines
Your doctor will tell you when you can resume driving or using dangerous machines after the use of Rocuronium bromide.

Rocuronium bromide contains sodium

Each vial/ampoule contains 8.2 mg (0.36 mmol) of sodium.
This medicine contains less than 1 mmol sodium (23 mg) per vial/ampoule, that is to say essentially 'sodium-free'.

3. How to use Rocuronium bromide

Dosage
Your doctor will determine the dosage of Rocuronium bromide, based on:
- which type of anaesthetic is used
- the expected length of the surgical procedure
- other medicines you are using
- your age and state of health.

You will be given Rocuronium bromide before and/or during a surgical procedure. The normal dose is 0.6 mg rocuronium bromide per kilo of body weight and the effect lasts 30 to 40 minutes. During the procedure, it will be checked whether Rocuronium bromide is still working. You will be given additional doses, if needed.

How Rocuronium bromide is given
Rocuronium bromide is not intended for self-administration. Rocuronium bromide will be injected as a solution into a vein. It will be given by a single injection or via an infusion.

The injections must be administered by a doctor or nurse.

If you use more Rocuronium bromide than you should
As the medical staff will be monitoring your condition carefully, it is unlikely that you will be given too much Rocuronium bromide. However if this happens, artificial respiration will be continued until you can breathe again on your own. It is possible to counter the effects of (too much) Rocuronium bromide and speed up your recovery, by giving you a medicine that counteracts the effects of Rocuronium bromide.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. If these side effects occur during anaesthesia, they will be seen and treated by your doctor.
The following side effects may occur:

Common (may affect less than 1 in 10 people)
- rapid heartbeat (tachycardia) in children (newborn babies up to adolescents).

Uncommon/rare (may affect less than 1 in 100/1 000 people)
- rapid heartbeat (tachycardia) in adults
- reduced blood pressure (hypotension)
- Rocuronium bromide has no effect, or is too effective or not effective enough
- pain at the injection site
- redness or itching at the injection site
- prolongation of the muscle-relaxant effect of Rocuronium bromide
- delayed recovery from anaesthesia.

Very rare (may affect less than 1 in 10 000 people)
- allergic reactions, such as breathing difficulties, changes in blood pressure or heart rate, shock (sharp drop in blood pressure) due to insufficient circulating blood, or skin changes (e.g. fluid accumulation, redness or rash)
- shortness of breath due to spasms of the airway muscles (bronchospasm)
- muscle weakness or paralysis
- long-term muscle disorder normally seen after use of Rocuronium bromide in combination with corticosteroids (anti-inflammatory medicines) in intensive care among seriously ill patients (steroid myopathy)
- sudden fluid accumulation in the skin and mucous membranes (e.g. throat or tongue), breathing difficulties and/or itching or rash, often as an allergic reaction (angioedema)
- fluid accumulation (oedema) in the face
- airway problems due to the anaesthetic
- rash, sometimes with severe itching and whealing (hives or urticaria)
- skin redness
- flushing.

Not known (frequency cannot be estimated from the available data)
- severe allergic coronary blood vessels spasm (Kounis syndrome) resulting in chest pain (angina) or heart attack (myocardial infarction)
- dilated pupils (mydriasis) or fixed pupils that do not change its size with light or other stimuli.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via
For UK: Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
For IE: HPRA Pharmacovigilance, Website: www.hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Rocuronium bromide

Keep this medicine out of the sight and reach of children.
Store in a refrigerator (2°C – 8°C).

Rocuronium bromide should be used immediately after opening the vial or ampoule.

The diluted product is physically and chemically stable for 72 hours at 28°C – 32°C or 72 hours at 2°C – 8°C. From a microbiological point of view, the product should be used immediately after dilution. If not used immediately, in –use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C – 8°C, unless dilution has taken place in controlled and validated aseptic conditions.
Do not use this medicine after the expiry date which is stated on the carton, the label of the ampoule and the vial after EXP. The expiry date refers to the last day of that month.

The medicinal product should be visually inspected prior to use. The solution should only be used if it is clear, practically free from particles and if the container is undamaged.
Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Rocuronium bromide contains
- The active substance is rocuronium bromide.

Each mL of solution contains 10 mg rocuronium bromide.

- The other ingredients are sodium acetate trihydrate, sodium chloride, acetic acid glacial and water for injections.

What Rocuronium bromide looks like and contents of the pack
Rocuronium bromide is a clear colourless to pale yellow solution for injection or infusion, containing 10 mg rocuronium bromide per millilitre.

Rocuronium bromide comes in 3 presentations:
- Glass vials with 50 mg rocuronium bromide (10 or 50 vials per pack)
- Glass ampoules with 50 mg rocuronium bromide (10 or 50 ampoules per pack)
- Plastic ampoules with 50 mg rocuronium bromide (10 or 50 ampoules per pack)

Not all pack sizes may be marketed.

Marketing Authorization Holder and Manufacturer

Marketing Authorisation Holder: Noridem Enterprises Limited, Evagorou & Makariou, Mitsi Building 3, Office 115, 1065 Nicosia, Cyprus.

Manufacturer: DEMO S.A., PHARMACEUTICAL INDUSTRY, 21st km National Road Athens-Lamia, 14568 Krioneri, Attiki, Greece, **T:** +30 210 8161802, **F:** +30 210 8161587.

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Netherlands:	Rocuroniumbromide Noridem 10 mg/ml oplossing voor injectie/infusie
Cyprus:	ROCUDEM 10 mg / mL Solution for injection / infusion
Germany:	Rocuroniumbromid Noridem 10 mg/ml Injektions-/Infusionslösung
Greece:	ROCUDEM 10 mg / mL Διάλυμα για ένεση / έγχυση
France:	ROCURONIUM NORIDEM 10 mg/mL, solution injectable/pour perfusion
Belgium:	Rocuronium bromide Noridem 10 mg / mL solution injectable / pour perfusion – oplossing voor injectie / infusie – Injektions-/Infusionslösung
Ireland:	Rocuronium bromide 10 mg / mL Solution for injection / infusion
United Kingdom (Northern Ireland):	Rocuronium bromide 10 mg / mL Solution for injection / infusion

This leaflet was last revised in 07/2024.

The following information is intended for healthcare professionals only:

Preparation and handling

Incompatibilities

Rocuronium bromide is physically incompatible with solutions of the following medicinal products: amphotericin, amoxicillin, azathioprine, cefazolin, cloxacillin, dexamethasone, diazepam, enoximone, erythromycin, famotidine, furosemide, hydrocortisone sodium succinate, insulin, methohexital, methylprednisolone, prednisolone sodium succinate, thiopental, trimethoprim and vancomycin. Rocuronium bromide is also incompatible with soybean oil.

This medicinal product must not be mixed with other medicinal products except those mentioned in section "Method of administration".

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

Posology and method of administration

In adults, the following dosage recommendations serve as a general guideline for tracheal intubation and muscle relaxation in short- to long-lasting surgical procedures and for use in intensive care.

Surgical procedures

Tracheal intubation
The standard intubation dose during routine induction is 0.6 $mg.kg^{-1}$ rocuronium bromide, after which adequate intubation conditions are reached within 60 seconds in nearly all patients. To facilitate tracheal intubation during rapid induction of anaesthesia, 1 $mg.kg^{-1}$ rocuronium bromide is recommended, after which adequate intubation conditions are also reached within 60 seconds in nearly all patients. If a dosage of 0.6 $mg.kg^{-1}$ rocuronium bromide is used for rapid induction of anaesthesia, it is advisable to intubate the patient only after 90 seconds after administration of rocuronium bromide.

Caesarean section
Dosages of 0.6 $mg.kg^{-1}$ rocuronium bromide have no influence on the Apgar score, foetal muscle tone or cardiorespiratory adaptation. In umbilical cord blood samples, it has been demonstrated that only limited amounts of rocuronium bromide cross the placenta, which do not lead to clinical adverse effects in the neonate.
Dosages of 1 $mg.kg^{-1}$ have been investigated during rapid induction of anaesthesia, but not in patients undergoing Caesarean section.

Higher dosages
If there is reason to select a higher dosage: patients have been given initial dosages of up to 2 $mg.kg^{-1}$ rocuronium bromide without any adverse cardiovascular effects having been observed. The use of a higher dosage shortens the onset time and prolongs the duration of action.

Maintenance dosage
The recommended maintenance dosage is 0.15 $mg.kg^{-1}$ rocuronium bromide; in long-term inhalational anaesthesia, this should be reduced to 0.075 – 0.1 $mg.kg^{-1}$ rocuronium bromide. The maintenance doses should preferably be given when twitch height has recovered to 25% of the control value, or when 2 to 3 responses to train-of-four (TOF) stimulation are present.

Continuous infusion

If rocuronium bromide is administered by continuous infusion, it is recommended to start with an initial bolus dose of 0.6 $mg.kg^{-1}$ rocuronium bromide. Administration by continuous infusion can be started when twitch height starts to recover. The infusion rate should be such that twitch response remains at 10% of the control value and 1 to 2 responses to TOF stimulation remain present. In adults under intravenous anaesthesia, this equates to an infusion rate of 0.3 – 0.6 $mg.kg^{-1}.h^{-1}$ and for those under inhalational anaesthesia to an infusion rate of 0.3 – 0.4 $mg.kg^{-1}.h^{-1}$. Continuous monitoring of neuromuscular blockade is recommended, since the required amount varies from patient to patient and is dependent on the method of anaesthesia used.

Paediatric population
For neonates (0 – 27 days), infants (28 days – 2 months), toddlers (3 – 23 months), children (2 – 11 years) and adolescents (12 – 17 years), the recommended intubation dose during routine anaesthesia and the maintenance dosage are similar to those in adults.
However, in neonates and infants, the duration of action of the single intubation dose will be longer than in children.

For continuous infusion in paediatric patients, the infusion rate, with the exception of children (2 – 11 years), is the same as for adults. For children aged 2 to 11 years inclusive, a higher infusion rate may be necessary.

Thus, the initial dosage for children (2 – 11 years) is the same as for adults and must be subsequently adjusted, so that twitch response remains at 10% of the control value or 1 or 2 responses to TOF stimulation remain present.

Experience with rocuronium bromide during rapid induction in paediatric patients is limited. Rocuronium bromide is therefore not recommended for facilitating tracheal intubation conditions during rapid induction in paediatric patients.

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 induction of anaesthesia is 0.6 $mg.kg^{-1}$ rocuronium bromide. In patients in whom a prolonged duration of action is expected, a dosage of 0.6 $mg.kg^{-1}$ rocuronium bromide should be considered for rapid induction of anaesthesia. Regardless of the anaesthetic technique used, the recommended maintenance dosage for these patients is 0.075 – 0.1 $mg.kg^{-1}$ rocuronium bromide, and the recommended infusion rate is 0.3 – 0.4 $mg.kg^{-1}.h^{-1}$ (see 'Continuous infusion').

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 and calculated on the basis of ideal body weight.

Short term use in intensive care

Tracheal intubation
For tracheal intubation, the same dosage recommendations as for surgical procedures apply.

Maintenance dosage
The use of an initial bolus dose of 0.6 $mg.kg^{-1}$ rocuronium bromide is recommended, followed by a continuous infusion as soon as twitch height recovers to 10 %, or when 1 to 2 twitches to TOF stimulation are present. The dosage should always be titrated to effect in the individual patient. The recommended initial infusion rate for adults to obtain 80 – 90 % neuromuscular blockade (1 to 2 twitches to TOF stimulation) is 0.3 – 0.6 $mg.kg^{-1}.h^{-1}$ during the first hour of administration. The infusion rate should be reduced during the subsequent 6 to 12 hours, depending on the individual response. Thereafter, individual dose requirements remain relatively constant. The use of Rocuronium bromide must be for short term; however the total duration must not exceed 7 days, due to the lack of sufficient long-term data.

Wide variability in infusion rates has been seen in clinical studies. The mean infusion rate ranged from 0.2 – 0.5 $mg.kg^{-1}.h^{-1}$, depending on the nature and extent of organ failure, concomitant medication and the individual patient's condition. To meet the needs of the individual patient as far as possible, monitoring of neuromuscular transmission is highly recommended. Administration for a maximum of 7 days has been investigated.

Special populations
Rocuronium bromide is not recommended for facilitating mechanical ventilation in paediatric and geriatric patients, due to a lack of data on safety and efficacy.

Method of administration
Rocuronium bromide is administered intravenously as a bolus injection or continuous infusion. Compatibility studies have been performed with the following infusions: Rocuronium bromide at nominal concentrations of 0.5 mg / mL and 2 mg / mL is compatible with 0.9 % NaCl, 5 % glucose, 5 % glucose in 0.9 % NaCl, sterile water for injections, lactated Ringer's solution and Haemaccel. Administration should commence immediately after mixing and should be complete within 24 hours.

For single use only.
Bring the glass vials to room temperature before piercing so as to decrease the potential for fragmentation. Unused solutions must be discarded.

Special precautions for storage
Store in a refrigerator (2ºC – 8ºC).

Rocuronium bromide contains no preservatives and should be used immediately after opening the vial or ampoule.

The diluted product is physically and chemically stable for 72 hours at 28°C – 32°C or 72 hours at 2°C – 8°C. From a microbiological point of view, the product should be used immediately after dilution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C – 8ºC, unless dilution has taken place in controlled and validated aseptic conditions.

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

Overdose
In the event of overdose and prolonged neuromuscular blockade, the patient must continue to receive ventilation and sedation. In this situation, there are two options for the reversal of neuromuscular blockade: (1) In adults, sugammadex can be used for reversal of intense (total) and deep blockade. The dosage of sugammadex administered depends on the intensity of neuromuscular blockade.
(2) An acetylcholinesterase inhibitor (e.g. neostigmine, edrophonium, pyridostigmine) or sugammadex can be used once spontaneous recovery has started and should be administered at the correct dosage. If administration of an acetylcholinesterase inhibitor fails to reverse the neuromuscular effects of rocuronium bromide, ventilation should be continued until spontaneous breathing is restored. Repeated administration of an acetylcholinesterase inhibitor can be dangerous.

In animal studies, severely impaired cardiovascular function, ultimately leading to heart failure, became apparent only at a cumulative dose of 750 x ED_{90} (135 $mg.kg^{-1}$ rocuronium bromide).