SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

VECUBLOC 10 mg Powder and Solvent for Solution for I.V. Injection

Sterile

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance: 1 vial contains 10 mg vecuronium bromide which corresponds to 1 mg vecuronium bromide per ml.

Excipients: 1 vial contains 16.25 mg dibasic sodium phosphate anhydrate, 20.75 mg citric acid anhydrate and 97.0 mg mannitol.

Solvent ampoule contains 10 ml water for injection.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

VECUBLOC 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

Posology/frequency and duration of administration

As with other neuromuscular blocking agents, vecuronium bromide should only be administered by, or under supervision of, experienced clinicians who are familiar with the action and use of these drugs.

As with all other neuromuscular blocking agents, the dosage of VECUBLOC should be individualized 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 technique is recommended to monitor neuromuscular block and recovery.

Inhalational anaesthetics potentiate the neuromuscular blocking effects of VECUBLOC. 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, the dose of vecuronium bromide should be adjusted by administering smaller doses at more frequent intervals or by using lower infusion rates 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 intubating dose during routine anaesthesia is 80 to 100 micrograms vecuronium bromide per kg body weight, after which adequate intubation conditions are established within 90 to 120 seconds in nearly all patients.

Dosages of VECUBLOC for surgical procedures after intubation with suxamethonium:
Recommended doses are 30 to 50 micrograms vecuronium bromide per kg body weight.

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

Maintenance dose:
The recommended maintenance dose is 20 to 30 micrograms vecuronium bromide per kg body weight. These maintenance doses should best be given when twitch height has recovered to 25% of control twitch height.

Dose required for administration of VECUBLOC by continuous infusion:
If VECUBLOC 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 VECUBLOC 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 0.8 to 1.4 micrograms vecuronium bromide/kg/min. For neonates and infants see below. Repeat monitoring of neuromuscular block is recommended since infusion rate requirements vary from patient to patient and with the anaesthetic method used.

Additional information on special populations:
Renal/Hepatic failure:
Because vecuronium is excreted in bile and in urine, VECUBLOC should be used with caution in

patients with clinically significant hepatic and/or biliary diseases and/or renal failure (See section 4.4).

Geriatric population:
The same intubation and maintenance doses as for younger adults (80 – 100 micrograms/kg and 20 -30 micrograms/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.

Pediatric 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 section 5.1 "Pediatric patients"). However, the same intubation and maintenance doses as for adults (80 – 100 micrograms/kg and 20-30 micrograms/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 the possible variations of the sensitivity of the neuromuscular junction, especially in neonates and probably in infants up to 4 months of age, an initial test dose of 10-20 micrograms 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 100 micrograms/kg.

Dose requirements in older infants (5-23 months) are the same as in adults. However, since the onset time of Vecuronium bromide 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 vecuronium bromide is longer in neonates and infants than in children and adults, maintenance doses are required less frequently (see 'Pediatric 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.

Continuous infusion in pediatric patients

There are insufficient data concerning continuous infusion of vecuronium in pediatric patients, therefore, no dosing 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 150 micrograms up to 300 micrograms vecuronium bromide per kg body weight have been administered during surgery both under halothane and neuroleptic anesthesia without adverse cardiovascular effects being noted as long as ventilation is properly maintained. The use of these high dosages of vecuronium bromide pharmacodynamically decreases the onset time and increases the duration of action. In caesarean section (see also section 4.6) and neonatal surgery the dose should not exceed 100 micrograms/kg.

Method of administration

VECUBLOC should be administered following reconstitution with water for injections. VECUBLOC is administered intravenously either as a bolus injection or as a continuous infusion (see also section 6.6).

4.3. Contraindications

Hypersensitivity to vecuronium or the bromide ion or to any of the excipients of VECUBLOC.

4.4. Special warnings and precautions for use

Since VECUBLOC 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 neuromuscular blockade has been reported for vecuronium bromide. In order to prevent complications resulting from residual neuromuscular blockade, it is recommended to extubate only after the patient has recovered sufficiently from neuromuscular block. Other factors which could cause residual neuromuscular blockade 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 neuromuscular blockade is more likely to occur.

High rates of cross-sensitivity between neuromuscular blocking agents have been reported. Therefore, where possible, before administering VECUBLOC, hypersensitivity to other neuromuscular blocking agents should be excluded. VECUBLOC should only be used when absolutely essential in susceptible patients. Patients who experience a hypersensitivity reaction under general anaesthesia should be tested subsequently for hypersensitivity to other neuromuscular

blockers.

Since vecuronium bromide 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, ophthalmic, abdominal or anorectal surgery, etc.).

In general, following long term use of neuromuscular blocking agents 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 neuromuscular blocking agents. In addition, patients should receive adequate analgesia and sedation. Furthermore, muscle relaxants 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-depolarizing 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 VECUBLOC:

Hepatic and/or biliary tract disease and renal failure.
Because vecuronium is excreted in bile and in urine, VECUBLOC 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 (200 micrograms/kg body weight) were administered in patients with hepatic disease.

Prolonged circulation time
Conditions associated with prolonged circulation time such as cardiovascular disease, old age, edematous 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, VECUBLOC 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 myasthenic (Eaton Lambert) syndrome, small doses of vecuronium bromide may have profound effects and vecuronium bromide should be titrated to the response.

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

Obesity
Like other neuromuscular blocking agents, VECUBLOC 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.

Other conditions which may increase the effects of vecuronium bromide are:
Hypokalemia (e.g. after severe vomiting, diarrhea, and diuretic therapy), hypermagnesaemia, hypocalcaemia (after massive transfusions), hyperproteinemia, dehydration, acidosis, hypercapnia, cachexia.

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

This medicinal product contains less than 1 mmol (23 mg) of sodium per dose; no effects associated with sodium are expected.

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 VECUBLOC
Increased effect:
Halogenated volatile anaesthetics potentiate the neuromuscular block of VECUBLOC. 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 vecuronium bromide in the ICU may result in prolonged duration of neuromuscular block or myopathy (see also section 4.4 and 4.8).
Other medicines:

- Antibiotics: aminoglycoside, lincosamide and polypeptide antibiotics, acylamino-penicillin antibiotics.
- Diuretics, quinidine, magnesium salts, calcium channel blocking agents, lithium salts, cimetidine, lidocaine 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 and magnesium salts (see section 4.4).

Decreased effect:
Prior chronic administration of phenytoin or carbamazepine
Calcium chloride, potassium chloride.

Variable effect:
Administration of other non-depolarizing neuromuscular blocking agents in combination with VECUBLOC 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 VECUBLOC may produce potentiation or attenuation of the neuromuscular blocking effect of VECUBLOC.

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

Additional information on special populations
No interaction study has been performed in special populations.

Pediatric population
No interaction study has been performed in pediatric populations.

4.6. Pregnancy and lactation
General recommendation
Pregnancy category: C

Women with childbearing potential/Contraception
Women with childbearing potential should use effective birth control methods.

Pregnancy
There are insufficient data on the use of VECUBLOC during animal or human pregnancy to assess potential harm to the fetus. VECUBLOC should be given to a pregnant woman only when the attending physician decides that the benefits outweigh the risks.

Caesarean section:
Studies with vecuronium bromide, administered in doses up to 100 micrograms/kg, have shown its safety for use in caesarean section. In caesarean section the dose should not exceed 100 micrograms/kg.

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

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

Lactation
It is unknown whether vecuronium bromide is excreted in human breast milk. The excretion of vecuronium bromide in milk has not been studied in animals. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with vecuronium bromide should be made taking into account the benefit of breast-feeding to the child and the benefit of vecuronium bromide therapy to the woman.

Reproductive ability/Fertility
Animal studies do not indicate an effect on fertility.

4.7. Effects on ability to drive and use machines
Since VECUBLOC is used as an adjunct to general anaesthesia, the usual precautionary measures after a general anaesthesia 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.
Very common (≥ 1/10); common (≥ 1/100 to< 1/10); uncommon (≥ 1/1,000 to< 1/100); rare≥ 1/10,000 to< 1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data)

Immunity system disorders
Very rare: Hypersensitivity, Anaphylactic reaction, Anaphylactoid reaction, Anaphylactic shock, Anaphylactoid shock

Nervous system disorders
Very rare: Flaccid paralysis

Cardiac disorders
Uncommon: Tachycardia

Vascular disorders
Uncommon: Hypotension
Very rare: Circulatory collapse and shock, flushing

Respiratory, thoracic and mediastinal disorders
Very rare: Bronchospasm

Skin and subcutaneous tissue disorders
Very rare: Angioneurotic edema, urticaria, rash, erythematous rash

Musculoskeletal and connective tissue disorders
Very rare: Muscle weakness*, steroid myopathy*

General Disorders and Administration Site Conditions
Uncommon: Drug ineffective, decreased drug effect/therapeutic response, increased drug effect/therapeutic response Face oedema, injection site pain, injection site reaction

Injury and poisoning
Uncommon: Prolonged neuromuscular block, delayed recovery from anaesthesia
Very rare: Airway complication of anaesthesia

*after long-term use in the ICU.
Frequencies are estimates derived from post-marketing surveillance reports and data from the general literature.

Prolonged Neuromuscular block
The most frequent adverse reaction to nondepolarising 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 vecuronium bromide was used in the ICU in combination with corticosteroids (see section 4.4).

Anaphylactic reactions
Although very rare, severe anaphylactic reactions to neuromuscular blocking agents, including vecuronium bromide, 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 generalized 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 vecuronium bromide 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 vecuronium bromide. Nevertheless, such cases have rarely been reported during large scale use of vecuronium bromide.

4.9. Overdose

In the event of overdosage 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. (2) An acetylcholinesterase inhibitor (e.g. Neostigmine, edrophonium, pyridostigmine) in adequate doses can be used once spontaneous recovery starts. When administration of an acetylcholinesterase inhibiting agent fails to reverse the neuromuscular effects of VECUBLOC, ventilation must be continued until spontaneous breathing is restored. Repeated dosage of an acetyl-cholinesterase inhibitor can be dangerous.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Muscle relaxant, peripherally acting agents
ATC Code: M03AC03

VECUBLOC (vecuronium bromide) is a non-depolarizing neuromuscular blocking agent, chemically designated as the aminosteroid 1(3α,17β-diacetoxy-2βpiperidino-5α-androstan-16β-yl)-1 methylpiperidinium bromide.

VECUBLOC blocks the 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 depolarizing neuromuscular blocking agents, such as suxamethonium, VECUBLOC does not cause muscle fasciculation.

Within the clinical dosage range, vecuronium does not block the sympathetic nicotinic receptors, and thus exerts no ganglion blocking activity. In addition, in this dose range vecuronium does not block the parasympathetic muscarinic receptors, and thus exerts no vagolytic activity.

Tracheal intubation
Within 90 to 120 seconds following intravenous administration of a dose of 80 to 100 micrograms vecuronium bromide per kg body weight, good to excellent conditions for endotracheal 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 vecuronium bromide, onset time to maximal block is shortened and duration of action is prolonged.

Continuous intravenous infusion:
When VECUBLOC is administered by continuous intravenous infusion, a steady state neuromuscular block 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.
Vecuronium bromide 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.

These properties allow the use of VECUBLOC in short, medium and long lasting surgical procedures.

Reversal of neuromuscular block:
Administration of acetylcholinesterase inhibitors, such as neostigmine, pyridostigmine or edrophonium, antagonises the action of vecuronium bromide.

Special Populations
Pediatric patients:
Neonates and infants:
In neonates and infants, the ED_{95} dose of vecuronium under balanced anesthesia was found to be approximately the same (approx. 47 µg/kg body weight) as in adults.
The onset time of vecuronium bromide 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 vecuronium bromide is longer in neonates and infants than in adults. Maintenance doses of VECUBLOC should therefore be less frequently administered.

Children:
In children the ED_{95} dose of vecuronium bromide under balanced anaesthesia was found to be higher than in adults (81 vs 43 micrograms/kg bodyweight, respectively). In comparison to adults, the duration of action and recovery time with vecuronium bromide 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 and administered at 25% recovery of control twitch height are not observed in pediatric patients.

5.2. Pharmacokinetic properties

General properties
Absorption: For intravenous administration.

Distribution After intravenous administration of 100–150 micrograms/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 0.18-0.51 l.kg in adult patients.

Biotransformation The extent of metabolism of vecuronium is relatively low. In humans, a 3hydroxy derivative having approximately 50% less neuromuscular blocking potency than vecuronium is formed in the liver. In patients not suffering from renal or hepatic failure, the plasma concentration of this derivative is below detection limit, and does not contribute to the neuromuscular block occurring after administration of vecuronium bromide.

Elimination: The plasma clearance of vecuronium amounts to 3.0-6.4 ml/kg/min and its plasma elimination half-life is 36-117 minutes.

Biliary excretion is the main elimination route. It is estimated that within 24 hours after intravenous administration of vecuronium bromide, 40 to 60% of the dose administered is excreted into the bile as monoquaternary compounds. Approximately 95% of this compound is unchanged vecuronium and less than 5% is 3-OH 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 compounds excreted in the urine collected by intravesical catheter for 24 hours following VECUBLOC administration is 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.

Special Populations

Pediatric population
There are limited pharmacokinetic data for vecuronium in the pediatric population. After intravenous administration, vecuronium plasma clearance is similar across neonates, infants and children (2.8-9.0 ml.kg) and not different from the clearance in adults. Volume of distribution at steady state (Vdss), 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, embryo toxic 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
Dibasic sodium phosphate anhydrate
Mannitol
Sodium hydroxide and/or Phosphoric acid (for pH adjustment)
Water for injection

6.2. Incompatibilities
As is the case for many other drugs, incompatibility has been documented for vecuronium bromide when added to thiopental.

Except for those solutions with which vecuronium bromide has been shown to be compatible, it is not recommended to mix vecuronium bromide with other solutions, or drugs in the same syringe or bag (See section 6.6).

If vecuronium bromide 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% sodium chloride) between administration of vecuronium bromide and drugs for which incompatibility with vecuronium bromide has been demonstrated or for which compatibility with vecuronium bromide has not been established.

6.3. Shelf-life
24 months.

VECUBLOC may be stored in its packaging under specified conditions until the end of shelf-life.
After reconstitution, it is stable at 2-8°C for 24 hours. After reconstitution, it maintains its physical and chemical stability for 24 hours at room temperature and in daylight. From a microbiological point of view, the product should be used immediately after opening. In addition, physical and chemical

compatibility with 5% dextrose solution, 5% dextrose/0.9% NaCl solution, lactated ringer solution has been demonstrated at room temperature for 12 hours.
Shake/spin until product is completely dissolved during reconstitution.

From a microbiological point of view, the product should be used immediately after opening. 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 2-8°C, unless reconstitution/dilution (etc.) has taken place in controlled and validated aseptic conditions.
"Date of Expiry" on the vial label indicates that VECUBLOC could be used until that day.

6.4. Special precautions for storage
Store at room temperature below 25°C and in original packaging in order to protect from light. After reconstitution, it maintains its physical and chemical stability for 24 hours at room temperature and in daylight.

For storage conditions of the reconstituted solution see Section 6.3.

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

6.5. Nature and contents of container
Each packaging contains a vial and an ampoule.

Vial: Colorless Type I glass vial sealed with bromobutyl rubber stopper and transparent flip-off cap.
Ampoule: Colorless, type I glass ampoule

6.6. Special precautions for disposal and other handling
VECUBLOC is for intravenous route only and should be used after being reconstituted. VECUBLOC may be diluted in 5% dextrose/water, 5% dextrose/0.9% NaCl, lactated Ringer solutions. Unused parts of infusion solutions should be disposed of immediately.

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

7. MARKETING AUTHORISATION HOLDER
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