Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Acuron 10mg/ml solution for Injection or Infusion 3ml.

2. Qualitative and quantitative composition

Each ml contains; Atracurium 10 mg as Atracurium Besylate USP solution for Injection or Infusion
For a full list of excipients (see section 6.1)

3. Pharmaceutical form

Solution for Injection/Infusion.
The product is a clear and colourless solution with a pH of 3.00 – 3.65 and an osmolality of 10 - 30 mOsmol/kg.

4. Clinical particulars

4.1 Therapeutic indications

Intravenous use during surgical and other procedures and in intensive care.
Atracurium besylate is used as an adjunct to general anaesthesia, to facilitate tracheal intubation and controlled ventilation.

4.2 Posology and method of administration

Use as an adjunct to general anaesthesia. Atracurium Besylate Injection should only be administered by intravenous injection. Do not give Atracurium Besylate Injection intramuscularly since this may result in tissue irritation and there are no clinical data to support this route of administration.
Monitoring of neuromuscular function is recommended during the use of atracurium besylate in order to individualise dosage requirements.

Posology

Adults

Use as an injection

Atracurium besylate 10 mg/ml solution for injection/infusion is administered by intravenous injection and must not be administered intramuscularly.

Relaxation

The dosage range recommended for adults is 0.3 to 0.6 mg atracurium besylate/kg (depending on the duration of full block required). This dose will provide adequate relaxation for about 15 to 35 minutes.

Intubation

Endotracheal intubation can usually be accomplished within 90

seconds from the intravenous injection of 0.5 to 0.6 mg atracurium besylate /kg.

Repeated dose

Full block can be prolonged with supplementary doses of 0.1 to 0.2 mg atracurium besylate /kg. Generally, the first maintenance dose is required 20 to 45 minutes after the initial bolus injection, then typically at 15 to 25 minute intervals, however, the need for maintenance doses should be determined by the individual patient's requirements and responses.

Successive supplementary dosing does not produce accumulation in neuromuscular blocking effect.

As measured by the restoration of the tetanic response to 95% of normal neuromuscular function, spontaneous recovery occurs about 35 minutes after a full block.

Once evidence of spontaneous recovery is present, the neuromuscular block produced by atracurium besylate can be rapidly reversed by standard doses of anticholinesterase agents, such as neostigmine and edrophonium, accompanied or preceded by atropine or glycopyrrolate, with no evidence of recurarisation.

Use as an infusion in adults

Atracurium besylate 10 mg/ml is hypotonic and must not be administered via the infusion system of a blood transfusion. In this case atracurium besylate has to be administered via a separate infusion line.

Initial bolus doses for intubation an initial atracurium besylate dose of 0.3 to 0.6 mg/kg (depending on the duration of full block required), given as an intravenous bolus injection, is recommended. This will provide adequate relaxation for about 15 to 35 minutes. Maximum neuromuscular blockade is generally achieved approximately 3 to 5 minutes after administration. Spontaneous recovery from the end of full block occurs in about 35 minutes as measured by the restoration of the tetanic response to 95% of normal neuromuscular function. Although atracurium is potentiated by (approximately 35%) isoflurane or enflurane anaesthesia, the same initial atracurium besylate dose (0.3 to 0.6 mg/kg) may be used for intubation if given prior to the administration of these inhalation agents.

However if the initial atracurium dose is administered after steady state anaesthesia with isoflurane or enflurane has been achieved, the dose of atracurium should be reduced by approximately one-third. Smaller dosage reductions may be considered with concomitant halothane anaesthesia since it has only a marginal (approximately 20%) potentiating effect on atracurium

After an initial bolus dose of 0.3 to 0.6 mg/kg, atracurium besylate, administered as a continuous infusion at rates of 0.3 to 0.6 mg/kg/hour, can be used for maintenance of neuromuscular blockade during long surgical procedures.

Atracurium besylate can be administered by infusion during cardiopulmonary bypass surgery at the recommended infusion rates.

Induced hypothermia with body temperature of 25° to 26° C reduces the rate of degradation of atracurium besylate, therefore full neuromuscular block may be maintained with approximately half the original infusion rate.

Reversal of neuromuscular blockade

The neuromuscular blockade induced by atracurium can be reversed with an anticholinesterase agent such as neostigmine or pyridostigmine, usually in conjunction with an anticholinergic agent such as atropine or glycopyrronium to prevent the adverse muscarinic effects of the anticholinesterase. Under balanced anaesthesia, reversal can usually be attempted approximately 20 to 35 minutes after the initial atracurium dose, or approximately 10 to 30 minutes after the last atracurium maintenance dose, when recovery of muscle twitch has started. Complete reversal of neuromuscular blockade is usually achieved within 8 to 10 minutes after administration of the reversing agents.

Rare instances of breathing difficulties, possibly related to incomplete reversal, have been reported following attempted pharmacological antagonism of atracurium induced neuromuscular blockade. As with other agents in this class, the tendency for residual neuromuscular block is increased if reversal is attempted at deep levels of blockade or if inadequate doses of reversal agents are employed.

Use in children, in the elderly, in patients with reduced renal and/or hepatic function, in patients with cardiovascular disease, in patients suffering from burns and in patients in intensive care units (ICU)

Use in children:

On a bodyweight basis the dosage in children over the age of one month is similar to that in adults.

Use in Neonates:

The use of atracurium besylate is not recommended in neonates since there are insufficient data available (see section 5.1). In case of a necessary neuromuscular blockade also in newborn or premature newborn the dose has to be significantly lowered.

Use in the elderly:

Atracurium besylate may be used at standard dosage in elderly patients. It is recommended, however, that the initial dose be at the lower end of the range and that it be administered slowly.

Use in patients with reduced renal and/or hepatic function:

Atracurium besylate may be used at standard dosage at all levels of renal or hepatic function, including end-stage failure.

Use in patients with cardiovascular disease:

Patients with severe cardiovascular diseases may react more sensitively

to transient states of hypotony (see also section 4.4). In these patients, atracurium besylate should therefore be administered slowly and/or in divided doses over 1 - 2 minutes.

Use in patients suffering from burns:

As with other non-depolarising neuromuscular blocking agents, resistance may develop in patients suffering from burns. Such patients may require increased doses dependent on the time elapsed since the burn injury and the extent of the burn.

Use in patients in intensive care units (ICU):

When there is a need of atracurium besylate for long-term mechanical ventilation in intensive care units, the benefit to risk ratio of neuromuscular block must be considered.

After an optional initial bolus dose of 0.3 - 0.6 mg/kg, Atracurium besylate can be used to maintain neuromuscular block by administration of a continuous infusion of between 11 and 13 micrograms/kg/min (0.66 - 0.78 mg/kg/h). There is, however, a great variety of dosage requirements between patients. Patients may require infusion rates of as low as 4.5 micrograms/kg/min (0.27 mg/kg/h) or as high as 29.5 micrograms/kg/min (1.77 mg/kg/h). Dosage requirements may change over time. Therefore, the rate of infusion should be adjusted by peripheral nerve monitoring.

The speed of spontaneous recovery from neuromuscular block after infusion of atracurium besylate in ICU patients is independent of the duration of administration. Spontaneous recovery can be expected of a train-of-four ratio of more than 0.75 (the ratio of the peak of the fourth to the first contraction in a train of four) which occurs on average in approximately 60 minutes with a range of 32 - 108 minutes (n = 6) observed in clinical trials.

The few findings currently available regarding long-term use of atracurium besylate indicate only minor influence of haemofiltration and haemodialysis on the plasma levels of atracurium besylate and its metabolites.

The effect of the haemoperfusion on the level of atracurium besylate and its metabolites in plasma is not known.

Method of administration

For intravenous administration as a bolus injection or as a continuous infusion.

Atracurium Besylate solution for injection/infusion should not be mixed in the same syringe, or administered simultaneously through the same needle, with alkaline solutions (e.g., barbiturate solutions) (see section 4.4).

When a small vein is selected as the injection site, Atracurium solution for injection/infusion should be flushed through the vein with physiological saline after injection. When other anaesthetic drugs are

administered through the same indwelling needle or cannula as Atracurium solution for injection/infusion, it is important that each drug is flushed through with an adequate volume of physiological saline.

Atracurium besylate 10 mg/ml diluted to 0.5mg/ml or 5mg/ml with the infusion solutions in section 6.6 and stored at 30°C protected from light, were shown to be stable.

4.3 Contraindications

• Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
• Hypersensitivity to cisatracurium (see section 4.4)

4.4 Special warnings and precautions for use

Atracurium has no known effect on consciousness, pain threshold, or cerebration. In surgery, it should be used only with adequate general anaesthesia.

Anaphylactic reactions
Anaphylactic reactions to neuromuscular blocking agents in general have been reported (sometimes severe, such as shock, cardiac arrest). Although these phenomena only occur rarely with atracurium, precautions should always be taken to prevent the possible occurrence of these reactions (see also section 4.8).

Special precautions should be taken in patients with known anaphylactic reactions to neuromuscular blocking agents, as cross-reactivity may be possible with this product.

During administration of Atracurium Besylate solution for injection/infusion, special attention should be paid to patients with a history of hypersensitivity to other neuromuscular blocking agents, as high levels of crossed allergic reactions (greater than 50%) between neuromuscular blocking agents have been reported (see section 4.3).

In common with other neuromuscular blocking agents, the potential for histamine release exists in susceptible patients during administration of Atracurium Besylate solution for injection/infusion. Caution should be exercised in patients with a history suggestive of an increased sensitivity to the effects of histamine. Bronchospasms may occur, particularly in patients with a history of allergy or asthma. Caution is also recommended in atopic and asthmatic patients.

Do not give Atracurium Besylate solution for injection/infusion by intramuscular administration.

Atracurium Besylate solution for injection/infusion has an acid pH and therefore should not be mixed with alkaline solutions (e.g., barbiturate solutions) in the same syringe or administered simultaneously during intravenous infusion through the same needle. Depending on the resultant pH of such mixtures, Atracurium Besylate solution for injection/infusion may be inactivated, and a free acid may be precipitated.

Atracurium Besylate solution for injection/infusion may have profound effects in patients with myasthenia gravis, Eaton-Lambert syndrome, or other neuromuscular diseases in which potentiation of non-depolarising agents has been noted. A reduced dosage of Atracurium Besylate solution for injection/infusion and the use of a peripheral nerve stimulator for assessing neuromuscular blockade is especially important in these patients. Similar precautions should be taken in patients with severe electrolyte disorders.

Atracurium Besylate solution for injection/infusion does not have significant vagal or ganglion blocking properties in the recommended dosage range. Consequently, Atracurium Besylate solution for injection/infusion will not counteract the bradycardia produced by many anaesthetic agents or by vagal stimulation during surgery. Therefore, bradycardia during anaesthesia may be more common with Atracurium Besylate solution for injection/infusion than with other muscle relaxants.

As with other non-depolarising neuromuscular blocking agents, resistance to Atracurium Besylate solution for injection/infusion may develop in patients suffering from burns. Such patients may require increased doses of Atracurium Besylate solution for injection/infusion depending on the time elapsed since the burn injury and the extent of the burn.

Atracurium Besylate solution for injection/infusion should be administered over a period of at least 60 seconds to patients who may be unusually sensitive to falls in arterial blood pressure, for example those who are hypovolaemic.

Atracurium Besylate solution for injection/infusion is hypotonic and must not be applied into the infusion line of a blood transfusion.
Monitoring of serial creatine phosphokinase (CPK) values should be considered in asthmatic patients receiving high dose corticosteroids and neuromuscular blocking agents in intensive care units.

Intensive care unit (ICU) patients
The administration of laudanosine, the atracurium and cisatracurium metabolite, at high doses to laboratory animals has been accompanied by transient hypotension and in some species, cerebral excitatory effects.

In the most sensitive animal species, these effects occurred for plasma laudanosine concentrations identical to those observed in ICU patients after prolonged infusion of atracurium.

There have been rare reports of seizures in ICU patients who had received Atracurium Besylate solution for injection/infusion concurrently with several other agents. These patients usually had one or more medical conditions predisposing to seizures (e.g., cranial trauma, cerebral oedema, viral encephalitis, hypoxic encephalopathy, uraemia). In clinical trials, there appeared to be no correlation between plasma laudanosine concentration and the occurrence of seizures.

After prolonged administration of Atracurium Besylate solution for injection/infusion in severely ill patients under intensive care, some incidences of muscle weakness and/or myopathy occurred. Most patients were concomitantly treated with corticosteroids. A causal relationship with Atracurium Besylate solution for injection/infusion therapy has not been established.

4.5 Interaction with other medicinal products and other forms of interaction

As with other non-depolarising neuromuscular blocking agents, the magnitude and/or duration of the effects of Atracurium Besylate solution for injection/infusion may be increased as a result of an interaction with the following agents.

Inhalation anaesthetics: atracurium is potentiated by isoflurane, desflurane, sevoflurane and enflurane anaesthesia, and only marginally potentiated by halothane anaesthesia.

Antibiotics: including the aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincosamides (e.g., lincomycin, clindamycin), vancomycin and telithromycin.

Anticonvulsants (acute administration only): phenytoin, carbamazepine.
Local anaesthetics: lidocaine.

Antiarrhythmic drugs: lidocaine, procainamide, quinidine.

Beta-blockers: propranolol, oxprenolol.

Antirheumatic drugs: chloroquine, d-penicillamine.

Calcium channel blockers: diltiazem, nicardipine, nifedipine, verapamil.

Diuretics: furosemide, thiazides, acetazolamide and possibly mannitol.

Ganglion blocking agents: trimetaphan, hexamethonium.

Others: dantrolene, parenteral magnesium sulphate, chlorpromazine, steroids, ketamine, lithium salts and quinine.

Rarely, some of the above drugs may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome. In these situations a consequent increased sensitivity to Atracurium Besylate solution for injection/infusion would be expected.
The administration of combinations of non-depolarising neuromuscular blocking agents in conjunction with Atracurium Besylate solution for injection/infusion may produce a degree of neuromuscular blockade in excess of that which might be expected were an equipotent total dose of Atracurium Besylate solution for injection/infusion administered. Any synergistic effect may vary between different drug combinations.

Administration of anticholinesterases, usually used in the treatment of Alzheimer's disease, such as donepezil, may decrease the duration and intensity of the neuromuscular block induced by Atracurium Besylate solution for injection/infusion.

A depolarising muscle relaxant such as suxamethonium chloride should not be administered to prolong the neuromuscular blocking effects of non-depolarising blocking agents such as Atracurium Besylate solution for injection/infusion, as this may result in a prolonged and complex block which can be difficult to reverse with anticholinesterase drugs.

The prior use of suxamethonium reduces the onset (to maximum blockade) by approximately 2 to 3 minutes and may increase the depth of neuromuscular blockade induced by Atracurium Besylate solution for injection/infusion. Therefore, the initial Atracurium Besylate solution for injection/infusion dose should be reduced, and the reduced dose should not be administered until the patient has recovered from the neuromuscular blocking effects of suxamethonium.

The use of intravenous corticosteroids with neuromuscular blocking agents has been reported to antagonise neuromuscular blockades. In addition, prolonged co-administration of these agents may increase the risk and/or severity of myopathy resulting in prolonged flaccid paralysis following discontinuation of the neuromuscular blocking agent. The myopathy is usually reversible with recovery in several months.

The onset of neuromuscular blockade is likely to be lengthened and the duration of blockade shortened in patients receiving chronic anticonvulsant therapy (e.g., carbamazepine, phenytoin). However, if the anticonvulsants are given acutely, the neuromuscular blocking effects may be increased.
In principle, maintaining neuromuscular monitoring until complete reversal of neuromuscular blockade should permit detection of most

interactions. Nevertheless, recurrence of neuromuscular blockade may occur, for example, upon treatment with post-surgical antibiotics.
Aminoglycosides, colistin and lincosamides
Potentiation of muscular blockade may occur when the antibiotic is administered parenterally and/or peritoneally before, during or after the neuromuscular blocking agent. Monitor the level of neuromuscular blockade at the end of anaesthesia.

4.6 Pregnancy and Lactation

Pregnancy
Atracurium crosses the placenta but there have been no demonstrated adverse effects in the foetus or newborn infant. Animal studies have indicated that atracurium has no adverse effects on foetal development. As with all neuromuscular blocking agents, the use of Atracurium Besylate solution for injection/infusion in the first three months of pregnancy should be avoided and it should not be used during the second and third trimesters unless clearly necessary.

Atracurium Besylate solution for injection/infusion is suitable for maintenance of muscle relaxation during caesarean section as it does not cross the placenta in clinically significant amounts following recommended doses. In an open-label study, atracurium besylate (0.3 mg/kg) was administered to 26 pregnant women during delivery by caesarean section. No harmful effects were attributable to atracurium in any of the newborn infants, although small amounts of atracurium were shown to cross the placental barrier. The possibility of respiratory depression in the newborn infant should always be considered following caesarean section during which a neuromuscular blocking agent has been administered.

Anaesthesia during the third trimester of pregnancy exposes the mother to Mendelson syndrome (acid pneumopathy due to gastric acid aspiration). If a muscle relaxant is used at induction of anaesthesia, one should be chosen with a short onset and duration of action and low placental transfer and used in the lowest dose required to induce adequate neuromuscular relaxation. In patients receiving magnesium sulphate, the reversal of neuromuscular blockade may be unsatisfactory and the Atracurium Besylate solution for injection/infusion dose should be lowered as indicated.

Breast-feeding
Atracurium has a relatively high molecular weight and is highly ionized at physiologic pH, both factors that markedly reduce transfer into milk. In addition, even though milk is slightly more acidic than plasma, any atracurium transferred into milk would be rapidly degraded. Nevertheless, in view of the potential respiratory depressant effect on the neonate, especially if premature, breast-feeding should be discontinued

for 24 hours after administration of Atracurium Besylate solution for injection/infusion.

Fertility
No fertility data are available.

4.7 Effects on ability to drive and use machines

Atracurium Besylate solution for injection/infusion in combination with other anaesthetic agents can have major influence on the ability to drive and use machines. It is not recommended to use potentially dangerous machinery or drive a car within 24 hours after full recovery from the neuromuscular blocking action of atracurium.

4.8 Undesirable effects

The adverse effects are reported in decreasing order of frequency within each system order class (SOC).

As with most neuromuscular blocking agents, the potential exists for undesirable effects suggestive of histamine release in susceptible patients. In clinical trials (875 patients) reports of skin flushing ranged from 1% at doses up to 0.3 mg/kg, to 29% at doses of 0.6 mg/kg or greater. The incidence of transient hypotension ranged from 1% to 14% respectively for the corresponding dosages.

Table for frequency of adverse reactions for Atracurium Besylate solution for injection/infusion.

System organ class	**Common (≥ 1/100 to < 1/10)**	**Uncommon (≥ 1/1,000 to < 1/100)**	**Rare (≥ 1/10,000 to < 1/1,000**	**Very rare (< 1/10,000)**	**Not known (cannot be estimated from the available data)**
Immune system disorders				Anaphylactic shock,. anaphylactic reaction, anaphylactoid reaction	
Cardiac disorders	Tachycardia, bradycardia		Cardiac arrest, cardiac failure*		
Vascular disorders	Hypertension, hypotension, vasodilatation (flushing)				
Respiratory, thoracic and mediastinal disorders	Wheezing	Bronchospasm	Dyspnoea, laryngospasm	Hypoxemia	Bronchial secretions
Skin and subcutaneous	Localised skin	Generalised erythema, hives	Angioneurotic oedema, urticaria		

tissue disorders	reactions, rash, itching				
General disorders and administration site conditions	Reaction at injection site				
Injury, poisoning and procedural complications					

Reporting of suspected adverse reactions. Healthcare professonals are asked to report any suspected adverse reactions via pharmacy and poisons board, Parmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Prolonged muscle paralysis and its consequences are the main signs of overdose. There is limited experience with Acuron (Atracurium Besylate Injection USP) overdosage following parenteral administration. The possibility of iatrogenic overdosage can be minimised by carefully monitoring muscle twitch response to peripheral nerve stimulation.

Excessive doses of atracurium are likely to produce symptoms consistent with extensions of the usual pharmacological effects.

Overdosage may increase the risk of histamine release and adverse cardiovascular effects, especially hypotension. If cardiovascular support is necessary, this should include proper positioning, fluid administration, and the use of vasopressor agents if necessary. It is essential to maintain a potent airway with assisted positive pressure ventilation until spontaneous respiration is adequate. Full sedation will be required since consciousness is not impaired. The duration of neuromuscular blockade may be prolonged and a peripheral nerve stimulator should be used to monitor recovery.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: muscle relaxants, peripherally acting agents; Other quaternary ammonium components

ATC code: M03A C04.

Atracurium besylate 10 mg/ml is a non-depolarising muscle relaxant with medium duration of action.

The active substance, atracurium besylate, interacts specifically with neurophysiological processes at the motor end-plate by competitively displacing acetylcholine from its receptor sites.

As a result of end-plate occupation by atracurium besylate, further depolarisation is inhibited. Subsequently, skeletal muscles are paralysed since stimulation by motor nerves cannot be transmitted to the muscles.

Once recovery from atracurium's neuromuscular blocking effect begins, it proceeds more rapidly than recovery from tubocurarine, alcuronium, and pancuronium. Regardless of the atracurium dose, the time from start of recovery (from complete block) to complete recovery is approximately 30 minutes under balanced anaesthesia. Repeated doses have no cumulative effect on recovery rate.

Through inhibition of acetylcholine degradation by means of cholinesterase inhibitors, e.g. neostigmine or edrophonium, an increase of acetylcholine concentration is achieved at all cholinergic synapses. The balance between atracurium besylate (antagonist) and acetylcholine (agonist) is shifted in favour of the latter. As a result, stimulation of the muscle can reoccur.

Paediatric population:
The limited data in neonates from literature reports suggest variability in the time to onset and duration of atracurium in this population as compared to children (see section 4.2).

5.2 Pharmacokinetic properties

The onset and duration of effect of atracurium besylate are dose-dependent.

In man, following the administration of 0.3 mg atracurium besylate/kg, plasma concentrations of 3 micrograms/ml were measured after 3 minutes.

Atracurium besylate is inactivated by:

1. Hofmann elimination, a non-enzymatic process which occurs at physiological pH and temperature,

2. Ester hydrolysis catalysed by non-specific esterases.

Variations in the blood pH and body temperature in patients within the physiological range will not significantly alter the duration of action of atracurium besylate.

Tests with plasma from patients with low levels of pseudocholinesterase show that the inactivation of atracurium besylate proceeds unaffected.

Plasma protein binding

The plasma protein binding of atracurium besylate is about 82%. Plasma proteins neither influence the rate nor the mode of atracurium besylate catabolism.

Elimination

Elimination half-life for atracurium besylate is 20 to 30 minutes. As the termination of the neuromuscular blocking action of atracurium besylate is not dependent on its hepatic or renal metabolism or excretion, its duration of action, therefore, is unlikely to be affected by impaired renal, hepatic or circulatory function.

When given to laboratory animals, cerebral excitatory effects have been associated with a metabolite of atracurium besylate, laudanosine. Although seizures have been observed in patients in ICUs who were receiving atracurium besylate, they were not attributed in any case to laudanosine or to atracurium besylate, even after weeks of continuous infusion.

The metabolites are present at higher concentrations in intensive care patients with limited renal and/or hepatic function. However, these metabolites have no effect on the muscle relaxant action.

5.3 Preclinical safety data

Genotoxicity:
Atracurium besylate was not mutagenic in bacteria and in myeloid cells of rats. In vitro, minor mutagenic activity in mammalian cells was observed only in cytotoxic concentrations.

Carcinogenicity:
Carcinogenicity studies have not been performed.

Embryotoxicity/ Foetotoxicity:
From the results of animal experiments, it appears that atracurium besylate has no significant effect on embryonic development. Studies of the effects on the foetal development phase were not carried out.

Fertility:
Fertility studies were not carried out.

6. Pharmaceutical Particulars

6.1 List of Excipients

Water for injections
Benzene sulfonic acid

6.2 Incompatibilities

Atracurium besylate is inactivated by high pH and so must not be mixed in the same syringe with thiopentone or any alkaline agent.

Therefore, the cannula has to be flushed between infusion of atracurium besylate and thiopentone in order to avoid the formation of aggregates, which might cause an anaphylactoid reaction.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf-Life

Unopened ampoules: 18 months

Opened ampoules:

The product should be used immediately after opening the ampoule.

Prepared infusion solutions:

Chemical and physical in-use stability has been demonstrated in Sodium Chloride Intravenous Infusion BP for up to 24 hours at 30° C and in other common infusion fluids for up to 4 or 8 hours, respectively (see section 6.6).

Infusion Solution	**Period of Stability**
1. Sodium Chloride Intravenous Infusion BP (0.9% w/v)	24 hours
2. Glucose Intravenous Infusion BP (5% w/v)	8 hours
3. Ringer's Injection USP	8 hours
4. Sodium Chloride (0.18% w/v) and Glucose (4% w/v) Intravenous Infusion BP	8 hours
5. Compound Sodium Lactate Intravenous Infusion BP (Hartmann's Solution for Injection)	4 hours

Intravenous Infusion BP

(Hartmann's Solution for Injection)

When diluted in these solutions to administer atracurium besylate concentrations of 0.5 mg/ml and above, the resultant solutions will be stable in daylight for the stated periods at temperatures of up to 30° C.

From a microbiological point of view, the product should be used immediately. 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 to 8° C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special Precautions for storage

Store in a refrigerator (2° C - 8° C).
Do not freeze.
Keep the ampoules in the outer carton in order to protect from light.
For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and Content of container

Acuron (Atracurium Besylate Injection USP) Injection IV is available in 5 x 3ml (30mg/Ampoule) Pack.

6.6 Special precautions for disposal and other handling

Atracurium besylate 10 mg/ml can be used for intravenous injection or infusion.

The product should be inspected visually prior to administration (also after dilution). If it is not clear, colourless and free of particles or if the container is damaged the product should be discarded.

For single dose use only.

Any unused solution from opened ampoules should be discarded.

Atracurium besylate 10 mg/ml is compatible with the following solutions for infusion:

Infusion Solution	**Period of Stability**
1. Sodium Chloride Intravenous Infusion BP (0.9% w/v)	24 hours
2. Glucose Intravenous Infusion BP (5% w/v)	8 hours
3. Ringer's Injection USP	8 hours

4. Sodium Chloride (0.18% w/v) and Glucose (4% w/v) Intravenous Infusion BP	8 hours
5. Compound Sodium Lactate Intravenous Infusion BP (Hartmann's Solution for Injection)	4 hours

Compound Sodium Lactate Intravenous Infusion BP

(Hartmann's Solution for Injection)

7. Marketing Authorization Holder

Brookes Pharma (Private) Limited

8. Marketing Authorization Number

CTD8368

9. Date of first authorization/renewal of the authorization

17/01/2025

10. Date of revision of the text

05/05/2025