

**Package Leaflet: Information for the Patient**

**Atracurium besilate 10mg/ml Solution for injection/infusion**

# **atracurium besilate**

**Read all of this leaflet carefully before you start having 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.
- 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 Atracurium besilate Solution for injection/infusion is and what it is used for
2. What you need to know before you have Atracurium besilate Solution for injection/infusion
3. How to have Atracurium besilate Solution for injection/infusion
4. Possible side effects
5. How to store Atracurium besilate Solution for injection/infusion
6. Contents of the pack and other information

## **1. What Atracurium besilate Solution for injection/infusion is and what it is used for**

Atracurium besilate Solution for injection/infusion contains a medicine called atracurium besilate. This belongs to a group of medicines called muscle relaxants.

Atracurium besilate Solution for injection/infusion is used:

- to relax muscles during operations on adults and children over 1 month of age
- to help insert a tube into the windpipe (tracheal intubation), if a person needs help to breathe
- to relax the muscles of adults in intensive care.

Ask your doctor if you would like more explanation about this medicine.

## **2. What you need to know before you have Atracurium besilate Solution for injection/infusion**

**Do not have Atracurium besilate Solution for injection/infusion if:**

- you are allergic to atracurium besilate, any other muscle relaxant or any of the other ingredients in atracurium (listed in section 6)

- you have reacted badly to an anaesthetic before.

Do not have this medicine if any of the above apply to you. If you are not sure, talk to your doctor, nurse or pharmacist before you have this medicine.

### **Warnings and precautions**

Talk to your doctor, pharmacist or nurse before having this medicine if:

- you have muscle weakness, tiredness or difficulty in co-ordinating your movements (myasthenia gravis)
- you have a neuromuscular disease, such as a muscle wasting disease, paralysis, motor neurone disease or cerebral palsy
- you have a severe electrolyte imbalance
- you have a lower than normal volume of blood (hypovolaemia)
- you have a burn which requires medical treatment
- you have ever had an allergic reaction to any muscle relaxant which was given as part of an operation
- you have a history of sensitivity to histamine. In particular, spasm of the airways may occur if you have a history of allergy or asthma.

If you are not sure if any of the above apply to you, talk to your doctor, nurse or pharmacist before you are given this medicine.

### **Other medicines and atracurium**

Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, including herbal medicines. This is because these medicines can affect how well this medicine works or can cause side effects.

In particular tell your doctor, nurse or pharmacist if you are taking any of the following:

- anaesthetics (used to reduce sensation and pain during surgical procedures)
- antibiotics (used to treat infections)
- medicines for heart conditions
- medicines for high blood pressure
- water tablets (diuretics), such as furosemide
- medicines for fits (epilepsy), such as phenytoin or carbamazepine
- medicines containing magnesium, such as those to treat indigestion and heart burn
- drugs for Alzheimer's disease (anticholinesterases e.g. donepezil)
- medicines for mental illness, such as lithium
- medicines for inflammation of the joints, such as chloroquine or D-penicillamine
- steroids.

### **Pregnancy and breast-feeding**

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

### **Driving and using machines**

It can be dangerous to drive or operate machinery too soon after having had an operation. Your doctor will tell you how long to wait before you can drive and use machinery.

### **3. How to have Atracurium besilate Solution for injection/infusion**

#### **How your injection is given**

You will never be expected to give yourself this medicine. It will always be given to you by a person who is qualified to do so.

This medicine can be given:

- as a single injection into your vein (intravenous bolus injection)
- as a continuous infusion into your vein. This is where the drug is slowly given to you over a long period of time.

Your doctor will decide the way you are given the drug and the dose you will receive. It will depend on:

- your body weight
- the amount and duration of muscle relaxation required
- your expected response to the medicine.

Children less than 1 month old should not have this medicine.

#### **If you receive more Atracurium besilate Solution for injection/infusion than you should**

This medicine will always be given under carefully controlled conditions. However, if you think that you have been given more than you should tell your doctor or nurse immediately.

### **4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following effects may happen with this medicine:

#### **Allergic reactions including anaphylactic shock**

If you have an allergic reaction, tell your doctor or nurse straight away. The signs may include:

#### **Common side effects (may affect up to 1 in 10 people)**

- decrease in blood pressure
- reddening of your skin

#### **Uncommon side effects (may affect up to 1 in 100 people)**

- wheezing or coughing

#### **Rare side effects (may affect up to 1 in 1,000 people)**

- a lumpy skin rash or 'hives' anywhere on your body

#### **Very Rare side effects (may affect up to 1 in 10,000 people)**

- sudden wheeziness, chest pain or chest tightness
- swelling of your eyelids, face, lips, mouth or tongue
- decrease in heart rate
- shock, circulatory failure, cardiac arrest

Very rarely a severe allergic reaction can occur when given one or more anaesthetic agent.

**Other side effects (unknown frequency) that you may experience are:**

- seizures
- muscle disease (myopathy) or muscle weakness

**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 the Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

**5. How to store Atracurium besilate Solution for injection/infusion**

- Keep out of the sight and reach of children
- Do not use this medicine after the expiry date which is stated on the pack after EXP. The expiry date refers to the last day of that month
- Store between 2 and 8°C. Do not freeze
- Keep in the outer carton in order to protect from light
- When this medicine is made up it should be used straight away. Any unused solution should be thrown away

**6. Contents of the pack and other information**

**What this medicine contains**

- The active substance is atracurium besilate
- The other ingredients are benzene sulfonic acid and Water for Injections.

**What this medicine looks like and contents of the pack**

Atracurium besilate Solution for injection/infusion comes in boxes of 5 by 2.5 ml and 5 ml glass ampoules or 2 by 25 ml glass vials.  
Each vial/ampoule contains 10 mg/ml of the active ingredient atracurium besilate.

**Marketing authorisation holder and manufacturer**

Marketing authorisation Holder:

Aspen Pharma Trading Limited, 3016 Lake Drive, City West Business Campus, Dublin 24, Ireland  
Service-Tel: 0800 008 7392 (+ 44 1748 828 391)

Manufacturer (ampoules and vials):  
GlaxoSmithKline Manufacturing S.p.A.,  
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**Other formats**

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000 (UK only)

Please be ready to give the following information:

<b>Product name</b>	<b>Atracurium besilate 10mg/ml Solution for</b>
<b>injection/infusion</b>	
Reference number	PL 39699/0091

This is a service provided by the Royal National Institute of Blind People

This leaflet was revised in September 2023

## Package Leaflet: Information for Healthcare Professions

### Atracurium besilate 10mg/ml Solution for injection/infusion

# atracurium besilate

Please refer to the Summary of Product Characteristics for complete prescribing information.

#### Presentation

Atracurium besilate Solution for injection/infusion is a clear, colourless to slightly yellow, sterile aqueous solution in a glass ampoule or vial containing 10 mg atracurium besilate per ml. Each 2.5 ml ampoule contains 25 mg atracurium besilate, each 5 ml ampoule contains 50 mg atracurium besilate and each 25 ml vial contains 250 mg atracurium besilate.

#### Uses

Atracurium besilate is a highly selective, competitive or non-depolarising neuromuscular blocking agent. It is used as an adjunct to general anaesthesia or sedation in the Intensive Care Unit (ICU), to relax skeletal muscles, and to facilitate tracheal intubation and mechanical ventilation.

#### Dosage and administration

**Use by injection in adults:** this medicine is administered by intravenous injection.

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

Endotracheal intubation can usually be accomplished within 90 seconds from the intravenous injection of 0.5 to 0.6 mg/kg.

Full block can be prolonged with supplementary doses of 0.1 to 0.2 mg/kg as required. Successive supplementary dosing does not give rise to accumulation of neuromuscular blocking effect.

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.

The neuromuscular block produced by this medicine can be rapidly reversed by standard doses of anticholinesterase agents, such as neostigmine and edrophonium, accompanied or preceded by atropine, with no evidence of recurarisation.

**Use as an infusion in adults:** After an initial bolus dose of 0.3 to 0.6 mg/kg, this medicine can be used to maintain neuromuscular block during long surgical procedures by administration as a continuous infusion at rates of 0.3 to 0.6 mg/kg/hour.

This medicine can be administered by infusion during cardiopulmonary bypass surgery at the recommended infusion rates. Induced hypothermia to a body temperature of 25° to 26°C reduces the rate of inactivation of atracurium, therefore full neuromuscular block may be maintained by approximately half the original infusion rate at these low temperatures.

This medicine is compatible with the following infusion solutions for the times stated below:

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

When diluted in these solutions to give atracurium besilate 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.

**Use in children:** The dosage in children over the age of one month is similar to that in adults on a body weight basis.

**Use in neonates:** The use of this medicine is not recommended in neonates since there are insufficient data available (see section 5.1 Summary of Product Characteristics).

**Use in the elderly:** This medicine 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:** This medicine may be used at standard dosage at all levels of renal or hepatic function, including end stage failure.

**Use in patients with cardiovascular disease:** In patients with clinically significant cardiovascular disease, the initial dose of this medicine should be administered over a period of 60 seconds.

**Use in Intensive Care Unit (ICU) patients:** After an optional initial bolus dose of this medicine of 0.3 to 0.6 mg/kg, this medicine can be used to maintain neuromuscular block by administering a continuous infusion at rates of between 11 and 13 micrograms/kg/min (0.65 to 0.78 mg/kg/hr). There may be wide inter-patient variability in dosage requirements and these may increase or decrease with time. Infusion rates as low as 4.5 microgram/kg/min (0.27 mg/kg/hr) or as high as 29.5 microgram/kg/min (1.77 mg/kg/hr) are required in some patients.

The rate of spontaneous recovery from neuromuscular block after infusion of this medicine in ICU patients is independent of the duration of administration. Spontaneous recovery to a train-of-four ratio >0.75 (the ratio of the height of the fourth to the first twitch in a train-of-four) can be expected to occur in approximately 60 minutes. A range of 32 to 108 minutes has been observed in clinical trials.

**Monitoring: In common with all neuromuscular blocking agents, monitoring of neuromuscular function is recommended during the use of this medicine in order to individualise dosage requirements.**

## Contraindications

This medicine is contraindicated in patients known to be hypersensitive to atracurium, cisatracurium or benzene sulfonic acid.

### **Special warnings and precautions for use**

**Precautions: In common with all the other neuromuscular blocking agents, this medicine paralyzes the respiratory muscles as well as other skeletal muscles but has no effect on consciousness. This medicine should be administered only with adequate general anaesthesia and only by or under the close supervision of an experienced anaesthetist with adequate facilities for endotracheal intubation and artificial ventilation.**

The potential for histamine release exists in susceptible patients during atracurium besilate administration. Caution should be exercised in administering this medicine to patients with a history suggestive of an increased sensitivity to the effects of histamine. In particular, bronchospasm may occur in patients with a history of allergy and asthma.

High rates of cross-sensitivity between neuromuscular blocking agents have been reported. Therefore, where possible, before administering atracurium, hypersensitivity to other neuromuscular blocking agents should be excluded. Atracurium 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.

Monitoring of serial creatinine phosphate (cpk) values should be considered in asthmatic patients receiving high dose corticosteroids and neuromuscular blocking agents in ICU.

This medicine does not have significant vagal or ganglionic blocking properties in the recommended dosage range. Consequently, this medicine has no clinically significant effects on heart rate in the recommended dosage range and it will not counteract the bradycardia produced by many anaesthetic agents or by vagal stimulation during surgery.

In common with other non-depolarising neuromuscular blocking agents, increased sensitivity to atracurium may be expected in patients with myasthenia gravis and other forms of neuromuscular disease.

As with other neuromuscular blocking agents severe acid-base and/or serum electrolyte abnormalities may increase or decrease the sensitivity of patients to atracurium.

As with other non-depolarising neuromuscular blockers hypophosphataemia may prolong recovery. Recovery may be hastened by correcting this condition.

This medicine should be administered over a period of 60 seconds to patients who may be unusually sensitive to falls in arterial blood pressure, for example those who are hypovolaemic.

This medicine is inactivated by high pH and so must not be mixed in the same syringe with thiopental or any alkaline agent.

When a small vein is selected as the injection site, this medicine should be flushed through the vein with physiological saline after injection. When other anaesthetic drugs are administered through the same in-dwelling needle or cannula as this medicine it is important that each drug is flushed through with an adequate volume of physiological saline.

Atracurium is hypotonic and must not be administered into the infusion line of a blood transfusion.

Studies in malignant hyperthermia in susceptible animals (swine) and clinical studies in patients susceptible to malignant hyperthermia indicate that this medicine does not trigger this syndrome.



In common 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.

**Intensive Care Unit (ICU) patients:** When administered to laboratory animals, in high doses, laudanosine, a metabolite of atracurium has been associated with transient hypotension and, in some species, cerebral excitatory effects. Although seizures have been seen in ICU patients receiving atracurium, a causal relationship to laudanosine has not been established (see *Undesirable effects*).

### **Drug interactions**

The neuromuscular block produced by this medicine may be increased by the concomitant use of inhalational anaesthetics such as halothane, isoflurane and enflurane.

In common with all non-depolarising neuromuscular blocking agents the magnitude and/or duration of a non-depolarising neuromuscular block may be increased as a result of interaction with: antibiotics, including the aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin and clindamycin; antiarrhythmic drugs: propranolol, calcium channel blockers, lidocaine, procainamide and quinidine; diuretics: furosemide and possibly mannitol, thiazide diuretics and acetazolamide; magnesium sulphate; ketamine; lithium salts; ganglion blocking agents: trimetaphan, hexamethonium.

Rarely, certain drugs may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome; increased sensitivity to this medicine would be consequent on such a development. Such drugs include various antibiotics, beta-blockers (propranolol, oxprenolol), antiarrhythmic drugs (procainamide, quinidine), antirheumatic drugs (chloroquine, D-penicillamine), trimetaphan, chlorpromazine, steroids, phenytoin and lithium. The onset of non-depolarising neuromuscular block is likely to be lengthened and the duration of block shortened in patients receiving chronic anticonvulsant therapy.

The administration of combinations of non-depolarising neuromuscular blocking agents in conjunction with this medicine may produce a degree of neuromuscular blockade in excess of that which might be expected were an equipotent total dose of this medicine administered. Any synergistic effect may vary between different drug combinations.

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, as this may result in a prolonged and complex block which can be difficult to reverse with anticholinesterase drugs.

Treatment with anticholinesterases, commonly used in the treatment of Alzheimer's disease e.g. donepezil, may shorten the duration and diminish the magnitude of neuromuscular blockade with atracurium.

### **Undesirable effects**

The most commonly reported adverse reactions during treatment are hypotension (mild, transient) and skin flushing, these events are attributed to histamine release. Very rarely, severe anaphylactoid or anaphylactic reactions have been reported in patients receiving atracurium in conjunction with one or more anaesthetic agents.

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common > 1/10, common >1/100 and < 1/10, uncommon >1/1,000 and < 1/100, rare >1/10,000 and < 1/1,000, very rare < 1/10,000.

Very common, common and uncommon frequencies were determined from clinical trial data. Rare and very rare frequencies were generally derived from spontaneous data. The frequency classification "Not known" has been applied to those reactions where a frequency could not be estimated from the available data.

#### **Clinical Trial Data:**

##### **Vascular Disorders**

Common Hypotension (mild, transient)#, Skin flushing#

##### **Respiratory, thoracic and mediastinal disorders**

Uncommon Bronchospasm#

#### **Post-Marketing Data:**

##### **Immune system disorders**

Very rare Anaphylactic reaction, anaphylactoid reaction including anaphylactic shock, circulatory failure and cardiac arrest

Very rarely severe anaphylactoid or anaphylactic reactions have been reported in patients receiving atracurium in conjunction with one or more anaesthetic agents

##### **Nervous system disorder**

Not known Seizures

There have been reports of seizures in ICU patients who have been receiving atracurium 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). A causal relationship to laudanosine has not been established. In clinical trials, there appears to be no correlation between plasma laudanosine concentration and the occurrence of seizures.

##### **Skin and subcutaneous tissue disorders**

Rare Urticaria

##### **Musculoskeletal and connective tissue disorders**

Not known Myopathy, muscle weakness

There have been some reports of muscle weakness and/or myopathy following prolonged use of muscle relaxants in severely ill patients in the ICU. Most patients were receiving concomitant corticosteroids. These events have been seen infrequently in association with atracurium and a causal relationship has not been established.

Events which have been attributed to histamine release are indicated by a hash (#)

Description of selected adverse reactions:

**Anaphylactic reaction, anaphylactoid reaction including anaphylactic shock:** Very rarely, severe anaphylactoid or anaphylactic reactions including anaphylactic shock have been reported in patients receiving atracurium in conjunction with one or more anesthetic agents.

#### **Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare

professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).

### **Fertility, pregnancy and lactation**

**Fertility:** Fertility studies have not been performed.

**Pregnancy:** Animal studies have indicated that this medicine has no significant effects on foetal development.

In common with all neuromuscular blocking agents, this medicine should be used during pregnancy only if the potential benefit to the mother outweighs any potential risk to the foetus. This medicine is suitable for maintenance of muscle relaxation during Caesarean section as it does not cross the placenta in clinically significant amounts following recommended doses.

**Breast-feeding:** It is not known whether atracurium besilate is excreted in human milk.

### **Ability to drive and use machines**

This precaution is not relevant to the use of atracurium. Atracurium will always be used in combination with a general anaesthetic and therefore the usual precautions relating to performance of tasks following general anaesthesia apply.

### **Toxicity and treatment of overdose**

**Signs:** Prolonged muscle paralysis and its consequences are the main signs of overdose.

**Management:** It is essential to maintain a patent airway together with assisted positive pressure ventilation until spontaneous respiration is adequate. Full sedation will be required since consciousness is not impaired. Recovery may be hastened by the administration of anticholinesterase agents accompanied by atropine or glycopyrrolate, once evidence of spontaneous recovery is present.

### **Pharmaceutical precautions**

Store at temperatures between 2° to 8°C. Do not freeze. Keep container in the outer carton in order to protect from light. Any unused atracurium besilate from opened ampoules should be discarded.

### **Legal category**

POM

### **Package quantities**

Box of 5 x 2.5 ml ampoules (each ampoule containing 25 mg atracurium besilate).

Box of 5 x 5 ml ampoules (each ampoule containing 50 mg atracurium besilate).

Box of 2 x 25 ml vials (each vial containing 250 mg atracurium besilate).

### **Further information**

This medicine is inactivated by Hofmann elimination, a non-enzymatic process which occurs at physiological pH and temperature, and by ester hydrolysis catalysed by non-specific esterases.

The termination of the neuromuscular blocking action of this medicine 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.

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

This medicine has no direct effect on intra-ocular pressure, and is therefore suitable for use in ophthalmic surgery.

Variations in the blood pH and body temperature of the patient within the physiological range will not significantly alter the duration of action of this medicine.

Haemofiltration and haemodiafiltration have a minimal effect on plasma levels of atracurium and its metabolites, including laudanosine. The effects of haemodialysis and haemoperfusion on plasma levels of atracurium and its metabolites are unknown.

**Product licence number**

PL 39699/0091

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