Atracurium 10mg/ml Solution for Injection/Infusion
Atracurium besilate

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 symptoms 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.
• The full name of this medicine is Atracurium 10mg/ml Solution for Injection/Infusion but within the leaflet it will be referred to as Atracurium.

What is in this leaflet
1. What Atracurium is and what it is used for
2. What you need to know before you use Atracurium
3. How to use Atracurium
4. Possible side effects
5. How to store Atracurium
6. Contents of the pack and other information

1. What Atracurium is and what it is used for
Atracurium belongs to a group of medicines called muscle relaxants. It is used to relax muscles during surgery.

Atracurium is used:
• during surgery, other procedures and in intensive care
• during general anaesthesia to ease tracheal intubation (a tube into the windpipe) and controlled ventilation.

2. What you need to know before you use Atracurium
Do not use Atracurium
• if you are allergic (hypersensitive) to atracurium, cisatracurium or benzenesulfonic acid.

Warnings and Precautions
Talk to your doctor before using Atracurium. Tell your doctor if you have:
• a disease that affects the muscles and/or their nervous control (neuromuscular disease such as myasthenia gravis or Eaton-Lambert syndrome)
• an electrolyte imbalance (changes to the body’s normal levels of certain chemicals)
• cancer that has spread to different parts of the body (carinomatosis)
• allergy to any other muscle relaxant
• a recent burn that has required medical attention
• a history of asthma, hay fever or allergies that give you a rash, itching or shortness of breath (histamine hypersensitivity)
• heart diseases and low blood pressure

Other medicines and Atracurium
Tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This is especially important with the following medicines as they may interact with Atracurium:

- antibiotics (e.g. aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin, clindamycin and vancomycin)
- antiarrhythmic medicines (used to control the rhythm of the heart e.g. lidocaine, procainamide, quinidine)
- diuretics (water tablets) (e.g. furosemide, thiazides and mannitol)
- medicines used to control blood pressure, angina or other heart problems (e.g. propranolol, oxprenolol, diltiazem, nicardipine, nifedipine and verapamil)
- antiepileptic medicines (e.g. carbamazepine, phenytoin)
- drugs used to treat rheumatism (e.g. chloroquine, D-penicillamine)
- steroids
- trimetaphan, hexamethonium (used to lower blood pressure during surgery)
- dantrolene (a muscle relaxant)
- acetazolamide (treatment of glaucoma)
- magnesium sulphate
- ketamine (an anaesthetic drug)
- lithium, chlorpromazine (treatment of mental illness)
- medicines used in the treatment of Alzheimer’s disease (anticholinesterases e.g. donepezil)

It may still be all right for you to be given Atracurium and your doctor will be able to decide what is suitable for you.

**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 using this medicine.

There is no adequate data on the use of atracurium besilate during pregnancy. Atracurium should only be administered during pregnancy after careful risk-benefit assessment.

The use of the recommended dose in caesarean section showed no harmful effects on the newborn infants. Therefore Atracurium is also suitable for maintenance of muscle relaxation during caesarean section.

It is not known whether atracurium besilate passes into breast milk. As precaution you should restart breast-feeding 24 hours after administration of Atracurium, when the effect of the medicine has worn off.

**Driving and using machines**

You should not drive, operate machinery or work in exposed situations soon after having had an operation. The time factor should be decided individually by the physician.

You should be accompanied on your way home and you should not drink alcoholic drinks.

**3. How to use Atracurium**

Atracurium should only be used by a physician.
Dosage
Atracurium is used during procedures that require that the patient is fully anaesthetised (unconscious), or heavily sedated. The dosing will be worked out by the doctor. Atracurium must be given only by injection directly into a vein (intravenous use). Atracurium must not be injected into a muscle.

Use in children:
The use of Atracurium is not recommended in neonates (children under the age of one month). In the case of necessary treatment in newborn or premature newborn the dose has to be significantly lowered.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist. Information for medical or healthcare professionals is provided at the end of this leaflet.

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them. The frequency of possible side effects listed below is defined using the following convention:

Very common: affects more than 1 user in 10
Common: affects 1 to 10 users in 100
Uncommon: affects 1 to 10 users in 1,000
Rare: affects 1 to 10 users in 10,000
Very rare: affects less than 1 user in 10,000
Not known: frequency cannot be estimated from the available data

Common:
• tachycardia (rapid heartbeat)
• temporary hypotension (low blood pressure)
• wheezing
• bronchospasm (asthma-like symptoms)
• skin flushing
• urticaria (nettle rash)

Very rare:
• myasthenia and/or myopathy (weak or nonworking muscles)
• severe allergic reactions including shock, circulatory failure and heart attack in patients receiving atracurium with one or more anaesthetic drugs
• seizures (fits) when taken with other drugs in at-risk patients
• laryngospasm (spasm of the vocal cords)

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

5. How to store Atracurium
Keep this medicine out of the sight and reach of children.

Do not use Atracurium after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

**Storage conditions**
Store in a refrigerator (2°C – 8°C). Keep the ampoules in the outer carton.

**Shelf life after opening the ampoule**
The solution has to be used immediately after opening the ampoule.

When Atracurium is diluted in compatible solutions, the resultant solutions will be stable in daylight for 4 to 24 hours at temperatures of up to 30°C, depending on the type of diluent (see Dilution instructions in section ‘The following information is intended for medical or healthcare professionals only’ at the end of this leaflet). 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 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Prior to administration a healthcare professional should inspect the product visually and discard any product where the usual appearance of the product has changed or if the container is damaged. Only clear solutions practically free from particles should be used.

The product is for single use only. Any unused solution should be discarded.

Do not throw away any medicines via wastewater or household waste. 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 Atracurium contains:**
The active substance is atracurium besilate.
1 ml solution contains 10mg atracurium besilate.
One ampoule with 2.5 ml solution contains 25mg atracurium besilate.
One ampoule with 5 ml solution contains 50mg atracurium besilate.
One ampoule with 25 ml solution contains 250mg atracurium besilate

The other ingredients are: Benzensulphonic acid, Water for injection.

**What Atracurium looks like and contents of the pack**
Solution for injection and Concentrate for solution for infusion

Clear and colourless solution

Box of 1 ampoule with 2.5 ml
Box of 5 ampoules with 2.5 ml
Box of 10 ampoules with 2.5 ml
Box of 5x5 ampoules with 2.5 ml
Box of 5x10 ampoules with 2.5 ml
Box of 1 ampoule with 5 ml
Box of 5 ampoules with 5 ml
Box of 10 ampoules with 5 ml
Box of 5x5 ampoules with 5 ml
Box of 5x10 ampoules with 5 ml
Box of 1 ampoule with 25 ml
Box of 2 ampoules with 25 ml
Box of 5 ampoules with 25 ml

Not all pack sizes may be marketed.

**Marketing Authorisation Holder:**
Actavis Group PTC ehf
Reykjavikurvegur 76-78,
220 Hafnarfjordur
Iceland

**Manufacturers:**
Actavis Group PTC ehf.
Reykjavikurvegur 76-78
220 Hafnarfjordur
Iceland

**This leaflet was last revised in June 2016**

If you would like a leaflet with larger text, please contact 01271 311257.

The following information is intended for medical or healthcare professionals only:
Preparation and administration of Atracurium 10mg/ml solution for injection and concentrate for solution for infusion.

It is important that you read the entire contents of this guide prior to the preparation of this medicinal product.

Please refer to Summary of Product Characteristics for full prescribing and other information.

**Incompatibility**
Atracurium 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 and thiopentone in order to avoid the formation of aggregates, which might cause an anaphylactoid reaction.

**Dilution instructions**
Atracurium can be diluted with the following solutions for infusion:

*Solution for infusion 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
When diluted in these solutions to give atracurium besilate concentrations of 0.5mg/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 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

**Posology and method of administration**
The product is for single use only. Any unused solution should be discarded.

Prior to administration it is recommended to inspect the product visually and discard any product where the usual appearance of the product has changed or if the container is damaged.

Only clear solutions practically free from particles should be used.

In common with all neuromuscular blocking agents, monitoring of neuromuscular function is recommended during the use of atracurium besilate, in order to individualise dosage requirements.

**Use in anaesthesia**
*In adults: Use as an injection*
Atracurium besilate is administered by intravenous injection and must not be applied intramuscularly.

**Relaxation**
The dosage range recommended for adults is 0.3 to 0.6mg atracurium besilate/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 0.6mg atracurium besilate/kg.

**Repeated dose**
Full block can be prolonged with supplementary doses of 0.1 to 0.2mg atracurium besilate/kg. Generally, the first maintenance dose is required 20 to 45 minutes after the initial bolus dose, then typically at 15 to 25 minutes 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.

The neuromuscular block produced by atracurium besilate 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.
In adults: Use as an infusion
Atracurium besilate is hypotonic and must not be administered via the infusion system of a blood transfusion. In this case atracurium besilate has to be administered via a separate infusion line.

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

Atracurium besilate 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 besilate, therefore full neuromuscular block may be maintained with approximately half the original infusion rate.

Atracurium can be diluted with the solutions for infusion listed above.

Use in paediatric population
On a bodyweight basis the dosage in children over the age of 1 month is similar to that in adults.

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

Use in special populations
Use in the elderly:
Atracurium besilate 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 besilate may be used at standard dosage at all levels of renal or hepatic function, including endstage failure.

Use in patients with cardiovascular disease:
Patients with severe cardiovascular diseases may react more sensitively to transient states of hypotony (see section 4.4). In these patients, atracurium besilate 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 besilate for long-term mechanical ventilation in intensive care units, the benefit to risk ratio of neuromuscular block must be considered. After an initial bolus dose of 0.3 - 0.6mg/kg, Atracurium besilate can be used to maintain neuromuscular block by administration of a continuous infusion of between 11 and 13 micrograms/kg/min (0.65 - 0.78mg/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 (0.27mg/kg/h) or as high as 29.5 micrograms/kg/min (1.77mg/kg/h). Dosage requirements may change over time. The speed of spontaneous recovery from neuromuscular block after infusion of atracurium besilate 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 approximately 32 – 108 minutes (n = 6).