PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Atracurium besilate 10 mg/ml solution for injection/infusion

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.
- 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 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 ARE GIVEN ATRACURIUM

You should not be given Atracurium:
- if you are **allergic** to **atracurium besilate** or **any of the other ingredients of this medicine** (listed in section 6). An allergic reaction may include rash, itching, difficulty of breathing or swelling of the face, lips, throat or tongue. You may know this from earlier experience.

Warnings and precautions
Before you receive 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)
- a severe electrolyte disorder
- cancer spread widely from a primary source (carcinomatosis)
- a sensitivity to histamine
- asthma-like symptoms (a history of allergy, asthma or bronchospasm)
- burns
- lack of adequate circulatory filling (hypovolaemia)

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. Ask your doctor if you have any further questions.

Other medicines and Atracurium
Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines This is especially important with the following medicines as they may interact with your 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, acetazolamide 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)
- corticosteroids (used to treat inflammation)
- trimetaphan, hexamethonium (used to lower blood pressure during surgery)
- dantrolene (a muscle relaxant)
- magnesium sulphate
- ketamine (an anaesthetic drug)
- lithium, chlorpromazine (treatment of mental illness)
- quinine (treatment of malaria or leg cramps)

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
Atracurium should not be given to pregnant women unless medically justified. Mothers should stop breast-feeding for 24 hours after receiving Atracurium. 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 taking this medicine.

Driving and using machines
After you have been given Atracurium, you must not drive, operate machinery, or work in dangerous situations. You should not go home alone and should **not drink alcohol until fully recovered**.

3. HOW ATRACURIUM IS GIVEN

Atracurium must only be given by an experienced doctor under carefully controlled conditions.

Dosage
Atracurium is used during procedures that require that the patient is fully anaesthetized (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.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been reported:

Common (may affect up to 1 in 10 people)
- tachycardia (rapid heartbeat)
- temporary hypotension (low blood pressure)
- wheezing
- bronchospasm (asthma-like symptoms)
- skin flushing
- urticaria (nettle rash)

Very rare (may affect up to 1 in 10,000 people)
- myasthenia and/or myopathy (weak or non-working 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 sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label and the carton after "Exp". The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C - 8°C). Do not freeze. Keep the ampoules in the outer carton in order to protect from light.
- After first opening the medicinal product should be used immediately.
- Shelf life of prepared infusion solutions for infusion: 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 Dilution instructions at the end of this leaflet 'The following information is intended for healthcare professionals only)'. 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.
- The product should be inspected visually prior to administration (also after dilution.) Do not use Atracurium if you notice the solution is not clear, colourless and free of particles or if the container is damaged.
- Any unused solution from opened ampoules should be discarded.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Atracurium contains
The active substance is atracurium besilate.
1 ml of Atracurium contains 10 mg of atracurium besilate.
One ampoule with 2.5 ml solution contains 25 mg atracurium besilate
One ampoule with 5.0 ml solution contains 50 mg atracurium besilate.

The other ingredients are water for injections and benzenesulfonic acid.

What Atracurium looks like and the content of the pack
Atracurium is a clear and colourless solution for injection/infusion.

3 ml or 5 ml clear glass ampoules
Box of 5 ampoules with 2.5 or 5 ml
Box of 10 ampoules with 2.5 or 5 ml
Box of 5 x 10 ampoules with 2.5 or 5 ml

Not all pack sizes may be marketed.

Marketing authorisation holder
hameln pharma ltd
Nexus, Gloucester Business Park
Gloucester, GL3 4AG
United Kingdom

Manufacturer
Siegfried Hameln GmbH
Langes Feld 13
31789 Hameln
Germany

This medicinal product is authorised in the Member States of the EEA under the following names:

DE: Atracurium-hameln 10 mg/ml Injektions-/Infusionslösung
IT: Atracurium-hameln 10 mg/ml soluzione iniettabile o per infusione
NL: Atracurium-hameln 10 mg/ml oplossing voor injectie/infusie
ES: Besilato de Atracurio-hameln 10 mg/ml solución inyectable y para perfusión EFG
SE: Atracurium-hameln 10 mg/ml injektions-/infusions vätska, lösning
UK: Atracurium besilate 10 mg/ml solution for injection/infusion

This leaflet was last revised in November 2022

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The following information is intended for healthcare professionals only:

Preparation and administration of Atracurium besilate 10 mg/ml solution for injection/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.

Incompatibilities

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

Dilution instructions

Atracurium besilate is compatible with the following solutions for infusions:

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 administer 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.

Posology and method of administration

Atracurium is used for intravenous injection or infusion.
For single dose use only. Any unused solution from opened ampoules should be discarded.

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

- Use as an injection in adults

Atracurium 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 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 0.6 mg atracurium besilate/kg.

Repeated dose
Full block can be prolonged with supplementary doses of 0.1 to 0.2 mg atracurium besilate/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 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.

- Use as an infusion in adults

Atracurium 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 0.6 mg/kg, atracurium besilate, administered as a continuous infusion at rates of 0.3 to 0.6 mg/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 infusion solutions listed above.

- 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 besilate 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 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 end-stage failure.

Use in patients with cardiovascular disease
Patients with severe cardiovascular diseases may react more sensitively to transient states of hypotony. 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 optional initial bolus dose of 0.3 - 0.6 mg/kg, atracurium besilate can be used to maintain neuromuscular block by administration of a continuous infusion of between 11 and 13 micrograms/kg/min (0.66 - 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 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 32 - 108 minutes (n = 6) observed in clinical trials.