Package leaflet: Information for the patient

Tracrium 10 mg/ml solution for injection or 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, nurse or pharmacist.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Tracrium is and what it is used for

Tracrium contains a medicine called atracurium besilate. This belongs to a group of medicines called muscle relaxants.

Tracrium 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.

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

2. What you need to know before you use Tracrium

Do not use Tracrium if:
- you are allergic to atracurium besilate, cisatracurium (another muscle relaxant) or any of the other ingredients in Tracrium (listed in Section 6)
- you have reacted badly to an anaesthetic before.

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

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using this medicine if:
- you are allergic to any other muscle relaxant
- 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 form of cancer called carcinomatosis
- you have severe cardiovascular disease
- you have a burn which requires medical treatment
- you have a tendency towards allergies or have asthma. If so, you may have an increased sensitivity to the effects of histamine
- you are elderly.

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

Other medicines and Tracrium
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 Tracrium works or can cause side effects.

In particular tell your doctor, nurse or pharmacist if you are taking any of the following:
- anaesthetics such as ketamine, ether, enflurane, isoflurane and halothane (used to reduce sensation and pain during surgical procedures)
- muscle relaxants such as suxamethonium chloride
- antibiotics such as aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin and clindamycin (used to treat infections)
- medicines for uneven heart beats such as propranolol (also used to treat high blood pressure), lidocaine, procainamide, quinidine and calcium channel blockers (anti-arrhythmics)
- water tablets (diuretics), such as furosemide, thiazides, mannitol and acetazolamide
- medicines for inflammation of the joints, such as chloroquine or d-penicillamine
- steroids
- medicines for fits (epilepsy), such as phenytoin
- medicines for mental illness, such as lithium or chlorpromazine (which can also be used for sickness)
- medicines containing magnesium, such as those to treat indigestion and heart burn
- ganglion blocking drugs such as trimetaphan and hexamethonium
- medicines for chest pain (angina) such as oxprenolol (also used to treat high blood pressure)
- medicines called anticholinesterases (e.g. donepezil), commonly used in the treatment of Alzheimer's disease.

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 taking this medicine.

Driving and using machines
Do not drive or operate machinery after having this medicine. Your doctor will tell you when it is safe to do so again. It is recommended that you arrange for someone to accompany you home from the hospital.

3. How to use Tracrium

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.

Tracrium 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 Tracrium than you should
Tracrium 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, Tracrium can cause side effects, although not everybody gets them.

The following effects may happen with this medicine:

Allergic reactions (may affect up to 1 in 10,000 people)
If you have an allergic reaction, tell your doctor or nurse straight away. The signs may include:
- sudden wheeziness, chest pain or chest tightness
- swelling of your eyelids, face, lips, mouth or tongue
- a lumpy skin rash or 'hives' anywhere on your body
- decrease in heart rate
- decrease in blood pressure
- a rash or redness of your skin
- wheezing or coughing.

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

Talk to your doctor, nurse or pharmacist if you notice any of the following:

Common (may affect up to 1 in 10 people)
- low blood pressure
- reddening of the skin.

Uncommon (may affect up to 1 in 100 people)
- difficulty in breathing and chest tightness (bronchospasm).

Rare (may affect up to 1 in 1,000 people)
- a lumpy skin rash or 'hives' anywhere on your body (urticaria).

Not known (frequency cannot be estimated from the available data)
- fits
- 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 HPRA Pharmacovigilance Website: www.hpra.ie.

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

5. How to store Tracrium

- Keep this medicine out of the sight and reach of children.
- Do not use Tracrium after the expiry date which is stated on the carton and the label after "EXP". The expiry date refers to the last day of the month.
- Store between 2 and 8°C. Do not freeze.
- Store in the original package, to protect from light.
- Tracrium is a clear, colorless to slightly yellow solution. Do not use it if it looks different to normal.
- When Tracrium is made up it should be used straight away (please see section headed 'the following information is intended for healthcare professionals only' for further information).
- Any waste material should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What Tracrium contains
- The active substance is atracurium besilate
- The other ingredients are benzenesulfonic acid and Water for Injections.

What Tracrium looks like and contents of the pack
Tracrium is a clear, colorless to slightly yellow solution.
Tracrium 10 mg/ml solution for injection or infusion (ampoules) comes in boxes of 5 by 2.5 ml or 5 ml glass ampoules. Each 2.5 ml ampoule contains 25 mg of atracurium besilate. Each 5 ml ampoule contains 50 mg of atracurium besilate.
Tracrium 10 mg/ml solution for injection or infusion (vial) comes in boxes of 2 by 25 ml glass vials. Each 25 ml vial contains 250 mg atracurium besilate.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder: Aspen Pharma Trading Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland.

Manufacturer (ampoules and vials):
GlaxoSmithKline Manufacturing S.p.A., Strada Provinciale Asolana 90, 43056 San Polo di Torrile, Parma, Italy.

Aspen Pharma Ireland Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland

Manufacturer (ampoules):
Aspen Bad Oldesloe GmbH, Industriestrasse 32-36, 23843 Bad Oldesloe, Germany

Medical Information Enquiries
For any Medical Information enquiries about this product, please contact:
Tel: 00353 1 630 8400

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THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS ONLY

(Please refer to the Summary of Product Characteristics for further information)

Pharmaceutical forms

Tracrium 10 mg/ml solution for injection or infusion, ampoules
Tracrium 10 mg/ml solution for injection or infusion, vials

Posology and method of administration

Injection:
Tracrium is administered by intravenous injection. The dosage range for adults is 0.3 to 0.6 mg/kg (depending on the duration of full block required) and will provide adequate relaxation for 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.

Caesarean Section:
Tracrium is suitable for maintenance of muscle relaxation during Caesarean section as it does not cross the placenta in clinically significant amounts following recommended doses (0.3 to 0.6 mg/kg).

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 Tracrium 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.

Continuous infusion:
Normothermia: After an initial bolus dose of 0.3 to 0.6 mg/kg, Tracrium 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.

Tracrium can be administered by infusion during cardiopulmonary bypass surgery at the recommended infusion rates. Induced hypothermia to a body temperature of 25^{o}C to 26^{o}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.

Paediatric populations: The dosage in children over the age of 1 month is the same as that in adults on a body weight basis.

Neonates: The use of Tracrium is not recommended in neonates since there are insufficient data available (see section 5.1 of the SmPC).

Elderly: Tracrium 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.

Renal and/or hepatic impairment: Tracrium may be used at standard dosage at all levels of renal or hepatic function, including endstage failure.

Cardiovascular disease: In patients with clinically significant cardiovascular disease, the initial dose of Tracrium should be administered over a period of 60 seconds.

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

Overdose

Symptoms and Signs
Prolonged muscle paralysis and its consequences are the main signs of overdosage.

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.

Shelf life and special precautions for storage

Unopened: 2 years.

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 reconstitution/dilution has taken place in controlled and validated aseptic conditions.

Store at temperatures between 2ºC and 8ºC. Store in the original package in order to protect from light. Do not freeze.

Please see ‘Instructions for use and handling’ for further information regarding in-use shelf life and storage precautions

Instructions for use and handling

In-use: must be used immediately. Any unused Tracrium from opened ampoules/vials should be discarded immediately after use.

No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

In-use following dilution: Chemical and physical in-use stability for Tracrium has been demonstrated with the following infusion solutions, for the times stated below at 30°C:

Infusion Solution	Period of Stability at 30°C
- Sodium Chloride Intravenous Infusion British Pharmacopoeia (BP) (0.9% w/v)	24 hours
- Glucose Intravenous Infusion British Pharmacopoeia (BP) (5% w/v)	8 hours
- Ringer's Injection United States Pharmacopoeia (USP)	8 hours
- Sodium Chloride (0.18% w/v) and Glucose (4% w/v) Intravenous Infusion British Pharmacopoeia (BP)	8 hours
- Compound Sodium Lactate Intravenous Infusion British Pharmacopoeia (BP) (Hartmann's Solution for Injection)	4 hours

Please see ‘Shelf life and special precautions for storage’ for microbiological in-use information.

Ampoules

Instructions to open the ampoule:

Ampoules are equipped with the OPC (One Point Cut) opening system and must be opened following the below instructions:

- Hold with the hand the bottom part of the ampoule.
- Put the other hand on the top of the ampoule positioning the thumb above the coloured point and press.