

Date: 27 Aug 2020

Important information for healthcare professionals

**Supply of Tracrium 10mg/ml Solution for Injection or Infusion, amps (50mg/5ml).
- PA 1691/029/001**

**Batch: RP3G
Exp: 01-Nov-2020
Quantity: 2130 packs**

This letter must remain with the pack at all times until the point of administration.

Ampoules must not be taken out of the outer carton until the point of administration.

Dear Healthcare Professional,

I am writing to you with regards to supply of the above referenced product.

We are currently unable to supply Irish licensed packs and have obtained approval from the Health Products Regulatory Authority (HPRA) to supply Ukrainian-labelled packs for a limited period, due to a large increase in demand.

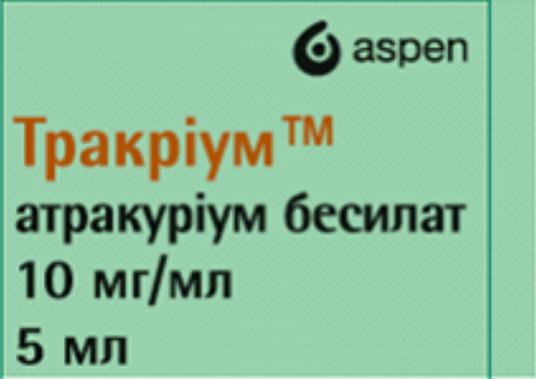
The Ukrainian packs are labelled with Batch No. RP3G and have an expiry date of 01-Nov-2020. Product from this batch will be supplied as a temporary measure until we resume supply of Irish stock.

The pharmaceutical composition and specifications of Ukrainian product are equivalent to Irish licenced product.

Use of the product should be carried out in-line with the Irish SmPC as usual, which can be found on the HPRA or medicines.ie website. We have also provided a label text comparison, copy of the Irish carton, and Patient Information Leaflet at the end of this letter. The Ukrainian Patient Information Leaflet should be discarded.

Please ensure all relevant staff members are made aware of the content of this letter and that the information is communicated to patients.

This communication has been agreed with the HPRA.

Label on the product Ukrainian language	English translation
 <p>Тракриум™ атракуріум бесилат 10 мг/мл 5 мл</p>	<p>"Tracrium Atracurium besilate 10 mg/ml 5 ml"</p>

Aspen Pharma Trading Limited, 3016 Lake Drive,
Citywest Business Campus, Dublin 24, Ireland
Tracrium is a trade mark of the Aspen group.
© 2017 Aspen group of companies. All rights reserved.
PA 1691/029/001. Medicinal product subject to medical prescription.



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BREAK SECURITY SEAL TO OPEN

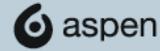
PUSH

Tracrium

10 mg/ml
solution for
injection or infusion
atracurium besilate
50 mg in 5 ml

5 AMPOULES

Injection containing
50 mg of
atracurium besilate
in 5 ml (10 mg/ml)
solution for injection
or infusion



PUSH

BREAK SECURITY SEAL TO OPEN

**50 mg
in
5 ml**

Dose: As directed by physician. Read the package leaflet before use.
For intravenous administration only.
Storage: Store in a refrigerator at 2-8°C. Do not freeze. Store in original package in order to protect from light,
Discard any remaining contents immediately after use.
Precautions: Any portion of the contents remaining after use should be discarded.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

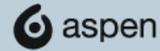
**50 mg
in
5 ml**

Tracrium

10 mg/ml
solution for
injection or infusion
atracurium besilate
50 mg in 5 ml

5 AMPOULES

Injection containing
50 mg of
atracurium besilate
in 5 ml (10 mg/ml)
solution for injection
or infusion



Each ml of solution contains
10 mg of atracurium besilate
Each 5 ml ampoule contains
50 mg of atracurium besilate
Also contains:
Benzenesulfonic acid
Water for Injections

**50 mg
in
5 ml**



Tracrium 10 mg/ml
solution for injection or infusion
atracurium besilate
50 mg in 5 ml
5 AMPOULES



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
2. What you need to know before you use Tracrium
3. How to use Tracrium
4. Possible side effects
5. How to store Tracrium
6. Contents of the pack and other information

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.



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°C 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.

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.

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 anaesthetic 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:

Ireland

HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie

Malta

ADR Reporting

Website: www.medicinesauthority.gov.mt/adrportal

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, 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, 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. Tel: +353 1 6 308 400

Manufacturer:

Aspen Pharma Ireland Limited, One George's Quay Plaza, Dublin 2, Ireland.

Medical Information Enquiries

For any Medical Information enquiries about this product, please contact:

Ireland

Tel: 00353 1 630 8400

Malta

Tel: 00356 21497982

Leaflet date: January 2019

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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 2°C and 8°C. 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:

<u>Infusion Solution</u>	<u>Period of Stability at 30°C</u>
- 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.