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Atracurium besylate



1

Generic names & Trade names :

No	Brand Name	Manufacturer	Type
1	<u>Acris (10 mg)</u>	Zydus Cadila (German Remedies).	Injection
2	<u>Acris (25 mg)</u>	Zydus Cadila (German Remedies).	Injection
3	<u>Arium (25 mg)</u>	Celon Laboratories Ltd.	Injection
4	<u>Arium (50 mg)</u>	Celon Laboratories Ltd.	Injection
5	<u>Artacil (25 mg)</u>	Neon Laboratories Limited	Injection
6	<u>Artacil (50 mg)</u>	Neon Laboratories Limited	Injection
7	<u>Atcurium (25 mg)</u>	Chandra Bhagat Pharma Pvt. Ltd.	Injection
8	<u>Atrelax (25 mg)</u>	Abbott Healthcare Pvt Ltd (AHPL)	Injection
9	<u>Tracrium (25 mg)</u>	GlaxoSmithKline Pharmaceuticals Ltd	Injection
10	<u>Troycurium (25 mg)</u>	Troikaa Pharmaceuticals Ltd.	Injection

Pharmacological class :

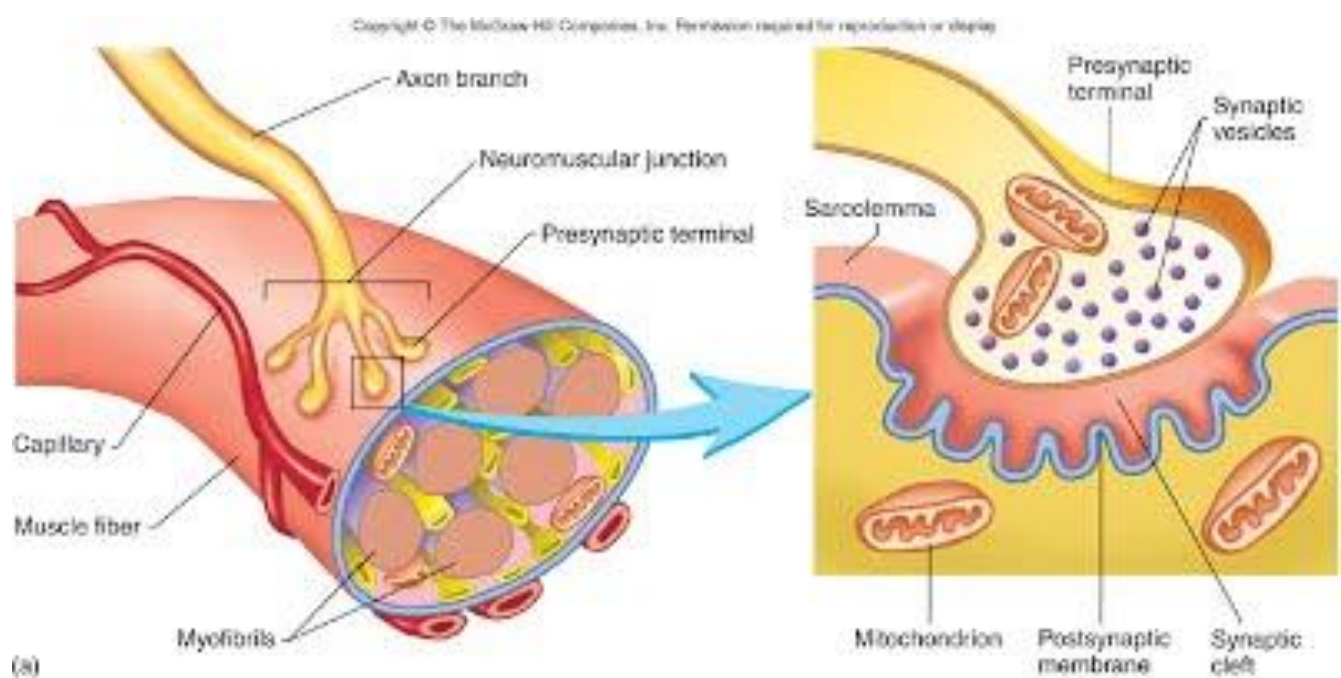
Anesthesia

Neuromuscular blocker (nondepolarizing).

Mechanism of action :

Atracurium antagonizes the neurotransmitter action of acetylcholine by binding competitively with cholinergic receptor sites on the motor end-plate. This antagonism is inhibited, and neuromuscular block reversed, by acetylcholinesterase inhibitors such as neostigmine, edrophonium, and pyridostigmine.

Neuromuscular blocking agents work by interfering with the transmission of acetylcholine. Under normal conditions, acetylcholine crosses the neuromuscular junction cleft and stimulates the receptors upon receiving the nerve impulse. Then, acetylcholine is broken down by the acetylcholinesterase enzyme that presides in the junction cleft as well. The postsynaptic receptors are located on the side of the junction where the acetylcholine was released. When it binds to these receptors, sodium and calcium move into the muscle and potassium leaves.



There are two different types of neuromuscular blocking agents that affect these acetylcholine receptors: depolarizing and nondepolarizing. Atracurium has a nondepolarizing mechanism of action. Nondepolarizing neuromuscular blocking agents act as competitive inhibitors with acetylcholine to bind to the postsynaptic receptors. By binding to these receptors, the channel will not open to allow movement of ions, thus rendering the muscle limp.

Pharmacological actions :

Atracurium is susceptible to degradation by Hofmann elimination and ester hydrolysis as components of the in vivo metabolic processes. The initial in vitro studies appeared to indicate a major role for ester hydrolysis but, with accumulation of clinical data over time, the preponderance of evidence indicated that Hofmann elimination at physiological pH is the major degradation pathway vindicating the premise for the design of atracurium to undergo an organ-independent metabolism.

Atracurium is a nondepolarizing skeletal muscle relaxant. Atracurium can be used most advantageously if muscle twitch response to peripheral nerve stimulation is monitored to assess degree of muscle relaxation. The duration of neuromuscular block produced by Atracurium is approximately one third to one half the duration of block by d-tubocurarine, metocurine, and pancuronium at initially equipotent doses. As with other nondepolarizing neuromuscular blockers, the time to onset of paralysis decreases and the duration of maximum effect increases with increasing doses of Atracurium. Repeated administration of maintenance doses of Atracurium has no cumulative effect on the duration of neuromuscular block if recovery is allowed to begin prior to repeat dosing. Moreover, the time needed to recover from repeat doses does not change with additional doses. Repeat doses can therefore be administered at relatively regular intervals with predictable results .

Therapeutic uses (doses and regimen) :

An initial atracurium besilate dose of 0.3 to 0.6 mg/kg (depending on the duration of full block required), given as an intravenous bolus injection, is recommended. This will provide adequate relaxation for about 15 to 35 minutes.

Endotracheal intubation can usually be accomplished within 90 to 120 seconds of the intravenous injection of 0.5 to 0.6 mg/kg. Maximum neuromuscular blockade is generally achieved approximately 3 to 5 minutes after administration. 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.

Atracurium Besilate Injection 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, and therefore full neuromuscular block may be maintained with approximately half the original infusion rate at these temperatures.

Dosage considerations :

Use in children: The dosage in children over the age of 1 month is similar to that in adults on a body weight basis, however, large individual variability in the neuromuscular response in paediatric patients indicates that neuromuscular monitoring is essential.

Use in neonates: The use of Atracurium is not recommended .

Adverse effects :

1-10%

Skin flush (5%)

<1%

Erythema (0.6%)

Wheezing (0.2%)

Increased bronchial secretions (0.2%)

Pruritus (0.2%)

Urticaria (0.1%)

Postmarketing Reports

Wheals

Erythema at injection site

Bronchospasm (0.01%)
Cyanosis (0.001%)
Changes in heart rate (0.6-2.1%)
Mean arterial pressure (1.9%)
Diastolic arterial pressure changes
Systemic vascular resistance changes
Cardiac index changes
Cardiac output changes
Cardiac arrest (0.001%)

Drug interactions :

As with other non-depolarising neuromuscular blocking agents, the magnitude and/or duration of atracurium's effects may be increased as a result of an interaction with the following agents.

Inhalation anaesthetics: atracurium is potentiated by isoflurane, desflurane, sevoflurane and enflurane anaesthesia, and only marginally potentiated by halothane anaesthesia.

Antibiotics: including the aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin, clindamycin and vancomycin.

Anticonvulsants (acute administration only): phenytoin, carbamazepine.

Antiarrhythmic drugs: local anaesthetics such as lidocaine, procainamide, quinidine.

Beta-blockers: propranolol, oxprenolol

Antirheumatic drugs: chloroquine, d-penicillamine

Calcium channel blockers: diltiazem, nicardipine, nifedipine, verapamil.

Diuretics: frusemide, thiazides, acetazolamide and possibly mannitol.

Ganglion blocking agents: trimetaphan, hexamethonium.

Others: dantrolene, parenteral magnesium sulphate, chlorpromazine, steroids, ketamine, lithium salts and quinine.

Rarely, some of the above drugs may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome. In these situations a consequent increased sensitivity to atracurium would be expected.

The administration of combinations of non-depolarising neuromuscular blocking agents in conjunction with atracurium may produce a degree of neuromuscular blockade in excess of that which might be expected were an equipotent total dose of atracurium 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.

The prior use of suxamethonium reduces the onset (to maximum blockade) by approximately 2 to 3 minutes and may increase the depth of neuromuscular blockade induced by atracurium. Therefore, the initial atracurium dose should be reduced and the reduced dose should not be administered until the patient has recovered from the neuromuscular blocking effects of suxamethonium.

The use of intravenous corticosteroids with neuromuscular blocking agents has been reported to antagonise neuromuscular blockades. In addition, prolonged co-administration of these agents may increase the risk and/or severity of myopathy resulting in prolonged flaccid paralysis following discontinuation of the neuromuscular blocking agent. The myopathy is usually reversible with recovery in several months.

The onset of neuromuscular blockade is likely to be lengthened and the duration of blockade shortened in patients receiving chronic anticonvulsant therapy (e.g. carbamazepine, phenytoin). However, if the anticonvulsants are given acutely, the neuromuscular blocking effects may be increased.

In principle, maintaining neuromuscular monitoring until complete reversal of neuromuscular blockade should permit detection of most interactions. Nevertheless,

recurrence of neuromuscular blockade may occur, for example, upon treatment with post surgical antibiotics.

Precautions and contraindications :

Atracurium Besilate Injection should be used only by those skilled in the management of artificial respiration and only when facilities are immediately available for endotracheal intubation and for providing adequate ventilation support, including the administration of oxygen under positive pressure and the elimination of carbon dioxide. The clinician must be prepared to assist or control ventilation, and anticholinesterase agents should be immediately available for reversal of neuromuscular blockade.

Atracurium has no known effect on consciousness, pain threshold, or cerebation. In surgery, it should be used only with adequate general anaesthesia.

In common with other neuromuscular blocking agents, the potential for histamine release exists in susceptible patients during administration of atracurium besilate. Caution should be exercised in patients with a history suggestive of an increased sensitivity to the effects of histamine.

Do not give Atracurium Besilate Injection by intramuscular administration.

Atracurium Besilate Injection has an acid pH and therefore should not be mixed with alkaline solutions (e.g. barbiturate solutions) in the same syringe or administered simultaneously during intravenous infusion through the same needle. Depending on the resultant pH of such mixtures, Atracurium Besilate Injection may be inactivated and a free acid may be precipitated.

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

Atracurium may have profound effects in patients with myasthenia gravis, Eaton-Lambert syndrome, or other neuromuscular diseases in which potentiation of non-depolarising agents has been noted. A reduced dosage of atracurium and the use of a peripheral nerve stimulator for assessing neuromuscular blockade is especially important in these patients. Similar precautions should be taken in patients with severe electrolyte disorders.

Atracurium does not have significant vagal or ganglion blocking properties in the recommended dosage range. Consequently, atracurium will not counteract the bradycardia produced by many anaesthetic agents or by vagal stimulation during surgery. Therefore, bradycardia during anaesthesia may be more common with atracurium than with other muscle relaxants.

As with other non-depolarising neuromuscular blocking agents, resistance to atracurium may develop in patients suffering from burns. Such patients may require increased doses of atracurium depending on the time elapsed since the burn injury and the extent of the burn.

Atracurium Besilate Injection should be administered over a period of at least 60 seconds to patients who may be unusually sensitive to falls in arterial blood pressure, for example those who are hypovolaemic.

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

Monitoring of serial creatine phosphokinase (CPK) values should be considered in asthmatic patients receiving high dose corticosteroids and neuromuscular blocking agents in intensive care units.

Special precautions should be taken in patients with known anaphylactic reactions to curares, as cross-reactivity may be possible with this product.

Contraindications :

Hypersensitivity to the active substance or any of the excipients listed in section 6.1.

References :

1. "Atracurium Besylate". The American Society of Health-System Pharmacists. Archived from the original on 21 December 2016. Retrieved 8 December 2016.
2. "WHO Model List of Essential Medicines (19th List)" (PDF). World Health Organization. April 2015. Archived (PDF) from the original on 13 December 2016. Retrieved 8 December 2016.
3. "Atracurium". International Drug Price Indicator Guide. Retrieved 8 December 2016.
4. "Atracurium Besylate". <https://pubchem.ncbi.nlm.nih.gov/compound/47320> .
5. "Atracurium (RX)". <https://reference.medscape.com/drug/atracurium-343103>.
6. Siler JN, Mager JG Jr, Wyche MQ Jr (May 1985). "Atracurium: hypotension, tachycardia and bronchospasm". *Anesthesiology*. **62** (5): 645–646 .
7. Jooste E, Klafter F, Hirshman CA, Emala CW (Apr 2003). "A mechanism for rapacuronium-induced bronchospasm: M2 muscarinic receptor antagonism". *Anesthesiology*. **98** (4): 906–911.