years of age at an initial rate equivalent to cisatracurium 3 micrograms/kg per minute followed by a rate of 1 to 2 micrograms/kg per minute after stabilisation.

◊ Reviews.

1. Bryson HM, Faulds D. Cisatracurium besilate: a review of its pharmacology and clinical potential in anaesthetic practice. *Drugs* 1997; **53:** 848–66.

Administration in infants and children. Children generally require larger doses of competitive neuromuscular blockers on a weight basis than adolescents or adults to achieve similar degrees of neuromuscular blockade and may recover more quickly. In contrast, neonates and infants under 1 year of age are more sensitive and usual doses may produce prolonged neuromuscular blockade (see also above for some suggested doses).

References.

1. Brandom BW, Fine GF. Neuromuscular blocking drugs in pediatric anesthesia. *Anesthesiol Clin North America* 2002; **20:** 45–58.

ECT. Competitive neuromuscular blockers have been used to reduce the intensity of muscle contractions and minimise trauma in patients receiving ECT, but suxamethonium (p.1912) is generally preferred because of its short duration of action.

Intravenous regional anaesthesia. Competitive neuromuscular blockers and/or opioid analgesics have been added to the local anaesthetic used in intravenous regional anaesthesia (p.1853) to improve the quality of anaesthesia. However atracurium (see Tourniquets under Precautions, above) and mivacurium (see Tourniquets, p.1907) might be unsuitable for such use.

Shivering. Various drugs have been tried in the treatment of postoperative shivering (p.1779). There are reports of neuromuscular blockers being used to treat shivering after cardiac surgery in order to reduce cardiovascular stress;[1] one study[2] has suggested that vecuronium might be preferable to pancuronium as it does not increase myocardial work and may be associated with fewer complications.

1. Cruise C, *et al.* Comparison of meperidine and pancuronium for the treatment of shivering after cardiac surgery. *Can J Anaesth* 1992; **39:** 563–8.
2. Dupuis J-Y, *et al.* Pancuronium or vecuronium for the treatment of shivering after cardiac surgery. *Anesth Analg* 1994; **79:** 472–81.

Tetanus. For a comment on the role of competitive neuromuscular blockers in the management of muscle spasms caused by tetanus, see p.1901.

Preparations

USP 31: Atracurium Besylate Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Gelolagar; Nimbex†; Nimbium; Tracrium; Tracurix; Tracuron; ***Austral.:*** Nimbex; Tracrium; ***Austria:*** Nimbex; Tracrium; ***Belg.:*** Nimbex; Tracrium; ***Braz.:*** Abbottracurium; Nimbium; Sitrac†; Tracrium; Tracur; ***Canad.:*** Nimbex; ***Chile:*** Nimbex; Tracrium; ***Cz.:*** Nimbex; Tracrium; ***Denm.:*** Nimbex; Tracrium†; ***Fin.:*** Nimbex; ***Fr.:*** Nimbex; Tracrium; ***Ger.:*** Nimbex; Tracrium; ***Gr.:*** Nimbex; Tracrium; ***Hong Kong:*** Nimbex; Tracrium; ***Hung.:*** Nimbex; Tracrium; ***India:*** Tracrium; ***Indon.:*** Notrixum; Tracrium; Tramus; ***Irl.:*** Nimbex; Tracrium; ***Israel:*** Mycurium; Tracrium; ***Ital.:*** Acurmil; Nimbex; Tracrium; ***Malaysia:*** Nimbex; Tracrium; ***Mex.:*** Ifacur†; Nimbex; Relatrac; Trablok; Tracrium; ***Neth.:*** Nimbex; Tracrium; ***Norw.:*** Nimbex; ***NZ:*** Tracrium; ***Philipp.:*** Tracrium; ***Pol.:*** Abbocurium; Nimbex; Tracrium; ***Port.:*** Faulcurium; Nimbex; Tracrium; ***Rus.:*** Nimbex (Нимбекс); Tracrium (Тракриум); ***S.Afr.:*** Nimbex; Tracrium; ***Singapore:*** Nimbex†; Tracrium; ***Spain:*** Laurak; Nimbex; Tracrium; ***Swed.:*** Nimbex; Tracrium; ***Switz.:*** Nimbex; Tracrium; ***Thai.:*** Nimbex; Tracrium; ***Turk.:*** Dematrac; Nimbex; Tracrium; ***UK:*** Nimbex; Tracrium; ***USA:*** Nimbex; Tracrium.

Doxacurium Chloride *(BAN, USAN, rINN)*

BW-A938U; Cloruro de doxacurio; Doksakuriumkloridi; Doxacurii Chloridum; Doxacurium, Chlorure de; Doxakuriumklorid. A mixture of the (*1R,1′S,2S,2′R*), (*1R,1′R,2S,2′S*), and (*1S,1′S,2R,2′R*) stereoisomers (a *meso* isomer and two enantiomers respectively) of 1,1′,2,2′,3,3′,4,4′-octahydro-6,6′,7,7′,8,8′-hexamethoxy-2,2′-dimethyl-1,1′-bis(3,4,5-trimethoxybenzyl)-2,2′-[butanedioylbis(oxytrimethylene)]di-isoquinolinium dichloride, all of which are in a *trans* configuration at the 1 and 2 positions of the isoquinolinium rings.

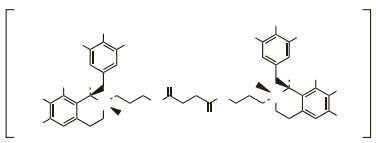
Доксакурия Хлорид

$C_{56}H_{78}Cl_2N_2O_{16}$ = 1106.1.

CAS — 133814-18-3 (doxacurium); 106819-53-8 (doxacurium chloride, meso isomer); 83348-52-1 (doxacurium chloride, total racemate).

ATC — M03AC07.

ATC Vet — QM03AC07.



Profile

Doxacurium chloride is a benzylisoquinolinium competitive neuromuscular blocker (see Atracurium, p.1902). It has been used for endotracheal intubation and to provide muscle relaxation in general anaesthesia for surgical procedures and to aid controlled ventilation. Doxacurium has little histamine-releasing activity and causes negligible vagal or sympathetic blockade so that significant cardiovascular adverse effects are not a problem.

Preparations

Proprietary Preparations (details are given in Part 3)
Canad.: Nuromax†; ***USA:*** Nuromax†.

Gallamine Triethiodide *(BANM, rINN)*

Benzcurine Iodide; Galamin Trietiyodür; Galamino trietjodidas; Gallamiinitrietjodidi; Gallamine, triéthiodure de; Gallamini triethiodidum; Gallamin-triethojodid; Gallamintrietjodid; Gallamin-trietjodid; Gallamone Triethiodide; Trietioduro de galamina. 2,2′,2″-(Benzene-1,2,3-triyltrioxy)tris(tetraethylammonium) tri-iodide.

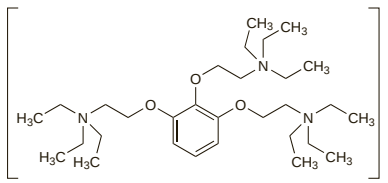
Галламина Триэтйодид

$C_{30}H_{60}I_3N_3O_3$ = 891.5.

CAS — 153-76-4 (gallamine); 65-29-2 (gallamine triethiodide).

ATC — M03AC02.

ATC Vet — QM03AC02.



Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, and *US.*

Ph. Eur. 6.2 (Gallamine Triethiodide). A white, or almost white, hygroscopic powder. Very soluble in water; slightly soluble in alcohol; practically insoluble in dichloromethane. Store in airtight containers. Protect from light.

USP 31 (Gallamine Triethiodide). A white, hygroscopic, odourless, amorphous powder. Very soluble in water; sparingly soluble in alcohol; very slightly soluble in chloroform. pH of a 2% solution in water is between 5.3 and 7.0. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

As for competitive neuromuscular blockers in general (see Atracurium, p.1902). Tachycardia often develops due to the vagolytic action of gallamine triethiodide and blood pressure may be raised. It has a small histamine-releasing effect; occasional anaphylactoid reactions have been reported. It should be avoided in patients hypersensitive to iodine and in severe renal impairment. Although competitive muscle relaxants have been given with great care to patients with myasthenia gravis (see Neuromuscular Disorders, p.1903), UK licensed product information for gallamine triethiodide recommended that it should not be used in such patients.

Cardiopulmonary bypass. Alterations in the pharmacokinetics of competitive neuromuscular blockers in patients undergoing surgery involving cardiopulmonary bypass usually necessitate the use of reduced doses (see p.1903). However, the pharmacokinetics of gallamine in patients undergoing cardiopulmonary bypass appear not to differ significantly from those in control patients.[1]

1. Shanks CA, *et al.* Gallamine disposition in open-heart surgery involving cardiopulmonary bypass. *Clin Pharmacol Ther* 1983; **33:** 792–9.

Renal impairment. Gallamine triethiodide is excreted unchanged in the urine and UK licensed product information considered that it should be avoided in severe renal impairment since prolonged paralysis may occur. Significantly prolonged elimination half-life and reduced clearance have been reported[1] in patients with chronic renal failure given gallamine triethiodide in initial doses of 2 mg/kg intravenously.

1. Ramzan MI, *et al.* Gallamine disposition in surgical patients with chronic renal failure. *Br J Clin Pharmacol* 1981; **12:** 141–7.

Interactions

For interactions associated with competitive neuromuscular blockers, see Atracurium, p.1903.

Pharmacokinetics

After intravenous use gallamine triethiodide is distributed throughout body tissues. It is not metabolised, and is excreted in the urine as unchanged drug.

Uses and Administration

Gallamine triethiodide is a benzylisoquinolinium competitive neuromuscular blocker (see Atracurium, p.1905). Muscle relaxation occurs within about 1 to 2 minutes after intravenous injection and lasts for about 20 to 30 minutes. It has been used to provide muscle relaxation in general anaesthesia for surgical procedures (see Anaesthesia, p.1900) and to aid controlled ventilation (see Intensive Care, p.1901).

Doses of neuromuscular blockers need to be carefully titrated for individual patients according to response, and may vary with the procedure, the other drugs given, and the state of the patient; monitoring of the degree of block is recommended in order to reduce the risk of overdosage. An initial test dose of 20 mg may be given intravenously to the patient before anaesthesia to determine undue sensitivity. In the UK, initial doses of 80 to 120 mg by intravenous injection have been recommended, with further doses of 20 to 40 mg as required. In children, a dose of 1.5 mg/kg has been recommended, reduced to 600 micrograms/kg for neonates.

In some other countries lower doses have generally been used; an initial dose of 1 mg/kg intravenously, up to a maximum of 80 mg, with additional doses of 0.5 to 1 mg/kg after about 50 to 60 minutes if required.

Gallamine triethiodide has also been given intramuscularly, with or without hyaluronidase.

Preparations

BP 2008: Gallamine Injection;
USP 31: Gallamine Triethiodide Injection.

Proprietary Preparations (details are given in Part 3)
UK: Flaxedil†.

Metocurine Iodide *(USAN)*

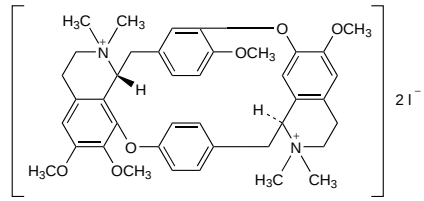
Dimethyl Tubocurarine Iodide; (+)-*O,O′*-Dimethylchondrocurarine Di-iodide; Dimethyltubocurarine Iodide; Dimetiltubocurarinio, ioduro de; Metocurini Iodidum; Metokuriinijodidi; Metokurinjodid; Trimethyltubocurarine Iodide. (+)-6,6′,7′,12′-Tetramethoxy-2,2,2′,2′-tetramethyltubocuraranium di-iodide.

$C_{40}H_{48}I_2N_2O_6$ = 906.6.

CAS — 5152-30-7 (metocurine); 7601-55-0 (metocurine iodide).

ATC — M03AA04.

ATC Vet — QM03AA04.



Profile

Metocurine iodide is a benzylisoquinolinium competitive neuromuscular blocker (see Atracurium, p.1905) that has been used to provide muscle relaxation in surgical and other procedures.

Metocurine iodide has a moderate risk of inducing histamine release; it also has some ganglion blocking activity.

Mivacurium Chloride *(BAN, USAN, rINN)*

BW-B1090U; Cloruro de mivacurio; Mivacurii Chloridum; Mivacurium, Chlorure de; Mivakuriumklorid; Mivakuriumkloridi; Mivakuryum Klorür. A mixture of the stereoisomers of (*E*)-1,1′,2,2′,3,3′,4,4′-octahydro-6,6′,7,7′-tetramethoxy-2,2′-dimethyl-1,1′-bis(3,4,5-trimethoxybenzyl)-2,2′-[oct-4-enedioylbis(oxytrimethylene)]di-isoquinolinium dichloride.

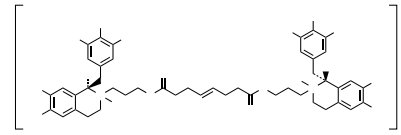
Мивакурия Хлорид

$C_{58}H_{80}Cl_2N_2O_{14}$ = 1100.2.

CAS — 106861-44-3 (mivacurium chloride, total racemate).

ATC — M03AC10.

ATC Vet — QM03AC10.



Incompatibility. See under Atracurium, p.1902 for details regarding the incompatibility of neuromuscular blockers.

Adverse Effects, Treatment, and Precautions

As for competitive neuromuscular blockers in general (see Atracurium, p.1902). Mivacurium chloride has no significant vagal or ganglion blocking activity at recommended doses. It may induce histamine release especially when given in large doses rapidly.

Mivacurium should be used with caution, if at all, in patients with plasma cholinesterase deficiency, since its duration of action will be prolonged in such patients.

Burns. In common with other competitive muscle relaxants patients with burns may develop resistance to mivacurium and require increased doses (see under Atracurium, p.1903). However, as these patients may also have reduced plasma cholinesterase activity dosage requirements could also be reduced. Licensed