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.

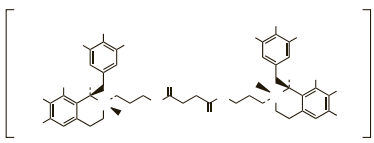
Доксакурия Хлорид

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

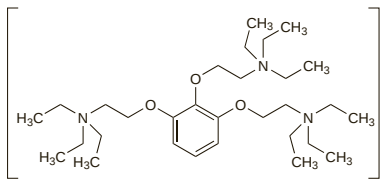
Галламина Триэтйодид

$C_{30}H_{60}I_3N_3O_3$ = 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)*

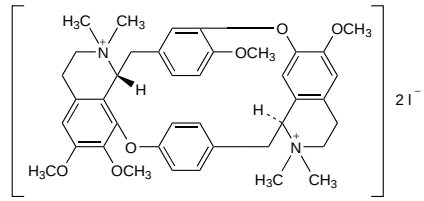
Dimethyl Tubocurarine Iodide; (+)-*O,O′*-Dimethylchondrocurarine Di-iodide; Dimethyltubocurarine Iodide; Dimetiltubocurarinio, ioduro de; Metocurini Iodidum; Metokuriinijodidi; Metokurinjodid; Trimethyltubocurarine Iodide. (+)-6,6′,7′,12′-Tetramethoxy-2,2,2′,2′-tetramethyltubocuraranium di-iodide.

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

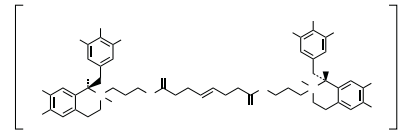
Мивакурия Хлорид

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

product information recommends that such patients should be given a test dose of 15 to 20 micrograms/kg with subsequent dosage adjustments being guided by monitoring of the block.

Neuromuscular disorders. Neuromuscular blockade was successfully achieved with mivacurium in an obese elderly patient with myasthenia gravis requiring surgery.[1] Only about half the usual dose was required and even then recovery was delayed. See Atracurium, p.1903 for a discussion of the use of competitive neuromuscular blockers in patients with neuromuscular disorders.

1. Seigne RD, Scott RPF. Mivacurium chloride and myasthenia gravis. *Br J Anaesth* 1994; **72:** 468–9.

Plasma cholinesterase deficiency. There have been reports of prolonged neuromuscular block produced by mivacurium in patients with plasma cholinesterase deficiency.[1-4] Time to full recovery varied; one patient required up to 8 hours.

1. Goudsouzian NG, *et al.* Prolonged neuromuscular block from mivacurium in two patients with cholinesterase deficiency. *Anesth Analg* 1993; **77:** 183–5.
2. Sockalingam I, Green DW. Mivacurium-induced prolonged neuromuscular block. *Br J Anaesth* 1995; **74:** 234–6.
3. Fox MH, Hunt PCW. Prolonged neuromuscular block associated with mivacurium. *Br J Anaesth* 1995; **74:** 237–8.
4. Zimmer S. Mivacurium and prolonged neuromuscular block. *Br J Anaesth* 1995; **75:** 823.

Tourniquets. Mivacurium might be unsuitable for neuromuscular blockade of a limb which has been isolated with a tourniquet in order to provide a bloodless field for surgery.[1] It is largely inactivated by the enzymatic action of plasma cholinesterase and would therefore continue to degrade locally leading to a loss of blockade in the limb, which could not be corrected by further doses unless the tourniquet was deflated. However, as for other competitive neuromuscular blockers, the use of mivacurium to supplement regional anaesthesia has produced prolonged muscle weakness well beyond cuff deflation.[2] This suggests that mivacurium is not broken down in the ischaemic limb and that recovery is not dependent on plasma concentrations of mivacurium.

See also Local Anaesthetics, under Interactions of Atracurium, p.1904, for a report of symptoms suggestive of local anaesthetic toxicity when prilocaine and mivacurium were used together.

1. Shannon PF. Neuromuscular block and tourniquets. *Br J Anaesth* 1994; **73:** 726.
2. Torrance JM, *et al.* Low-dose mivacurium supplementation of prilocaine i.v. regional anaesthesia. *Br J Anaesth* 1997; **78:** 222–3.

Interactions

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

Metoclopramide. Metoclopramide, an inhibitor of plasma cholinesterase, was found to significantly prolong the duration of action of mivacurium in patients undergoing surgery, although in this study only marginal inhibition of plasma cholinesterase by metoclopramide occurred.[1]

1. Skinner HJ, *et al.* Influence of metoclopramide on plasma cholinesterase and duration of action of mivacurium. *Br J Anaesth* 1999; **82:** 542–5.

Pharmacokinetics

Mivacurium is a mixture of 3 stereoisomers, 2 of which (*cis-trans* and *trans-trans*) are considered to account for most of the neuromuscular blocking effect. All 3 isomers are inactivated by plasma cholinesterase. Renal and hepatic mechanisms are involved in their elimination with excretion in urine and bile.

◊ Reviews.

1. Atherton DPL, Hunter JM. Clinical pharmacokinetics of the newer neuromuscular blocking drugs. *Clin Pharmacokinet* 1999; **36:** 169–89.

Uses and Administration

Mivacurium chloride is a benzylisoquinolinium competitive neuromuscular blocker (see Atracurium, p.1905).

On intravenous injection muscle relaxation occurs within 1.5 to 2.5 minutes, depending on the dose with a duration of action of about 10 to 20 minutes. It is used for endotracheal intubation and 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. Mivacurium is given as the chloride although doses are expressed in terms of mivacurium base. The initial dose by intravenous injection is 70 to 250 micrograms/kg. Doses up to 150 micrograms/kg may be given over 5 to 15 seconds but higher doses should be given over 30 seconds. In patients with asthma or cardiovascular disease, or those who are sensitive to falls in arterial blood pressure, it should be given over 60 seconds. To give a dose of 250 micrograms/kg for tracheal intubation, an injection of 150 micrograms/kg may be followed 30 seconds later by an injection of 100 micrograms/kg. Maintenance doses of 100 micrograms/kg may be given at intervals of 15 minutes. In children aged 2 to 6 months an initial dose of 150 micrograms/kg has been given; in children aged 7 months to 12 years, an initial dose of 200 micrograms/kg has been given. A maintenance dose of 100 micrograms/kg may be given every 6 to 9 minutes for children aged 2 months to 12 years.

Mivacurium chloride may also be given by continuous intravenous infusion for maintenance of block. For adults the initial rate is 8 to 10 micrograms/kg per minute adjusted every 3 minutes if necessary by increments of 1 microgram/kg per minute to a usual rate of 6 to 7 micrograms/kg per minute; in children aged 2 months to 12 years the usual dose is 11 to 14 micrograms/kg per minute.

Reduced doses may be required in the elderly and in patients with hepatic or renal impairment (see below).

◊ Reviews.

1. Mirakhur RK. Newer neuromuscular blocking drugs: an overview of their clinical pharmacology and therapeutic use. *Drugs* 1992; **44:** 182–99.
2. Frampton JE, McTavish D. Mivacurium: a review of its pharmacology and therapeutic potential in general anaesthesia. *Drugs* 1993; **45:** 1066–89.
3. Feldman S. Mivacurium. *Br J Hosp Med* 1997; **57:** 199–201.

Action. Mivacurium has a shorter duration of action than most other competitive neuromuscular blockers. Studies[1-3] suggest that it is a useful alternative to suxamethonium for the production of neuromuscular block of short duration and has the advantage that its block can be reversed with an anticholinesterase. For a discussion of the choice of anticholinesterase for reversal of neuromuscular block produced by short-acting blockers such as mivacurium, see under Neostigmine, p.633. Although its onset of action may be accelerated by giving a priming dose,[4] mivacurium has a slower onset than suxamethonium and so may not be a suitable alternative[5] when rapid intubation is required. For a general review of neuromuscular blockers, see Anaesthesia, p.1900.

1. Brandom BW, *et al.* Comparison of mivacurium and suxamethonium administered by bolus and infusion. *Br J Anaesth* 1989; **62:** 488–93.
2. Caldwell JE, *et al.* Comparison of the neuromuscular block induced by mivacurium, suxamethonium or atracurium during nitrous oxide-fentanyl anaesthesia. *Br J Anaesth* 1989; **63:** 393–9.
3. Goldberg ME, *et al.* Comparison of tracheal intubating conditions and neuromuscular blocking profiles after intubating doses of mivacurium chloride or succinylcholine in surgical outpatients. *Anesth Analg* 1989; **69:** 93–9.
4. Haxby EJ, *et al.* Mivacurium priming intervals. *Br J Anaesth* 1994; **72:** 485P.
5. Anonymous. Mivacurium—a new neuromuscular blocker. *Med Lett Drugs Ther* 1992; **34:** 82.

Administration in the elderly. In a study[1] comparing the effects of mivacurium in elderly and young adults, the duration of neuromuscular effects was prolonged in elderly patients by about 30%. The mean infusion requirement in elderly patients was 3.67 micrograms/kg per minute compared with 5.5 micrograms/kg per minute in young adults.

Licensed product information states that elderly patients may require decreased infusion rates or smaller or less frequent maintenance bolus doses.

1. Maddineni VR, *et al.* Neuromuscular and haemodynamic effects of mivacurium in elderly and young adult patients. *Br J Anaesth* 1994; **73:** 608–12.

Administration in hepatic or renal impairment. The pharmacokinetics of mivacurium have been studied in patients with renal[1-3] or hepatic impairment.[1,4,5] The duration of relaxation produced by mivacurium was about 1.5 times greater than normal in patients with end-stage renal disease and up to about 3 times greater than normal in patients with end-stage liver disease. Reduced plasma-cholinesterase activity in the patients with hepatic impairment may have played an important part in this effect. Although an anticholinesterase such as neostigmine hastens recovery by only a few minutes in healthy subjects, its use may be indicated in patients in whom recovery is delayed.[2]

Licensed product information recommends that in patients with end-stage renal or liver disease, the dose should be adjusted according to individual clinical response.

1. Cook DR, *et al.* Pharmacokinetics of mivacurium in normal patients and in those with hepatic or renal failure. *Br J Anaesth* 1992; **69:** 580–5.
2. Phillips BJ, Hunter JM. Use of mivacurium chloride by constant infusion in the anephric patient. *Br J Anaesth* 1992: **68:** 492–8.
3. Head-Rapson AG, *et al.* Pharmacokinetics and pharmacodynamics of the three isomers of mivacurium in health, in end-stage renal failure and in patients with impaired renal function. *Br J Anaesth* 1995; **75:** 31–6.
4. Devlin JC, *et al.* Pharmacodynamics of mivacurium chloride in patients with hepatic cirrhosis. *Br J Anaesth* 1993; **71:** 227–31.
5. Head-Rapson AG, *et al.* Pharmacokinetics of the three isomers of mivacurium and pharmacodynamics of the chiral mixture in hepatic cirrhosis. *Br J Anaesth* 1994; **73:** 613–18.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Mivacron; ***Austral.:*** Mivacron; ***Austria:*** Mivacron; Novacrium; ***Belg.:*** Mivacron; ***Braz.:*** Mivacron†; ***Canad.:*** Mivacron†; ***Chile:*** Mivacron; ***Cz.:*** Mivacron; ***Denm.:*** Mivacron; ***Fin.:*** Mivacron; ***Fr.:*** Mivacron; ***Ger.:*** Mivacron; ***Gr.:*** Mivacron; ***Hong Kong:*** Mivacron; ***Hung.:*** Mivacron; ***Irl.:*** Mivacron; ***Israel:*** Mivacron†; ***Ital.:*** Mivacron; ***Malaysia:*** Mivacron; ***Neth.:*** Mivacron; ***Norw.:*** Mivacron; ***NZ:*** Mivacron; ***Pol.:*** Mivacron; ***Port.:*** Mivacron; ***Rus.:*** Mivacron (Мивакрон); ***S.Afr.:*** Mivacron; ***Singapore:*** Mivacron; ***Spain:*** Mivacron; ***Swed.:*** Mivacron; ***Switz.:*** Mivacron; ***Turk.:*** Mivacron; ***UK:*** Mivacron; ***USA:*** Mivacron†.

Pancuronium Bromide *(BAN, USAN, rINN)*

Bromuro de pancuronio; NA-97; Org-NA-97; Pancuronii bromidum; Pancuronium, bromure de; Pankuronio bromidas; Pankuroniowy bromek; Pankuroniumbromid; Pankuronium-bromid; Pankuroniumbromidi; Pankuronyum Bromür. 1,1′-(3α,17β-Diacetoxy-5α-androstan-2β,16β-ylene)bis(1-methylpiperidinium) dibromide.

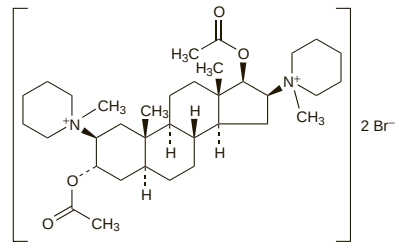
Панкурония Бромид

$C_{35}H_{60}Br_2N_2O_4$ = 732.7.

CAS — 15500-66-0.

ATC — M03AC01.

ATC Vet — QM03AC01.



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

Ph. Eur. 6.2 (Pancuronium Bromide). White, yellowish-white, or slightly pink, hygroscopic crystalline powder. Very soluble to freely soluble in water; freely soluble in alcohol; very soluble in dichloromethane. Store in airtight containers. Protect from light.

USP 31 (Pancuronium Bromide). A white, yellowish-white, or slightly pink, crystalline hygroscopic powder. Freely soluble in water, in alcohol, and in dichloromethane. Store in airtight containers at a temperature of 15° to 25°. Protect from light.

Adverse Effects, Treatment, and Precautions

As for competitive neuromuscular blockers in general (see Atracurium, p.1902).

Pancuronium has vagolytic and sympathomimetic action, which may cause tachycardia and hypertension, but does not produce ganglionic blockade. It has little histamine-releasing effect. Hypersensitivity reactions are relatively rare but bradycardia, bronchospasm, hypotension, and cardiovascular collapse have been reported. Pancuronium has been associated with excessive salivation in some patients.

Pancuronium should be used with caution in patients with raised catecholamine concentrations, or in those who are receiving drugs with sympathomimetic effects, as cardiovascular adverse effects are more likely in these patients.

Effects on the ears. A study[1] found that neonates who survived congenital diaphragmatic hernia were more likely to suffer from sensorineural hearing loss after prolonged use of pancuronium bromide during the neonatal period. However, the authors commented that the association is not necessarily causal and that further investigation is required.

1. Cheung P-Y, *et al.* Prolonged use of pancuronium bromide and sensorineural hearing loss in childhood survivors of congenital diaphragmatic hernia. *J Pediatr* 1999; **135:** 233–9.

Hypersensitivity. Reports of anaphylactoid or anaphylactic reactions associated with pancuronium bromide.

See also under Suxamethonium Chloride, p.1910.

1. Brauer FS, Ananthanarayan CR. Histamine release by pancuronium. *Anesthesiology* 1978; **49:** 434–5.
2. Patriarca G, *et al.* Pancuronium allergy: a case report. *Br J Anaesth* 1989; **62:** 210–12.
3. Moneret-Vautrin DA, *et al.* Simultaneous anaphylaxis to thiopentone and a neuromuscular blocker: a study of two cases. *Br J Anaesth* 1990; **64:** 743–5.
4. Sanchez-Guerrero IM, *et al.* Anaphylactoid reaction induced by pancuronium during general anaesthesia. *Eur J Anaesthesiol* 1998; **15:** 613–14.

Postoperative complications. Because of its prolonged duration of action, pancuronium may be more likely than other neu-