

romuscular blockers to produce residual neuromuscular block; such residual block is associated with an increased incidence of postoperative respiratory complications.^{1,2}

1. Berg H, *et al.* Residual neuromuscular block is a risk factor for postoperative pulmonary complications: a prospective, randomised, and blinded study of postoperative pulmonary complications after atracurium, vecuronium and pancuronium. *Acta Anaesthesiol Scand* 1997; **41**: 1095–1103.
2. Bissinger U, *et al.* Postoperative residual paralysis and respiratory status: a comparative study of pancuronium and vecuronium. *Physiol Res* 2000; **49**: 455–62.

Interactions

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

Pharmacokinetics

On intravenous injection pancuronium bromide is rapidly distributed into body tissues; about 80% may be bound to plasma proteins. A small proportion is metabolised in the liver to metabolites with weak neuromuscular blocking activity. It is largely excreted in urine as unchanged drug and metabolites; a small amount is excreted in bile. The plasma elimination half-life is about 2 hours. It crosses the placenta in small amounts.

Pregnancy. In 15 patients undergoing caesarean section¹ given pancuronium bromide 100 micrograms/kg intravenously with other agents, mean maternal arterial and umbilical venous serum concentrations of pancuronium bromide and metabolites were 520 and 120 nanograms/mL, respectively at delivery (mean of 13 minutes after injection), giving a fetal to maternal ratio of 0.23.

1. Wingard LB, *et al.* Modified fluorometric quantitation of pancuronium bromide and metabolites in human maternal and umbilical serums. *J Pharm Sci* 1979; **68**: 914–15.

Uses and Administration

Pancuronium bromide is an aminosteroidal competitive neuromuscular blocker (see Atracurium, p.1905). Muscle relaxation occurs within about 1.5 to 2 minutes of intravenous injection and lasts for about 45 to 60 minutes.

Pancuronium bromide 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. The initial dose for intubation is usually 50 to 100 micrograms/kg by intravenous injection, with maintenance doses of 10 to 20 micrograms/kg. Children may be given similar doses. Some manufacturers recommend a reduction in the initial dose to 20 to 60 micrograms/kg when pancuronium is given following suxamethonium. Doses of 30 to 40 micrograms/kg initially have been suggested in neonates, with maintenance doses of 10 to 20 micrograms/kg as necessary; in the UK, the *BNFC* suggests that higher doses may be used for neonates in some cases. In the USA, dosage based on an initial test dose of 20 micrograms/kg has been advocated for the neonate.

Adult patients under intensive care who require assisted ventilation for conditions such as intractable status asthmaticus or tetanus may be given 60 micrograms/kg intravenously every 1 to 1½ hours or less frequently.

Care should be taken when giving pancuronium to patients with hepatic or renal impairment, see below.

Administration in hepatic impairment. Prolonged neuromuscular blockade may occur in patients with liver disease given pancuronium bromide since increased elimination half-life with increased volume of distribution and reduced clearance has been reported.¹ However, the expanded distribution volume may necessitate an increase in the dose of pancuronium in these patients^{1,2} and may be interpreted as resistance to the neuromuscular blocking effects of pancuronium.

1. Duvaldestin P, *et al.* Pancuronium pharmacokinetics in patients with liver cirrhosis. *Br J Anaesth* 1978; **50**: 1131–6.
2. Ward ME, *et al.* Althesin and pancuronium in chronic liver disease. *Br J Anaesth* 1975; **47**: 1199–1204.

Administration in renal impairment. Prolonged neuromuscular blockade may occur when pancuronium is given to patients with severe renal impairment. Pancuronium distributes rapidly into extracellular fluid after intravenous injection and the initial neuromuscular blockade produced will depend upon the

peak drug concentration in this fluid. Since extracellular fluid volume is increased in chronic renal failure such patients may require a larger initial dose of pancuronium and a 45% increase in dose requirement has been reported¹ in patients with end-stage renal failure. Renal excretion is the main route of elimination and prolonged elimination half-life with reduced clearance may be expected in renal failure; total dose requirements may be reduced. The main infusion rate of pancuronium to maintain 90% blockade in patients with end-stage renal failure was reported to be 61.5% less than for patients with normal renal function.

1. Gramstad L. Atracurium, vecuronium and pancuronium in end-stage renal failure. *Br J Anaesth* 1987; **59**: 995–1003.

Fetal paralysis. Pancuronium bromide 100 micrograms/kg of the estimated fetal-weight, given into the umbilical vein, produced fetal paralysis for about 40 minutes during intravascular exchange transfusion.¹ A dose of 200 to 300 micrograms/kg produced fetal paralysis for about 1 to 8 hours for more complicated transfusion procedures.² No adverse effects were reported.

1. Coppel JA, *et al.* The use of intravenous pancuronium bromide to produce fetal paralysis during intravascular transfusion. *Am J Obstet Gynecol* 1988; **158**: 170–1.
2. Moise KJ, *et al.* Intravenous pancuronium bromide for fetal neuromuscular blockade during intrauterine transfusion for red-cell alloimmunization. *Obstet Gynecol* 1989; **74**: 905–8.

Neuroleptic malignant syndrome. Pancuronium is one of several drugs for which there have been isolated reports¹ of success in the management of neuroleptic malignant syndrome (p.972).

1. Sangal R, Dimitrijevic R. Neuroleptic malignant syndrome: successful treatment with pancuronium. *JAMA* 1985; **254**: 2795–6.

Preparations

BP 2008: Pancuronium Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Bemicon; Pancuron; Pavulon; Plumger; **Austral.:** Pavulon; **Braz.:** Pancuron; Pavulon; **Chile:** Pavulon; **Cz.:** Pavulon; **Denm.:** Pavulon; **Fin.:** Pavulon; **Fr.:** Pavulon; **Gr.:** Pavulon; **Hong Kong:** Pavulon; **Hung.:** Pavulon; **India:** Panconium; **Indon.:** Pavulon; **Irl.:** Pavulon; **Israel:** Pavulon; **Ital.:** Pavulon; **Jpn.:** Mioblock; **Malaysia:** Pavulon; **Mex.:** Bromurex; Panlem; **Neth.:** Pavulon; **Norw.:** Pavulon; **Philipp.:** Pavulon; **Port.:** Pancurox; Pavulon; **S.Afr.:** Curron-B; Pavulon; **Singapore:** Pavulon; **Spain:** Pavulon; **Swed.:** Pavulon; **Switz.:** Pavulon; **Thai.:** Pavulon; **Turk.:** Pavulon; **USA:** Pavulon; **Venez.:** Panuron; Pavulon; Pesium.

Pipecuronium Bromide (BAN, USAN, rINN)

Bromuro de pipecuronio; Pipecurium Bromide; Pipecuronii Bromidum; Pipécuronium, Bromure de; Pipecuroniumbromid; Pipecuroniumbromidi; RGH-1106. 1,1,1',1'-Tetramethyl-4,4'-(3 α ,17 β -diacetoxo-5 α -androstan-2 β ,16 β -diyl)dipiperazinium dibromide.

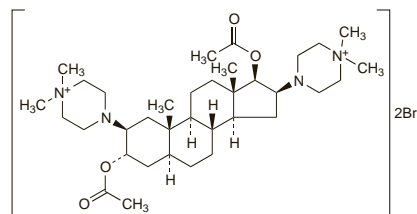
Пипекурония Бромид

$C_{35}H_{62}Br_2N_4O_4 = 762.7$.

CAS — 52212-02-9 (anhydrous pipecuronium bromide); 68399-57-5 (pipecuronium bromide dihydrate).

ATC — M03AC06.

ATC Vet — QM03AC06.



Profile

Pipecuronium bromide is an aminosteroidal competitive neuromuscular blocker (see Atracurium, p.1902). Pipecuronium is reported to have no significant cardiovascular adverse effects or histamine-related effects. On intravenous injection muscle relaxation occurs within 2.5 to 3 minutes with a duration of action of about 30 minutes to 2 hours, depending on the dose.

Pipecuronium bromide has been used for endotracheal intubation and to provide muscle relaxation in general anaesthesia for surgical procedures (see Anaesthesia, p.1900) and to aid mechanical 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. Initial doses of 80 to 100 micrograms/kg intravenously have been recommended, with subsequent doses of 10 to 20 micrograms/kg. Lower initial doses are given following suxamethonium or in patients at high risk: 50 to 60 micrograms/kg has been recommended, or 35 micrograms/kg for caesarean section.

◊ Reviews and studies.

1. Mirakhr RK. Newer neuromuscular blocking drugs: an overview of their clinical pharmacology and therapeutic use. *Drugs* 1992; **44**: 182–99.
2. Tassonyi E, *et al.* Pharmacokinetics of pipecuronium in infants, children and adults. *Eur J Drug Metab Pharmacokinet* 1995; **20**: 203–8.

3. Melloni C. Farmacologia clinica del pipecuronio: studio comparativo della sua durata clinica in anestesia bilanciata (propofol/fentanyl) vs isoflurano. *Minerva Anestesiologica* 1995; **61**: 491–500.

4. Meretoja OA, Erkola O. Pipecuronium revisited: dose-response and maintenance requirement in infants, children, and adults. *J Clin Anesth* 1997; **9**: 125–9.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Arplon; **Cz.:** Arduan; **Hung.:** Arduan; **Pol.:** Arduan; **Rus.:** Aperiomid (Аперимид); Arduan (Ардуан).

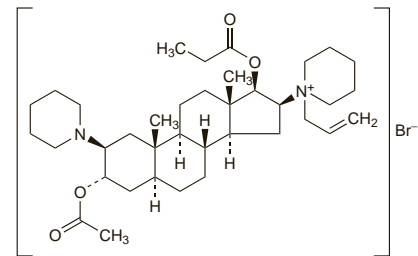
Rapacuronium Bromide (BAN, USAN, rINN)

Bromuro de rapacuronio; Org-9487; Rapacuronii Bromidum; Rapacuronium, Bromure de. 1-(3 α -Acetoxo-2 β -piperidino-17 β -propionyloxy-5 α -androstan-16 β -yl)-1-allylpiperidinium bromide; 1-Allyl-1-(3 α ,17 β -dihydroxy-2 β -piperidino-5 α -androstan-16 β -yl)piperidinium bromide, 3-acetate 17-propionate.

Рапакурония Бромид

$C_{37}H_{61}BrN_2O_4 = 677.8$.

CAS — 156137-99-4.



Profile

Rapacuronium bromide, an analogue of vecuronium (p.1913), is an aminosteroidal competitive neuromuscular blocker (see Atracurium, p.1905). It was used to provide muscle relaxation in general anaesthesia for surgical procedures and for endotracheal intubation, but was withdrawn from the market after reports of severe bronchospasm, including fatalities.

◊ Reviews.

1. Wight WJ, Wright PMC. Pharmacokinetics and pharmacodynamics of rapacuronium bromide. *Clin Pharmacokinet* 2002; **41**: 1059–76.

Rocuronium Bromide (BAN, USAN, rINN)

Bromuro de rocuronio; Org-9426; Rocuronii bromidum; Rocuronium, bromure de; Rokuronioowy bromek; Rokuroniumbromid; Rokuronium-bromid; Rokuroniumbromidi; Rokuronium Bromür. 1-Allyl-1-(3 α ,17 β -dihydroxy-2 β -morpholino-5 α -androstan-16 β -yl)pyrrolidinium bromide 17-acetate; 1-(17 β -Acetoxo-3 α -hydroxy-2 β -morpholino-5 α -androstan-16 β -yl)-1-allylpyrrolidinium bromide.

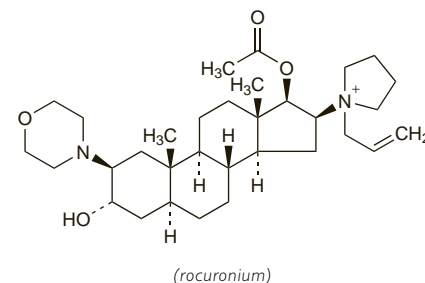
Рокурония Бромид

$C_{32}H_{53}BrN_2O_4 = 609.7$.

CAS — 119302-91-9.

ATC — M03AC09.

ATC Vet — QM03AC09.



Pharmacopoeias. In *Eur.* (see p.viii).

Ph. Eur. 6.2 (Rocuronium Bromide). An almost white or pale yellow, slightly hygroscopic, powder. Freely soluble in water and in dehydrated alcohol. A 1.0% solution in water has a pH of 8.9 to 9.5. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

As for competitive neuromuscular blockers in general (see Atracurium, p.1902). Rocuronium is reported to