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 section[1] 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 reported[1] 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. Copel 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 reports[1] 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.: Bemicin; 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.:*** Curon-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; Pipekuroniumbromid; Pipekuroniumbromidi; RGH-1106. 1,1,1′,1′-Tetramethyl-4,4′-(3α,17β-diacetoxy-5α-androstan-2β,16β-diyl)dipiperazinium dibromide.

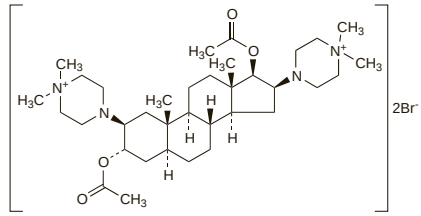
Пипекурония Бромид

$C_{35}H_{62}Br_2N_4O_4$ = 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. Mirakhur 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 pipecuronium; studio comparativo della sua durata clinica in anestesia bilanciata (propofol/fentanyl) vs isoflurano. *Minerva Anestesiol* 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: Arpilon†; ***Cz.:*** Arduan; ***Hung.:*** Arduan; ***Pol.:*** Arduan; ***Rus.:*** Aperomid (Аеромид)†; Arduan (Ардуан).

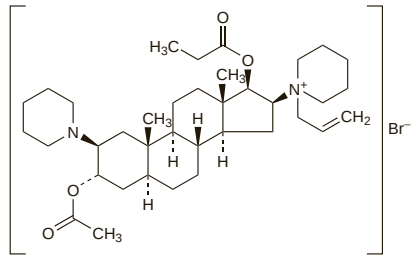
Rapacuronium Bromide *(BAN, USAN, rINN)*

Bromuro de rapacuronio; Org-9487; Rapacuronii Bromidum; Rapacuronium, Bromure de. 1-(3α-Acetoxy-2β-piperidino-17β-propionyloxy-5α-androstan-16β-yl)-1-allylpiperidinium bromide; 1-Allyl-1-(3α,17β-dihydroxy-2β-piperidino-5α-androstan-16β-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; Rokuroniowy bromek; Rokuroniumbromid; Rokuronium-bromid; Rokuroniumbromidi; Rokuronyum Bromür. 1-Allyl-1-(3α,17β-dihydroxy-2β-morpholino-5α-androstan-16β-yl)pyrrolidinium bromide 17-acetate; 1-(17β-Acetoxy-3α-hydroxy-2β-morpholino-5α-androstan-16β-yl)-1-allylpyrrolidinium bromide.

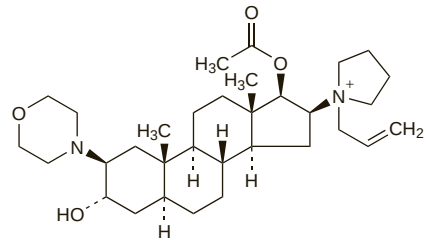
Рокурония Бромид

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

CAS — 119302-91-9.

ATC — M03AC09.

ATC Vet — QM03AC09.



(rocuronium)

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

have minimal cardiovascular and histamine-releasing effects. High doses (greater than 900 micrograms/kg of rocuronium bromide) have mild vagolytic activity. It should be used with caution in patients with biliary disease or hepatic or renal impairment.

Hepatic impairment. There have been conflicting reports of the pharmacokinetics and pharmacodynamics of rocuronium in patients with hepatic impairment. In contrast to earlier studies[1,2] one group of workers[3] found a significant reduction in the plasma clearance of rocuronium in patients with cirrhosis. The elimination half-life has been variously reported to be unchanged[1] or prolonged[2,3] with delayed recovery.[3] Some studies[2,3] found that the onset of action was not affected while one group of workers[1] reported a delay.

Licensed product information recommends that care should be taken when giving rocuronium to patients with clinically significant hepatic impairment (see also under Uses and Administration, below).

1. Khalil M, *et al.* Pharmacokinetics and pharmacodynamics of rocuronium in patients with cirrhosis. *Anesthesiology* 1994; **80:** 1241–7.
2. Magorian T, *et al.* The pharmacokinetics and neuromuscular effects of rocuronium bromide in patients with liver disease. *Anesth Analg* 1995; **80:** 754–9.
3. van Miert MM, *et al.* The pharmacokinetics and pharmacodynamics of rocuronium in patients with hepatic cirrhosis. *Br J Clin Pharmacol* 1997; **44:** 139–44.

Hypersensitivity. Although rocuronium is considered to have minimal histamine-releasing effects, histaminoid reactions have been reported[1] on induction of anaesthesia in 3 patients who had been given rocuronium. An increased incidence of severe hypersensitivity reactions (particularly anaphylactic shock) has been reported with rocuronium compared with other neuromuscular blockers available in France.[2] Fatalities have occurred.[3]

See also the discussion of the relative risks of hypersensitivity associated with neuromuscular blockers, under Suxamethonium Chloride, p.1910.

1. Neal SM, *et al.* Histaminoid reactions associated with rocuronium. *Br J Anaesth* 2000; **84:** 108–11.
2. Mayer M. Information importante de pharmacovigilance: Esméron et manifestations allergiques. Available at: http://agmed.sante.gouv.fr/htm/10/filltrpsc/letesmer.pdf (accessed 28/05/04)
3. Baillard C, *et al.* Anaphylaxis to rocuronium. *Br J Anaesth* 2002; **88:** 600–602.

Pain on administration. Severe transient burning pain associated with injection of rocuronium was considered[1] to be responsible for the spontaneous movement sometimes seen in the arm or wrist into which rocuronium is given. It is recommended that rocuronium should be given only when a deep stage of unconsciousness has been achieved.

1. Borgeat A, Kwiatkowski D. Spontaneous movements associated with rocuronium: is pain on injection the cause? *Br J Anaesth* 1997; **79:** 382–3.

Renal impairment. In a study[1] of the pharmacokinetics and neuromuscular effects of rocuronium, the clearance of rocuronium was reduced in patients with renal failure when compared with healthy patients, but the accompanying increase in duration of clinical relaxation did not reach statistical significance. However, it was recommended that rocuronium should be used with caution in the presence of renal failure as there were large interpatient variations in both clinical response and pharmacokinetic parameters. It has been suggested[2] that chronic renal failure may have played a role in the prolongation of neuromuscular blockade in a 47-year-old woman given rocuronium 1 mg/kg. Although this dose is within the recommended adult dose range, it was criticised[3] as being excessive for a patient with renal impairment.

For recommendation that care should be taken when giving rocuronium to patients with renal failure, see under Uses and Administration, below.

1. Cooper RA, *et al.* Time course of neuromuscular effects and pharmacokinetics of rocuronium bromide (ORG 9426) during isoflurane anaesthesia in patients with and without renal failure. *Br J Anaesth* 1993; **71:** 222–6.
2. Lewis KS, *et al.* Prolonged neuromuscular blockade associated with rocuronium. *Am J Health-Syst Pharm* 1999; **56:** 1114–18.
3. Cozanitis DA, Booij HD. Muscle relaxants and renal failure. *Am J Health-Syst Pharm* 2000; **57:** 1713–14.

Interactions

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

Pharmacokinetics

On intravenous use plasma concentrations of rocuronium follow a three-compartment open model. There is an initial distribution phase with a half-life of 1 to 2 minutes followed by a slower distribution phase with a half-life of 14 to 18 minutes. It is reported to be about 30% bound to plasma proteins. The elimination half-life is about 1.2 to 1.4 hours. Up to 40% of a dose may be excreted in the urine within 24 hours; rocuronium is also excreted in the bile. The main metabolite of rocuronium, 17-desacetylrocuronium, is reported to have a weak neuromuscular blocking effect.

◊ References.

1. Khuenl-Brady KS, Sparr H. Clinical pharmacokinetics of rocuronium bromide. *Clin Pharmacokinet* 1996; **31:** 174–83.
2. McCoy EP, *et al.* Pharmacokinetics of rocuronium after bolus and continuous infusion during halothane anaesthesia. *Br J Anaesth* 1996: **76:** 29–33.
3. Wierda JMKH, *et al.* Pharmacokinetics and pharmacokinetic-dynamic modelling of rocuronium in infants and children. *Br J Anaesth* 1997; **78:** 690–5.
4. Atherton DPL, Hunter JM. Clinical pharmacokinetics of the newer neuromuscular blocking drugs. *Clin Pharmacokinet* 1999; **36:** 169–89.
5. Proost JH, *et al.* Urinary, biliary and faecal excretion of rocuronium in humans. *Br J Anaesth* 2000; **85:** 717–23.

Intensive care. The pharmacokinetics of rocuronium appear to differ between intensive care patients given prolonged dosage and surgical patients.[1] The volume of distribution at steady state may be increased, the plasma clearance decreased, and the terminal half-life prolonged. Recovery time on stopping may also be longer.

1. Sparr HJ, *et al.* Pharmacodynamics and pharmacokinetics of rocuronium in intensive care patients. *Br J Anaesth* 1997; **78:** 267–73.

Pregnancy. The mean concentration of rocuronium in venous plasma of 32 patients given a dose of 600 micrograms/kg before undergoing caesarean section was 2412 nanograms/mL at delivery;[1] the ratio of mean concentrations of rocuronium in umbilical venous plasma to maternal venous plasma at this time was 0.16. In 12 of these patients the mean concentration of rocuronium in umbilical arterial plasma was 271 nanograms/mL giving a ratio of 0.62 for the mean concentration of rocuronium in arterial to venous umbilical plasma. The concentration of 17-desacetylrocuronium in maternal venous plasma was 178 nanograms/mL and was less than 25 nanograms/mL in umbilical plasma.

1. Abouleish E, *et al.* Rocuronium (Org 9426) for Caesarean section. *Br J Anaesth* 1994; **73:** 336–41.

Uses and Administration

Rocuronium bromide is an aminosteroidal competitive neuromuscular blocker (see Atracurium, p.1905). After intravenous injection it produces muscle relaxation within 1 to 2 minutes with a duration of about 30 to 50 minutes. Rocuronium 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. A usual initial dose is 600 micrograms/kg by intravenous injection; however, higher doses of 1 mg/kg are recommended for intubation during rapid sequence induction of anaesthesia. Usual maintenance doses are 150 micrograms/kg by injection, although these should be reduced to 75 to 100 micrograms/kg if prolonged inhalational anaesthesia is planned. Maintenance may also be by infusion at a rate of 300 to 600 micrograms/kg per hour although higher rates have been used in the USA. Similar doses to those used in adults have been used in the UK in infants and children older than one month but maintenance doses may be required more frequently. In the USA, rocuronium is licensed for use in children aged 3 months and over; again doses are similar to those used in adults.

For obese patients weighing more than 30% over their ideal body-weight UK licensed product information recommends that doses should be calculated according to lean body-mass; in the USA it is recommended that dosage should be based on actual body-weight. UK product information also recommends reduced maintenance doses of 75 to 100 micrograms/kg by injection in the elderly. For doses in hepatic or renal impairment, see below.

◊ Reviews and discussions.

1. Mirakhur RK. Newer neuromuscular blocking drugs: an overview of their clinical pharmacology and therapeutic use. *Drugs* 1992; **44:** 182–9.
2. Hunter JM. Rocuronium: the newest aminosteroid neuromuscular blocking drug. *Br J Anaesth* 1996; **76:** 481–3.

Administration in children. In a study involving 70 children, conditions for intubation were judged to be good to excellent within one minute of intravenous doses of rocuronium 600 or 900 micrograms/kg, with a trend to better conditions with the higher dose.[1]

1. Fuchs-Buder T, Tassonyi E. Intubating conditions and time course of rocuronium-induced neuromuscular block in children. *Br J Anaesth* 1996; **77:** 335–8.

INTRAMUSCULAR ROUTE. Intramuscular injection of rocuronium 1 mg/kg into the deltoid muscle permitted tracheal intubation to be carried out in lightly anaesthetised infants after 2.5 minutes.[1] In children a dose of 1.8 mg/kg enabled tracheal intubation after 3 minutes. However, the mean time to initial recovery after these large doses was 57 minutes in infants and 70 minutes in children. This prolonged duration of action may limit intramuscular use for brief procedures, particularly in children.

1. Reynolds LM, *et al.* Intramuscular rocuronium in infants and children: dose-ranging and tracheal intubating conditions. *Anesthesiology* 1996; **85:** 231–9.

Administration in hepatic or renal impairment. UK licensed product information recommends a reduced maintenance dose of 75 to 100 micrograms/kg in patients with hepatic or biliary-tract disease, or renal failure. Initial doses remain unaltered.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Zemuron†; ***Austral.:*** Esmeron; ***Austria:*** Esmeron; ***Belg.:*** Esmeron; ***Braz.:*** Esmeron; Rocuron; ***Canad.:*** Zemuron; ***Chile:*** Esmeron; ***Cz.:*** Esmeron; ***Denm.:*** Esmeron; ***Fin.:*** Esmeron; ***Fr.:*** Esmeron; ***Ger.:*** Esmeron; ***Gr.:*** Esmeron; ***Hong Kong:*** Esmeron; ***Hung.:*** Esmeron; ***Indon.:*** Esmeron; Roculax; ***Irl.:*** Esmeron; ***Israel:*** Esmeron; ***Ital.:*** Esmeron; ***Jpn:*** Eslax; ***Malaysia:*** Esmeron; ***Mex.:*** Esmeron; ***Neth.:*** Esmeron; ***Norw.:*** Esmeron; ***NZ:*** Esmeron; ***Philipp.:*** Esmeron; ***Pol.:*** Esmeron; ***Port.:*** Esmeron; ***Rus.:*** Esmeron (Эсмерон); ***S.Afr.:*** Esmeron; ***Singapore:*** Esmeron; ***Spain:*** Esmeron; ***Swed.:*** Esmeron; ***Switz.:*** Esmeron; ***Thai.:*** Esmeron; ***Turk.:*** Esmeron; ***UK:*** Esmeron; ***USA:*** Zemuron; ***Venez.:*** Esmeron.

Suxamethonium Chloride *(BAN, pINN)*

Choline Chloride Succinate; Cloruro de suxametonio; Succicurarium Chloride; Succinylcholine Chloride; Suksametonio chloridas; Suksametoniowy chlorek; Suksametoniumkloridi; Süksinilkolin Klorür; Suxamethonii chloridum; Suxamethonii Chloridum Dihydricum; Suxamethonium chlorid dihydrát; Suxaméthonium, chlorure de; Suxametoniumklorid; Suxametonklorid; Szuxametóniumklorid. 2,2′-Succinyldioxybis(ethyltrimethylammonium) dichloride dihydrate.

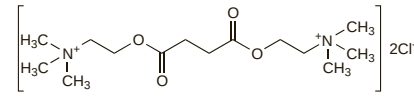
Суксаметония Хлорид

$C_{14}H_{30}Cl_2N_2O_4,2H_2O$ = 397.3.

CAS — 306-40-1 (suxamethonium); 55-94-7 (suxamethonium bromide); 71-27-2 (anhydrous suxamethonium chloride); 6101-15-1 (suxamethonium chloride dihydrate); 541-19-5 (suxamethonium iodide).

ATC — M03AB01.

ATC Vet — QM03AB01.



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

Ph. Eur. 6.2 (Suxamethonium Chloride). A white or almost white, hygroscopic, crystalline powder. Freely soluble in water; slightly soluble in alcohol. A 0.5% solution in water has a pH of 4.0 to 5.0. Protect from light.

USP 31 (Succinylcholine Chloride). A white, odourless, crystalline powder. The anhydrous form is hygroscopic. Soluble 1 in 1 of water and 1 in 350 of alcohol; slightly soluble in chloroform; practically insoluble in ether. Its solutions in water have a pH of about 4. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Incompatibility. Incompatibilities of neuromuscular blockers are discussed under Atracurium, p.1902.

Stability. A study of the loss of potency of suxamethonium chloride 20 mg/mL in water indicated that decomposition occurred at a considerably higher rate at 40° than at 25° and that the pH range of maximum stability was 3.75 to 4.50 for unbuffered solutions.[1] Assuming the usual conditions of manufacturing, transit, and storage the total loss of potency was estimated to be 7% and 9% respectively for injections kept at room temperature for 4 and 6 weeks. If unbuffered, suxamethonium chloride injection complying with USP 31 pH limits (3.0 to 4.5) must be stored at room temperature; it should not be kept for longer than 4 weeks.

1. Boehm JJ, *et al.* Shelf life of unrefrigerated succinylcholine chloride injection. *Am J Hosp Pharm* 1984; **41:** 300–2.

Adverse Effects

The neuromuscular blocking action of suxamethonium chloride is terminated by the enzyme plasma cholinesterase and prolonged apnoea may occur in patients with an atypical enzyme or with low enzyme activity. Apnoea may also occur following development of phase II block (see Uses and Administration, below) after high or repeated doses of suxamethonium chloride, although tachyphylaxis may also occur with repeated doses.

Transient fasciculations occur during the onset of depolarising block. Rhabdomyolysis, myoglobinae-