have occurred when used in anaesthetic regimens with *propofol* and opioids such as *fentanyl*.
See also under Interactions of Atracurium, p.1904.
1. Laurence AS, Henderson P. Serum myoglobin after suxamethonium administration to children: effect of pretreatment before iv and inhalation induction. *Br J Anaesth* 1986; **58:** 126P.

Histamine H_2 antagonists. See under Atracurium, p.1904.

Lithium. See under Atracurium, p.1904.

Local anaesthetics. *Procaine*, *cocaine*, and *chloroprocaine* are ester-type local anaesthetics which are hydrolysed by plasma cholinesterase and may competitively enhance the neuromuscular blocking activity of suxamethonium. See also Antiarrhythmics under Atracurium, p.1903.

Magnesium salts. See under Atracurium, p.1904.

MAOIs. Reduction of plasma cholinesterase activity by *phenelzine* has been reported[1] to cause significant prolongation of suxamethonium paralysis. Enzyme activity may be reduced to 10% of normal and recovery can take up to a month. The dosage of suxamethonium may need to be substantially reduced or a competitive neuromuscular blocker used.
1. Bodley PO, *et al.* Low serum pseudocholinesterase levels complicating treatment with phenelzine. *BMJ* 1969; **3:** 510–12.

Metoclopramide. Dose-dependent prolongation of suxamethonium-induced neuromuscular blockade has been reported in patients given metoclopramide.[1,2] The potent inhibitory effect of metoclopramide on plasma cholinesterase may account for this interaction.
1. Turner DR, *et al.* Neuromuscular block by suxamethonium following treatment with histamine type 2 antagonists or metoclopramide. *Br J Anaesth* 1989; **63:** 348–50.
2. Kao YJ, *et al.* Dose-dependent effect of metoclopramide on cholinesterases and suxamethonium metabolism. *Br J Anaesth* 1990; **65:** 220–4.

Neuromuscular blockers. See under Atracurium, p.1905.

Sex hormones. *Oestrogens* and oestrogen-containing *oral contraceptives* reduce plasma cholinesterase activity[1] possibly due to suppression of hepatic synthesis of the enzyme, but little prolongation of suxamethonium paralysis may be expected since activity is reduced by only about 20%. See also under Atracurium, p.1905.
1. Robertson GS, Aberd MB. Serum protein and cholinesterase changes in association with contraceptive pills. *Lancet* 1967; **i:** 232–5.

Sympathomimetics. *Bambuterol* can inhibit plasma cholinesterase activity and so prolong the activity of suxamethonium.[1] Phase II block has been reported in some patients with abnormal plasma cholinesterase.[2]
1. Staun P, *et al.* The influence of 10 mg and 20 mg bambuterol on the duration of succinylcholine-induced neuromuscular blockade. *Acta Anaesthesiol Scand* 1990; **34:** 498–500.
2. Bang U, *et al.* The effect of bambuterol on plasma cholinesterase activity and suxamethonium-induced neuromuscular blockade in subjects heterozygous for abnormal plasma cholinesterase. *Acta Anaesthesiol Scand* 1990; **34:** 600–604.

Pharmacokinetics

After injection, suxamethonium is rapidly hydrolysed by plasma cholinesterase. One molecule of choline is split off rapidly to form succinylmonocholine which is then slowly hydrolysed to succinic acid and choline. About 10% of suxamethonium is excreted unchanged in the urine. Succinylmonocholine has weak muscle-relaxant properties mainly of a competitive nature.

The gene responsible for the expression of plasma cholinesterase exhibits polymorphism and enzyme activity varies between individuals (see under Precautions, above).

Small amounts of suxamethonium cross the placenta.

◊ Reviews.
1. Booij LHDJ, Vree TB. Skeletal muscle relaxants: pharmacodynamics and pharmacokinetics in different patient groups. *Int J Clin Pract* 2000; **54:** 526–34.

Uses and Administration

Suxamethonium is a depolarising neuromuscular blocker used to produce muscle relaxation. It combines with cholinergic receptors of the motor end-plate to produce depolarisation but is resistant to breakdown by acetylcholinesterase. This prevents repolarisation and subsequent depolarisation, and a flaccid muscle paralysis occurs. This initial depolarisation block is commonly known as a **phase I block.** The muscles that produce fine rapid movements such as those of the face are the first to be affected followed by those of the limbs, abdomen, and chest; the diaphragm is affected last. Recovery occurs in reverse order. When excessive amounts of suxamethonium accumulate at the neuromuscular junction, for example after high or prolonged dosage, the nature of the block may change to one with characteristics similar to competitive block. This is commonly termed **phase II block** or **dual block** and may be associated with prolonged neuromuscular blockade and apnoea.

After intravenous injection suxamethonium chloride acts in about 30 to 60 seconds and has a duration of action of about 2 to 6 minutes. After intramuscular injection it acts in 2 to 3 minutes and has a duration of action of about 10 to 30 minutes.

Suxamethonium is used in surgical and other procedures in which a rapid onset and brief duration of muscle relaxation is needed (see Anaesthesia, p.1900), including intubation, endoscopies, and ECT. It is used as suxamethonium chloride, and is normally given by intravenous injection. The content of preparations of suxamethonium chloride may be described in terms of either the dihydrate or the anhydrous form, depending on the country of origin, and this should be borne in mind when evaluating the literature although the differences are small (anhydrous suxamethonium chloride 1 mg is equivalent to about 1.1 mg of the dihydrate).

Suxamethonium should be given after induction of general anaesthesia because paralysis is usually preceded by painful muscle fasciculations. A competitive neuromuscular blocker may sometimes be given before suxamethonium to try to reduce some of the adverse effects on the muscles (see Effects on the Muscles, above). Premedication with an antimuscarinic may be of value in reducing bradycardia and excessive salivation. Assisted ventilation is necessary.

An initial test dose of 100 micrograms/kg, or 5 to 10 mg, of suxamethonium chloride may be given intravenously if increased sensitivity is suspected. 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 response to suxamethonium varies considerably and the usual single dose of suxamethonium chloride for an adult is 0.3 to 1.1 mg/kg by intravenous injection. Supplementary doses of 50 to 100% of the initial dose may be given at 5 to 10 minute intervals if required but the total dose given by repeated intravenous injection or continuous infusion (see below) should not exceed 500 mg/hour. Infants and children are more resistant to suxamethonium than adults. A recommended intravenous dose for infants under one year of age is 2 mg/kg; a dose of 1 mg/kg is recommended for children 1 to 12 years old.

When a suitable vein is inaccessible suxamethonium chloride has been given by intramuscular injection in a dose of 3 to 4 mg/kg to a maximum total dose of 150 mg. The intramuscular dose for infants is up to 4 to 5 mg/kg and for older children up to 4 mg/kg to a maximum total dose of 150 mg.

For prolonged procedures in adults sustained relaxation may be obtained by continuous intravenous infusion of a 0.1 to 0.2% solution. A rate of 2.5 to 4 mg/minute is usually adequate but may be adjusted as necessary. The total dose given by repeated intravenous injection (see above) or continuous infusion should not exceed 500 mg/hour.

Suxamethonium bromide and suxamethonium iodide have also been used.

ECT. Suxamethonium chloride is used to decrease the muscular contractions associated with electrically induced convulsions. It temporarily paralyses muscles during ECT, preventing violent muscle contractions which can potentially result in broken bones and fractures.

Suxamethonium chloride remains the most commonly used neuromuscular blocker in ECT. However, patients with a history of malignant hyperthermia, neuroleptic malignant syndrome, catatonic schizophrenia, and organophosphate poisoning are more susceptible to adverse effects.[1] Mivacurium has been used, with satisfactory results, in at-risk-patients, although histamine release and hypotension may be a problem. Other competitive neuromuscular blockers tried include atracurium and vecuronium.

1. Ding Z, White PF. Anesthesia for electroconvulsive therapy. *Anesth Analg* 2002; **94:** 1351–64.

Preparations

BP 2008: Suxamethonium Chloride Injection;
USP 31: Succinylcholine Chloride for Injection; Succinylcholine Chloride Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Actirelax; Fosfitone; Succi†; ***Austral.:*** Scoline; ***Austria:*** Lysthenon; ***Belg.:*** Myoplegine†; ***Braz.:*** Quelicin; Succitrat; Succnil Colin; ***Canad.:*** Quelicin; ***Fin.:*** Sukolin; ***Fr.:*** Celocurine†; ***Ger.:*** Lysthenon; Pantolax; ***Gr.:*** Lycitrope; ***India:*** Midarine; ***Indon.:*** Quelicin; ***Irl.:*** Anectine; ***Israel:*** Succinyl; ***Ital.:*** Midarine; Myotenlis†; ***Malaysia:*** Ethicoline; Succinyl†; ***Mex.:*** Anectine; Uxicolin; ***Neth.:*** Curalest; ***Norw.:*** Curacit; ***NZ:*** Ethicholine†; ***Pol.:*** Chlorsuccillin; ***Port.:*** Mioflex; ***Rus.:*** Lysthenon (Листенон); ***S.Afr.:*** Scoline; ***Singapore:*** Ethicholine; ***Spain:*** Anectine; Mioflex; ***Swed.:*** Celocurin; ***Switz.:*** Lysthenon; Midarine; Succinolin; ***Thai.:*** Succinyl; ***Turk.:*** Lysthenon; ***UK:*** Anectine; ***USA:*** Anectine; Quelicin.

Tubocurarine Chloride *(BAN, rINN)*

Cloruro de tubocurarina; *d*-Tubocurarine Chloride; (+)-Tubocurarine Chloride Hydrochloride Pentahydrate; Tubocurarine, chlorure de; Tubocurarini chloridum; Tubocurarinii Chloridum Pentahydricum; Tubokurariinikloridi; Tubokurarinium-chlorid pentahydrát; Tubokurarinklorid; Tubokurarin-klorid; Tubokurarino chloridas. (+)-7′,12′-Dihydroxy-6,6′-dimethoxy-2,2′,2′-trimethyltubocuraranium dichloride pentahydrate.

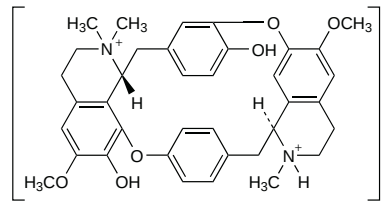
Тубокурарина Хлорид

$C_{37}H_{42}Cl_2N_2O_6,5H_2O$ = 771.7.

CAS — 57-95-4 (tubocurarine); 57-94-3 (anhydrous tubocurarine chloride); 6989-98-6 (tubocurarine chloride, pentahydrate).

ATC — M03AA02.

ATC Vet — QM03AA02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Tubocurarine Chloride). A white or slightly yellowish crystalline powder. Soluble in water and in alcohol; practically insoluble in acetone; dissolves in solutions of alkali hydroxides. A 1% solution in water has a pH of 4.0 to 6.0. Store in airtight containers.
USP 31 (Tubocurarine Chloride). A white or yellowish-white to greyish-white, crystalline powder. Soluble 1 in 20 of water and 1 in 45 of alcohol. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for competitive neuromuscular blockers in general (see Atracurium, p.1902). A transient fall in blood pressure commonly occurs, due in part to ganglionic blockade and the release of histamine; there may be an increase in heart rate. Tubocurarine has a greater propensity to cause histamine release than other competitive neuromuscular blockers in clinical use. Tubocurarine should be used with caution in patients with renal impairment. Resistance to the effect of tubocurarine may occur in patients with hepatic impairment.

Interactions

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

Pharmacokinetics

Tubocurarine chloride is a quaternary ammonium compound and absorption from the gastrointestinal tract is extremely poor. Absorption is slow and irregular when given intramuscularly. After intravenous injection tubocurarine is widely distributed throughout body tissues; less than 50% is bound to plasma proteins. After a single dose extensive redistribution to tissues is responsible for the termination of activity, but after a large single dose or repeated small doses tissue saturation occurs and renal excretion becomes the main determinant of duration. When given in usual doses it does not pass the blood-brain barrier, and does not appear to cross the placenta in significant amounts. Up to 75% of a dose is excreted unchanged in the urine in 24 hours, and up to 12% in bile. Biliary excretion is increased in renal impairment. A small proportion of a dose is metabolised in the liver.

Uses and Administration

Tubocurarine is a benzylisoquinolinium competitive neuromuscular blocker (see Atracurium, p.1905). It may be obtained from extracts of the stems of *Chondodendron tomentosum* (Menispermaceae) and is one of the active principles of curare, by which name it is sometimes referred to in anaesthetic literature. Tubocurarine chloride is the chloride of (+)-tubocurarine. After intravenous injection of tubocurarine chloride neuromuscular block appears within 1 minute and lasts for about 30 minutes; the maximum effect is attained within 2 to 5 minutes.

Tubocurarine chloride has been used similarly to other competitive neuromuscular blockers to produce muscle relaxation in various procedures but has largely been replaced by other drugs with fewer cardiovascular effects and a lower potential for histamine release.

Doses used have varied according to the degree of muscle relaxation required. 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 dose of 6 to 9 mg intravenously has been suggested followed by 3 to 4.5 mg after 3 to 5 minutes if necessary; additional doses of 3 mg may be given as required for prolonged procedures. Higher doses have been given in some countries. It has also been given intramuscularly but absorption is slow and erratic. Tubocurarine should be given with caution in reduced doses to patients with renal impairment; if large or repeated doses are given neuromuscular block may be prolonged.

Tubocurarine chloride has also been used to control the muscle spasms of tetanus (p.1901).

Preparations

USP 31: Tubocurarine Chloride Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Decurin; ***Israel:*** Curarine†; Tubarine†.

Vecuronium Bromide *(BAN, USAN, rINN)*

Bromuro de vecuronio; Org-NC-45; Vecuronii bromidum; Vécuronium, bromure de; Vekuroniumbromid; Vekuronium-bromid; Vekuroniumbromidi; Vekuronyum Bromür; Wekuroniowy bromek. 1-(3α,17β-Diacetoxy-2β-piperidino-5α-androstan-16β-yl)-1-methylpiperidinium bromide.

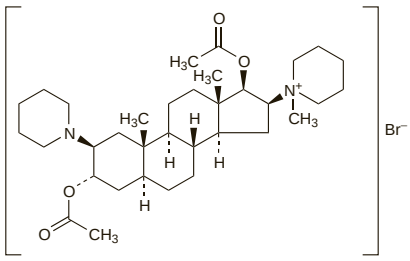
Векурония Бромид

$C_{34}H_{57}BrN_2O_4$ = 637.7.

CAS — 50700-72-6.

ATC — M03AC03.

ATC Vet — QM03AC03.



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

Ph. Eur. 6.2 (Vecuronium Bromide). White or almost white crystals or crystalline powder. Slightly soluble in water; sparingly soluble in dehydrated alcohol and in acetonitrile; freely soluble in dichloromethane. Store in airtight containers. Protect from light and moisture.

USP 31 (Vecuronium Bromide). White or creamy white crystals, or a crystalline powder. Slightly soluble in water and in acetone; sparingly soluble in alcohol. Store in airtight containers.

Incompatibility. A solution containing vecuronium bromide 1 mg/mL was found to be visually incompatible with furosemide.[1] For incompatibilities of competitive neuromuscular blockers in general, see under Atracurium on p.1902.

1. Chiu MF, Schwartz ML. Visual compatibility of injectable drugs used in the intensive care unit. *Am J Health-Syst Pharm* 1997; **54:** 64–5.

Adverse Effects, Treatment, and Precautions

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

Vecuronium bromide has little histamine-releasing activity although a local reaction at the site of injection has been reported; bronchospasm and anaphylactoid reactions have been rarely reported. It also has little vagolytic or ganglion-blocking activity and produces no significant adverse cardiovascular effects at usual doses.

Caution may be needed in patients with hepatic or renal impairment (see under Uses and Administration, below); dosage adjustments may be required in renal failure.

The elderly. It has been recommended that neuromuscular function should be monitored in elderly patients receiving vecuronium since there may be a risk of prolonged block.[1]

1. Slavov V, *et al.* Comparison of duration of neuromuscular blocking effect of atracurium and vecuronium in young and elderly patients. *Br J Anaesth* 1995; **74:** 709–11.

Pregnancy. The proportion of vecuronium crossing the placenta after doses of 60 to 80 micrograms/kg was considered clinically insignificant and its use during obstetric anaesthesia was considered safe for the newborn.[1]

1. Demetriou M, *et al.* Placental transfer of Org NC 45 in women undergoing caesarean section. *Br J Anaesth* 1982; **54:** 643–5.

Interactions

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

Pharmacokinetics

On intravenous injection vecuronium is rapidly distributed. It is taken up by the liver and partly metabolised; the metabolites have some neuromuscular blocking activity. It is excreted mainly in bile as unchanged drug and metabolites; some is also excreted in urine. The plasma elimination half-life is reported to range from about 30 to 80 minutes.

Uses and Administration

Vecuronium bromide is an aminosteroidal competitive neuromuscular blocker (see Atracurium, p.1905).

After intravenous injection muscle relaxation occurs within about 1.5 to 2 minutes and lasts for about 20 to 30 minutes.

Vecuronium 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 usual initial dose for intubation is 80 to 100 micrograms/kg by intravenous injection, although reduced initial doses of 30 to 50 micrograms/kg are suggested following the use of suxamethonium. Higher initial doses ranging from 150 to 300 micrograms/kg have sometimes been used for other procedures. However, it is recommended that the dose should not exceed 100 micrograms/kg in caesarean section or neonatal surgery. Maintenance doses of 20 to 30 micrograms/kg may be given as required during prolonged procedures; in the USA a lower maintenance dose of 10 to 15 micrograms/kg is recommended. Neuromuscular blockade may also be maintained with an intravenous infusion given at a rate of 0.8 to 1.4 micrograms/kg per minute but should be preceded by an initial bolus injection of 40 to 100 micrograms/kg. UK licensed product information recommends that in obese patients the dosage of vecuronium should be reduced taking into account lean body-mass.

Children older than 5 months can be given adult doses but children up to 1 year may have a more rapid response and the high initial dose for intubation may not be necessary. Neonates and infants below 5 months of age may be more sensitive to vecuronium and it is recommended that they should be given an initial test dose of 10 to 20 micrograms/kg, followed by increments according to response. The duration of action and recovery is longer in neonates and infants than in children and adults and they may require smaller maintenance doses given less frequently.

Administration in hepatic impairment. Although the manufacturers make no specific recommendations for dosage reduction in hepatic impairment, the duration of action of vecuronium was reported to be significantly prolonged in patients with cholestasis[1] or cirrhosis with oesophageal varices[2] given a dose of 200 micrograms/kg intravenously. Plasma clearance was significantly reduced and the elimination half-life significantly increased from a mean of 58 to 98 minutes.[1] A dose of 150 micrograms/kg was found to have a similar onset and duration of action in patients with hepatic impairment and healthy controls,[2] but a dose of 100 micrograms/kg had a slower onset and slightly shorter duration of action in those with liver disturbance.[3] After a dose of vecuronium, rapid and extensive hepatic uptake occurs, which largely determines its short duration of action. However, as the dose increases this mechanism becomes saturated, and hepatic elimination becomes more important in terminating activity. This would help to explain the variation in results seen with the different doses. Caution is needed if large single doses or repeated doses are given to patients with hepatic impairment.

1. Lebrault C, *et al.* Pharmacokinetics and pharmacodynamics of vecuronium in patients with cholestasis. *Br J Anaesth* 1986; **58:** 983–7.
2. Hunter JM, *et al.* The use of different doses of vecuronium in patients with liver dysfunction. *Br J Anaesth* 1985; **57:** 758–64.
3. Bell CF, *et al.* Use of atracurium and vecuronium in patients with oesophageal varices. *Br J Anaesth* 1985; **57:** 160–8.

Administration in renal impairment. A small proportion of vecuronium bromide is excreted in urine and it may be given in usual doses to patients with renal failure.[1,2] No clinically significant difference in elimination half-life, clearance, or duration of action were reported[1] between patients with renal failure and those with normal renal function. The onset of neuromuscular block may be slightly slower in renal failure[2] and these patients may require an increase of around 20% in the initial dose of vecuronium.[3] However, the dosage requirement for maintenance of neuromuscular block may be reduced by about 20%[3] and slight prolongation of block may occur if dosage is not adjusted, but reversal of residual block with neostigmine is prompt and effective.[2]

Resistance to vecuronium has been reported[2] in 2 anephric patients. Total doses of 620 and 660 micrograms/kg produced maximum neuromuscular block of 77% and 36%, respectively but, despite the high doses used, there were no adverse effects or residual curarisation.

1. Fahey MR, *et al.* Pharmacokinetics of Org NC 45 (Norcuron) in patients with and without renal failure. *Br J Anaesth* 1981; **53:** 1049–53.
2. Hunter JM, *et al.* Comparison of vecuronium, atracurium and tubocurarine in normal patients and in patients with no renal function. *Br J Anaesth* 1984; **56:** 941–51.
3. Gramstad L. Atracurium, vecuronium and pancuronium in end-stage renal failure: dose-response properties and interactions with azathioprine. *Br J Anaesth* 1987; **59:** 995–1003.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Galaren; Gobbicuronio; Norcuron†; Rivecrum; Vecural; Vecuron; ***Austral.:*** Norcuron; ***Austria:*** Norcuron; ***Belg.:*** Norcuron; ***Braz.:*** Norcuron; Vecuron; ***Canad.:*** Norcuron†; ***Chile:*** Norcuron; ***Cz.:*** Norcuron; ***Fin.:*** Norcuron; ***Fr.:*** Norcuron; ***Ger.:*** Norcuron; ***Gr.:*** Norcuron; ***Hong Kong:*** Norcuron; ***Hung.:*** Norcuron; ***India:*** Norcuron; ***Indon.:*** Norcuron; ***Irl.:*** Norcuron†; ***Israel:*** Norcuron; ***Ital.:*** Norcuron; ***Jpn:*** Musculax; ***Malaysia:*** Norcuron; ***Mex.:*** Bromivec; Curlem; Norcuron; ***Neth.:*** Norcuron; ***Norw.:*** Norcuron; ***NZ:*** Norcuron; ***Philipp.:*** Norcuron; ***Pol.:*** Norcuron; ***Port.:*** Norcuron; ***Rus.:*** Norcuron (Норкурон); ***S.Afr.:*** Norcuron; ***Singapore:*** Norcuron; ***Spain:*** Norcuron; ***Swed.:*** Norcuron; ***Switz.:*** Norcuron; ***Thai.:*** Norcuron; ***Turk.:*** Norcuron; ***UK:*** Norcuron; ***USA:*** Norcuron; ***Venez.:*** Norcuron†; Prorelax; Vecuron.