M.p. 81° to 83°. Soluble 1 in 100 of water at 25°, 1 in 20 of water at 80°, 1 in 20 of glycerol; freely soluble in alcohol, in chloroform, in ether, and in solutions of fixed alkali hydroxides. Its solutions are acid to litmus. Store in airtight containers. Protect from light.

Profile
Vanillin is used as a flavour and in perfumery.

Preparations
BP 2008: Tolu-flavour Solution.

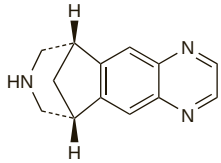
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Belg.:*** Pulmex; Pulmex Baby; ***Turk.:*** Musilaks.

Varenicline *(BAN, rINN)*

Vareniclina; Varénicline; Vareniclinum. 7,8,9,10-Tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline.

Варениклин

$C_{13}H_{13}N_3$ = 211.3.
CAS — 249296-44-4.
ATC — N07BA03.
ATC Vet — QN07BA03.



Varenicline Tartrate *(BANM, USAN, rINNM)*

CP-526555-18; Tartrato de vareniclina; Varénicline, Tartrate de; Vareniclini Tartras.

Варениклина Тартрат

$C_{13}H_{13}N_3,C_4H_6O_6$ = 361.3.
CAS — 375815-87-5.
ATC — N07BA03.
ATC Vet — QN07BA03.

Adverse Effects and Precautions
The most common adverse effect of varenicline is nausea; other adverse effects also commonly reported are headache, dizziness, somnolence, fatigue, sleep disturbances, increased appetite, and gastrointestinal disturbances including vomiting, constipation, and flatulence. There have been reports of neuropsychiatric symptoms as well as exacerbation of pre-existing psychiatric illness in patients who have taken varenicline. Patients should be monitored for such symptoms, including suicidal ideation or behaviour, agitation, depression, or other changes in behaviour.

Dizziness and somnolence may affect the performance of skilled tasks such as driving.

Pharmacokinetics
Varenicline is well absorbed from the gastrointestinal tract, reaching peak plasma concentrations within 3 to 4 hours; bioavailability is high. Steady state concentrations are reached within 4 days of multiple oral dosing. Metabolism is minimal and about 92% of a dose is excreted unchanged in the urine; the elimination half-life is about 24 hours.

◊ References.

1. Faessel HM, *et al.* Single-dose pharmacokinetics of varenicline, a selective nicotinic receptor partial agonist, in healthy smokers and nonsmokers. *J Clin Pharmacol* 2006; **46:** 991–8.
2. Burstein AH, *et al.* Pharmacokinetics, safety, and tolerability after single and multiple oral doses of varenicline in elderly smokers. *J Clin Pharmacol* 2006; **46:** 1234–40.
3. Burstein AH, *et al.* Pharmacokinetics, safety, and tolerability after single and multiple oral doses of varenicline in elderly smokers. *J Clin Pharmacol* 2006; **46:** 1234–40.
4. Faessel HM, *et al.* Multiple-dose pharmacokinetics of the selective nicotinic receptor partial agonist, varenicline, in healthy smokers. *J Clin Pharmacol* 2006; **46:** 1439–48.

Uses and Administration
Varenicline is a selective nicotinic receptor partial agonist that is used as an aid for smoking cessation.

Varenicline is given orally as the tartrate with doses expressed in terms of the equivalent amount of varenicline; 1.71 mg of varenicline tartrate is equivalent to about 1 mg of varenicline. An initial dose equivalent to 500 micrograms varenicline is given once daily for the first 3 days, increasing to 500 micrograms twice daily for the next 4 days. The dose from the eighth day for the remainder of the course is 1 mg twice daily. The dose may be reduced to 500 micrograms twice daily if adverse effects are intolerable. Patients are advised to set a date to stop smoking and start varenicline 1 to 2 weeks before. Treatment is normally given for 12 weeks; in patients who successfully stop smoking, a further 12 weeks of treatment has been recommended to reduce the risk of relapse. For doses in renal impairment, see below.

◊ Reviews.

1. Zierler-Brown SL, Kyle JA. Oral varenicline for smoking cessation. *Ann Pharmacother* 2007; **41:** 95–9.
2. Potts LA, Garwood CL. Varenicline: the newest agent for smoking cessation. *Am J Health-Syst Pharm* 2007; **64:** 1381–4.
3. Hays JT, *et al.* Efficacy and safety of varenicline for smoking cessation. *Am J Med* 2008; **121** (suppl 1): S32–S42.
4. Anonymous. Varenicline for smoking cessation. *Drug Ther Bull* 2008; **46:** 33–6.

Administration in renal impairment. In patients with severe renal impairment (creatinine clearance less than 30 mL/minute) licensed product information recommends a starting dose of 500 micrograms daily increased if necessary after 3 days to a maximum dose of 500 micrograms twice daily (in the USA) or 1 mg once daily (in the UK). In patients with end-stage renal disease undergoing haemodialysis, a maximum dose of 500 micrograms once daily may be given provided that this is well tolerated. No dosage adjustment is considered to be needed in patients with lesser degrees of impairment.

Smoking cessation. Varenicline is an α4β2 nicotinic acetylcholine receptor partial agonist that is used as an aid for smoking cessation (p.2354). Results from 2 randomised controlled studies[1,2] show greater efficacy than placebo as well as favourable results compared with bupropion, a standard treatment for smoking cessation. However, these studies also showed that nausea was reported in almost 30% of participants in the varenicline group; abnormal dreams were also a problem. A further 12 weeks of treatment with varenicline improved abstinence at 24 weeks in patients who stopped smoking in the first 12 weeks of treatment; after stopping all treatment, the reduced relapse rate was maintained in this group up to 28 weeks later (i.e. 1 year from the start of treatment).[3]

1. Gonzales D, *et al.* Varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. *JAMA* 2006; **296:** 47–55.
2. Jorenby DE, *et al.* Efficacy of varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. *JAMA* 2006; **296:** 56–63. Correction. *ibid.*; 1355.
3. Tonstad S, *et al.* Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. *JAMA* 2006; **296:** 64–71.

Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Champix; ***Braz.:*** Champix; ***Cz.:*** Champix; ***Fr.:*** Champix; ***Gr.:*** Champix; ***Hung.:*** Champix; ***NZ:*** Champix; ***Port.:*** Champix; ***UK:*** Champix; ***USA:*** Chantix.

Vascular Endothelial Growth Factor

Сосудистого Эндотелиального Фактора Роста; Фактор Роста Эндотелия Сосудов

Profile
Vascular endothelial growth factor is a family of structurally related proteins involved in angiogenesis and vasculogenesis. VEGF-A, the first member of the family to be discovered and still often referred to as simply VEGF, is thought to provide most of the angiogenic effect of this family. Other members described to date include: VEGF-B, VEGF-C, VEGF-D, VEGF-E, and placental growth factor.

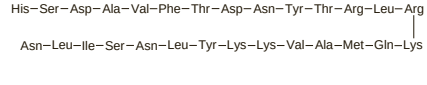
A gene therapy product supplying the gene for vascular endothelial growth factor D via an adenoviral vector is under investigation for the prevention of stenosis in synthetic grafts used in haemodialysis.

Vasoactive Intestinal Peptide

Péptido vasoactivo intestinal; PIV; Vasoactive Intestinal Polypeptide; VIP.

Вазоактивный Пептид Кишечника

CAS — 37221-79-7.



Aviptadil *(BAN, rINN)*

Aviptadilum; Vasoactive Intestinal Octacosapeptide (Swine).

Авиптадил

$C_{147}H_{238}N_{44}O_{42}S$ = 3325.8.
CAS — 40077-57-4.

Profile
Vasoactive intestinal peptide acts as a hormone and neurotransmitter in various parts of the body; it is a potent relaxant of smooth muscle and has vasodilator and bronchodilator properties as well as stimulating the gastrointestinal tract to increased secretion. It is available as a synthetic analogue, aviptadil. It has been tried in the management of acute oesophageal food impaction, and for the treatment of acute respiratory distress syndrome, pulmonary arterial hypertension, acute lung injury, and chronic thromboembolic pulmonary hypertension. Aviptadil has been tried as a combination product with phentolamine for erectile dysfunction (p.2179).

◊ Vasoactive intestinal peptide has potential therapeutic applications in immunological disorders since it appears to inhibit inflammatory responses; it modulates the function of inflammatory cells via specific receptors affecting both innate and adaptive immunity.[1] It also appears to have endogenous neuroprotective properties within the CNS, possibly through influencing the expression and secretion of glial-cell derived neuroprotective factors. Consequently, it may have therapeutic potential in neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease, and stroke.[2]

1. Delgado M, *et al.* The significance of vasoactive intestinal peptide in immunomodulation. *Pharmacol Rev* 2004; **56:** 249–90.
2. Dejda A, *et al.* Neuroprotective potential of three neuropeptides PACAP, VIP and PHI. *Pharmacol Rep* 2005; **57:** 307–20.

Preparations
Proprietary Preparations (details are given in Part 3)
NZ: Invicorp.

Vasopressin *(rINNM)*

ADH; Antidiuretic Hormone; Beta-Hypophamine; Vasopresina; Vasopressiini; Vasopressine; Vasopressinum; Vazopresin.

Вазопрессин

CAS — 11000-17-2 (vasopressin injection).
ATC — H01BA01.
ATC Vet — QH01BA01.

NOTE. Vasopressin Injection is *rINN*.

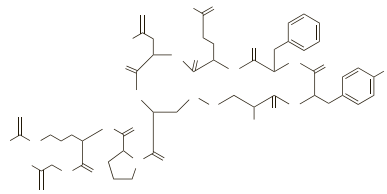
Pharmacopoeias. In *US*, which includes both argipressin and lypressin in this title.
An injection is included in *Jpn*.
USP 31 (Vasopressin). A polypeptide hormone having the properties of causing the contraction of vascular and other smooth muscles, and of antidiuresis. It is prepared by synthesis or obtained from the posterior lobe of the pituitary of healthy, domestic animals used for food by humans. Its vasopressor activity is not less than 300 USP units/mg. Store in airtight containers at 2° to 8°.

Argipressin *(BAN, rINN)*

[8-Arginine]vasopressin; Argipresina; Argipressine; Argipressinum; AVP. Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly-NH_2 cyclic (1→6) disulphide.

Аргипрессин

$C_{46}H_{65}N_{15}O_{12}S_2$ = 1084.2.
CAS — 113-79-1.
ATC — H01BA06.
ATC Vet — QH01BA06.



Description. Argipressin is a form of vasopressin obtained from most mammals including man but excluding pig. It is usually prepared synthetically. Lypressin (see below) is vasopressin from pig.

Argipressin Tannate *(BANM, USAN, rINNM)*

8-L-Arginine-vasopressin Tannate; Argipressine, Tannate d'; Argipressini Tannatum; CI-107; Tanato de argipresina. Tannins compound with argipressin.

Аргипрессина Таннат

ATC — H01BA06.
ATC Vet — QH01BA06.

Units
8.2 units of argipressin for bioassay are contained in approximately 20 micrograms of synthetic peptide acetate (with human albumin 5 mg and citric acid) in one ampoule of the first International Standard (1978).