ingredient herbal preparation promoted for weight loss; one patient required emergency liver transplantation.[1]

1. Sanchez W, *et al.* Severe hepatotoxicity associated with use of a dietary supplement containing usnic acid. *Mayo Clin Proc* 2006; **81:** 541–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Dr Grandel Granobil†; Tetesept Hals-activ; ***Ital.:*** Vidermina; Zeta N.

Multi-ingredient: ***Indon.:*** Scabicid; ***Ital.:*** Foot Zeta; Micofoot; Steril Zeta.

Valepotriates

Valepotriatos.

Acevaltrate *(rINN)*

Acévaltrate; Acevaltrato; Acevaltratum. 4-Acetoxymethyl-(1 or 6)-3-(acetoxy-3-methylbutyryloxy)-1,6,7,7a-tetrahydro-(6 or 1)-isovaleryloxycyclopenta[*c*]pyran-7-spiro-2′-oxiran.

Ацевалтрат

$C_{24}H_{32}O_{10}$ = 480.5.
CAS — 25161-41-5.

Didrovaltrate *(rINN)*

Didrovaltrato; Didrovaltratum. 6-Acetoxy-1,4a,5,6,7,7a-hexahydro-1-isovaleryloxy-4-isovaleryloxymethylcyclopenta[*c*]pyran-7-spiro-2′-oxiran.

Дидровальтрат

$C_{22}H_{32}O_8$ = 424.5.
CAS — 18296-45-2.

Valtrate *(pINN)*

Valtrato; Valtratum. 4-Acetoxymethyl-1,6-di-isovaleryloxy-1,6,7,7a-tetrahydrocyclopenta[*c*]pyran-7-spiro-2′-oxiran.

Вальтрат

$C_{22}H_{30}O_8$ = 422.5.
CAS — 18296-44-1.

Profile

Valepotriates are epoxy-iridoid esters, isolated from valerian (see below). They include acevaltrate, didrovaltrate, and valtrate. On prolonged storage and drying they are hydrolysed to yield isovaleric acid.

A mixture stated to contain acevaltrate, didrovaltrate, and valtrate has been used as a sedative and as an anxiolytic. Concern has been expressed over the potential toxicity of valepotriates which have been reported to have cytotoxic properties *in vitro*.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Valmane; ***Gr.:*** Valmane.

Multi-ingredient: ***Arg.:*** SDN 200.

Valerian

Baldrianwurzel; Korzeń kozłka; Kozlíkový kořen; Macskagyökér; Valer; Valeriaananjuuri; Valerian Rhizome; Valerian Root; Valeriana; Valerianae radix; Valerianarot; Valériane, racine de; Valerijonų šaknys.

CAS — 8057-49-6 (valerian extract).
ATC — N05CM09.
ATC Vet — QN05CM09.

Pharmacopoeias. In *Eur.* (see p.vii) and *US. Eur.* also includes valerian dry hydroalcoholic extract and tincture. *US.* includes the powdered form.

Jpn has Japanese Valerian from *V. fauriei*.

Ph. Eur. 6.2 (Valerian Root; Valerian BP 2008). The yellowish-grey to pale brownish-grey whole underground parts of *Valeriana officinalis*, including the rhizome surrounded by the roots and stolons, or by fragments of these parts. It contains not less than 0.4% v/w of essential oil for the whole drug and not less then 0.3% v/w for the cut drug, both calculated with reference to the dried drug. Protect from light.

USP 31 (Valerian). The subterranean parts of *Valeriana officinalis* (Valerianaceae), including the rhizome, roots, and stolons. It contains not less than 0.5% of volatile oil and not less than 0.05% of valerenic acid, calculated on the dried basis. Store in airtight containers. Protect from light.

Profile

Valerian has sedative properties and is used as an extract, infusion, or tincture, or occasionally as the dried root, in preparations for anxiety states. It has also been used as a carminative. Valerian oil is used in aromatherapy. The odour of valerian may be removed from the skin and from hard surfaces with sodium bicarbonate.

◊ References.

1. Houghton P. Valerian. *Pharm J* 1994; **253:** 95–6.
2. Houghton PJ. The scientific basis for the reputed activity of valerian. *J Pharm Pharmacol* 1999; **51:** 505–12.
3. Plushner SL. Valerian: valeriana officinalis. *Am J Health-Syst Pharm* 2000; **57:** 328–35.
4. Stevinson C, Ernst E. Valerian for insomnia: a systematic review of randomized clinical trials. *Sleep Med* 2000; **1:** 91–9.
5. Bent S, *et al.* Valerian for sleep: a systematic review and meta-analysis. *Am J Med* 2006; **119:** 1005–12.

Adverse effects. Liver damage[1] was reported in 4 patients who took herbal stress remedies that contained valerian. Cardiac complications and delirium in a 58-year-old man may have been caused by the withdrawal of prolonged therapy with a valerian root extract preparation.[2]

1. MacGregor FB, *et al.* Hepatotoxicity of herbal remedies. *BMJ* 1989; **299:** 1156–7.
2. Garges HP, *et al.* Cardiac complications and delirium associated with valerian root withdrawal. *JAMA* 1998; **280:** 1566–7.

Preparations

Ph. Eur.: Valerian Dry Hydroalcoholic Extract; Valerian Tincture;
USP 31: Valerian Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Nervisatis; Sedante Nativa†; ***Austral.:*** Herbal Sleep Formula†; ***Austria:*** Baldrinetten†; ***Belg.:*** Dormiplant; Relaxine; Valdispert†; Valerial; ***Braz.:*** Noctaval; Recalm; Sonoripan; Traminer; Valdorm; Valeriane; Valerimed; Valerin; Valerix; Valezen; Valmane; ***Canad.:*** Nytol Natural Source; Sleep-Eze V Natural; Unisom Natural Source†; ***Chile:*** Sominex; ***Cz.:*** Koren Kozliku Lekarskeho†; Kozlik; Valdispert†; ***Fin.:*** Valrian; ***Ger.:*** Baldorm; Baldriparan Stark†; Baldrivit; Baldurat; Cefaluna†; Cefan; Dolestan; Euvegal Balance; Kytta-Sedativum; Luvased mono; Phytodorma†; Recvalysat†; Sedonium; Sporal mono; Valdispert†; ***Hong Kong:*** Cirku Sed†; ***Israel:*** Relaxine; Valeton; ***Ital.:*** Ticalma; Val-Uno†; ***Mex.:*** Neolaikan; ***Neth.:*** Dormiplant; Sedonium; Valdispert; ***Pol.:*** Cirkused; Relana Forte; Valerin; ***Port.:*** Valdispert; Valditas; ***Rus.:*** Novo-Passit (Ново-Пассит); ***S.Afr.:*** Calmettes; ***Spain:*** Ansiokey; Cirkused†; Coenrelax; Tauval†; Valdispert; Valeriana Orto; Valsedan; ***Swed.:*** Baldrian-Dispert; Neurol; Valerecen; ***Switz.:*** Baldriparan pour la nuit; Baldrisedon†; Natu-Seda; Plantival Mono†; ReDormin; Sedasol eco natura; Sedonium; Sirop pour le sommeil†; Valdispert; Valverde Sommeil†; ***UK:*** Niteherb; Phytorelax; Sedonium; ***Venez.:*** Floral Pas.

Multi-ingredient: ***Arg.:*** Armonil; Calmtabs†; Dioxicolagol; Erbonda Noche†; Herbaccion Sedante†; Incaico Serenidad; Insomnal†; Nervocalm; SDN 200; Sedanat; Sedante Arceli†; Sedante Dia; Serenil; Sigmasedan; Top Life Relax†; Trixol†; Valeriana Diates; Valeriana Oligoplex; Valeriana Relax Diates; ***Austral.:*** Calmo; Coleus Complex; Dan Shen Compound; Executive B; Extralife Sleep-Care; Goodnight Formula†; Humulus Compound; Lifesystem Herbal Plus Formula 2 Valerian†; Macro Anti-Stress†; Multi-Vitamin Day & Night†; Natural Deep Sleep; Pacifenity†; Passiflora Complex†; Passionflower Plus; Prosed-X†; ReDormin; Relaxaplex†; Valerian Plus Herbal Plus Formula 12†; Valerian†; ***Austria:*** Baldracin; Baldrian AMA; Eryval; Euvekan; Hova; Nervenruh; Nerventee St Severin; Sedadom; Sedogelat; Songha; Species nervinae; Thymoval; Valin Baldrian; Wechselstee St Severin; ***Belg.:*** Natudor; Seneuval; Songha; ***Braz.:*** Anevrase†; Passicalm†; Remilev; Sominex; Sonhare; ***Canad.:*** Herbal Nerve; Herbal Sleep Well†; Relax and Sleep; ***Chile:*** Armonyl; Recalm; Valupass; ***Cz.:*** Baldracin; Bio-Strath†; Contraspan†; Dr Theiss Rheuma Creme†; Dr Theiss Schwedenbitter; Euvekan; Hertz- und Kreislauftee†; Hova; Klosterfrau Beruhigungs Forte†; Nervova Cajova Smes; Novo-Passit; Persen; Sanason; Schlaf-Nerventee N†; Songha Night†; Species Nervinae Planta; Valofyt Neo; Visinal†; ***Fr.:*** Anxoral†; Biocarde; Euphytose; Mediflor Tisane Calmante Troubles du Sommeil No 14; Mediflor Tisane Circulation du Sang No 12; Neuroflorine; Palpipax†; Passinevryl; Phytocalm†; Spasmine; Sympaneurol; Tranquital; ***Ger.:*** Alluna Nacht; Ardeysedon; Avedorm duo; Baldrian-Dispert Nacht; Baldriparan N Stark†; Biosedon†; Boxocalm; Cefasedativ†; Cor-Select†; Dormarist†; Dormeasan; Dormo-Sern†; Dormoverlan; Dr. Scheffler Bergischer Krautertee Nerven- und Beruhigungstee; Dreierlei; Euvegal; Euvegal Entspannungs- und Einschlafdragees†; Euvegal Entspannungs- und Einschlaftropfen; Gutnacht†; Habstal-Nerv N†; Heumann Beruhigungstee Tenerval; Hingfong-Essenz Hofmanns; Hyperesa; JuDorm†; Kavosporal comp†; Kneipp Gute Nacht; Kytta-Sedativum; Leukona-Beruhigungsbad†; Lomasleep†; Luvased; Majocarmin mite†; Moradorm S; Mutellon; Nervendragees†; Nervenkapseln; Nervoregin forte†; Nervoregin phyto; Nervosana†; Neurapas; Nitrangin compositum†; Oxacant N†; Oxacant-sedativ; Pascosedon; Phytonoctu; Plantival novo; Presselin Nerven K I N†; Pronervon Phyto; Psychotonin-sed; Rhoival†; RubieSed†; Schlaf- und Nerventee; Schwedentrunk Elixier; Seda-Plantina†; Sedacur; Sedariston Konzentrat; Sedariston plus; Sedaselect D; Sedasyx†; Sedinfant N†; Selon; Sensinerv forte†; Somnuvis S†; Tornix; Valdispert comp†; Valeriana comp novum; Valeriana forte N†; Valeriana mild†; Valverde Baldrian Hopfen bei Einschlafstorungen und zur Beruhigung†; Vivinox Day; ***Hong Kong:*** Epizon†; ***Hung.:*** Euvekan; Hova; ReDormin; Sedacur; ***India:*** Well-Beeing†; ***Indon.:*** Slip-iZZZ; ***Israel:*** Calmanervin; Nerven-Dragees; Passiflora; Passiflora Compound; Songha Night; ***Ital.:*** Anevrasi; Bianco Val†; Biocalm; Calmason; Camomilla (Specie Composta)†; Dormiplant; Fitosonno; Florelax; Glicero-Valerovit; Melissa (Specie Composta)†; Noctis; Parvisedil; Reve; Sedatol; Sedopuer F; Val-Plus†; Valeriana (Specie Composta)†; ***Mex.:*** Ivel; Nervinetas; Pasinordin; Plantival; ***Pol.:*** Calmina; Cardiol C; Cardiotonic; Cholitol; Dormiplant; Fortestomachicae; Guttae Stomachicae; Hova; Kalms; Krople Zoladkowe; Lekosen; Lumewal; Neocardina; Neospasmina; Neospasmol; Nervendragees; Nervomix; Nervosol; Nerwobonisol; Passispasmin; Passispasmol; Persen; Prostapol; Relana; Sedomix; Tabletki Uspokajajace; Uroprost; Vallup; Valused; ***Port.:*** Antispasmina Colica; Gabisedil†; Neurocardol†; Songha†; Valesono†; ***Rus.:*** Doppelherz Vitalotonik (Доппельгерц Виталотоник); Herbion Drops for the Heart (Гербион Сердечные Капли); Insti (Инсти); Passifit (Пассифит); Persen (Персен); Sanason (Санасон); ***S.Afr.:*** Avena Sativa Comp; Biral; Entressdruppels HM; Helmontskruie; Krampdruppels; Restin; Stuidruppels; Wonderkroonessens; ***Spain:*** Dormiplant; Melival; Natusor Somnisedan†; Nervikan; Relana; Sedasor†; Sedonat; Valdispert Complex; ***Switz.:*** Baldriparan; Baldrisedon plus†; Dicalm†; Dormeasan; Dormiplant; Dragees pour la detente nerveuse; Dragees pour le coeur et les nerfs; Dragees pour le sommeil; Dragees sedatives Dr Welti; Hova; Nervinetten; Perpector†; Phytomed Somni†; ReDormin; Relaxane; Relaxo; Songha Night; Soporin; Strath Gouttes pour le nerfs et contre l'insomnie; Tisane calmante pour les enfants; Tisane pour le sommeil et les nerfs; Tisane relaxante N†; Valverde Coeur; Valverde Detente dragees; Valverde Sommeil; Valviska; Zeller Sommeil; ***UK:*** Avena Sativa Comp; Bio-Strath Valerian Formula; Daily Tension & Strain Relief; Digestive; Gerard House Serenity; Gerard House Somnus; Herbal Indigestion Naturtabs; Herbal Pain Relief; HRI Calm Life; HRI Golden Seal Digestive; HRI Night; Indigestion and Flatulence; Kalms; Kalms Sleep; Laxative Tablets; Menopause Relief; Modern Herbals Stress; Natrasleep; Natural Herb Tablets; Newrelax; Niteherb Plus; Nodoff; Nytol Herbal; Period Pain Relief; PMT Formula; Prementaid; Quiet Days; Quiet Life; Quiet Nite; Quiet Tyme; Relax B ; Scullcap & Gentian Tablets; Sominex Herbal; Stressless; SuNerven; Sure-Lax (Herbal); Tranquil; Unwind Herbal Nytol; Valerina Day Time; Valerina Night-Time; Vegetable Cough Remover; Wellwoman; Wind & Dyspepsia Relief; ***Venez.:*** Cratex†; Equaliv; Eufytose†; Euvekan; Femendol; Insocaps; Lupassin; Nervinetas; Pasidor; Pasifluidina; Rendetil; Sedival.

Valspodar *(BAN, USAN, rINN)*

PSC-833; SDZ-PSC-833; Valspodarum. Cyclo{[(2*S*,4*R*,6*E*)-4-methyl-2-(methylamino)-3-oxo-6-octenoyl]-L-valyl-*N*-methylglycyl-*N*-methyl-L-leucyl-L-valyl-*N*-methyl-L-leucyl-L-alanyl-D-alanyl-*N*-methyl-L-leucyl-*N*-methyl-L-leucyl-*N*-methyl-L-valyl}.

Вальсподар

$C_{63}H_{111}N_{11}O_{12}$ = 1214.6.
CAS — 121584-18-7.

Profile

Valspodar is an analogue of ciclosporin (p.1822). It inhibits P-glycoprotein, which is associated with multidrug resistance. Valspodar is being investigated in various neoplasms to restore sensitivity of resistant tumour cells to anticancer drugs, but results have been disappointing.

Valspodar inhibits the cytochrome P450 isoenzyme CYP3A4, and may reduce the metabolism and clearance of other drugs.

◊ References.

1. Advani, R, *et al.* Treatment of poor prognosis AML patients using PSC833 (valspodar) plus mitoxantrone, etoposide, and cytarabine (PSC-MEC). *Adv Exp Med Biol* 1999; **457:** 47–56.
2. Sparreboom A, Nooter K. Does P-glycoprotein play a role in anticancer drug pharmacokinetics? *Drug Resist Updat* 2000; **3:** 357–63.
3. Kang MH, *et al.* The P-glycoprotein antagonist PSC 833 increases the plasma concentrations of 6α-hydroxypaclitaxel, a major metabolite of paclitaxel. *Clin Cancer Res* 2001; **7:** 1610–17.
4. Fracasso PM, *et al.* Phase II study of paclitaxel and valspodar (PSC 833) in refractory ovarian carcinoma: a gynecologic oncology group study. *J Clin Oncol* 2001; **19:** 2975–82.
5. Baekelandt M, *et al.* Phase I/II trial of the multidrug-resistance modulator valspodar combined with cisplatin and doxorubicin in refractory ovarian cancer. *J Clin Oncol* 2001; **19:** 2983–93.
6. Baer MR, *et al.* Phase 3 study of the multidrug resistance modulator PSC-833 in previously untreated patients 60 years of age and older with acute myeloid leukemia: Cancer and Leukemia Group B Study 9720. *Blood* 2002; **100:** 1224–32.
7. Ma MK, *et al.* Pharmacokinetic study of infusional valspodar. *J Clin Pharmacol* 2002; **42:** 412–18.
8. Greenberg PL, *et al.* Mitoxantrone, etoposide, and cytarabine with or without valspodar in patients with relapsed or refractory acute myeloid leukemia and high-risk myelodysplastic syndrome: a phase III trial (E2995). *J Clin Oncol* 2004; **22:** 1078–86. Correction. *ibid.*; 2747.
9. van der Holt B, *et al.* The value of the MDR1 reversal agent PSC-833 in addition to daunorubicin and cytarabine in the treatment of elderly patients with previously untreated acute myeloid leukemia (AML), in relation to MDR1 status at diagnosis. *Blood* 2005; **106:** 2646–54.
10. Friedenberg WR, *et al.* Phase III study of PSC-833 (valspodar) in combination with vincristine, doxorubicin, and dexamethasone (valspodar/VAD) versus VAD alone in patients with recurring or refractory multiple myeloma (E1A95): a trial of the Eastern Cooperative Oncology Group. *Cancer* 2006; **106:** 830–8.

Vanilla

Baunilha; Vainilla; Vanilla Beans; Vanilla Pods.

Pharmacopoeias. In *USNF*.

USNF 26 (Vanilla). The cured, full-grown, unripe fruit of *Vanilla planifolia*, often known in commerce as Mexican, Bourbon, or Madagascar vanilla, or of *V. tahitensis*, known in commerce as Tahitian vanilla (Orchidaceae). Vanilla that has become brittle should not be used. Store in airtight containers at a temperature not exceeding 8°.

Profile

Vanilla is used as a flavour and in perfumery. However, the odour and flavour of vanilla are not entirely due to vanillin (see below) but depend on the presence of other aromatic substances. Preparations of vanilla have been used in aromatherapy.

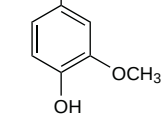
Preparations

USNF 26: Vanilla Tincture.

Vanillin

Vainillina; Vaniliini; Vanilin; Vanilinas; Vanillic Aldehyde; Vanilline; Vanillinum; Wanilina. 4-Hydroxy-3-methoxybenzaldehyde.

$C_8H_8O_3$ = 152.1.
CAS — 121-33-5.



Pharmacopoeias. In *Eur.* (see p.vii) and *Viet.* Also in *USNF*.

Ph. Eur. 6.2 (Vanillin). White or slightly yellowish crystalline needles or powder. M.p. 81° to 84°. Slightly soluble in water; freely soluble in alcohol and in methyl alcohol; it dissolves in dilute solutions of alkali hydroxides. Protect from light.

USNF 26 (Vanillin). Fine, white to slightly yellow crystals, usually needle-like, having an odour and taste suggestive of vanilla.

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.

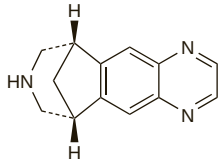
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Belg.:*** Pulmex; Pulmex Baby; ***Turk.:*** Musilaks.

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.

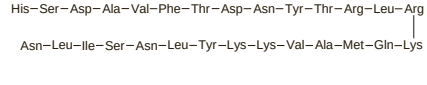
A gene therapy product supplying the gene for vascular endothelial growth factor D via an adenoviral vector is under investigation for the prevention of stenosis in synthetic grafts used in haemodialysis.

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*.

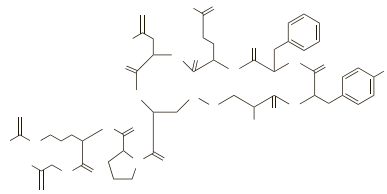
Pharmacopoeias. In *US*, which includes both argipressin and lypressin in this title.
An injection is included in *Jpn*.
USP 31 (Vasopressin). A polypeptide hormone having the properties of causing the contraction of vascular and other smooth muscles, and of antidiuresis. It is prepared by synthesis 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).