

ingredient herbal preparation promoted for weight loss; one patient required emergency liver transplantation.<sup>1</sup>

- 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.:** Scabidid; **Ital.:** Foot Zeta; Micofoot; Steril Zeta.

### Valepotriates

Valepotriates.

### Acevaltrate (rINN)

Acévaltrate; Acevaltrato; Acevaltratum. 4-Acetoxyethyl-(1 or 6)-3-(acetoxy-3-methylbutyryloxy)-1,6,7,7a-tetrahydro-(6 or 1)-isovaleryloxy-cyclopenta[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-isovaleryloxy-methylcyclopenta[c]pyran-7-spiro-2'-oxiran.

Дидровальтрат

$C_{22}H_{30}O_8$  = 424.5.

CAS — 18296-45-2.

### Valtrate (pINN)

Valtrato; Valtratum. 4-Acetoxyethyl-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 kozłki; Kozlikový kořen; Macskagyökér; Valer; Valerianaanijuri; Valerian Rhizome; Valerian Root; Valeriana; Valeriana radix; Valerianarot; Valériane, racine de; Valerijonų šaknis.

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% w/w of essential oil for the whole drug and not less than 0.3% w/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 valeric 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

- Houghton P. Valerian. *Pharm J* 1994; **253**: 95–6.
- Houghton PJ. The scientific basis for the reputed activity of valerian. *J Pharm Pharmacol* 1999; **51**: 505–12.
- Plushner SL. Valerian: valeriana officinalis. *Am J Health-Syst Pharm* 2000; **57**: 328–35.

- Stevinson C, Ernst E. Valerian for insomnia: a systematic review of randomized clinical trials. *Sleep Med* 2000; **1**: 91–9.
- Bent S, et al. Valerian for sleep: a systematic review and meta-analysis. *Am J Med* 2006; **119**: 1005–12.

**Adverse effects.** Liver damage<sup>1</sup> 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.<sup>2</sup>

- MacGregor FB, et al. Hepatotoxicity of herbal remedies. *BMJ* 1989; **299**: 1156–7.
- 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:** Baldrinet; **Belg.:** Dormiplant; Relaxine; Valdispert; Valeria; **Braz.:** Noctaval; Re calm; Sonoripant; Traminer; Valdorm; Valeriane; Valerimex; Valerian; Valerian; Valezen; Valmane; **Canad.:** Nytol Natural Source; Sleep-Eze V Natural; Unisom Natural Source; **Chile:** Somnax; **Cz.:** Koren Kozliku Lekarstevni; Kozlik; Valdispert; **Fin.:** Valin; **Ger.:** Baldorm; Baldriparan Stark; Baldriwt; Baldurat; Cefaluna; Cefan; Dolestan; Euvegal Balance; Kytta-Sedativum; Luvased mono; Phytodormat; Recvalysat; Sedonium; Sporal mono; Valdispert; **Hong Kong:** Cirku Sed; **Israel:** Relaxine; Valerion; **Ital.:** Ticalma; Val-Uno; **Mex.:** Neolaikan; **Neth.:** Dormiplant; Sedonium; Valdispert; **Pol.:** Cirkused; Relana Forte; Valerian; **Port.:** Valdispert; Valditas; **Rus.:** Novo-Passit (Hobo-Flaccor); **S.Afr.:** Calmettes; **Spain:** Ansoyker; Cirkused; Coenrelax; Tauval; Valdispert; Valeriana Orto; Valse-dan; **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.:** Armonik; Calmtabs; Dioxicolagol; Erbonda Noche; Herbacion Sedante; Incaico Serenidad; Insomnal; Nervocalm; SDN 200; Sedanet; Sedante Arcefi; 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; Pacifenty; Passiflora Complex; Passionflower Plus; Prosed-X; ReDormin; Relaxaplex; Valerian Plus Herbal Plus Formula 12; Valerian; **Austria:** Baldracin; Baldrian AMA; Eryval; Euvekan; Hova; Nerveneruh; Nerventee St Severin; Sedadom; Sedogelat; Songha; Species nervinae; Thymoval; Valin Baldrian; Wechseltsee St Severin; **Belg.:** Natudor; Seneval; Songha; **Braz.:** Anevrax; Passicalm; Remilev; Somnax; Sonhare; **Canad.:** Herbal Nerve; Herbal Sleep VWell; Relax and Sleep; **Chile:** Armony; Re calm; Valupass; **Cz.:** Baldracin; Bio-Strath; Contrapan; Dr Theiss Rheuma Creme; Dr Theiss Schwedenbitter; Euvekan; Hertz- und Kreislauftee; Hova; Klosterfrau Beruhigungsforte; Nervova Cajova Smes; Novo-Passit; Persen; Sanason; Schlaf-Nerventee Nj; Songha Night; Species Nervinae Planta; Valofyt Neo; Vinalif; **Fr.:** Anxoral; Biocard; Euphytose; Mediflor Tisane Calmante Tribules du Sommeil No 14; Mediflor Tisane Circulation du Sang No 12; Neuroflorine; Palipaxat; Passinevryl; Phytocalm; Spasmine; Sympaneuro; Tranquital; **Ger.:** Alluna Nacht; Ardeyседon; Avsedorm 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 Entspannung- und Einschlafdragees; Euvegal Entspannung- und Einschlaftröpfchen; Gutmacht; Habstalt-Nerv Nj; Heumann Beruhigungstee Teneval; Hingfong-Essenz Hofmanns; Hypersea; JuDorm; Kavosporal comp; Kneipp Gute Nacht; Kytta-Sedativum; Leukona-Beruhigungsbad; Lomasleep; Luvased; Majocamin mitef; Moradorm S; Mutellon; Nervendragees; Nervenkapseln; Nervoregin forte; Nervoregin phyto; Nervosana; Neurapas; Nitrangin compositum; Oxacant Nj; Oxacant-sedativ; Pasosedon; Phytocactu; Plantival novo; Presselin Nerv K I Nj; Pronerven Phyto; Psychotonin-sed; Rhovalif; RubieSed; Schlaf- und Nerventee; Schweden-trunk Elxier; Seda-Plantina; Sedacur; Sedariston Konzentrat; Sedariston plus; Sedaselect D; Sedasyct; Sedinfant Nj; Selon; Sensinerv forte; Somnux S; Tormix; Valdispert comp; Valeriana comp novum; Valeriana forte Nj; Valeriana mild; Valverde Baldrian Hopfen bei Einschlafstörungen und zur Beruhigung; Vinox Day; **Hong Kong:** Epizon; **Hung.:** Euvekan; Hova; ReDormin; Sedacur; **India:** Well-Being; **Indon.:** Slip-iZZZ; **Israel:** Calmanervin; Nerven-Dragees; Passiflora; Passiflora Compound; Songha Night; **Ital.:** Anevrax; 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; Fortestomachica; Guttae Stomachicae; Hova; Kalms; Kropke Zoladkowie; Leko-sen; Lumeval; Neocardina; Neospasmina; Neospasmol; Nervendragees; Nervomix; Nervosol; Nervobonisol; Passipasmin; Passipasmol; Persen; Prostopal; Relana; Sedomix; Tabletki Uspokajajace; Uproprost; Vallup; Valused; **Port.:** Antispasmina Colica; Gabisedil; Neurocardol; Songha; Valasonj; **Rus.:** Doppelherz Vitalotonik (Допльгерц Виталотоник); Herbon 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; Natu-sor Somnisedant; Nervikan; Relana; Sedasor; Sedonax; 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; Nervinette; Perceptor; 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 Nj; Valverde Coeur; Valverde Detente dragees; Valverde Sommeil; Valvika; Zeller Sommeil; **UK:** Avena Sativa Comp; Bio-Strath Valerian Formula; Daily Tension & Strain Relief; Digestive; Gerard House Serenity; Gerard House Somnus; Herbal Indigestion Naturtats; 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 Tyne; Relax B; Scullcap & Gentian Tablets; Somnax Herbal; Stressless; SuNerven Sure-Lax (Herbal); Tranquil; Unwind Herbal Nytol; Valeriana Day Time; Valeriana Night-Time; Vegetable Cough Remover; Wellwomn; Wind & Dyspepsia Relief; **Venez.:** Cratex; Equaliv; Eufytose; Euvekan; Femendol; Inscaps; Lupassin; Nervinetas; Pasidor; Passifludina; Rendetil; Sedval.

### Valspodar (BAN, USAN, rINN)

PSC-833; SDZ-PSC-833; Valspodarum. Cyclo[[[(2S,4R,6E)-4-methyl-2-(methylamino)-3-oxo-6-octenoil]-L-valyl-N-methylglycyl-L-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

- Advani, R, et al. Treatment of poor prognosis AML patients using PSC833 (valsopodar) plus mitoxantrone, etoposide, and cytarabine (PSC-MEC). *Adv Exp Med Biol* 1999; **457**: 47–56.
- Sparreboom A, Nooter K. Does P-glycoprotein play a role in anticancer drug pharmacokinetics? *Drug Resist Updat* 2000; **3**: 357–63.
- Kang MH, et al. The P-glycoprotein antagonist PSC 833 increases the plasma concentrations of 6a-hydroxypaclitaxel, a major metabolite of paclitaxel. *Clin Cancer Res* 2001; **7**: 1610–17.
- Fracasso PM, et al. Phase II study of paclitaxel and valsopodar (PSC 833) in refractory ovarian carcinoma: a gynecologic oncology group study. *J Clin Oncol* 2001; **19**: 2975–82.
- Baekelandt M, et al. Phase III trial of the multidrug-resistance modulator valsopodar combined with cisplatin and doxorubicin in refractory ovarian cancer. *J Clin Oncol* 2001; **19**: 2983–93.
- 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.
- Ma MK, et al. Pharmacokinetic study of infusional valsopodar. *J Clin Pharmacol* 2002; **42**: 412–18.
- Greenberg PL, et al. Mitoxantrone, etoposide, and cytarabine with or without valsopodar 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.
- 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.
- Friedenberg WR, et al. Phase III study of PSC-833 (valsopodar) in combination with vincristine, doxorubicin, and dexamethasone (valsopodar/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

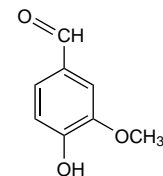
**USNF 26:** Vanilla Tincture.

### 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.