

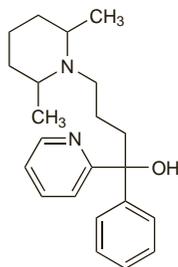
Pirmenol Hydrochloride (USAN, rINN)

CL-845; CL-845; Hidrocloruro de pimenol; Pirménol; Chlorhydrate de; Pirmenoli Hydrochloridum. (±)-*cis*-2,6-Dimethyl- α -phenyl- α -2-pyridyl-1-piperidinebutanol hydrochloride.

Пирменоло Гидрохлорид

$C_{22}H_{30}N_2O \cdot HCl = 374.9$.

CAS — 68252-19-7 (pirmenol); 61477-94-9 (pirmenol hydrochloride).



(pirmenol)

Profile

Pirmenol hydrochloride is an antiarrhythmic with class Ia activity (p.1153).

♦ References.

- Hampton EM, *et al.* Initial and long-term outpatient experience with pirmenol for control of ventricular arrhythmias. *Eur J Clin Pharmacol* 1986; **31**: 15–22.
- Stringer KA, *et al.* Enhanced pirmenol elimination by rifampin. *J Clin Pharmacol* 1988; **28**: 1094–7.
- Janiczek N, *et al.* Pharmacokinetics of pirmenol enantiomers and pharmacodynamics of pirmenol racemate in patients with premature ventricular contractions. *J Clin Pharmacol* 1997; **37**: 502–13.

Pitavastatin (rINN)

Itavastatin; Nisvastatin; NK-104; Pitavastatina; Pitavastatine; Pitavastatinum. (3*R*,5*S*,6*E*)-7-[2-Cyclopropyl-4-(*p*-fluorophenyl)-3-quinolyl]-3,5-dihydroxy-6-heptenoic acid.

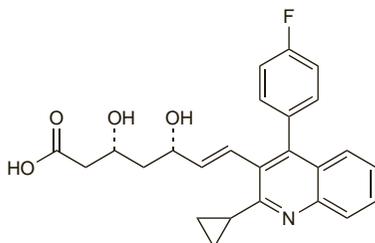
Питавастатин

$C_{25}H_{34}FNO_4 = 421.5$.

CAS — 147511-69-1 (pitavastatin); 147526-32-7 (pitavastatin calcium).

ATC — C10AA08.

ATC Vet — QC10AA08.

**Profile**

Pitavastatin, a hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (or statin), is a lipid regulating drug with similar properties to simvastatin (p.1390). It is used as the calcium salt in the treatment of hyperlipidaemias.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn: Livalo.

Plant Stanols and Sterols

Phytosterols.

Станолы и Стерины из Растений

Phytosterol

Fitosteroli; Fitoszterin; Fytosterol; Fytosteroli; Phytosterin; Phytostérol; Phytosterolum.

Фитостерин; Фитостерол

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

Ph. Eur. 6.2 (Phytosterol). A natural mixture of sterols obtained from plants of the genera *Hypoxis*, *Pinus*, and *Picea*. It contains not less than 70% β -sitosterol, calculated with reference to the dried substance. A white or almost white powder. Practically insoluble in water; soluble in tetrahydrofuran; sparingly soluble in ethyl acetate. Store in airtight containers. Protect from light.

The symbol † denotes a preparation no longer actively marketed

Sitostanol

Dihydro- β -sitosterol; Fucostanol; β -Sitostanol; Stigmastanol. (3 β ,5 α)-Stigmastan-3-ol.

Ситостанол

$C_{29}H_{52}O = 416.7$.

CAS — 83-45-4.

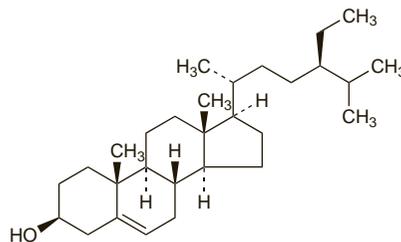
Sitosterol

β -Sitosterin; β -Sitosterol. (3 β)-Stigmast-5-en-3-ol.

Ситостерин; Ситостерол

$C_{29}H_{50}O = 414.7$.

CAS — 83-46-5.

**Profile**

Stanols and sterols occur naturally in plants and are chemically related to cholesterol. The term phytosterol is used to describe both unsaturated plant sterols and their saturated (hydrogenated) counterparts, plant stanols (phytostanols). Sitosterol, campesterol, and stigmasterol are the commonest phytosterols; their respective stanols are found in lower amounts naturally, but can be produced by hydrogenation of sterols.

Dietary phytosterols have a cholesterol-lowering action; they reduce cholesterol absorption from the intestine and may also have other mechanisms. Sitosterol has been used as a lipid regulating drug, and both sterol and stanol esters (formed by esterification with unsaturated fatty acids) have been incorporated into margarines and other food products for use in the dietary management of hypercholesterolaemia. Sitosterol, sitostanol, and other phytosterols, are also used in nutritional supplements.

Sitosterol is also used in benign prostatic hyperplasia (p.2178), although its mechanism of action is not clear. It is given orally in usual initial doses of 20 mg three times daily.

There have been reports of bleeding complications associated with supplements containing phytosterols.

♦ References.

- Wilt T, *et al.* Beta-sitosterols for benign prostatic hyperplasia. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 1999 (accessed 24/06/05).
- Law M. Plant sterol and stanol margarines and health. *BMJ* 2000; **320**: 861–4.
- Lichtenstein AH, Deckelbaum RJ. Stanol/sterol ester-containing foods and blood cholesterol levels: a statement for healthcare professionals from the Nutrition Committee of the Council on Nutrition, Physical Activity, and Metabolism of the American Heart Association. *Circulation* 2001; **103**: 1177–9. Also available at: <http://circ.ahajournals.org/cgi/reprint/103/8/1177.pdf> (accessed 01/06/08)
- Katan MB, *et al.* Efficacy and safety of plant stanols and sterols in the management of blood cholesterol levels. *Mayo Clin Proc* 2003; **78**: 965–78.
- Health Canada. Sterol and sterolin-containing products: hematologic adverse reactions. *Can Adverse React News* 2004; **14** (2): 1–2. Also available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/carn-bcei_v14n2-eng.pdf (accessed 19/08/08)
- Miettinen TA, Gylling H. Plant stanol and sterol esters in prevention of cardiovascular diseases: a review. *Int J Clin Pharmacol Ther* 2006; **44**: 247–50.
- Devaraj S, Jialal I. The role of dietary supplementation with plant sterols and stanols in the prevention of cardiovascular disease. *Nutr Rev* 2006; **64**: 348–54.
- Moruisi KG, *et al.* Phytosterols/stanols lower cholesterol concentrations in familial hypercholesterolemic subjects: a systematic review with meta-analysis. *J Am Coll Nutr* 2006; **25**: 41–8.
- Naruszewicz M, Kozłowska-Wojciechowska M. Plant sterols beyond low-density lipoprotein-cholesterol. *Br J Nutr* 2007; **98**: 454–5.
- Weingärtner O, *et al.* Pflanzliche Sterole als Nahrungsmitteladditiva zur Prävention kardiovaskulärer Erkrankungen. *Dtsch Med Wochenschr* 2008; **133**: 1201–4.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg: Prostacur; **Austria:** Harzol; **Ger:** Azuprostat; Flemun†; Harzol; Prostasal†; Sito-Land†; **It:** Sitosterin; **Trinastanol;** **Indon:** Cholbalance; **Pol:** Prostalizin; **Prosterol;** **Thai:** Mebo; **UAE:** Mebo.

Multi-ingredient Arg: Cholesterol Reducing Plan†; Sojasterol†; SX-22; **Fr:** Bakol; **Hong Kong:** Basikol; **Physiogel;** **Rus:** Herbion Urtica (Тербион Уртика); **UK:** Kolestop; **Lestrin;** **USA:** Better Cholesterol; Better Prostate†; Cholesterol Support; Prostate Support; Super Beta Prostate.

Plasminogen (BAN)

Plasminógeno.

CAS — 9001-91-6.

Profile

Plasminogen is the specific substance derived from plasma which, when activated to plasmin, has the property of lysing fibrinogen, fibrin, and some other proteins. Its role in the control of haemostasis is described further on p.1045. Plasminogen has been investigated as a thrombolytic and has been used with other blood products in wound-sealant preparations.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient Arg: Tissucol Duo Quick†; **Austria:** Tissucol; Tissucol Duo Quick; **Belg:** Tissucol Duo; **Canad:** Tisseel; **Cz:** Tissucol; **Denm:** Tisseel Duo Quick; **Fin:** Tisseel Duo Quick; **Fr:** Tissucol; **Ger:** Tissucol Duo S; **Tissucol-Kit;** **Hong Kong:** Tisseel; **Hung:** Tissucol-Kit; **Israel:** Tisseel; **Mex:** Tissucol†; **Spain:** Tissucol Duo; **Swed:** Tisseel Duo Quick; **Switz:** Tissucol; Tissucol Duo S; **UK:** Tisseel.

Policosanol

Поликосанол

CAS — 142583-61-7.

ATC — C10AX08.

ATC Vet — QC10AX08.

Octacosanol

Cluytl Alcohol; Montanyl Alcohol; Octacosyl Alcohol. 1-Octacosanol.

Октакосанол

$C_{28}H_{58}O = 410.8$.

CAS — 557-61-9.

Profile

Policosanol is a mixture of higher primary aliphatic alcohols (fatty alcohols) derived from plant waxes such as sugar cane wax; it is also found in beeswax and in wheat-germ oil (p.2415). The main component is octacosanol. Policosanol appears to have cholesterol-lowering properties and has been used in the treatment of hypercholesterolaemias, although its benefit has been disputed. Both policosanol and octacosanol are used in nutritional supplements.

♦ References.

- Gouni-Berthold I, Berthold HK. Policosanol: clinical pharmacology and therapeutic significance of a new lipid-lowering agent. *Am Heart J* 2002; **143**: 356–65.
- Pepping J. Policosanol. *Am J Health-Syst Pharm* 2003; **60**: 1112–5.
- Berthold HK, *et al.* Effect of policosanol on lipid levels among patients with hypercholesterolemia or combined hyperlipidemia: a randomized controlled trial. *JAMA* 2006; **295**: 2262–9.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg: Lipex; **Austral:** Polico; **Chile:** PPG; **Indon:** Polikos; **Mex:** Mercol; **S.Afr:** Phytacor; **Venez:** Dupla†.

Multi-ingredient Ital: Colesterase; Novostatin; **UK:** Chol-Aid; Octacosanol.

Polythiazide (BAN, USAN, rINN) ⊗

NSC-108161; P-2525; Politiazida; Polythiazidum; Polytiatsidi; Polytiiazid. 6-Chloro-3,4-dihydro-2-methyl-3-(2,2,2-trifluoroethylthiomethyl)-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

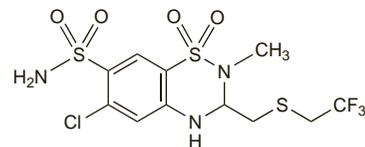
Политиазид

$C_{11}H_{13}ClF_3N_3O_3S_3 = 439.9$.

CAS — 346-18-9.

ATC — C03AA05.

ATC Vet — QC03AA05.

**Pharmacopoeias.** In *Br.*

BP 2008 (Polythiazide). A white or almost white, crystalline powder with an alliacious odour. Practically insoluble in water and in chloroform; sparingly soluble in alcohol.

Adverse Effects, Treatment, and Precautions

As for Hydrochlorothiazide, p.1307.

Interactions

As for Hydrochlorothiazide, p.1309.

Pharmacokinetics

Polythiazide is fairly readily absorbed from the gastrointestinal tract. The estimated plasma elimination half-life is about 26 hours. More than 80% may be bound to plasma proteins. It is

The symbol ⊗ denotes a substance whose use may be restricted in certain sports (see p.vii)

excreted mainly in the urine as unchanged polythiazide and metabolites.

References.

- Hobbs DC, Twomey TM. Kinetics of polythiazide. *Clin Pharmacol Ther* 1978; **23**: 241–6.

Uses and Administration

Polythiazide is a thiazide diuretic with actions and uses similar to those of hydrochlorothiazide (p.1310). It is given orally for hypertension (p.1171), and for oedema, including that associated with heart failure (p.1165).

Diuresis begins within about 2 hours of an oral dose, and lasts for 24 to 48 hours.

In the treatment of **hypertension** the usual dose is stated to be 2 to 4 mg daily, either alone or with other antihypertensives although doses of only 0.5 to 1 mg may be adequate. In the treatment of **oedema** the usual dose is 1 to 4 mg daily.

Preparations

BP 2008: Polythiazide Tablets.

Proprietary Preparations (details are given in Part 3)

Belg.: Renesef; **USA:** Renesef.

Multi-ingredient: **Ger.:** Polypress†; **USA:** Minizide†; Renese R†.

Potassium Canrenoate (BANM, rINN) ⓧ

Aldadiene Potassium; Canrenoate de Potassium; Canrenoate Potassium (USAN); Canrenoato de potasio; Kalii Canrenoas; Kaliumkanrenoatti; Kaliumkanrenoat; MF-465a; SC-14266. Potassium 17-hydroxy-3-oxo-17 α -pregna-4,6-diene-21-carboxylate.

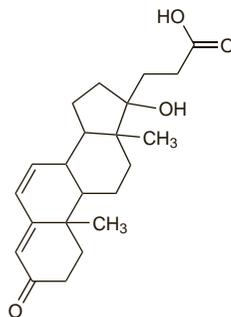
Калия Канреноат

$C_{22}H_{29}KO_4 = 396.6$.

CAS — 4138-96-9 (canrenoic acid); 2181-04-6 (potassium canrenoate).

ATC — C03DA02.

ATC Vet — QC03DA02.



(canrenoic acid)

Pharmacopoeias. In *Jpn*.

Adverse Effects and Precautions

As for Spironolactone, p.1400. Irritation or pain may occur at the site of injection.

Effects on endocrine function. A lower incidence of gynaecomastia has been reported in patients with hepatic cirrhosis and ascites during use of potassium canrenoate than with equivalent doses of spironolactone,¹ and spironolactone-induced gynaecomastia disappeared when spironolactone was replaced by potassium canrenoate in a patient with hyperaldosteronism.² This suggests that metabolites other than canrenone (a common metabolite of both canrenoate and spironolactone thought to be responsible for their activity) or possibly spironolactone itself may be responsible for the anti-androgenic effects of spironolactone.^{3,4}

- Bellati G, Ideo G. Gynaecomastia after spironolactone and potassium canrenoate. *Lancet* 1986; **i**: 626.
- Dupont A. Disappearance of spironolactone-induced gynaecomastia during treatment with potassium canrenoate. *Lancet* 1985; **ii**: 731.
- Gardiner P. Spironolactone and potassium canrenoate metabolism. *Lancet* 1985; **ii**: 1432.
- Ovendiek JWPM, Merkus FWHM. Spironolactone metabolism and gynaecomastia. *Lancet* 1986; **i**: 1103.

Interactions

As for Spironolactone, p.1401.

Uses and Administration

Potassium canrenoate is a potassium-sparing diuretic with actions and uses similar to those of spironolactone (p.1401). Canrenone (p.1239) is a metabolite common to both drugs, but its contribution to the pharmacological action is unclear. Potassium canrenoate is used in the treatment of refractory oedema associated with heart failure (p.1165) or hepatic disease when an injectable aldosterone antagonist is required. It may be given in doses of 200 to 400 mg daily, increasing to 800 mg daily in exceptional cases; it is given by slow intravenous injection over a period of 2 to 3 minutes for each 200 mg or by intravenous infusion in glucose 5% or sodium chloride 0.9%.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Aldactone; **Belg.:** Canrenol; Soldactone; **Cz.:** Aldactone; Canrenol†; **Fr.:** Soldactone; **Ger.:** Aldactone; Kalium-Car; **Hung.:** Aldactone†; **Ital.:** Dikantal; Diurek; Kanrenol; Luvin; Venactone†; **Neth.:** Soldactone; **Norw.:** Soldactone†; **Pol.:** Aldactone; **Switz.:** Soldactone.

Multi-ingredient: **Ital.:** Kadiur.

Prajmalium Bitartrate (BAN, rINN)

Bitartrato de prajmalio; GT-1012; NPAB; Prajmalii Bitartras; Prajmaline Bitartrate; Prajmalium, Bitartrate de. *N*-Propylajmalinium hydrogen tartrate.

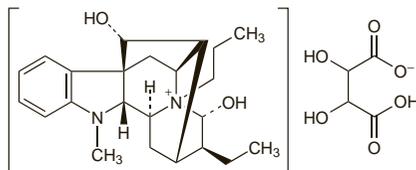
Праймалия Битартрат

$C_{23}H_{33}N_2O_2 \cdot C_4H_5O_6 = 518.6$.

CAS — 35080-11-6 (prajmalium); 2589-47-1 (prajmalium bitartrate).

ATC — C01BA08.

ATC Vet — QC01BA08.



Adverse Effects and Precautions

As for Ajmaline, p.1206.

Effects on the liver. Cholestatic jaundice associated with pruritus, chills, and eosinophilia¹ was attributed to an allergic reaction to prajmalium bitartrate in a patient 20 days after the start of treatment.

- Rotmensch HH, et al. Cholestatic jaundice: an immune response to prajmalium bitartrate. *Postgrad Med J* 1980; **56**: 738–41.

Effects on mental state. Confusion and disorientation in time and place¹ occurred on 2 occasions in a 67-year-old man given prajmalium bitartrate 100 mg daily for the control of tachycardia; the confusion rapidly disappeared when prajmalium was withdrawn.

- Lessing JB, Copperman JJ. Severe cerebral confusion produced by prajmalium bitartrate. *BMJ* 1977; **2**: 675.

Uses and Administration

Prajmalium is a class I antiarrhythmic (p.1153) and is the *N*-propyl derivative of ajmaline (p.1206). It is given orally as the bitartrate in the management of supraventricular and ventricular arrhythmias (p.1160) in initial doses of 60 to 80 mg daily. Maintenance doses of 20 to 40 mg daily in divided doses are used.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Neo-Gilurytmal; **Cz.:** Neo-Gilurytmal; **Ger.:** Neo-Gilurytmal; **Hung.:** Neo-Gilurytmal; **Indon.:** Neo-Gilurytmal; **Israel:** Neo-Gilurytmal†.

Multi-ingredient: **Spain:** Cresophene.

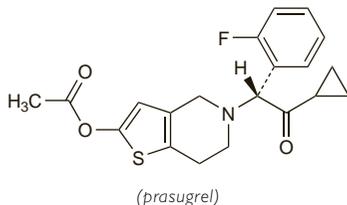
Prasugrel Hydrochloride (USAN, rINN)

LY-640315; Prasugrel, Chlorhydrate de; Prasugrel, hidroclocloruro de; Prasugreli Hydrochloridum. 5-[(1*R*)-2-Cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate hydrochloride.

Празугрела Гидрохлорид

$C_{20}H_{20}FNO_3 \cdot HCl = 409.9$.

CAS — 389574-19-0.



(prasugrel)

Profile

Prasugrel hydrochloride is a thienopyridine antiplatelet drug with similar properties to clopidogrel (p.1250). It is under development for cardiovascular disorders.

References.

- Wiviott SD, et al. Randomized comparison of prasugrel (CS-747, LY640315), a novel thienopyridine P2Y₁₂ antagonist, with clopidogrel in percutaneous coronary intervention: results of the Joint Utilization of Medications to Block Platelets Optimally (JUMBO)-TIMI 26 trial. *Circulation* 2005; **111**: 3366–73.

- Jakubowski JA, et al. A multiple dose study of prasugrel (CS-747), a novel thienopyridine P2Y₁₂ inhibitor, compared with clopidogrel in healthy humans. *Br J Clin Pharmacol* 2006; **63**: 421–30.
- Brandt JT, et al. A comparison of prasugrel and clopidogrel loading doses on platelet function: magnitude of platelet inhibition is related to active metabolite formation. *Am Heart J* 2007; **153**: 66.
- Wiviott SD, et al. TRITON-TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2007; **357**: 2001–15.
- Wiviott SD, et al. PRINCIPLE-TIMI 44 Investigators. Prasugrel compared with high loading- and maintenance-dose clopidogrel in patients with planned percutaneous coronary intervention: the Prasugrel in Comparison to Clopidogrel for Inhibition of Platelet Activation and Aggregation-Thrombolysis in Myocardial Infarction 44 trial. *Circulation* 2007; **116**: 2923–32.
- Antman EM, et al. Early and late benefits of prasugrel in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a TRITON-TIMI 38 (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction) analysis. *J Am Coll Cardiol* 2008; **51**: 2028–33.

Pravastatin Sodium (BANM, USAN, rINN)

CS-514; Eptastatin Sodium; 3 β -Hydroxycompactin Sodium; Natrii Pravastatinum; Pravastatininatrium; Pravastatin sodná sůl; Pravastatina sódica; Pravastatine sodique; Pravastatinnatrium; Pravastatino natrio druska; Pravastatinum natrium; Pravastatinnatrium; SQ-31000. Sodium (3*R*,5*R*)-7-[(1*S*,2*S*,6*S*,8*S*,8*R*)-1,2,6,7,8,8a-hexahydro-6-hydroxy-2-methyl-8-[(*S*)-2-methylbutyryloxy]-1-naphthyl]-3,5-dihydroxyheptanoate.

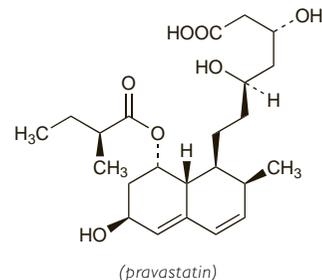
Натрий Правастатин

$C_{23}H_{35}O_7Na = 446.5$.

CAS — 81093-37-0 (pravastatin); 81131-70-6 (pravastatin sodium).

ATC — C10AA03.

ATC Vet — QC10AA03.



(pravastatin)

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

Ph. Eur. 6.2 (Pravastatin Sodium). A white to yellowish-white, hygroscopic, powder or crystalline powder. Freely soluble in water and in methyl alcohol; soluble in dehydrated alcohol. A 5% solution in water has a pH of 7.2 to 9.0. Store in airtight containers.

USP 31 (Pravastatin Sodium). A white to yellowish white hygroscopic powder. Freely soluble in water and in methyl alcohol; soluble in alcohol; practically insoluble in chloroform, in ether, and in ethyl acetate; very slightly soluble in acetonitrile. Store in airtight containers.

Adverse Effects and Precautions

As for Simvastatin, p.1390.

Interactions

The interactions of statins with other drugs are described under simvastatin (p.1392). Pravastatin is not significantly metabolised by the cytochrome P450 enzyme system and does not have the same interactions with enzyme inhibitors as simvastatin, although caution has been advised when such combinations are used. Increased plasma-pravastatin concentrations have been reported in some patients receiving ciclosporin and low doses should be used (see Uses and Administration, below).

Pharmacokinetics

Pravastatin is rapidly but incompletely absorbed from the gastrointestinal tract and undergoes extensive first-pass metabolism in the liver, its primary site of action. The absolute bioavailability of pravastatin is 17%. About 50% of the circulating drug is bound to plasma proteins. The plasma elimination half-life of pravastatin is 1.5 to 2 hours. About 70% of an oral dose of pravastatin is excreted in the urine.