

Profile

Pinacidil is a potassium-channel opener (p.1155) that produces direct peripheral vasodilatation of the arterioles. It has been used in the management of hypertension. It reduces blood pressure and peripheral resistance and produces fluid retention. Tachycardia and an increase in cardiac output occur mainly as a reflex response to the reduction in peripheral resistance.

◇ Reviews.

1. Friedel HA, Brogden RN. Pinacidil: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in the treatment of hypertension. *Drugs* 1990; **39**: 929–67.

Pindolol (BAN, USAN, rINN) ⊗

LB-46; Pindololi; Pindololis; Pindololum; Prindolol; Prinodolol. 1-(Indol-4-yloxy)-3-isopropylaminopropan-2-ol.

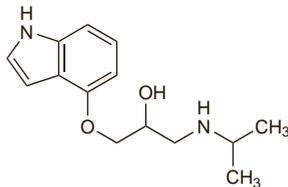
ПИНДОЛОЛ

$C_{14}H_{20}N_2O_2 = 248.3$.

CAS — 13523-86-9.

ATC — C07AA03.

ATC Vet — QC07AA03.



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

Ph. Eur. 6.2 (Pindolol). A white or almost white, crystalline powder. Practically insoluble in water; slightly soluble in methyl alcohol; dissolves in dilute mineral acids. Protect from light.

USP 31 (Pindolol). A white to off-white, crystalline powder with a faint odour. Practically insoluble in water; very slightly soluble in chloroform; slightly soluble in methyl alcohol. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Effects on lipid metabolism. Beta blockers can affect plasma-lipid concentrations, although this may be less of a problem with those that have intrinsic sympathomimetic activity. For reference to the lack of effect of pindolol, see p.1227.

Tremor. Fine tremor in the extremities of 5 patients during pindolol therapy was considered to have been due to its partial agonist activity.¹

1. Hod H, et al. Pindolol-induced tremor. *Postgrad Med J* 1980; **56**: 346–7.

Interactions

The interactions associated with beta blockers are discussed on p.1228.

Pharmacokinetics

Pindolol is almost completely absorbed from the gastrointestinal tract and peak plasma concentrations are obtained about 1 to 2 hours after an oral dose. It has a bioavailability of about 87%. About 40 to 60% is reported to be bound to plasma proteins. It is moderately lipid-soluble. Pindolol crosses the placenta and is distributed into breast milk. It is only partially metabolised in the liver and is excreted in the urine both unchanged and in the form of metabolites. A plasma elimination half-life of 3 to 4 hours has been reported in healthy adults. The half-life may be prolonged in elderly hypertensive patients and in patients with renal or hepatic impairment.

Uses and Administration

Pindolol is a non-cardioselective beta blocker (p.1225). It is reported to have intrinsic sympathomimetic activity but little membrane-stabilising activity.

Pindolol is used in the management of hypertension (p.1171), angina pectoris (p.1157), cardiac arrhythmias (p.1160), and other cardiovascular disorders. It is also used in glaucoma (p.1873).

In **hypertension** pindolol is usually given initially in an oral dosage of 5 mg two or three times daily, or 15 mg once daily, subsequently increased according to response. The usual maintenance dose is 15 to 30 mg once daily, but up to 45 mg daily, as a single dose or in divided doses, may be required. Additional benefit is rarely obtained from doses higher than 45 mg daily, although doses up to 60 mg daily have been given.

The usual oral dose for **angina pectoris** is 2.5 to 5 mg up to three times daily; however, doses of up to 40 mg daily have been used.

Eye drops containing pindolol 1% are used in the management of **glaucoma**.

Pindolol has also been given intravenously in the management of cardiac arrhythmias.

Psychiatric disorders. In addition to its beta-blocking properties, pindolol is also a partial agonist at serotonin 5-HT₁-receptors and has been used to augment the effects of SSRIs in patients with depression (p.373). Results have been conflicting,¹ but a meta-analysis² found that the time to response was shorter in patients given pindolol with an SSRI, although there was no effect on long-term outcomes. Small studies have also reported positive effects with pindolol augmentation of SSRIs in obsessive-compulsive disorder³ (p.952) and in panic disorder⁴ (p.952), although no effect was seen in social phobia.⁵ Another study⁶ found that pindolol augmentation of antipsychotic therapy reduced aggression in patients with schizophrenia (p.955).

1. Segrave R, Nathan PJ. Pindolol augmentation of selective serotonin reuptake inhibitors: accounting for the variability of results of placebo-controlled double-blind studies in patients with major depression. *Hum Psychopharmacol* 2005; **20**: 163–74.
2. Ballesteros J, Callado LF. Effectiveness of pindolol plus serotonin uptake inhibitors in depression: a meta-analysis of early and late outcomes from randomised controlled trials. *J Affect Disord* 2004; **79**: 137–47.
3. Dannon PN, et al. Pindolol augmentation in treatment-resistant obsessive compulsive disorder: a double-blind placebo controlled trial. *Eur Neuropsychopharmacol* 2000; **10**: 165–9.
4. Hirschmann S, et al. Pindolol augmentation in patients with treatment-resistant panic disorder: a double-blind, placebo-controlled trial. *J Clin Psychopharmacol* 2000; **20**: 556–9.
5. Stein MB, et al. Pindolol potentiation of paroxetine for generalized social phobia: a double-blind, placebo-controlled, crossover study. *Am J Psychiatry* 2001; **158**: 1725–7.
6. Caspi N, et al. Pindolol augmentation in aggressive schizophrenic patients: a double-blind crossover randomized study. *Int Clin Psychopharmacol* 2001; **16**: 111–5.

Preparations

BP 2008: Pindolol Tablets;

USP 31: Pindolol Tablets.

Proprietary Preparations (details are given in Part 3)

Austral.: Barloc; **Visken;** **Austria:** Visken; **Belg.:** Visken; **Braz.:** Visken; **Canada:** Apo-Pindol; Novo-Pindol; Nu-Pindol; **Visken;** **Cz.:** Apo-Pindol†; **Visken†;** **Denm.:** Hexapindol; **Visken;** **Fin.:** Pindocor; **Pinloc;** **Visken;** **Fr.:** **Visken;** **Ger.:** durapindol†; **Glauco-Stulln;** **Visken;** **Gr.:** **Visken;** **Hong Kong:** **Visken;** **Hung.:** **Visken;** **India:** **Visken;** **Irl.:** **Visken;** **Israel:** **Pinclen;** **Ital.:** **Visken;** **Mex.:** **Visken;** **Neth.:** **Visken;** **NZ:** **Pindol;** **Philipp.:** **Pyndale;** **Visken;** **Pol.:** **Visken;** **Rus.:** **Visken** (Вискен); **Swed.:** **Visken;** **Switz.:** **Viskene;** **Turk.:** **Visken;** **UK:** **Visken;** **USA:** **Visken;** **Venez.:** **Visken†.**

Multi-ingredient: **Austria:** **Visken†;** **Belg.:** **Viskaldix;** **Braz.:** **Viskaldix;** **Canada.:** **Viskazide;** **Chile:** **Viskaldix;** **Fr.:** **Viskaldix;** **Ger.:** **Viskaldix;** **Gr.:** **Viskaldix;** **Hung.:** **Viskaldix;** **Irl.:** **Viskaldix;** **Malaysia:** **Viskaldix;** **Neth.:** **Viskaldix;** **Philipp.:** **Viskaldix;** **Rus.:** **Viskaldix** (Вискалдикс); **Switz.:** **Viskaldix;** **Thai.:** **Viskaldix†;** **UK:** **Viskaldix;** **Venez.:** **Viskaldix†.**

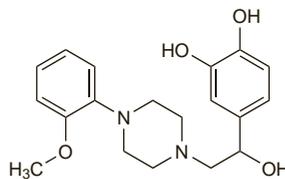
Pipratecol (rINN)

Pipratécol; Pipratecolum; 711-SE. 1-(3,4-Dihydroxyphenyl)-2-[4-(2-methoxyphenyl)piperazin-1-yl]ethanol.

Пипратекол

$C_{19}H_{24}N_2O_4 = 344.4$.

CAS — 15534-05-1.

**Profile**

Pipratecol is a vasodilator that has been given with raubasine (p.1386) in the treatment of cerebrovascular disorders.

Piretanide (BAN, USAN, rINN) ⊗

Hoe-118; Piretanid; Piretanida; Piretanidas; Pirétanide; Piretanidi; Piretanidium; 573-4118. 4-Phenoxy-3-(pyrrolidin-1-yl)-5-sulphamoylbenzoic acid.

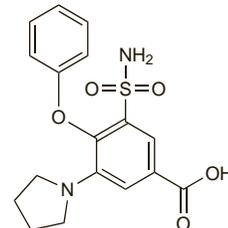
Пиретанид

$C_{17}H_{18}N_2O_5S = 362.4$.

CAS — 55837-27-9.

ATC — C03CA03.

ATC Vet — QC03CA03.



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

Ph. Eur. 6.2 (Piretanide). A yellowish-white to yellowish powder. It exhibits polymorphism. Very slightly soluble in water; sparingly soluble in dehydrated alcohol. Protect from light.

Adverse Effects

As for Furosemide, p.1292. Muscle cramps have been reported after high doses of piretanide.

Precautions

Piretanide's precautions and contra-indications, which are dependent on its effects on fluid and electrolyte balance, are similar to those of the thiazide diuretics (see Hydrochlorothiazide, p.1309). Patients with impaired micturition or prostatic hyperplasia may develop retention of urine with piretanide.

Interactions

As for Furosemide, p.1293.

Pharmacokinetics

Piretanide has been reported to be almost completely absorbed after oral doses. It is extensively bound to plasma proteins, and is reported to have a half-life of about 1 hour after an oral dose.

◇ References.

1. Beermann B, Grind M. Clinical pharmacokinetics of some newer diuretics. *Clin Pharmacokinet* 1987; **13**: 254–66.

Uses and Administration

Piretanide is a loop diuretic with actions and uses similar to those of furosemide (p.1294). It is used for oedema, including that associated with heart failure (p.1165), in oral doses of 3 to 6 mg daily. In the treatment of hypertension (p.1171) it is given in a usual oral dose of 6 to 12 mg daily. The sodium salt is given by injection.

◇ References.

1. Clissold SP, Brogden RN. Piretanide: a preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy. *Drugs* 1985; **29**: 489–530.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: **Arelis;** **Braz.:** **Arelis;** **Fr.:** **Eurelix;** **Ger.:** **Arelis;** **Irl.:** **Arelis;** **Ital.:** **Taulix;** **Mex.:** **Diural;** **S.Afr.:** **Spain:** **Perbilin;** **Switz.:** **Arelis.**

Multi-ingredient: **Austria:** **Trialex;** **Ger.:** **Arelis ACE;** **Aretensin;** **Betarelix;** **Irl.:** **Trialex;** **Ital.:** **Prilace;** **Switz.:** **Trialex.**

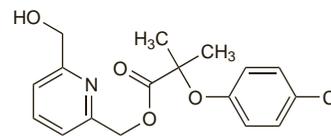
Pirifibrate (rINN)

EL-466; Pirifibrato; Pirifibratum. 6-Hydroxymethyl-2-pyridylmethyl 2-(4-chlorophenoxy)-2-methylpropionate.

Пирифибрат

$C_{17}H_{18}ClNO_4 = 335.8$.

CAS — 55285-45-5.

**Profile**

Pirifibrate, a fibric acid derivative (see Bezafibrate, p.1232), is a lipid regulating drug that has been used in the treatment of hyperlipidaemias.

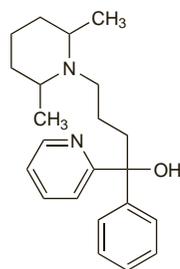
Pirmenol Hydrochloride (USAN, rINN)

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.

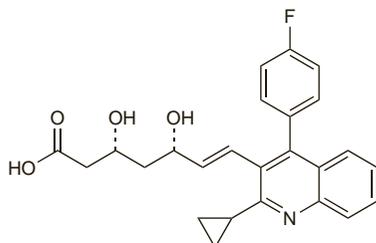
Питавастатин

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

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.

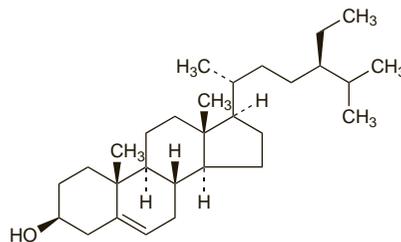
Sitosterol

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 stigmastanol 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.

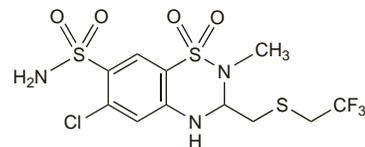
Политиазид

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

CAS — 346-18-9.

ATC — C03AA05.

ATC Vet — QC03AA05.

**Pharmacopoeias.** In *Br.*

BP 2008 (Polythiazide). A white or almost white, crystalline powder with an alliaceous 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)