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.

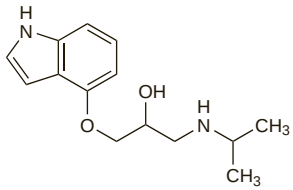
Пиндолол

$C_{14}H_{20}N_2O_2$ = 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-HT$_1$-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-analysis[2] 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 disorder[3] (p.952) and in panic disorder[4] (p.952), although no effect was seen in social phobia.[5] Another study[6] 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.: Barbloc; Visken; ***Austria:*** Visken; ***Belg.:*** Visken; ***Braz.:*** Visken; ***Canad.:*** 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:*** Pinden; ***Ital.:*** Visken; ***Mex.:*** Visken; ***Neth.:*** Viskeen; ***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:*** Viskenit; ***Belg.:*** Viskaldix; ***Braz.:*** Viskaldix; ***Canad.:*** 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†.

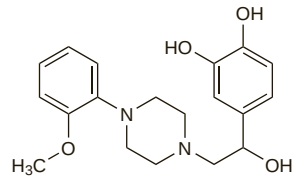
Pipratecol *(rINN)*

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; Piretanidum; S73-4118. 4-Phenoxy-3-(pyrrolidin-1-yl)-5-sulphamoylbenzoic acid.

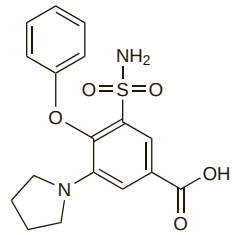
Пиретанид

$C_{17}H_{18}N_2O_5S$ = 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: Arelix; ***Braz.:*** Arelix; ***Fr.:*** Eurelix; ***Ger.:*** Arelix; ***Irl.:*** Arelix; ***Ital.:*** Tauliz; ***Mex.:*** Diural; ***S.Afr.:*** Arelix; ***Spain:*** Perbilen; ***Switz.:*** Arelix.

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

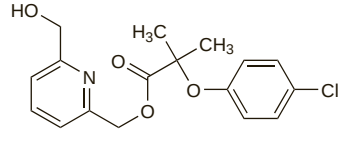
Pirifibrate *(rINN)*

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.