Phentolamine is given in the management of hypertensive crises, particularly those due to excessive catecholamine release associated with surgery for phaeochromocytoma (p.1179). It has been used for the differential diagnosis of phaeochromocytoma, but has largely been superseded by estimations of catecholamines in blood and urine.

Phentolamine is also used to prevent or treat dermal necrosis and sloughing associated with the intravenous infusion or extravasation of noradrenaline. It has been used in the treatment of erectile dysfunction (p.2179).

Phentolamine is given by injection as the mesilate.

In patients with hypertensive crises during surgery for **phaeochromocytoma**, a dose of 2 to 5 mg of phentolamine mesilate is given intravenously and repeated if necessary; blood pressure should be monitored. A dose of 1 mg intravenously is used for children. The intramuscular route may be used pre-operatively and for diagnostic procedures.

For prevention of **dermal necrosis** during intravenous infusion of noradrenaline, 10 mg of phentolamine mesilate is added to each litre of solution containing noradrenaline. For treatment of extravasation of noradrenaline, 5 to 10 mg of phentolamine mesilate in 10 mL of sodium chloride 0.9% is injected into the affected area.

For **erectile dysfunction**, phentolamine mesilate is given by injection into the corpora cavernosa of the penis. It is usually given with papaverine, but a preparation containing phentolamine with aviptadil (vasoactive intestinal peptide) may also be used. Phentolamine has also been tried orally.

Hyperhidrosis. Hyperhidrosis (p.1580) is usually treated with topical aluminium salts or topical antimuscarinics, but intradermal botulinum A toxin or procedures such as endoscopic transthoracic sympathectomy may be needed in severe cases. Phentolamine has been tried as an alternative. Improvement in symptoms has been reported[1] in 2 patients with generalised hyperhidrosis given 100 mg of phentolamine mesilate by intravenous infusion over 6 hours. Improvement lasted for 2 to 3 months and the infusion was repeated, in 1 patient several times.

1. McCleane G. The use of intravenous phentolamine mesilate in the treatment of hyperhidrosis. *Br J Dermatol* 2002; **146:** 533–4.

Pain. Sympathetic nerve block (p.1853) is used in a number of pain syndromes and usually involves injection of local anaesthetics. Phentolamine has been used as an alternative and beneficial results have been reported in pain associated with chronic pancreatitis,[1] pancreatic and other visceral cancers,[2,3] and chronic gastroparesis.[4]

Complete resolution of pain has also been reported in 2 patients with cutaneous leiomyomata given oral doxazosin.[5]

1. McCleane GJ. Phentolamine abolishes the pain of chronic pancreatitis. *Br J Hosp Med* 1996; **55:** 521.
2. McCleane GJ. Intravenous phentolamine mesylate alleviates the pain of pancreatic carcinoma. *Pain* 1997; **73:** 263–4.
3. Yasukawa M, *et al.* Intravenous phentolamine infusion alleviates the pain of abdominal visceral cancer, including pancreatic carcinoma. *J Anesth* 2007; **21:** 420–3.
4. Phillips WJ, *et al.* Relief of acute pain in chronic idiopathic gastroparesis with intravenous phentolamine. *Ann Pharmacother* 2006; **40:** 2032–6.
5. Batchelor RJ, *et al.* Successful treatment of pain in two patients with cutaneous leiomyomata with the oral alpha-1 adrenoceptor antagonist, doxazosin. *Br J Dermatol* 2004; **150:** 775–6.

Preparations

BP 2008: Phentolamine Injection;
USP 31: Phentolamine Mesylate for Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Regitina; ***Austral.:*** Regitine; ***Belg.:*** Regitine; ***Braz.:*** Herivyl; Regitina†; Vigamed; ***Canad.:*** Rogitine; ***Denm.:*** Regitin; ***Gr.:*** Regitine; Rogitine†; ***Hung.:*** Regitine; ***Israel:*** Regitine; ***Mex.:*** Z-Max†; ***Neth.:*** Regitine; ***NZ:*** Invicorp; Regitine; ***S.Afr.:*** Regitine†; ***Switz.:*** Regitine; ***UK:*** Rogitine; ***USA:*** Regitine†; ***Venez.:*** Regitina†.

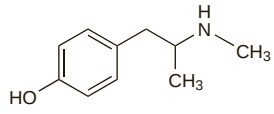
Multi-ingredient: ***Austria:*** Androskat; ***Neth.:*** Androskat; ***USA:*** Tri-Mix.

Pholedrine Sulfate *(rINNM)* ⊗

Isodrine Sulphate; Pholédrine, Sulfate de; Pholedrine Sulphate *(BANM)*; Pholedrini Sulfas; Sulfato de foledrina; Sympropaminum (pholedrine). 4-(2-Methylaminopropyl)phenol sulfate.

Фоледрина Сульфат

$(C_{10}H_{15}NO)_2,H_2SO_4$ = 428.5.
CAS — 370-14-9 (pholedrine); 6114-26-7 (pholedrine sulfate).



(pholedrine)

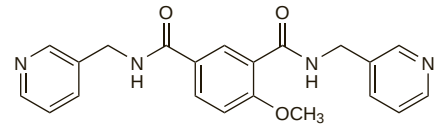
Profile
Pholedrine is a sympathomimetic (p.1407) used in the treatment of hypotensive states. It is usually given orally as the sulfate, often in combination with other drugs, and has also been included in preparations promoted for vascular disorders. Pholedrine eye drops have been used as an alternative to hydroxyamfetamine (p.2322) in the diagnosis of Horner's syndrome.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Ger.:*** Adyston†; Zellaforte N Plus†; ***Switz.:*** Ortho-Maren retard.

Picotamide *(BAN)*

G-137; Picotamida; Picotamide, monohydrate de; Picotamidmonohidrát; Picotamidum monohydricum; Pikotamid monohydrát; Pikotamidimonohydraatti; Pikotamidmonohydrat; Pikotamido monohidratas. 4-Methoxy-*N*,*N*′-bis(3-pyridinylmethyl)-1,3-benzenedicarboxamide monohydrate.

$C_{21}H_{20}N_4O_3,H_2O$ = 394.4.
CAS — 32828-81-2 (anhydrous picotamide); 80530-63-8 (picotamide monohydrate).
ATC — B01AC03.
ATC Vet — QB01AC03.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Picotamide Monohydrate). A white or almost white, polymorphic, crystalline powder. Slightly soluble in water; soluble in dehydrated alcohol and in dichloromethane; dissolves in dilute mineral acids.

Profile
Picotamide is a thromboxane synthase inhibitor and thromboxane receptor antagonist with antiplatelet activity. It is given by mouth in thromboembolic disorders (p.1187) in initial doses of 900 to 1200 mg daily in divided doses, reducing to a maintenance dose of 300 to 600 mg daily.

ACE inhibitor-induced cough. Cough is a recognised adverse effect of ACE inhibitors and has been treated with a number of drugs (see p.1194). Picotamide led to the disappearance of cough in 8 of 9 patients receiving enalapril for hypertension,[1] suggesting that thromboxanes may be involved in the aetiology of ACE inhibitor-induced cough.

1. Malini PL, *et al.* Thromboxane antagonism and cough induced by angiotensin-converting-enzyme inhibitor. *Lancet* 1997; **350:** 15–18.

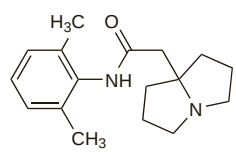
Preparations
Proprietary Preparations (details are given in Part 3)
Ital.: Plactidil.

Pilsicainide Hydrochloride *(rINNM)*

Hidrocloruro de pilsicainida; Pilsicaïnide, Chlorhydrate de; Pilsicainidi Hydrochloridum; SUN-1165. Tetrahydro-1*H*-pyrrolizine-7a(5*H*)-aceto-2′,6′-xylidide hydrochloride.

Пильсикаинида Гидрохлорид

$C_{17}H_{24}N_2O,HCl$ = 308.8.
CAS — 88069-67-4 (pilsicainide); 88069-49-2 (pilsicainide hydrochloride).



(pilsicainide)

Profile
Pilsicainide hydrochloride is an antiarrhythmic with class Ic activity (p.1153).

◊ References.
1. Takabatake T, *et al.* Pharmacokinetics of SUN 1165, a new antiarrhythmic agent, in renal dysfunction. *Eur J Clin Pharmacol* 1991; **40:** 411–14.
2. Okishige K, *et al.* Pilsicainide for conversion and maintenance of sinus rhythm in chronic atrial fibrillation: a placebo-controlled, multicenter study. *Am Heart J* 2000; **140:** 437–44.
3. Kumagai K, *et al.* Single oral administration of pilsicainide versus infusion of disopyramide for termination of paroxysmal atrial fibrillation: a multicenter trial. *Pacing Clin Electrophysiol* 2000; **23:** 1880–2.
4. Ogawa R, *et al.* Population pharmacokinetic and pharmacodynamic analysis of a class IC antiarrhythmic, pilsicainide, in patients with cardiac arrhythmias. *J Clin Pharmacol* 2006; **46:** 59–68.
5. Kumagai K, *et al.* Pilsicainide for atrial fibrillation. *Drugs* 2006; **66:** 2067–73.

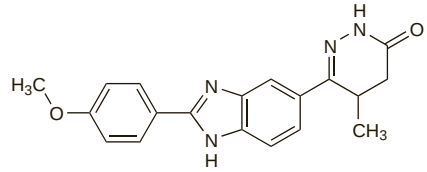
Preparations
Proprietary Preparations (details are given in Part 3)
Jpn: Sunrythm.

Pimobendan *(BAN, USAN, rINN)*

Pimobendaani; Pimobendán; Pimobendanas; Pimobendane; Pimobendanum; UDCG-115. 4,5-Dihydro-6-[2-(*p*-methoxyphenyl)-5-benzimidazolyl]-5-methyl-3(2*H*)-pyridazinone.

Пимобендан

$C_{19}H_{18}N_4O_2$ = 334.4.
CAS — 74150-27-9; 118428-36-7.
ATC Vet — QC01CE90.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Pimobendan). A white or slightly yellowish, hygroscopic powder. Practically insoluble in water; slightly soluble in acetone and in methyl alcohol; freely soluble in dimethylformamide. Store in airtight containers.

Profile
Pimobendan is a phosphodiesterase inhibitor with calcium-sensitising properties. It has positive inotropic and vasodilator activity and is used as an adjunct to standard therapy in the management of heart failure (p.1165). It is given orally in a dose of 1.25 to 2.5 mg twice daily.

Studies with other inotropic phosphodiesterase inhibitors have shown that their prolonged oral use can lead to an increased mortality rate.

◊ References.
1. Przechera M, *et al.* Pharmacokinetic profile and tolerability of pimobendan in patients with terminal renal insufficiency. *Eur J Clin Pharmacol* 1991; **40:** 107–11.
2. The Pimobendan in Congestive Heart Failure (PICO) Investigators. Effect of pimobendan on exercise capacity in patients with heart failure: main results from the Pimobendan in Congestive Heart Failure (PICO) trial. *Heart* 1996; **76:** 223–31.
3. Yoshikawa T, *et al.* Effectiveness of carvedilol alone versus carvedilol + pimobendan for severe congestive heart failure. *Am J Cardiol* 2000; **85:** 1495–7.
4. The EPOCH Study Group. Effects of pimobendan on adverse cardiac events and physical activities in patients with mild to moderate chronic heart failure: the effects of pimobendan on chronic heart failure study (EPOCH study). *Circ J* 2002; **66:** 149–57.

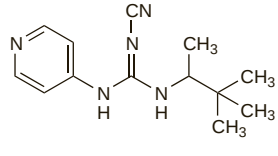
Preparations
Proprietary Preparations (details are given in Part 3)
Jpn: Acardi.

Pinacidil *(USAN, rINN)*

P-1134; Pinacidilum; Pinasidiili. (±)-2-Cyano-1-(4-pyridyl)-3-(1,2,2-trimethylpropyl)guanidine.

Пинацидил

$C_{13}H_{19}N_5$ = 245.3.
CAS — 60560-33-0 (anhydrous pinacidil); 85371-64-8 (pinacidil monohydrate).
ATC — C02DG01.
ATC Vet — QC02DG01.



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.

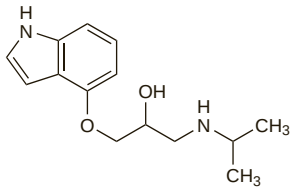
Пиндолол

$C_{14}H_{20}N_2O_2$ = 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†.

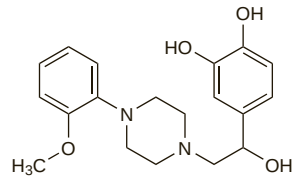
Pipratecol *(rINN)*

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.

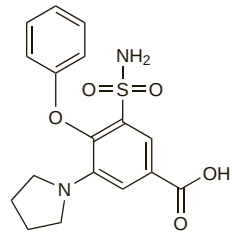
Пиретанид

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

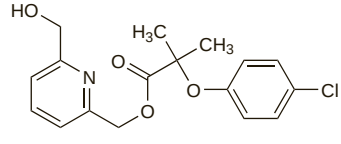
Pirifibrate *(rINN)*

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.