Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Nyal Dry Cough†; ***Austria:*** Atenos; Sedotussin; ***Belg.:*** Balsoclase Antitussivum; Tuclase; ***Cz.:*** Sedotussin†; ***Denm.:*** Toclase†; ***Fin.:*** Toclase; ***Fr.:*** Pectosan Toux Seche; Toclase Toux Seche; Vicks Pectoral; ***Ger.:*** Pertix-Solo-N, Pertix-T, Pertix-Z, and Pertix-L†; Sedotussin; ***Gr.:*** Tuclase; ***Hong Kong:*** Toclase; ***Hung.:*** Sedotussin; ***Ital.:*** Tuclase; ***Neth.:*** Balsoclase; Tuclase; ***Norw.:*** Toclase; ***Philipp.:*** Toclase; ***Swed.:*** Toclase; ***Thai.:*** Toclase; ***Turk.:*** Toclase; ***USA:*** Solotuss; ***Venez.:*** Carbin†.

Multi-ingredient: ***Arg.:*** Bio Grip Plus; Rynatus†; Wilpan Antigripal; Wilpan C†; ***Austral.:*** Vicks Cough Syrup; ***Austria:*** Tussoretardin; ***Belg.:*** Balsoclase Expectorans; ***Braz.:*** Alergo Glucalbet†; Coldrin; Gegrip†; Resprin; ***Fin.:*** Toclase Expectorant; ***Ger.:*** Sedotussin plus†; ***Hong Kong:*** Coci-Fedra; Marflu-X; Vida Cough; ***Neth.:*** Balsoclase Compositum; Balsoclase-E; ***S.Afr.:*** Vicks Acta Plus; ***Switz.:*** Sedotussin†; ***Turk.:*** Gayaben; ***USA:*** AMBI 1000/5; Aridex; BetaVent; C-Tanna 12D; Carb Pseudo-Tan; Carbatab; Diphen Tann/ PE Tann/ CT Tann; Duratuss CS; Dynex VR; Dytan-AT; Dytan-CD; Dytan-CS; Exratuss; Extendryl GCP; Levall; Levall 12; Oratuss; Pyrlex CB; Re-Tann; Rentamine Pediatric; Respi-Tann G; Ry-Tuss†; Rynatuss; Tannic-12; Tri-Tannate Plus Pediatric; Tuss-Tan; Tussi-12; Tussi-12 D; Tussi-12D S; Tussizone; Vazotan; XiraTuss; Xpect-AT; ***Venez.:*** Resprin; Tolmex; Yerba Santa.

Phenylephrine *(BAN, rINN)*

Fenilefrin; Fenilefrina; Fenilefrinas; Fenylefrin; Fenyyliefriini; Phénylephrine; Phenylephrinum; *m*-Synephrine. (1*R*)-1-(3-Hydroxyphenyl)-2-methylaminoethanol.

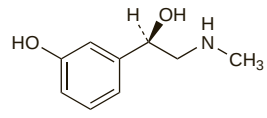
Фенилэфрин

$C_9H_{13}NO_2$ = 167.2.

CAS — 59-42-7.

ATC — C01CA06; R01AA04; R01AB01; R01BA03; S01FB01; S01GA05.

ATC Vet — QC01CA06; QR01AA04; QR01AB01; QR01BA03; QS01FB01; QS01GA05.



NOTE. Synephrine has been used as a synonym for oxedrine (p.1364). Care should be taken to avoid confusion with phenylephrine (*m*-synephrine).

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Phenylephrine). A white or almost white crystalline powder. Slightly soluble in water and in alcohol; sparingly soluble in methyl alcohol. It dissolves in dilute mineral acids and in solutions of alkali hydroxides. Store in airtight containers. Protect from light.

Phenylephrine Acid Tartrate

Phenylephrine Bitartrate *(rINNM)*; Bitartrato de fenilefrina; Phénylephrine, Bitartrate de; Phenylephrine Tartrate *(BANM)*; Phenylephrini Bitartras; Tartrato ácido de fenilefrina.

Фенилэфрина Битартрат

$C_9H_{13}NO_2.C_4H_6O_6$ = 317.3.

CAS — 13998-27-1.

ATC — C01CA06; R01AA04; R01AB01; R01BA03; S01FB01; S01GA05.

ATC Vet — QC01CA06; QR01AA04; QR01AB01; QR01BA03; QS01FB01; QS01GA05.

Pharmacopoeias. In *US*.
USP 31 (Phenylephrine Bitartrate). A white or almost white powder or colourless crystals. Freely soluble in water. pH of a 10% solution in water is between 3.0 and 4.0. Store in airtight containers. Protect from light.

Phenylephrine Hydrochloride *(BANM, rINNM)*

Fenilefrin Hidroklorür; Fenilefrin-hidroklorid; Fenilefrino hidrochloridas; Fenylefrin hydrochlorid; Fenylefrinhydroklorid; Fenylefryny chlorowodorek; Fenyyliefriinihydrokloridi; Hidrocloruro de fenilefrina; Mesatonum; Metaoxedrini Chloridum; Phénylephrine, chlorhydrate de; Phenylephrini hydrochloridum.

Фенилэфрина Гидрохлорид

$C_9H_{13}NO_2.HCl$ = 203.7.

CAS — 61-76-7.

ATC — C01CA06; R01AA04; R01AB01; R01BA03; S01FB01; S01GA05.

ATC Vet — QC01CA06; QR01AA04; QR01AB01; QR01BA03; QS01FB01; QS01GA05.

NOTE. PHNL is a code approved by the BP 2008 for use on single unit doses of eye drops containing phenylephrine hydrochloride where the individual container may be too small to bear all the appropriate labelling information. PHNCYC is a similar code approved for eye drops containing phenylephrine hydrochloride and cyclopentolate hydrochloride.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Phenylephrine Hydrochloride). A white or almost white, crystalline powder. Freely soluble in water and in alcohol.
USP 31 (Phenylephrine Hydrochloride). White or practically white, odourless, crystals. Freely soluble in water and in alcohol. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Incompatibility. Phenylephrine is stated to be incompatible with the local anaesthetic butacaine.

Adverse Effects and Precautions

As for Sympathomimetics, p.1407; phenylephrine has mainly alpha-agonist effects. It has a longer duration of action than noradrenaline and an excessive vasopressor response may cause a prolonged rise in blood pressure. It induces tachycardia or reflex bradycardia and should therefore be avoided in severe hyperthyroidism and used with caution in severe ischaemic heart disease. Patients with diabetes mellitus or prostatic hyperplasia should also avoid phenylephrine.

Since phenylephrine is absorbed through the mucosa systemic effects may follow application to the eyes or the nasal mucosa. In particular, phenylephrine 10% eye drops can have powerful systemic effects. They should be avoided or only used with extreme caution in infants, the elderly, and in patients with cardiac disease, significant hypertension, or advanced arteriosclerosis. Fatalities have been reported in patients with pre-existing cardiovascular disease.

Use of phenylephrine in the eye may liberate pigment granules from the iris, especially when given in high doses to elderly patients. Ophthalmic solutions of phenylephrine are contra-indicated in patients with angle-closure glaucoma. Corneal clouding may occur if corneal epithelium has been denuded or damaged.

Excessive or prolonged use of phenylephrine nasal drops can lead to rebound congestion.

Phenylephrine hydrochloride is irritant and may cause local discomfort at the site of application; extravasation of the injection may even cause local tissue necrosis.

Effects on the cardiovascular system. Systemic adverse effects have occurred after the use of phenylephrine as eye drops (particularly at a strength of 10%), or nasal drops.

Hypertension[1] and hypertension with pulmonary oedema[2] have been described in infants and children after the use of phenylephrine 10% eye drops. Hypertension with arrhythmias has also been reported in an 8-year-old child[3] and in an adult[4] after phenylephrine 10% eye drops had been used. Details have also been published on a series of 32 patients who had systemic cardiovascular reactions, including fatal myocardial infarctions, after the use of phenylephrine 10% solutions in the eye.[5] Severe cardiovascular adverse reactions have also been reported to the use of phenylephrine as topical 10% ocular[6] or 0.25% nasal[7] pledgets.

Although the incidence of such reactions seems low,[8] the use of lower concentrations[1,5] and caution in susceptible patients such as those with cardiovascular disorders or the elderly,[5] have been advocated. A reduction in the eye-drop volume has been found to produce adequate mydriasis and may reduce systemic absorption and the risk of adverse cardiovascular effects.[9,10]

1. Borromeo-McGrail V, *et al.* Systemic hypertension following ocular administration of 10% phenylephrine in the neonate. *Pediatrics* 1973; **51:** 1032–6.
2. Baldwin FJ, Morley AP. Intraoperative pulmonary oedema in a child following systemic absorption of phenylephrine eyedrops. *Br J Anaesth* 2002; **88:** 440–2.
3. Vaughan RW. Ventricular arrhythmias after topical vasoconstrictors. *Anesth Analg* 1973; **52:** 161–5.
4. Lai Y-K. Adverse effect of intraoperative phenylephrine 10%: case report. *Br J Ophthalmol* 1989; **73:** 468–9.
5. Fraunfelder FT, Scafidi AF. Possible adverse effects from topical ocular 10% phenylephrine. *Am J Ophthalmol* 1978; **85:** 447–53.
6. Fraunfelder FW, *et al.* Adverse systemic effects from pledgets of topical ocular phenylephrine 10%. *Am J Ophthalmol* 2002; **134:** 624–5.
7. Hecker RB, *et al.* Myocardial ischemia and stunning induced by topical intranasal phenylephrine pledgets. *Mil Med* 1997; **162:** 832–5.
8. Brown MM, *et al.* Lack of side effects from topically administered 10% phenylephrine eyedrops: a controlled study. *Arch Ophthalmol* 1980; **98:** 487–9.
9. Craig EW, Griffiths PG. Effect on mydriasis of modifying the volume of phenylephrine drops. *Br J Ophthalmol* 1991; **75:** 222–3.
10. Wheatcroft S, *et al.* Reduction in mydriatic drop size in premature infants. *Br J Ophthalmol* 1993; **77:** 364–5.

Effects on the eyes. Acute and chronic conjunctivitis has been reported[1] after use of over-the-counter ophthalmic decongestant preparations of phenylephrine, naphazoline, or tetryzoline. The conjunctival inflammation took several weeks to resolve in some cases. Dermatoconjunctivitis[2] has also been reported after use of phenylephrine eye drops.

1. Soparkar CN, *et al.* Acute and chronic conjunctivitis due to over-the-counter ophthalmic decongestants. *Arch Ophthalmol* 1997; **115:** 34–8.
2. Moreno-Ancillo A, *et al.* Allergic contact reactions due to phenylephrine hydrochloride in eyedrops. *Ann Allergy Asthma Immunol* 1997; **78:** 569–72.

Effects on mental function. Hallucinations and paranoid delusions have been reported[1] in a patient after excessive use of a nasal spray containing phenylephrine 0.5%. Mania has also followed the use of large oral doses.[2]

1. Snow SS, *et al.* Nasal spray 'addiction' and psychosis: a case report. *Br J Psychiatry* 1980; **136:** 297–9.
2. Waters BGH, Lapierre YD. Secondary mania associated with sympathomimetic drug use. *Am J Psychiatry* 1981; **138:** 837–40.

Hypersensitivity. Cross-sensitivity to phenylephrine has been reported in a patient hypersensitive to pseudoephedrine.[1] See also Effects on the Eyes, above.

1. Buzo-Sanchez G, *et al.* Stereoisomeric cutaneous hypersensitivity. *Ann Pharmacother* 1997; **31:** 1091.

Interactions

As for Sympathomimetics, p.1407. Phenylephrine has mainly direct alpha-agonist properties and is less liable than adrenaline or noradrenaline to induce ventricular fibrillation if used as a pressor agent during anaesthesia with inhalational anaesthetics such as cyclopropane and halothane; nevertheless, caution is necessary. Since phenylephrine is absorbed through the mucosa, interactions may also follow topical application, particularly in patients receiving an MAOI (including a RIMA). See also under Phenelzine (p.418) and Moclobemide (p.411).

Cardiovascular drugs. Hypertensive reactions have been reported in a patient stabilised on *debrisoquine* when given phenylephrine orally,[1] in patients receiving *reserpine* or *guanethidine* when given phenylephrine eye drops,[2] and a fatal reaction occurred in a patient receiving *propranolol* and *hydrochlorothiazide* also after the instillation of phenylephrine eye drops.[3]

1. Aminu J, *et al.* Interaction between debrisoquine and phenylephrine. *Lancet* 1970; **ii:** 935–6.
2. Kim JM, *et al.* Hypertensive reactions to phenylephrine eyedrops in patients with sympathetic denervation. *Am J Ophthalmol* 1978; **85:** 862–8.
3. Cass E, *et al.* Hazards of phenylephrine topical medication in persons taking propranolol. *Can Med Assoc J* 1979; **120:** 1261–2.

Pharmacokinetics

Phenylephrine has low oral bioavailability owing to irregular absorption and first-pass metabolism by monoamine oxidase in the gut and liver. When injected subcutaneously or intramuscularly it takes 10 to 15 minutes to act; subcutaneous and intramuscular injections are effective for up to about 1 hour and up to about 2 hours, respectively. Intravenous injections are effective for about 20 minutes.

Systemic absorption follows topical application.

Uses and Administration

Phenylephrine hydrochloride is a sympathomimetic (p.1408) with mainly direct effects on adrenergic receptors. It has mainly alpha-adrenergic activity and is without significant stimulating effects on the CNS at usual doses. Its pressor activity is weaker than that of noradrenaline (p.1360) but of longer duration. After injection it produces peripheral vasoconstriction and increased arterial pressure; it also causes reflex bradycardia. It reduces blood flow to the skin and to the kidneys.

Phenylephrine and its salts are most commonly used, either topically or by mouth, for the symptomatic relief of **nasal congestion** (p.1548). They are frequently included in preparations intended for the relief of cough and cold symptoms. For nasal congestion, a 0.25 to 1% solution may be instilled as nasal drops or a spray into each nostril every 4 hours as required, or phenylephrine hydrochloride may be given in usual oral doses of 10 mg every four hours (up to a maximum of 60 mg daily) or 12 mg up to four times daily.

In ophthalmology, phenylephrine hydrochloride is used as a **mydriatic** (p.1874) in concentrations of up to 10%; generally solutions containing 2.5 or 10% are used but systemic absorption can occur (see Effects on the Cardiovascular System, above) and the 10% strength, in particular, should be used with caution. The