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.

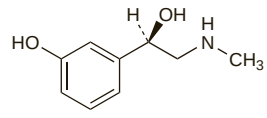
Фенилэфрин

$C_9H_{13}NO_2$ = 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

mydriatic effect can last several hours. Solutions containing 2.5% or more may cause intense irritation and a local anaesthetic other than butacaine (which is incompatible) should be instilled into the eye a few minutes beforehand.

Ocular solutions containing lower concentrations (usually 0.12% phenylephrine hydrochloride) are used as a **conjunctival decongestant** (see Conjunctivitis, p.564).

Phenylephrine has been used parenterally in the treatment of hypotensive states, such as those encountered during circulatory failure or spinal anaesthesia. Phenylephrine has also been used in orthostatic hypotension (see under Fludrocortisone, p.1530). For **hypotension**, an initial dose of phenylephrine hydrochloride 2 to 5 mg may be given as a 1% solution subcutaneously or intramuscularly with further doses of 1 to 10 mg if necessary, according to response. A dose of 100 to 500 micrograms by slow intravenous injection as a 0.1% solution, repeated as necessary after at least 15 minutes, has also been used. In severe hypotensive states, 10 mg in 500 mL of glucose 5% or sodium chloride 0.9% has been infused intravenously, initially at a rate of up to 180 micrograms/minute, reduced, according to the response, to 30 to 60 micrograms/minute.

For children's doses, see Administration in Children, below.

Phenylephrine hydrochloride has been given by intravenous injection to stop **paroxysmal supraventricular tachycardia** but other drugs are preferred (see Cardiac Arrhythmias, p.1160). The initial dose is usually not greater than 500 micrograms given as a 0.1% solution with subsequent doses gradually increased in increments of 100 to 200 micrograms up to 1 mg if necessary.

Phenylephrine hydrochloride has been used for its vasoconstrictor action as an **adjunct** to local anaesthetics.

Phenylephrine has also been used as the acid tartrate to prolong the bronchodilator effects of isoprenaline when given by inhalation. However, isoprenaline is now little used by this route.

Phenylephrine tannate has also been used.

Administration in children. Phenylephrine hydrochloride is used for the symptomatic relief of **nasal congestion**; however, over-the-counter cough and cold preparations containing sympathomimetic decongestants (including phenylephrine) should be used with caution in children and generally avoided in those under 2 years of age (see p.1547). In the USA, the following doses have been used in children:

- 2 to 6 years: 2 or 3 drops of a 0.125% or 0.16% solution into each nostril every four hours as needed
- 6 to 12 years: 2 or 3 drops, or 1 or 2 sprays, of a 0.25% solution may be instilled into each nostril every four hours as needed.

In the UK, oral preparations for nasal congestion associated with colds and hay fever are not licensed in children under 12 years of age.

Phenylephrine is used for **mydriasis** in diagnostic or therapeutic procedures. Solutions containing 2.5% are used in children as the 10% strength is contra-indicated owing to the risk of systemic effects.

For acute **hypotension**, the *BNFC* states that phenylephrine hydrochloride may be given subcutaneously or intramuscularly in the following doses:

- 1 to 12 years: 100 micrograms/kg every 1 to 2 hours as needed (to a maximum dose of 5 mg)
- 12 to 18 years: 2 to 5 mg, followed if necessary by further doses of 1 to 10 mg (maximum initial dose 5 mg)

Although the intravenous route is not licensed in the UK for such use in children, intravenous injection is preferred to the other parenteral routes; the *BNFC* recommends the following doses given as a 0.1% solution:

- 1 to 12 years: 5 to 20 micrograms/kg (maximum 500 micrograms), repeated as needed after at least 15 minutes.
- 12 to 18 years: 100 to 500 micrograms, repeated as needed after at least 15 minutes

For intravenous infusion, the solution is diluted with glucose 5% or sodium chloride 0.9% to a concentration of 20 micrograms/mL and given as a continuous infusion via a central venous catheter. The *BNFC* gives the following doses:

- 1 to 16 years: 100 to 500 nanograms/kg per minute, adjusted according to response
- 16 to 18 years: initially up to 180 micrograms/minute, reduced to 30 to 60 micrograms/minute according to response

Faecal incontinence. Topical application of phenylephrine gel has been shown to increase resting anal tone[1] and has been investigated in patients with faecal incontinence.[2] Although application of a 10% gel did not appear to be of clinical benefit in a double-blind crossover study in 36 patients with faecal incontinence caused by internal sphincter dysfunction,[3] continence was improved in another small study in patients with ileoanal pouches.[4]

1. Cheetham MJ, *et al.* Topical phenylephrine increases anal canal resting pressure in patients with faecal incontinence. *Gut* 2001; **48:** 356–9.
2. Cheetham M, *et al.* Drug treatment for faecal incontinence in adults. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2002 (accessed 04/01/07).
3. Carapeti EA, *et al.* Randomized controlled trial of topical phenylephrine in the treatment of faecal incontinence. *Br J Surg* 2000; **87:** 38–42.
4. Carapeti EA, *et al.* Randomized, controlled trial of topical phenylephrine for fecal incontinence in patients after ileoanal pouch construction. *Dis Colon Rectum* 2000; **43:** 1059–63.

Nasal congestion. A meta-analysis concluded that there was insufficient evidence that phenylephrine 10 mg was an effective oral decongestant.[1]

1. Hatton RC, *et al* Efficacy and safety of oral phenylephrine: systematic review and meta-analysis. *Ann Pharmacother* 2007; **41:** 381–90.

Priapism. Alpha agonists, including phenylephrine, may be used in the management of priapism (see under Metaraminol, p.1333). For reference to phenylephrine in low dosage and dilute solution being given by intracavernosal injection to reverse priapism, see under Alprostadil, p.2184.

Preparations

BP 2008: Phenylephrine Eye Drops; Phenylephrine Injection;
USP 31: Antipyrine, Benzocaine, and Phenylephrine Hydrochloride Otic Solution; Isoproterenol Hydrochloride and Phenylephrine Bitartrate Inhalation Aerosol; Phenylephrine Hydrochloride Injection; Phenylephrine Hydrochloride Nasal Jelly; Phenylephrine Hydrochloride Nasal Solution; Phenylephrine Hydrochloride Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Fadalefrina; Mydfrin†; Poen Efrina; Prefrin; Qura Nasal; ***Austral.:*** Actifed PE; Albalon Relief; Isopto Frin†; Neo-Synephrine; Nyal Decongestant; Nyal Sinus Relief†; Prefrin; Sudafed PE; Visopt†; ***Austria:*** Visadron; ***Belg.:*** Spraydil; Visadron; ***Braz.:*** Denason; ***Canad.:*** Ak-Dilate†; Dionephrine; Mydfrin; Neo-Synephrine; Prefrin; Triaminic Thin Strips Nasal Congestion; Triaminic Toddler Congestion; ***Chile:*** Mydfrin; ***Cz.:*** Humex Nosni; Neo-Synephrine; Visadron†; ***Fin.:*** Oftan Metaoksedrin†; ***Fr.:*** Auristan†; Neosynephrine; ***Ger.:*** Neo-Mydrial†; Neosynephrin-POS; Otriven Baby; Visadron; ***Hong Kong:*** Mydfrin; Prefrin; ***India:*** Drosyn; Pupiletto†; ***Irl.:*** Isopto Frin†; ***Israel:*** Af-Taf; Efrin; Neo-Synephrine; Prefrin†; ***Ital.:*** Isonefrine; Neo-Synephrine; Ribex Nasale†; Visadron†; ***Malaysia:*** Analux†; Isopto Frin†; Mydfrin; Prefrin†; ***Mex.:*** Dilufrin; Lefrine; Nefrin; Rinolan; Weiscalina†; ***Neth.:*** Boradrine; Visadron; ***NZ:*** Albalon Relief†; Isopto Frin†; Neosynephrine; Prefrin; ***Philipp.:*** Mydfrin; ***Port.:*** Davinefrina; Neo-Sinefrina; VibrocilFen; Visadron; ***Rus.:*** Irifrin (Ирифрин); Nazol Baby (Назол Бэби); Nazol Kids (Назол Кидс); ***S.Afr.:*** I-Glo; Naphensyl; Prefrin; ***Singapore:*** Isopto Frin†; Mydfrin; Prefrin†; ***Spain:*** ADA; Analux†; Boraline; Disneumon Mentol; Disneumon Pernasal; Mirazul; Rin Up†; Visadron; Vistafrin; ***Switz.:*** Gouttes nasales†; Rexophtal N; Spray nasal pour enfants; ***Turk.:*** Mydfrin; ***UK:*** Boots Decongestant Capsules; Fenox; Non-Drowsy Sudafed Congestion Relief; ***USA:*** AH-chew D; Ak-Dilate; Children's Nostril; Lusonal; Medicone†; Mydfrin; Nasop; Neo-Synephrine; Neofrin; Nostril; Ocu-Phrin; Pedia Care Childrens Decongestant; Phenoptic†; Phenyl-T; Prefrin†; Pretz-D†; Rectacaine; Relief; Rhinall; Sinex; Sudafed PE; Triaminic Infant Thin Strips Decongestant; Triaminic Thin Strips Cold; Tronolane.

Multi-ingredient: numerous preparations are listed in Part 3.

Used as an adjunct in: ***Braz.:*** Anestesico.

Phenylpropanolamine *(BAN, rINN)*

Fenilpropanolamina; Fennylpropanolamin; Fenyylipropanoliamiini; (±)-Norephedrine; Phénylpropanolamine; Phenylpropanolaminum. (1*RS*,2*SR*)-2-Amino-1-phenylpropan-1-ol.

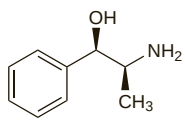
Фенилпропаноламин

$C_9H_{13}NO$ = 151.2.

CAS — 14838-15-4.

ATC — R01BA01.

ATC Vet — QG04BX91; QR01BA01.



(+)-Form

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of phenylpropanolamine: Pseudocaine.

Phenylpropanolamine Hydrochloride

(BANM, rINNM)

Fenilpropanolamin-hidroklorid; Fenilpropanolamino hidrochloridas; Fenylpropanolamin hydrochlorid; Fenylpropanolaminhydroklorid; Fenyylipropanoliamiinihydrokloridi; Hidrocloruro de fenilpropanolamina; Mydriatin; Phénylpropanolamine, chlorhydrate de; Phenylpropanolamini Hydrochloridum; Phenylpropanolamini hydrochloridum.

Фенилпропаноламина Гидрохлорид

$C_9H_{13}NO,HCl$ = 187.7.

CAS — 154-41-6.

ATC — R01BA01.

ATC Vet — QG04BX91; QR01BA01.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
US also includes phenylpropanolamine bitartrate.
Ph. Eur. 6.2 (Phenylpropanolamine Hydrochloride). A white or almost white, crystalline powder. Freely soluble in water and in alcohol; practically insoluble in dichloromethane.
USP 31 (Phenylpropanolamine Hydrochloride). A white crystalline powder, having a slight aromatic odour. Soluble 1 in 1.1 of water, 1 in 7.4 of alcohol, and 1 in 4100 of chloroform; insoluble in ether. pH of a 3% solution in water is between 4.2 and 5.5. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Ephedrine, p.1558.

Severe hypertensive episodes have followed phenylpropanolamine ingestion (see below). As with other indirect-acting sympathomimetics, tolerance to the therapeutic effects of phenylpropanolamine has been reported with prolonged use.

◊ An extensive and detailed review[1] of adverse effects attributed to phenylpropanolamine noted in 1990 that many of the adverse drug reactions reported in Europe described an alteration of mental status whereas those in North America were more often compatible with hypertension. The author suggested that this might be due to a difference in the isomers present in phenylpropanolamine preparations, based on earlier reports that *d*-norpseudoephedrine, the most potent of several isomeric forms as a stimulant of the CNS, was present in European preparations of phenylpropanolamine. However, later investigation suggests that currently the racemic mixture (±)-norephedrine (*d*,*l*-norephedrine) is the isomeric form present in commercial preparations in both Europe and the USA.[2]

The original review[1] concentrated on North American cases. The majority of products available were decongestants or cough or cold remedies; a small number were promoted as diet aids.

The data suggested that over-the-counter (OTC) products were more likely to be associated with an adverse reaction than a prescription medication; this may be because such OTC products were more likely to be overused and to be considered innocuous by the patient. It was also likely that drug interactions (below) rather than 'true overdosages' were involved in many of the adverse events, particularly as many OTC preparations contain other ingredients. (See also Abuse under Ephedrine, p.1558, for further discussion about the consequences of use of OTC preparations containing sympathomimetics, including phenylpropanolamine.)

The adverse reactions varied widely ranging from headache and elevated blood pressure to cardiopulmonary arrest, intracranial haemorrhage, and death. Mild reactions included blurred vision, dizziness, anxiety, agitation, tremor, confusion, and hypersensitivity reaction. Severe reactions included hypertensive crisis with hypertensive encephalopathy, seizures, arrhythmias, psychosis, and acute tubular necrosis. One unifying theme of many of the severe cases was that high blood pressure or symptoms suggestive of this were the presenting feature; an acute, persistent, severe headache was also noted in many cases.

It was pointed out that overall phenylpropanolamine was relatively safe. Although billions of doses were consumed annually, few cases of adverse drug reactions had been reported.

It was believed that certain groups may be at particular risk of adverse reactions to phenylpropanolamine: persons with elevated blood pressure, overweight persons (who are likely to be both hypertensive and to use diet aids), patients with eating disorders (who tend to abuse substances including diet aids), and the elderly (who may be multiple drug takers and likely to be hypertensive and at risk already of a stroke).

Subsequently, after a large case-control study in the USA which found an increased risk of haemorrhagic stroke associated with the use of preparations containing phenylpropanolamine (and in particular in women who used phenylpropanolamine as an appetite suppressant),[3] the FDA took steps to remove phenylpropanolamine from all drug products in the USA and requested that it no longer be marketed. Products containing phenylpropanolamine have also been withdrawn in some other countries. However, this study and the FDA decision have been criticised[4-6] notably on the basis that there was no evidence of an increased risk with the amount of phenylpropanolamine normally present in decongestant preparations and the study may have been subject to confounding. The UK CSM[7] considered that the evidence