Cough; Creo-Terpin; Creomulsion; Delsym; DexAlone; Diabe-Tuss DM; ElixSure Childrens Cough; Hold DM; Little Colds Cough Formula; PediaCare Childrens Long-Acting Cough; PediaCare Infants Long-Acting Cough; Robitussin Pediatric; Scot-Tussin DM Cough Chasers; Silphen DM; Simply Cough; Sucrets DM; Theraflu Cough; Triaminic Long Acting Cough; Trocal; Vicks 44 Cough Relief; ***Venez.:*** Bromodel†; Detofan†; Hidrofan†; Libolar; Metordex†; Mexobron†; Promedin; Tilodrin.

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

Dimemorfan Phosphate *(rINNM)*

AT-17; Dimémorfane, Phosphate de; Dimemorfani Phosphas; Fosfato de dimemorfano. (+)-3,9a-Dimethylmorphinan phosphate.

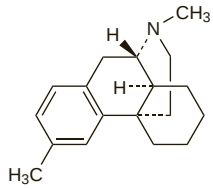
Димеморфана Фосфат

$C_{18}H_{25}N,H_3PO_4$ = 353.4.

CAS — 36309-01-0 (dimemorfan); 36304-84-4 (dimemorfan phosphate).

ATC — R05DA11.

ATC Vet — QR05DA11.



(dimemorfan)

Pharmacopoeias. In *Jpn.*

Profile

Dimemorfan phosphate is a centrally acting cough suppressant used for non-productive cough (p.1547). It is given orally in doses of 10 to 20 mg three or four times daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Tusben; ***Spain:*** Dastosin.

Dimethoxanate Hydrochloride *(BANM, rINNM)*

Diméthoxanate, Chlorhydrate de; Dimethoxanati Hydrochloridum; Hidrocloruro de dimetoxanato. 2-(2-Dimethylaminoethoxy)ethyl phenothiazine-10-carboxylate hydrochloride.

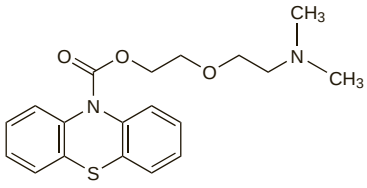
Диметоксаната Гидрохлорид

$C_{19}H_{22}N_2O_3S,HCl$ = 394.9.

CAS — 477-93-0 (dimethoxanate); 518-63-8 (dimethoxanate hydrochloride).

ATC — R05DB28.

ATC Vet — QR05DB28.



(dimethoxanate)

Profile

Dimethoxanate hydrochloride is a centrally acting cough suppressant used for non-productive cough (p.1547). It is given orally in usual doses of 37.5 mg three or four times daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Cotrane.

Dornase Alfa *(BAN, USAN, rINN)*

Deoxyribonuclease; Desoxyribonuclease; DNase I; Dornasa alfa; Dornasum Alfa; Dornaz Alfa; rhDNase. Deoxyribonuclease I (human recombinant).

Дорназа Альфа

$C_{1321}H_{1995}N_{339}O_{396}S_9$ = 29249.6.

CAS — 143831-71-4; 132053-08-8.

ATC — B06AA10; R05CB13.

ATC Vet — QB06AA10; QR05CB13.

Description. Dornase alfa is a recombinant enzyme having the same amino acid sequence and glycosylation pattern as human deoxyribonuclease I.

Adverse Effects

Common adverse effects with dornase alfa aerosol include pharyngitis, hoarseness of the voice, and chest pain. Occasionally laryngitis, conjunctivitis, and skin rashes and urticaria have been reported. There may be a transient decline in pulmonary function on beginning therapy with dornase alfa.

Uses and Administration

Dornase alfa acts as a mucolytic by hydrolysing DNA that has accumulated in sputum from decaying neutrophils. It is used as a nebulised solution in patients with cystic fibrosis; in the UK its indication is limited to patients with a forced vital capacity (FVC) greater than 40% of predicted value and to patients over 5 years of age, but in the USA it may also be given for advanced disease (FVC less than 40%) and to younger children. The usual dose is 2500 units (2.5 mg) of dornase alfa given once daily via a jet nebuliser. This dose may be given twice daily to patients over 21 years of age.

Bovine deoxyribonuclease has been used similarly. It has also been used topically, often with fibrinolysin, as a debriding agent for inflammatory and infected lesions. Bovine deoxyribonuclease has also been given by injection.

Administration in children. Although in some countries dornase alfa is not recommended for use in children under 5 years of age, a study[1] to assess the delivery of dornase alfa to the lungs of children with cystic fibrosis aged between 3 months and 5 years, showed that the amounts present in the lower airways were comparable to those in older children. It also appeared to be safe in these younger patients during the 2-week study period.

1. Wagener JS, *et al.* Aerosol delivery and safety of recombinant human deoxyribonuclease in young children with cystic fibrosis: a bronchoscopic study. *J Pediatr* 1998; **133:** 486–91.

Asthma. There are reports of the use of dornase alfa to liquefy mucus plugs and relieve an attack of acute severe asthma (p.1108) in children.[1-3] However, a randomised controlled study[4] found that adding a single dose of nebulised dornase alfa to standard emergency treatment has no benefits in children with moderate to severe acute asthma.

1. Greally P. Human recombinant DNase for mucus plugging in status asthmaticus. *Lancet* 1995; **346:** 1423–4.
2. Patel A, *et al.* Intratracheal recombinant human deoxyribonuclease in acute life-threatening asthma refractory to conventional treatment. *Br J Anaesth* 2000; **84:** 505–7.
3. Durward A, *et al.* Resolution of mucus plugging and atelectasis after intratracheal rhDNase therapy in a mechanically ventilated child with refractory status asthmaticus. *Crit Care Med* 2000; **28:** 560–2.
4. Boogaard R, *et al.* Recombinant human deoxyribonuclease for the treatment of acute asthma in children. *Thorax* 2008; **63:** 141–6.

Chronic obstructive pulmonary disease. A large phase III study in patients hospitalised for acute exacerbations of chronic bronchitis (p.1112) was halted prematurely because of a non-significant trend to increased mortality in patients given dornase alfa.[1]

1. Hudson TJ. Dornase in treatment of chronic bronchitis. *Ann Pharmacother* 1996; **30:** 674–5.

Cystic fibrosis. There is good evidence that inhalation therapy with dornase alfa can produce modest but useful improvement in lung function in some patients with cystic fibrosis (p.166). Most studies have concentrated on patients with mild or moderate disease (forced vital capacity at least 40% of the predicted value) in whom FEV_1 and forced vital capacity have shown improvements generally of the order of 5 to 10%,[1-3] and in whom more prolonged therapy (24 weeks) has been shown to reduce the risk of exacerbations of respiratory infections, and hence the need for intravenous antibacterial therapy.[3] There is also evidence that benefit may occur in patients with more severe disease.[4] A systematic review[5] of studies concluded that there is evidence to show that dornase alfa therapy over a 1-month period is associated with improved lung function. Furthermore, a randomised, multicentre, placebo-controlled study[6] in children showed that dornase alfa maintained lung function and reduced the risk of exacerbations over a period of 96 weeks. However, only a minority of patients, perhaps about one-third,[7] benefit from the drug, and at present there is no way of identifying those who will respond other than by a therapeutic trial.[8,9]

Given the high cost of therapy, which is not entirely recouped by savings in acute care, there has been some controversy about the appropriate use of dornase alfa:[10-13] it seems to be generally felt that it should be reserved for specialist use in cystic fibrosis clinics, but that patients should not be denied a trial where appropriate. Most responders with mild to moderate impairment of lung function will show improvements within 2 weeks, although in more severely affected patients a 6-week trial is advocated.[8] A review of the use of dornase alfa in cystic fibrosis concluded that dosing on alternate days would be as effective as daily dosing, and would reduce costs and treatment time.[14]

1. Ramsey BW, *et al.* Efficacy and safety of short-term administration of aerosolized recombinant human deoxyribonuclease in patients with cystic fibrosis. *Am Rev Respir Dis* 1993; **148:** 145–51.
2. Ranasinha C, *et al.* Efficacy and safety of short-term administration of aerosolised recombinant human DNase I in adults with stable stage cystic fibrosis. *Lancet* 1993; **342:** 199–202.
3. Fuchs H, *et al.* Effect of aerosolized recombinant human DNase on exacerbations of respiratory symptoms and on pulmonary function in patients with cystic fibrosis. *N Engl J Med* 1994; **331:** 637–42.
4. McCoy K, *et al.* Effects of 12-week administration of dornase alfa in patients with advanced cystic fibrosis lung disease. *Chest* 1996; **110:** 889–95.
5. Jones AP, *et al.* Dornase alpha for cystic fibrosis. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2003 (accessed 15/07/08).
6. Quan JM, *et al.* A two-year randomized, placebo-controlled trial of dornase alfa in young patients with cystic fibrosis with mild lung function abnormalities. *J Pediatr* 2001; **139:** 813–20.
7. Davis PB. Evolution of therapy for cystic fibrosis. *N Engl J Med* 1994; **331:** 672–3.
8. Conway SP, Littlewood JM. rhDNase in cystic fibrosis. *Br J Hosp Med* 1997; **57:** 371–2.
9. Ledson MJ, *et al.* Targeting of dornase alpha therapy in adult cystic fibrosis. *J R Soc Med* 1998; **91:** 360–4.
10. Anonymous. Dornase alfa for cystic fibrosis. *Drug Ther Bull* 1995; **33:** 15–16.
11. Spencer D, Weller P. Dornase-alfa for cystic fibrosis. *Lancet* 1995; **345:** 1307.
12. Bush A, *et al.* Dornase alfa for cystic fibrosis. *BMJ* 1995; **310:** 1533.
13. Robert G, *et al.* Dornase alfa for cystic fibrosis. *BMJ* 1995; **311:** 813.
14. Suri R. The use of human deoxyribonuclease (rhDNase) in the management of cystic fibrosis. *BioDrugs* 2005; **19:** 135–44.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Pulmozyme; ***Austral.:*** Pulmozyme; ***Austria:*** Pulmozyme; ***Belg.:*** Pulmozyme; ***Braz.:*** Pulmozyme; ***Canad.:*** Pulmozyme; ***Chile:*** Viscozyme; ***Cz.:*** Pulmozyme; ***Denm.:*** Pulmozyme; ***Fin.:*** Pulmozyme; ***Fr.:*** Pulmozyme; ***Ger.:*** Pulmozyme; ***Gr.:*** Pulmozyme; ***Hung.:*** Pulmozyme; ***Irl.:*** Pulmozyme; ***Israel:*** Pulmozyme; ***Ital.:*** Pulmozyme; ***Mex.:*** DNSM; Pulmozyme; ***Neth.:*** Pulmozyme; ***Norw.:*** Pulmozyme; ***NZ:*** Pulmozyme; ***Pol.:*** Pulmozyme; ***Port.:*** Pulmozyme; ***Rus.:*** Pulmozyme (Пульмозим); ***S.Afr.:*** Pulmozyme; ***Spain:*** Pulmozyme; ***Swed.:*** Pulmozyme; ***Switz.:*** Pulmozyme; ***Turk.:*** Pulmozyme; ***UK:*** Pulmozyme; ***USA:*** Pulmozyme.

Multi-ingredient: ***Arg.:*** Clorfibrase; ***Austria:*** Fibrolan; ***Braz.:*** Cauterex; Dermofibrin C†; Fibrabene; Fibrase; Fibrinase c/Cloranfenicol; Gino-Cauterex; Gino-Fibrase; Procutan†; ***Chile:*** Elase; ***Cz.:*** Fibrolan; ***Fr.:*** Elase; ***Ger.:*** Fibrolan†; ***Hung.:*** Fibrolan; ***Ital.:*** Elase†; ***Malaysia:*** Elase; ***Mex.:*** Fibrase; Fibrase SA; Ridasa; ***Pol.:*** Fibrolan; ***Switz.:*** Fibrolan.

Dropropizine *(BAN, rINN)*

Dropropitsiini; Dropropizin; Dropropizina; Dropropizinum; UCB-1967. 3-(4-Phenylpiperazin-1-yl)propane-1,2-diol.

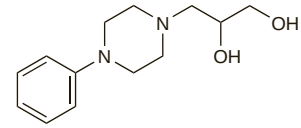
Дропропизин

$C_{13}H_{20}N_2O_2$ = 236.3.

CAS — 17692-31-8.

ATC — R05DB19.

ATC Vet — QR05DB19.



Levodropropizine *(BAN, rINN)*

DF-526; Levdropropizine; Levodropropitsiini; Levodropropizin; Levodropropizina; Levodropropizinas; Lévodropropizine; Levodropropizinum. The (–)-(*S*)-isomer of dropropizine.

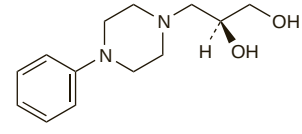
Леводропропизин

$C_{13}H_{20}N_2O_2$ = 236.3.

CAS — 99291-25-5.

ATC — R05DB27.

ATC Vet — QR05DB27.



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

Ph. Eur. 6.2 (Levodropropizine). A white or almost white powder. Slightly soluble in water and in alcohol; freely soluble in dilute acetic acid and in methyl alcohol. A 2.5% solution in water has a pH of 9.2 to 10.2. Protect from light.

Profile

Dropropizine is a cough suppressant reported to have a peripheral action in non-productive cough (p.1547). It is given orally usually in a dose of 30 mg three or four times daily. Levodropropiz-

ine, the (–)-(*S*)-isomer of dropropizine, is claimed to produce fewer CNS effects and is used similarly in an oral dose of 60 mg up to three times daily.

◊ References.

1. Catena E, Daffonchio L. Efficacy and tolerability of levodropropizine in adult patients with non-productive cough: comparison with dextromethorphan. *Pulm Pharmacol Ther* 1997; **10:** 89–96.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Perlatos; ***Belg.:*** Catabex; Levotuss; ***Braz.:*** Antux; Atossion; Ecos; Eritos; Flextoss; Neotoss; Percof; Tussiflex D; Vibral; Zyplo; ***Chile:*** Broncard; ***Cz.:*** Ditustat; Levopront; ***Ger.:*** Larylin Husten-Stiller; ***Gr.:*** Dropavix; Levotuss; ***Hung.:*** Levopront; ***Indon.:*** Levopront; ***Ital.:*** Danka; Domutussina; Levotuss; Rapitux†; Ribex Tosse; Salvituss; Tau-Tux; ***Mex.:*** Levocof; Troferit; Zyplo; ***Neth.:*** Levotuss; ***Philipp.:*** Levopront; ***Pol.:*** Levopront; ***Port.:*** Catabina; Levotuss; ***Singapore:*** Levopront†; ***Spain:*** Levotuss; Tautoss; ***Thai.:*** Levopront; ***Turk.:*** Levopront; ***Venez.:*** Antux; Levopront.

Multi-ingredient: ***Belg.:*** Catabex Expectorans†; ***Braz.:*** Notuss; ***Ital.:*** Elisir Terpina; Guaiacalcium Complex; Ribexen con Espettorante; Tiocalmina; Tussamag Complex; ***Port.:*** Catabina Expectorante.

Elecampane

Ala; Alant; Aunée; Énula; Énula campana; Helenio; Ínula; Inula.

Девясил Высокий

CAS — 97676-35-2 (elecampane oil).

Pharmacopoeias. In *Chin.* (which also includes various other species of *Inula*) and *Fr.*

Profile

Elecampane is the root of *Inula helenium* (Compositae). It has been used in herbal preparations for the treatment of cough for its supposed expectorant and cough suppressant properties. It is also used as a flavouring in foods and alcoholic beverages.

Elecampane contains sesquiterpene lactones including alantolactone (alant camphor; elecampane camphor; inula camphor; helenin), which was formerly used in the treatment of worm infections, and has also been an ingredient of some cough preparations.

Elecampane oil has been used in aromatherapy.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Brust- und Hustentee St Severin; ***Cz.:*** Klosterfrau Melisana; Species Cholagogae Planta; ***Fr.:*** Mediflor Tisane Digestive No 3; Mediflor Tisane Hepatique No 5; ***Ger.:*** Leber-Galle-Tropfen 83†; ***Pol.:*** Pectosol; ***Rus.:*** Original Grosser Bittner Balsam (Оригинальный Большой Бальзам Биттнера); ***S.Afr.:*** Wonderkroonessens; ***Spain:*** Bronpul†; Natusor Asmaten†; Natusor Broncopul†; ***Switz.:*** Hederix; Padmed Laxan; ***UK:*** Catarrh-eeze; Cough-eeze; Horehound and Aniseed Cough Mixture; Vegetable Cough Remover.

Ephedra ⊗

Efedra; Ma-huang.

Хвойник; Эфедра хвощевая (*Ephedra equisetina*)

Pharmacopoeias. In *Chin.*, *Ger.*, and *Jpn*.
Chin. also includes the roots of *Ephedra sinica* or *E. intermedia*.

Profile

Ephedra consists of the dried young branches of *Ephedra sinica*, *E. equisetina*, and *E. gerardiana* (including *E. nebrodensis*) (Ephedraceae), containing not less than 1.25% of alkaloids, calculated as ephedrine.

The action of ephedra is due to the presence of ephedrine (below) and pseudoephedrine (p.1571). It has been used chiefly as a source of these alkaloids. The FDA states that ephedra-containing dietary supplements are unsafe and the sale of these products is banned in the USA. Other countries have also banned the sale of ephedra-containing dietary supplements.

◊ For reference to the adverse effects of herbal products containing ephedra see Abuse under Ephedrine, below.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Canad.:*** Herbal Cold Relief†; ***Ger.:*** Cardibisana†; Cefadrin.

Ephedrine *(BAN)* ⊗

Efedriini; Efedrin; Efedrina; Efedrinas; Ephedrina; Éphédrine; (–)-Ephedrine; Ephedrinum. (1*R*,2*S*)-2-Methylamino-1-phenylpropan-1-ol.

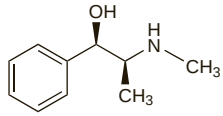
Эфедрин

$C_{10}H_{15}NO$ = 165.2.

CAS — 299-42-3 (anhydrous ephedrine); 50906-05-3 (ephedrine hemihydrate).

ATC — R01AA03; R01AB05; R03CA02; S01FB02.

ATC Vet — QG04BX90; QR01AA03; QR01AB05; QR03CA02; QS01FB02.



Description. Ephedrine is an alkaloid obtained from species of *Ephedra*, or prepared synthetically. It may exist in a hemihydrate form or as the anhydrous substance.
The following terms have been used as 'street names' (see p.vi) or slang names for various forms of ephedrine:
Trucker's Speed.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, and *US*, which have specifications, in either the same monograph or in separate monographs, for the anhydrous form and for the hemihydrate.
Ph. Eur. 6.2 (Ephedrine, Anhydrous). A white or almost white, crystalline powder or colourless crystals. Soluble in water; very soluble in alcohol. It melts at about 36°. Protect from light.
Ph. Eur. 6.2 (Ephedrine Hemihydrate; Ephedrine BP 2008). A white or almost white, crystalline powder or colourless crystals. Soluble in water; very soluble in alcohol. It melts at about 42°, determined without previous drying. Protect from light.
USP 31 (Ephedrine). It is anhydrous or contains not more than one-half molecule of water of hydration. It is an unctuous, practically colourless solid or white crystals or granules. It gradually decomposes on exposure to light. M.p. between 33° and 40°, the variability being the result of differences in the moisture content, anhydrous ephedrine having a lower melting-point than the hemihydrate. Soluble 1 in 20 of water and 1 in 0.2 of alcohol; soluble in chloroform and in ether; moderately and slowly soluble in liquid paraffin, the solution becoming turbid if the ephedrine contains more than about 1% of water. Its solutions are alkaline to litmus. Store in airtight containers at a temperature not exceeding 8°. Protect from light.

Ephedrine Hydrochloride *(BANM)* ⊗

Efedriinihydrokloridi; Efedrin Hidroklorür; Efedrin hydrochlorid; Efedrina, hidrocloruro de; Efedrin-hidroklorid; Efedrinhydroklorid; Efedrino hidrochloridas; Efedryny chlorowodorek; Ephedrinae Hydrochloridum; Éphédrine, chlorhydrate d'; Ephedrine Chloride; Ephedrini hydrochloridum; Ephedrinium Chloratum; *l*-Ephedrinum Hydrochloricum.

Эфедрина Гидрохлорид

$C_{10}H_{15}NO,HCl$ = 201.7.

CAS — 50-98-6.

ATC — R01AA03; R01AB05; R03CA02; S01FB02.

ATC Vet — QR01AA03; QR01AB05; QR03CA02; QS01FB02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet*.
Ph. Eur. 6.2 (Ephedrine Hydrochloride). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; soluble in alcohol. It melts at about 219°. Protect from light.
USP 31 (Ephedrine Hydrochloride). Fine, white, odourless crystals or powder. Soluble 1 in 3 of water and 1 in 14 of alcohol; insoluble in ether. Protect from light.

Ephedrine Sulfate ⊗

Efedrina, sulfato de; Ephedrine Sulphate *(BANM)*.

Эфедрина Сульфат

$(C_{10}H_{15}NO)_2,H_2SO_4$ = 428.5.

CAS — 134-72-5.

ATC — R01AA03; R01AB05; R03CA02; S01FB02.

ATC Vet — QR01AA03; QR01AB05; QR03CA02; QS01FB02.

Pharmacopoeias. In *Int.* and *US*.
USP 31 (Ephedrine Sulfate). Fine, white, odourless crystals or powder. It darkens on exposure to light. Soluble 1 in 1.3 of water and 1 in 90 of alcohol. Protect from light.

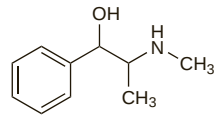
Racephedrine Hydrochloride *(BANM, USAN, rINNM)* ⊗

Efedriinihydrokloridi, raseeminen; Efedrinhydroklorid, racemisk; Efedrino (raceminio) hidrochloridas; Éphédrine (chlorhydrate d') racémique; *dl*-Ephedrine Hydrochloride; Ephedrini racemici hydrochloridum; *dl*-Ephedrinium Chloride; Hidrocloruro de racefedrina; Racém efedrin-hidroklorid; Racemic Ephedrine Hydrochloride; Racéphédrine, Chlorhydrate de; Racephedrini Hydrochloridum. (±)-2-Methylamino-1-phenylpropan-1-ol hydrochloride.

Рацефедрина Гидрохлорид

$C_{10}H_{15}NO,HCl$ = 201.7.

CAS — 90-81-3 (racephedrine); 134-71-4 (racephedrine hydrochloride).



(racephedrine)

Pharmacopoeias. In *Eur.*
Ph. Eur. 6.2 (Ephedrine Hydrochloride, Racemic; Racephedrine Hydrochloride BP 2008). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; soluble in alcohol; practically insoluble in ether. It melts at about 188°. Protect from light.

Adverse Effects

As for Sympathomimetics, p.1407. Ephedrine has both alpha- and beta-agonist effects and its commonest adverse effects are tachycardia, anxiety, restlessness, and insomnia. Tremor, dry mouth, impaired circulation to the extremities, hypertension, and cardiac arrhythmias may also occur.

Ephedrine may be used in labour to maintain blood pressure during spinal anaesthesia but can cause fetal tachycardia.

Paranoid psychosis, delusions, and hallucinations may also follow ephedrine overdosage. Prolonged use has no cumulative effect, but tolerance with dependence has been reported.

◊ For a discussion of the toxicity reported from the self-administration of ephedrine-containing dietary supplements or herbal stimulants, see Abuse, below.

Precautions

As for Sympathomimetics, p.1407. Ephedrine should be given with care to patients with hyperthyroidism, diabetes mellitus, ischaemic heart disease, hypertension, renal impairment, or angle-closure glaucoma. In patients with prostatic enlargement, ephedrine may increase difficulty with micturition.

Irritability and disturbed sleep have been reported in breast-fed infants.

Abuse. Although illicit use of ephedrine is primarily in the manufacture of street stimulants such as metamfetamine (p.2158), there is increasing evidence of the abuse of ephedrine preparations in some countries,[1] and the public health and social problems associated with its abuse appear to be significant, particularly in certain African countries. Ephedrine is also sold as a street substitute for 'Ecstasy' (Methylenedioxymethamfetamine, p.2159).

Adverse effects reported with illicit ephedrine use include cardiovascular toxicity[2,3] and chest pain.[4]

There is controversy over the abuse liability of over-the-counter (OTC) stimulants such as ephedrine:[5] some studies have indicated that ephedrine is, overall, a relatively weak reinforcer whereas others have suggested that the abuse potential may be high. Examination of the characteristics of 5 patients who had been taking ephedrine-containing OTC preparations in high doses for periods ranging from 8 months to 2 years, emphasised the reinforcing and, therefore, addictive potential of ephedrine; similar observations were made for 2 patients who had ingested phenylpropanolamine long term, combined with pseudoephedrine in one of these cases. The authors suggested that, for most people, OTC preparations containing weaker sympathomimetics will not be reinforcing at the recommended doses. However, these cases strengthen the research findings that high-dose use of an OTC stimulant increases its potency, and thus its effects become more like amfetamine (p.2150).

Toxicity has also been reported[6-8] from the self-administration of ephedrine-containing dietary supplements or herbal stimulants, usually based on ephedra (ma-huang) and marketed for a variety of purposes including weight loss and as an alternative to illegal drugs of abuse. Not all cases of ephedrine toxicity have arisen as a result of overt abuse but rather because of inadequate labelling of content and dosage instructions on some unlicensed products. A small study found that combinations of herbal caffeine and ephedra alkaloids taken in recommended amounts resulted in plasma ephedrine concentrations that exceeded the usual therapeutic range. Significant increases occurred in blood pressure and heart rate, and unfavourable effects on glucose and potassium homoeostasis were noted.[9] The use of ephedra-containing dietary supplements is now banned in the USA and some other countries.