Profile
Cilomilast is a phosphodiesterase type-4 inhibitor that has been investigated in the treatment of chronic obstructive pulmonary disease.

Clenbuterol Hydrochloride *(BANM, rINNM)* ⊗

Clenbutérol, chlorhydrate de; Clenbuteroli hydrochloridum; Hidrocloruro de clenbuterol; Klenbuterol hydrochlorid; Klenbuterol-hidroklorid; Klenbuterolhydroklorid; Klenbuterolihydrokloridi; Klenbuterolio hidrochloridas; NAB-365 (clenbuterol). 1-(4-Amino-3,5-dichlorophenyl)-2-*tert*-butylaminoethanol hydrochloride.

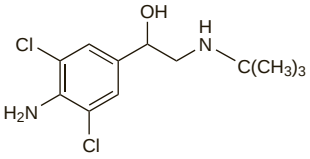
Кленбутерола Гидрохлорид

$C_{12}H_{18}Cl_2N_2O,HCl$ = 313.7.

CAS — 37148-27-9 (clenbuterol); 21898-19-1 (clenbuterol hydrochloride).

ATC — R03AC14; R03CC13.

ATC Vet — QR03AC14; QR03CC13.



(clenbuterol)

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of clenbuterol:
Angel Dust;
Clen.

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

Ph. Eur. 6.2 (Clenbuterol Hydrochloride). A white or almost white crystalline powder. Soluble in water and in alcohol; slightly soluble in acetone. A 5% solution in water has a pH of 5.0 to 7.0.

Profile
Clenbuterol hydrochloride is a direct-acting sympathomimetic with mainly beta-adrenergic activity and a selective action on $beta_2$ receptors (a $beta_2$ agonist). It has properties similar to those of salbutamol (p.1131). It is used as a bronchodilator in the management of reversible airways obstruction, as in asthma (p.1108) and in certain patients with chronic obstructive pulmonary disease (p.1112). A usual oral dose is 20 micrograms twice daily; doses of up to 40 micrograms twice daily have occasionally been given. Clenbuterol hydrochloride has also been given by inhalation. In patients with asthma, as-required beta agonist therapy is preferable to regular use. An increased need for, or decreased duration of effect of, clenbuterol indicates deterioration of asthma control and the need for review of therapy.

Abuse. Clenbuterol has been used illicitly in animal feeds in an attempt to promote weight gain and to increase muscle to lipid mass. Adverse effects typical of sympathomimetic activity have been attributed to such misuse both in farmers perpetrating such acts[1] and in innocent persons consuming meat products from affected animals.[2-5] Clenbuterol has been abused by sportsmen for its anabolic effects,[6] although it is doubtful as to whether it enhances performance.[7] Myocardial infarction was described in an otherwise healthy 17-year-old bodybuilder after abuse of clenbuterol.[8] Coronary artery spasm and/or temporary thrombosis were suggested as possible explanations for this adverse effect. Contamination of illicit heroin with clenbuterol has also been reported.[9]

1. Dawson J. β Agonists put meat in the limelight again. *BMJ* 1990; **301:** 1238–9.
2. Martínez-Navarro JF. Food poisoning related to consumption of illicit β-agonist in liver. *Lancet* 1990; **336:** 1311.
3. Maistro S, *et al.* Beta blockers to prevent clenbuterol poisoning. *Lancet* 1995; **346:** 180.
4. Brambilla G, *et al.* Food poisoning following consumption of clenbuterol-treated veal in Italy. *JAMA* 1997; **278:** 635.
5. Ramos F, *et al.* Proposed guidelines for clenbuterol food poisoning. *Am J Med* 2004; **117:** 362.
6. Anonymous. Muscling in on clenbuterol. *Lancet* 1992; **340:** 403.
7. Spann C, Winter ME. Effect of clenbuterol on athletic performance. *Ann Pharmacother* 1995; **29:** 75–7.
8. Kierzkowska B, *et al.* Myocardial infarction in a 17-year-old body builder using clenbuterol. *Circ J* 2005; **69:** 1144–6.
9. CDC. Atypical reactions associated with heroin use: five states, January-April 2005. *MMWR* 2005; **54:** 793–6. Correction. *ibid.*; 852.

Urinary incontinence. A systematic review of the use of adrenergic agonists, including clenbuterol, in urinary incontinence, found that there was weak evidence to suggest that their use was better than placebo.[1] Although only minor adverse effects were reported, the authors noted that there was still potential for rare but serious adverse effects reported elsewhere in the literature.

1. Alhasso A, *et al.* Adrenergic drugs for urinary incontinence in adults. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2005 (accessed 15/01/08).

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Bronq-C; Clembumar; Oxibron; ***Austria:*** Spiropent; ***Chile:*** Airum; Asmeren; Broncotosil†; ***Cz.:*** Spiropent; ***Ger.:*** Contraspasmin†; Spiropent; ***Gr.:*** Spiropent; ***Hong Kong:*** Clenasma†; ***Hung.:*** Spiropent; ***Indon.:*** Spiropent; ***Ital.:*** Clenasma†; Monores; Prontovent†; Spiropent; ***Jpn:*** Spiropent; ***Mex.:*** Novegam; Oxyflux; Spiropent; ***Philipp.:*** Spiropent; ***Port.:*** Broncoterol; Cesbron; ***Spain:*** Spiropent†; Ventolase; ***Venez.:*** Brodilan; Brodilin; Buclen; Clenbunal; Risopent.

Multi-ingredient: ***Arg.:*** Mucosolvon Compositum; Oxibron NF; ***Austria:*** Mucospas; ***Ger.:*** Spasmo-Mucosolvan; ***Mex.:*** Ambodil-C; Balsibron-C; Brogal Compositum; Bronolban-M; Brosolan C; Broxofar Compuesto; Broxol Plus; Broxolim-C; Ebromin P; Fludexol-CL; Loxorol; Mucosolvan Compositum; Mucovibrol C; Sekretovit Ex; Septacin Ex; Seraxol; Serbol; ***Port.:*** Clembroxol; Mucospas; Ventoliber; ***Venez.:*** Ambromuco Compositum; Arbixil; Clenbuxol; Litusix Compositum; Mucolin; Mucosolvan Compositum.

Diprophylline *(BAN, rINN)*

Dihydroxypropyltheophyllinum; Diprofilina; Diprofilinas; Diprofillin; Diprofylin; Diprofylliini; Diprofyllin; Diprophyllinum; Dyphylline; Glyphyllinum; Hyphylline. 7-(2,3-Dihydroxypropyl)-1,3-dimethylxanthine; 7-(2,3-Dihydroxypropyl)theophylline.

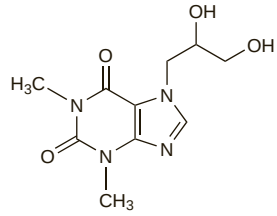
Дипрофиллин

$C_{10}H_{14}N_4O_4$ = 254.2.

CAS — 479-18-5.

ATC — R03DA01.

ATC Vet — QR03DA01.



Pharmacopoeias. In *Chin., Eur.* (see p.vii), and *US.*

Ph. Eur. 6.2 (Diprophylline). A white or almost white, crystalline powder. Freely soluble in water; slightly soluble in alcohol. Protect from light.

USP 31 (Dyphylline). A white, odourless, amorphous or crystalline solid. Freely soluble in water; sparingly soluble in alcohol and in chloroform; practically insoluble in ether. A 1% solution in water has a pH of 5.0 to 7.5. Store in airtight containers.

Adverse Effects, Treatment, and Precautions
As for Theophylline, p.1140. Diprophylline is primarily excreted unchanged in the urine and should therefore be used with caution in patients with renal impairment; dose adjustments may be required. However, unlike theophylline, plasma concentrations of diprophylline are not greatly affected by changes in liver function or hepatic enzyme activity such as those produced by smoking or age.

Breast feeding. In a study of 20 women given diprophylline by intramuscular injection,[1] diprophylline was found to concentrate in breast milk, with a milk to serum concentration ratio of about 2. However, it was felt that the quantity of diprophylline a breast-fed infant would ingest was unlikely to produce any pharmacological action unless the child was very sensitive. The American Academy of Pediatrics[2] also considers that the use of diprophylline is usually compatible with breast feeeding.

1. Jarboe CH, *et al.* Dyphylline elimination kinetics in lactating women: blood to milk transfer. *J Clin Pharmacol* 1981; **21:** 405–10.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 19/03/08)

Interactions
Since diprophylline does not undergo metabolism by hepatic microsomal cytochrome P450 it does not exhibit the numerous interactions seen with theophylline (p.1142). However, the possibility of synergistic effects should be borne in mind if it is prescribed with other xanthines.

Probenecid. Probenecid has been reported to decrease the clearance of diprophylline thus prolonging its half-life.[1-3]

1. May DC, Jarboe CH. Inhibition of clearance of dyphylline by probenecid. *N Engl J Med* 1981; **304:** 791.
2. May DC, Jarboe CH. Effect of probenecid on dyphylline elimination. *Clin Pharmacol Ther* 1983; **33:** 822–5.
3. Acara M, *et al.* Probenecid inhibition of the renal excretion of dyphylline in chicken, rat and man. *J Pharm Pharmacol* 1987; **39:** 526–30.

Pharmacokinetics
Diprophylline is rapidly absorbed from the gastrointestinal tract and from the site of intramuscular injections. Diprophylline is not converted to theophylline in the body. It is largely excreted unchanged in the urine with an elimination half-life of about 2 hours. Diprophylline is distributed into breast milk.

Uses and Administration
Diprophylline is a theophylline derivative which is used similarly to theophylline (p.1146) as a bronchodilator in reversible airways obstruction.

The usual oral dose of diprophylline is up to 15 mg/kg every 6 hours. It has also been given intramuscularly. Diprophylline is also an ingredient of preparations that have been promoted for coughs.

Action. Improvements in measurements of lung function after diprophylline in oral doses of 15 and 20 mg/kg were only one-third to one-half those obtained after oral theophylline 6 mg/kg.[1]

1. Furukawa CT, *et al.* Diphylline versus theophylline: a double-blind comparative evaluation. *J Clin Pharmacol* 1983; **23:** 414–18.

Preparations
USP 31: Dyphylline and Guaifenesin Elixir; Dyphylline and Guaifenesin Tablets; Dyphylline Elixir; Dyphylline Injection; Dyphylline Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Austrophyllin†; ***Gr.:*** Silbephylline†; ***Hong Kong:*** Syneophylline; ***Ital.:*** Katasma; ***Port.:*** Neufil; ***Turk.:*** Difilin; ***USA:*** Dilor†; Dylix; Lufyllin.

Multi-ingredient: ***Fr.:*** Ozothine a la Diprophylline; ***Israel:*** Philinal; Philinet; ***Ital.:*** Cort-Inal; ***Spain:*** Alergical Expect; Bronsal; Novofilin†; ***UK:*** Noradran; ***USA:*** Difil-G; Dilex-G; Dy-G; Dyflex-G; Dyline GG†; Dyphylline-GG; Jay-Phyl; Lufyllin-EPG†; Lufyllin-GG; Panfil G.

Doxofylline *(USAN, rINN)*

ABC 12/3; Doxofilina; Doxofyllinum. 7-(1,3-Dioxolan-2-ylmethyl)theophylline.

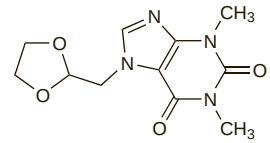
Доксофиллин

$C_{11}H_{14}N_4O_4$ = 266.3.

CAS — 69975-86-6.

ATC — R03DA11.

ATC Vet — QR03DA11.



Profile
Doxofylline is a theophylline derivative (p.1140) which is used as a bronchodilator in reversible airways obstruction. It is given in oral doses of up to 1200 mg daily. It may also be given by slow intravenous injection.

Preparations
Proprietary Preparations (details are given in Part 3)
Ital.: Ansimar; ***Mex.:*** Axofin; ***Philipp.:*** Ansimar; ***Thai.:*** Puroxan.

Etamiphylline Camsilate *(BANM, rINNM)*

Camsilato de etamifilina; Diétamiphylline Camphosulfonate; Étamiphylline, Camsilate d'; Etamiphylline Camsylate; Etamiphyllini Camsilas; Etamphyllin Camsylate. 7-(2-Diethylaminoethyl)-1,3-dimethylxanthine camphor-10-sulphonate; 7-(2-Diethylaminoethyl)theophylline camphor-10-sulphonate.

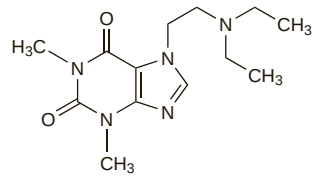
Этамифиллина Камзилат

$C_{23}H_{37}N_5O_6S$ = 511.6.

CAS — 314-35-2 (etamiphylline); 19326-29-5 (etamiphylline camsilate).

ATC — R03DA06.

ATC Vet — QR03DA06.



(etamiphylline)

Pharmacopoeias. In *BP(Vet).*

BP(Vet) 2008 (Etamiphylline Camsilate). A white or almost white powder. Very soluble in water; soluble in alcohol and in chloroform; very slightly soluble in ether. A 10% solution in water has a pH of 3.9 to 5.4.

Profile
Etamiphylline camsilate is a derivative of theophylline (p.1140) and has been used as a bronchodilator in reversible airways ob-

struction. Etamiphylline does not liberate theophylline in the body. Etamiphylline camsilate is used in veterinary medicine.

The hydrochloride salt has also been used.

Preparations

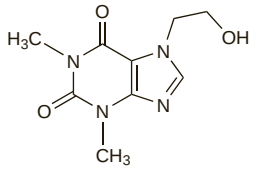
Proprietary Preparations (details are given in Part 3)
Spain: Solufilina.

Etofylline *(BAN, rINN)*

Aethophyllinum; Etofilina; Etofilinas; Etofillin; Etofylin; Etofylliini; Etofyllin; Étofylline; Etofyllinum; Hydroxyaethyltheophyllinum; Hydroxyéthylthéophylline; Oxyetophylline. 7-(2-Hydroxyethyl)-1,3-dimethylxanthine; 3,7-Dihydro-7-(2-hydroxyethyl)-1,3-dimethyl-1*H*-purine-2,6-dione; 7-(2-Hydroxyethyl)theophylline.

Этофиллин

$C_9H_{12}N_4O_3$ = 224.2.
CAS — 519-37-9.
ATC — C04AD04.
ATC Vet — QC04AD04.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Etofylline). A white or almost white, crystalline powder. Soluble in water; slightly soluble in alcohol. Protect from light.

Profile

Etofylline is a derivative of theophylline (p.1140) that is an ingredient of preparations promoted for respiratory and cardiovascular disorders. It is not converted to theophylline in the body.

Etofylline nicotinate has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Oxyphyllin.

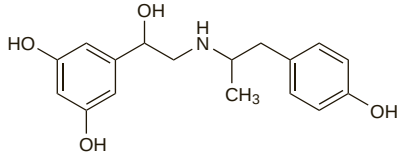
Multi-ingredient: ***Austria:*** Instenon; ***Cz.:*** Ersilan; Oxantil; ***Hong Kong:*** Instenon; ***India:*** Albutamol; Bronchilet†; Dericip; Deriphyllin; Etyofil†; Terphylin; ***Rus.:*** Instenon (Инстенон); ***S.Afr.:*** Actophlem; Alcophyllex; Dilinct; Solphyllex; Solphyllin; Theophen; Theophen Comp; ***Thai.:*** Instenon†.

Fenoterol *(BAN, USAN, rINN)* ⊗

Fénotérol; Fenoteroli; Fenoterolum. 1-(3,5-Dihydroxyphenyl)-2-(4-hydroxy-α-methylphenethylamino)ethanol.

Фенотерол

$C_{17}H_{21}NO_4$ = 303.4.
CAS — 13392-18-2.
ATC — G02CA03; R03AC04; R03CC04.
ATC Vet — QG02CA03; QR03AC04; QR03CC04.



Fenoterol Hydrobromide *(BANM, rINNM)* ⊗

Fénotérol, bromhydrate de; Fenoterol-hidrobromid; Fenoterol-hydrobromid; Fenoterol-hydrobromid; Fenoteroli hydrobromidum; Fenoterolihydrobromidi; Fenoterolio hidrobromidas; Fenoterolu bromowodorek; Hidrobromuro de fenoterol; TH-1165a. 1-(3,5-Dihydroxyphenyl)-2-(4-hydroxy-α-methylphenethylamino)ethanol hydrobromide.

Фенотерола Гидробромид

$C_{17}H_{21}NO_4$,HBr = 384.3.
CAS — 1944-12-3.
ATC — G02CA03; R03AC04; R03CC04.
ATC Vet — QG02CA03; QR03AC04; QR03CC04.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Fenoterol Hydrobromide). A white or almost white, crystalline powder. Soluble in water and in alcohol. A 4% solution in water has a pH of 4.2 to 5.2. Protect from light.

Adverse Effects and Precautions

As for Salbutamol, p.1131.

Increased mortality. Since the introduction of metered-dose aerosols of beta agonists there have been two reported epidemics of increased morbidity and mortality in asthmatic patients associated with their use. The first occurred in the 1960s and was linked with the use of high-dose isoprenaline inhalers.[1] The use of isoprenaline was subsequently largely stopped in favour of more selective beta$_2$ agonists.

The second epidemic occurred in New Zealand in the late 1970s and 1980s and was associated with the use of fenoterol.[1-5] When use of fenoterol fell in New Zealand, so too did the asthma mortality rate.[5] Heavy or regular use of fenoterol was implicated.[6,7] Fenoterol was also implicated in increased asthma morbidity and mortality in a study in Canada,[7] as was salbutamol, and results from Japan also suggested a relation between asthma deaths and excessive use of beta agonists, particularly fenoterol.[8] However, an analysis of the New Zealand deaths could not identify such a risk with beta agonists other than fenoterol.[5]

There is still debate about this second epidemic. The individual case control studies, including the one from Canada,[7] showed an increased morbidity and mortality in patients taking fenoterol, but a meta-analysis of the accumulated data to 1992 suggested that the increase in mortality in the patients taking beta$_2$ agonists was slight and only significant when they were given by nebulisation.[9] Also a working party of the UK CSM considered[10] that a causal link between asthma mortality and beta-agonist use could neither be confirmed nor refuted.

Not surprisingly there are different views on the cause of the increased asthma mortality. The cardiotoxicity of the beta agonist might have to be considered, although evidence for such an effect is felt by some to be slight.[11] The severity of the asthma might have been a factor in two different ways. One hypothesis is that patients used more fenoterol because they had severe asthma and were already at increased risk of dying.[12] Another proposes that heavy beta-agonist use led to an increase in asthma severity[13] which could be explained by a down regulation of beta receptors.[14]

This may appear to be only of historical interest since mortality rates have fallen and current recommendations for the use of short-acting beta$_2$ agonists, which are generally more selective than fenoterol, are for them to be taken as required rather than on a regular basis; indeed increasing use of such drugs is seen as an indication to amend the treatment schedule. Moreover, the dose of fenoterol has been reduced in recent years. However, controversy over regular use of short-acting beta$_2$ agonists continues to be fed by conflicting studies of their benefit. More recently 2 further observational studies have reported an association between use of short-acting beta$_2$ agonists and adverse effects on mortality.[15,16] A cohort study,[15] designed to evaluate the effect of respiratory medications on asthma death, found an association between the excessive use of short-acting beta$_2$ agonists and an increased risk of asthma death; no additional risk was found with fenoterol beyond the risk associated with beta$_2$ agonists as a class. It was unknown whether excessive use was a symptom or a cause of worsening asthma. A case-control study[16] similarly found a modestly increased risk of mortality associated with use of short-acting beta$_2$ agonists in the previous 1 to 5 years. However, the study had insufficient power to come to any conclusions regarding the effects of fenoterol, which was rarely prescribed alone, and concluded that evidence for a direct adverse effect of beta$_2$ agonists was inconclusive; other explanations might include lack of more appropriate asthma care, more severe disease or increasing severity of disease, or a tendency for patients whose disease was not responding to receive a wider range of treatments.

For discussion of similar concerns about the use of *long-acting* beta$_2$ agonists in asthma, see Salmeterol, p.1135.

1. Pearce N, *et al.* Beta agonists and asthma mortality: déjà vu. *Clin Exp Allergy* 1991; **21:** 401–10.
2. Crane J, *et al.* Prescribed fenoterol and death from asthma in New Zealand, 1981-83: case-control study. *Lancet* 1989; **i:** 917–22.
3. Pearce N, *et al.* Case-control study of prescribed fenoterol and death from asthma in New Zealand, 1977–81. *Thorax* 1990; **45:** 170–5.
4. Grainger J, *et al.* Prescribed fenoterol and death from asthma in New Zealand, 1981–7: a further case-control study. *Thorax* 1991; **46:** 105–111.
5. Pearce N, *et al.* End of the New Zealand asthma mortality epidemic. *Lancet* 1995; **345:** 41–4.
6. Sears MR, *et al.* Regular inhaled beta-agonist treatment in bronchial asthma. *Lancet* 1990; **336:** 1391–6.
7. Spitzer WO, *et al.* The use of β-agonists and the risk of death and near death from asthma. *N Engl J Med* 1992; **326:** 501–6.
8. Beasley R, *et al.* β-agonist therapy and asthma mortality in Japan. *Lancet* 1998; **351:** 1406–7.
9. Mullen M, *et al.* The association between β-agonist use and death from asthma: a meta-analytic integration of case control studies. *JAMA* 1993; **270:** 1842–5.
10. Committee on Safety of Medicines. Beta-agonist use in asthma: report from the CSM Working Party. *Current Problems 33* 1992. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024451&RevisionSelectionMethod=LatestReleased (accessed 15/01/08)
11. Sears MR, Taylor DR. The β -agonist controversy: observations, explanations and relationship to asthma epidemiology. *Drug Safety* 1994; **11:** 259–83.
12. Fuller RW. Use of β agonists in asthma: much ado about nothing? *BMJ* 1994; **309:** 795–6.
13. Sears MR. Asthma deaths in New Zealand. *Lancet* 1995; **345:** 655–6.
14. Tattersfield AE. Use of β agonists in asthma: much ado about nothing? *BMJ* 1994; **309:** 794–5.
15. Lanes SF, *et al.* Respiratory medications and risk of asthma death. *Thorax* 2002; **57:** 683–6.
16. Anderson HR, *et al.* Bronchodilator treatment and deaths from asthma: case-control study. Abridged version: *BMJ* 2005; **330:** 117. Full version: http://www.bmj.com/cgi/reprint/330/7483/117 (accessed 15/01/08)

Pulmonary oedema. Pulmonary oedema has occurred in women given beta agonists, including fenoterol,[1] for premature labour. The risk factors, the most important of which is fluid overload, are discussed under Precautions for Salbutamol, on p.1132.

1. Hawker F. Pulmonary oedema associated with β -sympathomimetic treatment of premature labour. *Anaesth Intensive Care* 1984; **12:** 143–51.

Interactions

As for Salbutamol, p.1132.

Pharmacokinetics

Fenoterol is incompletely absorbed from the gastrointestinal tract and is also subject to extensive first-pass metabolism by sulfate conjugation. It is excreted in the urine and bile almost entirely as the inactive sulfate conjugate. Fenoterol is distributed into breast milk.

◊ References.

1. Warnke K, *et al.* The pharmacokinetics of the beta 2-adrenoceptor agonist fenoterol in healthy women. *Eur J Clin Pharmacol* 1992; **43:** 663–5.
2. Hochhaus G, Möllmann H. Pharmacokinetic/pharmacodynamic characteristics of the beta-2-agonists terbutaline, salbutamol and fenoterol. *Int J Clin Pharmacol Ther Toxicol* 1992; **30:** 342–62.
3. Hildebrandt R, *et al.* Pharmacokinetics of fenoterol in pregnant and nonpregnant women. *Eur J Clin Pharmacol* 1993; **45:** 275–7.

Uses and Administration

Fenoterol is a direct-acting sympathomimetic with beta-adrenoceptor stimulant activity largely selective for beta$_2$ receptors (a beta$_2$ agonist). It has actions and uses similar to those of salbutamol (p.1133) and is used as a bronchodilator in the management of reversible airways obstruction, as occurs in asthma (p.1108) and in some patients with chronic obstructive pulmonary disease (p.1112). On inhalation, fenoterol acts rapidly (5 minutes) and has a duration of action of about 6 to 8 hours.

In the management of **reversible airways obstruction,** fenoterol hydrobromide may be given from a *metered-dose aerosol* in a dose of 1 or 2 inhalations of 100 micrograms up to 3 or 4 times daily, to a maximum of 800 micrograms daily. Current asthma guidelines recommend that inhaled short-acting beta$_2$ agonists such as fenoterol be used on an 'as-required', not regular, basis. In those patients requiring more than occasional use of fenoterol, anti-inflammatory therapy is also needed. An increased requirement for, or decreased duration of effect of, fenoterol indicates deterioration of asthma control and the need for increased anti-inflammatory therapy.

Fenoterol hydrobromide may be given as a *nebulised solution*; the usual dose for inhalation by this route is 0.5 to 1 mg. In more refractory cases up to 2.5 mg may be given. Treatment may be repeated every 6 hours as required.

Fenoterol hydrobromide may also be given *orally* for the relief of bronchospasm at a dose of 2.5 to 5 mg three times daily.

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

Fenoterol hydrobromide has also been used similarly to salbutamol, in the management of **premature labour** (see p.2003). A suggested dose, by intravenous infusion, has been 1 to 3 micrograms/minute, up to a maximum of 5 micrograms/minute, followed by oral doses of 5 mg every 3 to 6 hours.

Administration in children. In some countries fenoterol has been given via a metered-dose inhaler to children over 6 years of