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

The hydrochloride salt has also been used.

Preparations

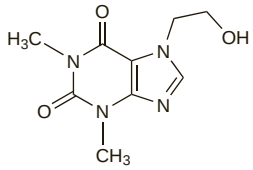
Proprietary Preparations (details are given in Part 3)
Spain: Solufilina.

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.

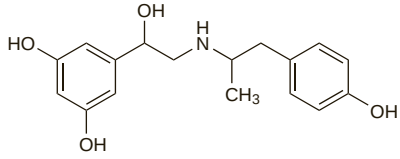
Multi-ingredient: ***Austria:*** Instenon; ***Cz.:*** Ersilan; Oxantil; ***Hong Kong:*** Instenon; ***India:*** Albutamol; Bronchilet†; Dericip; Deriphyllin; Etyofil†; Terphylin; ***Rus.:*** Instenon (Инстенон); ***S.Afr.:*** Actophlem; Alcophyllex; Dilinct; Solphyllex; Solphyllin; Theophen; Theophen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

age, at the same doses used in adults (see Uses and Administration, above).

Fenoterol hydrobromide is also given orally to children for the relief of bronchospasm in the following doses:

- children aged 1 to 3 years, 1.25 mg three times daily
- children aged 4 to 10 years, 2.5 mg three times daily
- children aged over 10 years, as for adults (see Uses and Administration, above)

Preparations

BP 2008: Fenoterol Pressurised Inhalation.

Proprietary Preparations (details are given in Part 3)
Arg.: Alveofen; Asmopul; Berotec; ***Austral.:*** Berotec†; ***Austria:*** Berotec; ***Belg.:*** Berotec; ***Braz.:*** Berotec; Bromifen; Bromotec; Febiotec†; Fenozan; ***Canad.:*** Berotec; ***Chile:*** Berotec†; Parsistene†; ***Cz.:*** Berotec; Partusisten†; ***Denm.:*** Berotec; ***Fin.:*** Berotec†; ***Ger.:*** Berotec; Partusisten; ***Hong Kong:*** Berotec†; ***Hung.:*** Berotec; ***Indon.:*** Berotec; ***Ital.:*** Dosberotec; ***Jpn:*** Berotec; ***Malaysia:*** Berotec; Feno; ***Mex.:*** Berotec†; Partusisten; ***Neth.:*** Berotec; Partusisten; ***Norw.:*** Berotec; ***Philipp.:*** Berotec; ***Pol.:*** Berotec; ***Port.:*** Berotec; ***Rus.:*** Berotec (Беротек); Partusisten (Партусистен); ***S.Afr.:*** Berotec; ***Singapore:*** Berotec; ***Spain:*** Berotec†; ***Swed.:*** Berotec†; ***Switz.:*** Berotec; ***Thai.:*** Berotec; ***Venez.:*** Berotec†; Segamol.

Multi-ingredient: ***Arg.:*** Berodual; Duotec†; Ipradual; ***Austria:*** Berodual; Berodualin; Ditec; ***Belg.:*** Duovent; ***Braz.:*** Duovent; Fymnal†; ***Canad.:*** Duovent; ***Chile:*** Berodual; ***Cz.:*** Berodual; Ditec†; ***Denm.:*** Berodual; ***Fin.:*** Atrovent Comp; ***Fr.:*** Bronchodual; ***Ger.:*** Berodual; Ditec†; ***Gr.:*** Berodual; ***Hong Kong:*** Berodual†; ***Hung.:*** Berodual; Duotec†; ***India:*** Fenovent; ***Indon.:*** Berodual; ***Irl.:*** Duovent; ***Ital.:*** Duovent; Iprafen; ***Malaysia:*** Berodual; Duovent; ***Mex.:*** Berodual; Berosolvon; ***Neth.:*** Berodual; ***Philipp.:*** Berodual; ***Pol.:*** Berodual; ***Port.:*** Berodual; ***Rus.:*** Berodual (Бородуал); Ditec (Дитек); ***S.Afr.:*** Atrovent Beta; Berodual; Duovent; Sabax Nebrafen; ***Singapore:*** Berodual; Duovent; ***Spain:*** Berodual†; ***Switz.:*** Berodual; ***Thai.:*** Berodual; Inhalex; Punol; ***UK:*** Duovent; ***Venez.:*** Berodual; Berosolvon†; Duovent; Respidual.

Fenspiride Hydrochloride *(USAN, rINNM)*

Decaspiride; Fenspiride, Chlorhydrate de; Fenspiridi Hydrochloridum; Hidrocloruro de fenspirida; JP-428; NAT-333; NDR-5998A. 8-Phenethyl-1-oxa-3,8-diazaspiro[4.5]decan-2-one hydrochloride.

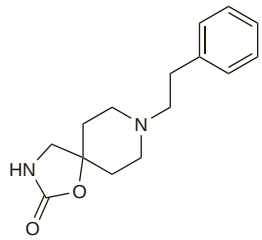
Фенспирида Гидрохлорид

$C_{15}H_{20}N_2O_2.HCl$ = 296.8.

CAS — 5053-06-5 (fenspiride); 5053-08-7 (fenspiride hydrochloride).

ATC — R03BX01; R03DX03.

ATC Vet — QR03BX01; QR03DX03.



(fenspiride)

Profile

Fenspiride is reported to have bronchodilator and anti-inflammatory properties. It is given as the hydrochloride in asthma (p.1108) and other respiratory disorders in usual oral doses of 160 to 240 mg daily in divided doses before meals. It has also been given rectally and by intramuscular or intravenous injection.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Pneumorel; ***Hong Kong:*** Pneumorel; ***Ital.:*** Pneumorel; ***Pol.:*** Eurespal; ***Port.:*** Fenspin†; Pneumorel; ***Rus.:*** Eurespal (Эреспал).

Formoterol Fumarate *(BANM, USAN, rINNM)* ⊗

BD-40A; CGP-25827A; Eformoterol Fumarat; Eformoterol Fumarate; Formoterol Fumarat; Formotérol, fumarate de; Formoterolfumarat; Formoterol-fumarát; Formoteroli fumaras; Formoterolifumaraatti; Formoterolio fumaratas; Formoterolu fumaran; Fumarato de formoterol; YM-08316. (±)-2′-Hydroxy-5′-[(*RS*)-1-hydroxy-2-{[(*RS*)-*p*-methoxy-α-methylphenethyl]amino}ethyl]formanilide fumarate.

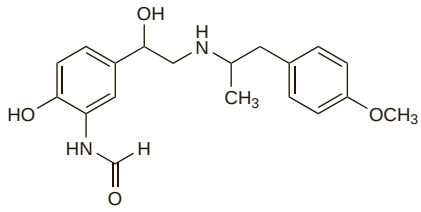
Формотерола Фумарат

$(C_{19}H_{24}N_2O_4)_2.C_4H_4O_4$ = 804.9.

CAS — 73573-87-2 (formoterol); 43229-80-7 (formoterol fumarate).

ATC — R03AC13.

ATC Vet — QR03AC13.



(formoterol)

Pharmacopoeias. In *Jpn. Eur.* (see p.vii) includes the dihydrate.

Ph. Eur. 6.2 (Formoterol Fumarate Dihydrate; Formoteroli Fumaras Dihydricus). A white or almost white or slightly yellow powder. Slightly soluble in water and in isopropyl alcohol; practically insoluble in acetonitrile; soluble in methyl alcohol. A 0.1% solution in water has a pH of 5.5 to 6.5. Protect from light.

Adverse Effects and Precautions

As for Salbutamol, p.1131. Inhalation of formoterol may be associated with paradoxical bronchospasm, and high doses have been associated with an increase in severe exacerbations of asthma. It should not be used in patients who are not also receiving an inhaled corticosteroid.

Long-acting $beta_2$ agonists such as formoterol are not appropriate for the treatment of acute bronchospasm.

Conjunctival irritation and eyelid oedema have been reported in isolated cases.

◊ References.

1. Wilton LV, Shakir SA. A post-marketing surveillance study of formoterol (Foradil): its use in general practice in England. *Drug Safety* 2002; **25:** 213–23.
2. Pauwels RA, *et al.* Formoterol as relief medication in asthma: a worldwide safety and effectiveness trial. *Eur Respir J* 2003; **22:** 787–94.

Asthma. A review of 3 controlled studies comparing inhaled formoterol with placebo, concluded that regular use of high-dose formoterol (48 micrograms daily) may be associated with more frequent serious asthma exacerbations.[1] The concomitant use of inhaled corticosteroids was allowed but not mandatory, and was not reported in the review, which led to debate on whether the results of the study would be applicable when current prescribing guidelines for asthma were followed.[2,3]

In contrast to this, a subsequent study,[4] designed to test the hypothesis of a dose-related increase in serious asthma exacerbations with formoterol therapy, did not show any increase in serious asthma exacerbations between different formoterol doses and placebo. Again, inhaled corticosteroid use was allowed but not mandatory, with 62.4% of patients reported as receiving regular anti-inflammatory therapy.

A systematic review[5] firmly concluded that the addition of a long-acting $beta_2$ agonist (such as formoterol) to low or high doses of inhaled corticosteroids reduced the risk of asthma exacerbations compared with ongoing treatment with similar doses of inhaled corticosteroids alone. The addition of a long-acting $beta_2$ agonist reduced by 19% the relative risk and by 5% the absolute risk of patients requiring systemic corticosteroids for an asthma exacerbation, over 4 to 54 weeks.

For discussion of serious adverse effects associated with long-acting $beta_2$ agonists in asthma, see Increased Mortality, under Salmeterol p.1135.

1. Mann M, *et al.* Serious asthma exacerbations in asthmatics treated with high-dose formoterol. *Chest* 2003; **124:** 70–4.
2. Rissmiller RW, *et al.* Asthma exacerbations and formoterol. *Chest* 2004; **125:** 1590–1.
3. van der Molen T. Formoterol and asthma exacerbations. *Chest* 2004; **125:** 1591.
4. Wolfe J, *et al.* Formoterol, 24μg bid, and serious asthma exacerbations: similar rates compared with formoterol, 12μg bid, with and without extra doses taken on demand, and placebo. *Chest* 2006; **129:** 27–38.
5. Ni Chroinin M, *et al.* Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids in children and adults with chronic asthma. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 15/01/08).

Effects on skeletal muscle. Myalgia and muscle weakness associated with elevated creatine kinase has been reported during formoterol therapy.[1] Subsequent muscle biopsy suggested mitochondrial dysfunction. No inflammatory changes were seen and symptoms resolved on withdrawal of formoterol.

1. Kiernan MC, *et al.* Mitochondrial dysfunction and rod-like lesions associated with administration of β2 adrenoceptor agonist formoterol. *Neuromuscul Disord* 2004; **14:** 375–7.

Tolerance. Regular use of formoterol produced bronchodilator desensitisation,[1-3] and tachyphylaxis to bronchoprotection against methacholine, effects that have been noted with other long-acting $beta_2$ agonists (see Salmeterol, p.1135) and short-acting $beta_2$ agonists (see Salbutamol, p.1132).

1. van der Woude HJ, *et al.* Decreased bronchodilating effect of salbutamol in relieving methacholine induced moderate to severe bronchoconstriction during high dose treatment with long acting β agonists. *Thorax* 2001; **56:** 529–35.
2. Jones SL, *et al.* Reversing acute bronchoconstriction in asthma: the effect of bronchodilator tolerance after treatment with formoterol. *Eur Respir J* 2001; **17:** 368–73.
3. Haney S, Hancox RJ. Tolerance to bronchodilation during treatment with long-acting beta-agonists, a randomised controlled trial. *Respir Res* 2005; **6:** 107. Also available at: http://respiratory-research.com/content/pdf/1465-9921-6-107.pdf (accessed 15/01/08)

Interactions

As for Salbutamol, p.1132.

Pharmacokinetics

Inhaled formoterol is rapidly absorbed. It is largely metabolised by glucuronidation and *O*-demethylation, with about 10% being excreted in the urine as unchanged drug. The mean terminal elimination half-life after inhalation is estimated to be 10 hours.

Stereoselectivity. Formoterol occurs as a racemic mixture, of which arformoterol (p.1115) is the *R,R*-enantiomer. Only the *R,R*-enantiomer is active.[1,2] It has been suggested that stereoselective metabolism and excretion may account for the individual variation in duration of effect seen with formoterol, although the exact mechanism remains unclear.[1,3]

1. Zhang M, *et al.* Stereoselective glucuronidation of formoterol by human liver microsomes. *Br J Clin Pharmacol* 2000; **49:** 152–7.
2. Lötvall J, *et al.* The effect of formoterol over 24 h in patients with asthma: the role of enantiomers. *Pulm Pharmacol Ther* 2005; **18:** 109–13.
3. Zhang M, *et al.* Stereoselective urinary excretion of formoterol and its glucuronide conjugate in human. *Br J Clin Pharmacol* 2002; **54:** 246–50.

Uses and Administration

Formoterol is a direct-acting sympathomimetic with mainly beta-adrenoceptor stimulant activity specific to $beta_2$ receptors (a $beta_2$ agonist). It has properties similar to those of salbutamol (p.1133), but like salmeterol (p.1135) it has a prolonged duration of action of up to 12 hours; it is therefore not considered suitable for the symptomatic relief of acute attacks of bronchospasm. It is used when the regular use of a long-acting $beta_2$ agonist is needed for management of reversible airways obstruction, as in chronic asthma (p.1108) or in some patients with chronic obstructive pulmonary disease (p.1112).

Formoterol is given by inhalation as the fumarate but how the dose is expressed may depend on the formulation.

- A usual dose is 12 micrograms of formoterol fumarate twice daily from inhalational capsules, increased to 24 micrograms twice daily if necessary in severe disease.
- Metered doses from a dry powder inhaler may be expressed as the amount delivered *into* the mouthpiece (multiples of 6 micrograms per inhalation) or the amount delivered *from* the mouthpiece (corresponding to multiples of 4.5 micrograms per inhalation). Usual doses, expressed as the amount delivered *into* the mouthpiece, are 6 or 12 micrograms once or twice daily, increased if necessary in severe disease to 24 micrograms twice daily.
- Metered doses from an aerosol inhaler may also be expressed as the amount delivered *into* the mouthpiece (12 micrograms per inhalation) or the amount delivered *from* the mouthpiece (corresponding to 10.1 micrograms per inhalation). Usual doses are 1 or 2 inhalations twice daily.

Treatment should be reassessed if this proves inadequate; in the UK, some preparations are licensed for additional short-term symptom relief, but such use is contrary to current asthma guidelines (see p.1108).

Formoterol fumarate may also be inhaled via a nebuliser in a dose of 20 micrograms twice daily. Oral doses of 80 micrograms have been given twice daily in adults.

For doses of formoterol fumarate used in children, see Administration in Children, below.