◊ Reviews.

1. Faulds D, *et al*. Formoterol: a review of its pharmacological properties and therapeutic potential in reversible obstructive airways disease. *Drugs* 1991; **42:** 115–37.
2. Bartow RA, Brogden RN. Formoterol: an update of its pharmacological properties and therapeutic efficacy in the management of asthma. *Drugs* 1998; **55:** 303–22.
3. Sovani MP, *et al*. A benefit-risk assessment of inhaled long-acting β -agonists in the management of obstructive pulmonary disease. *Drug Safety* 2004; **27:** 689–715.

Administration in children. Doses of formoterol fumarate inhaled from inhalational capsules in children aged 5 years or older are the same as those for adults, see Uses and Administration, above.

Formoterol fumarate may be given by metered-dose dry powder inhaler to children 6 years of age and over. The usual dose, expressed as the amount delivered *into* the mouthpiece, is 6 to 12 micrograms once or twice daily. Occasionally up to 48 micrograms daily may be required (maximum single dose should not exceed 12 micrograms).

In some countries, such as Japan, formoterol fumarate has been given orally to children from the age of 6 months at a dose of 4 micrograms/kg daily, in 2 or 3 divided doses.

Asthma. Formoterol is a long-acting beta$_2$ agonist (duration of action about 12 hours). Guidelines on the management of asthma, see p.1108, generally recommend that the use of long-acting beta$_2$ agonists be reserved for patients with chronic asthma who have already progressed to inhaled corticosteroids; it is not a substitute for corticosteroids. The exact dose of inhaled corticosteroid at which to add additional therapy, such as a long-acting beta$_2$ agonist, has yet to be determined. There is some evidence to suggest that, apart from in severe exacerbations, adding a long-acting beta$_2$ agonist to standard dose inhaled corticosteroid therapy may be more effective than increasing the dose of corticosteroid, or than combining a corticosteroid and an anti-leukotriene drug. Combinations of formoterol with an inhaled corticosteroid, used as both maintenance and reliever therapy, have also been studied. Results are seemingly encouraging, although what role such combinations should play in therapy is not yet clearly defined. Some asthma guidelines include this regimen as an option for adults at treatment step 3, see p.1108. Formoterol may also be useful in controlling persistent nocturnal asthma or preventing exercise-induced attacks. There is some evidence that after prolonged use, protection against bronchoconstriction is reduced (see Tolerance, above), and high-dose therapy may be associated with an increased rate of severe exacerbations (see Asthma under Adverse Effects and Precautions, above).

References.

1. van der Molen T, *et al*. Effects of the long acting β agonist formoterol on asthma control in asthmatic patients using inhaled corticosteroids. *Thorax* 1996; **52:** 535–9.
2. Pauwels RA, *et al*. Effect of inhaled formoterol and budesonide on exacerbations of asthma. *N Engl J Med* 1997; **337:** 1405–11. Correction. *ibid*.; 1998; **338:** 139.
3. O'Byrne PM, *et al*. Low dose inhaled budesonide and formoterol in mild persistent asthma: the OPTIMA randomized trial. *Am J Respir Crit Care Med* 2001; **164:** 1392–7.
4. Goldsmith DR, Keating GM. Budesonide/formoterol: a review of its use in asthma. *Drugs* 2004; **64:** 1597–1618.
5. Rabe KF, *et al*. Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomised controlled, double-blind study. *Lancet* 2006; **368:** 707–8.
6. Pedersen S. Budesonide plus formoterol for reliever therapy in asthma. *Lancet* 2006; **368:** 707–8.
7. Pohunek P, *et al*. Budesonide/formoterol improves lung function compared with budesonide alone in children with asthma. *Pediatr Allergy Immunol* 2006; **17:** 458–65. Correction. *ibid*.; 551.
8. Berger WE. The use of inhaled formoterol in the treatment of asthma. *Ann Allergy Asthma Immunol* 2006; **97:** 24–33. Correction. *ibid*.; 562. [dosage error in text]
9. Hermansen MN, *et al*. Acute relief of exercise-induced bronchoconstriction by inhaled formoterol in children with persistent asthma. *Chest* 2006; **129:** 1203–9.
10. Bateman ED, *et al*. Budesonide/formoterol and formoterol provide similar rapid relief in patients with acute asthma showing refractoriness to salbutamol. *Respir Res* 2006; **7:** 13.
11. O'Byrne PM, Parameswaran K. Pharmacological management of mild or moderate persistent asthma. *Lancet* 2006; **368:** 794–803.
12. O'Byrne PM, *et al*. Budesonide/formoterol combination therapy as both maintenance and reliever medication in asthma. *Am J Respir Crit Care Med* 2005; **171:** 129–36.

Stuttering. Inhaled formoterol 12 micrograms daily was reported to improve stuttering (p.1001) in 3 children between 14 and 20 years old. In 2 males, the onset of effect was about 6 weeks, but long-term follow-up was not possible. In the female patient there was early improvement that persisted during 45 weeks of treatment.[1]

1. Pešák J. Preliminary experience with formoterol for the treatment of stuttering. *Ann Pharmacother* 2004; **38:** 1323.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Fordilen; Oxis; Xanol; ***Austral.:*** Foradile; Oxis; ***Austria:*** Foradil; Oxis; ***Belg.:*** Foradil; Oxis; ***Braz.:*** Fluir; Foradil; Formocaps; Oxis; ***Canad.:*** Foradil; Oxeze; ***Cz.:*** Atimos; Foradil; Forair; Formano; Formovent; Oxis; ***Denm.:*** Delnil; Foradil; Oxis; ***Fin.:*** Foradil; Oxis; ***Fr.:*** Foradil; ***Ger.:*** Foradil; Forair; Formatris; FormoLich; Formotop; Oxis; ***Gr.:*** Broncoteril; Foradil; Forair; Forcap; Formopen; Formotil; Imotec; Oxez; ***Hong Kong:*** Foradil†; Oxis; ***Hung.:*** Atimos; Diffumax; Foradil; Fortofan; Oxis; ***India:*** Foratec; ***Irl.:*** Foradil; Oxis; ***Israel:*** Foradil; Oxis; ***Ital.:*** Atimos; Eolus; Foradil; Liferol; Oxis; ***Jpn:*** Atock; ***Malaysia:*** Foradil†; Oxis; ***Mex.:*** Foradil; Oxis; ***Neth.:*** Foradil; Oxis; ***Norw.:*** Foradil; Oxis; ***NZ:*** Foradil; Oxis; ***Philipp.:*** Atock; Foradil; Oxis; ***Pol.:*** Atimos; Diffumax; Foradil; Forastmin; Oxis; Oxodil; Zafiron; ***Port.:*** Asmatec; Atimos; Eformax; Foradil; Forair; Formaxa; Oxis; ***Rus.:*** Atimos (Атимос); Foradil (Форадил); Oxis (Оксис); ***S.Afr.:*** Foradil; Foratec; Oxis; ***Singapore:*** Foradil; Oxis; ***Spain:*** Broncoral; Foradil; Neblik; Oxis; ***Swed.:*** Foradil; Oxis; ***Switz.:*** Foradil; Oxis; ***Thai.:*** Oxis†; ***Turk.:*** Foradil; Oxis; ***UK:*** Atimos Modulite; Foradil; Oxis; ***USA:*** Foradil; Perforomist; ***Venez.:*** Fluir; Foradil; Formotec; Oxis†.

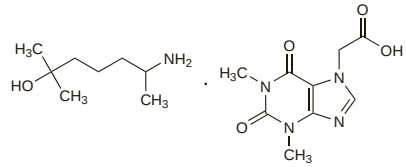
Multi-ingredient: ***Arg.:*** Neumoterol; Symbicort; ***Austral.:*** Symbicort; ***Austria:*** Symbicort; ***Belg.:*** Symbicort; ***Braz.:*** Alenia; Foraseq; Symbicort; ***Canad.:*** Symbicort; ***Chile:*** Symbicort; ***Cz.:*** Combair; Formodual; Symbicort; ***Denm.:*** Symbicort; ***Fin.:*** Symbicort; ***Fr.:*** Innovair; Symbicort; ***Ger.:*** Symbicort; ***Gr.:*** Symbicort; ***Hong Kong:*** Symbicort; ***Hung.:*** Symbicort; ***India:*** Duova; Foracort; ***Indon.:*** Symbicort; ***Irl.:*** Symbicort; ***Israel:*** Symbicort; ***Ital.:*** Assieme; Sinestic; Symbicort; ***Malaysia:*** Foracort; Symbicort; ***Mex.:*** Symbicort; ***Neth.:*** Assieme; Sinestic; Symbicort; ***Norw.:*** Symbicort; ***NZ:*** Symbicort; ***Philipp.:*** Symbicort; ***Pol.:*** Symbicort; ***Port.:*** Assieme; Formodual; Foster; Symbicort; ***Rus.:*** Simbicort (Симбикорт); ***S.Afr.:*** Symbicord; ***Singapore:*** Symbicort; ***Spain:*** Rilast; Symbicort; ***Swed.:*** Symbicort; ***Switz.:*** Symbicort; ***Thai.:*** Symbicort; ***Turk.:*** Symbicort; ***UK:*** Fostair; Symbicort; ***USA:*** Symbicort; ***Venez.:*** Foraseq; Symbicort.

Heptaminol Acefyllinate *(rINNM)*

Acefilinato de heptaminol; Acéfyllinate d'Heptaminol; Acefyllinum Heptaminolum; Heptaminol Acéfylline; Heptaminol Acephyllinate; Heptaminol Theophylline Ethanoate; Heptaminol Theophylline-7-acetate; Heptaminoli Acefyllinas. The 6-amino-2-methylheptan-2-ol salt of theophyllin-7-ylacetic acid .

Гептаминола Ацефилинат

$C_8H_{19}NO,C_9H_{10}N_4O_4$ = 383.4.
CAS — 5152-72-7; 10075-18-0.
ATC — C01DX08.
ATC Vet — QC01DX08.



Profile

Heptaminol acefyllinate is a derivative of theophylline (p.1140) that has been used for its bronchodilator and cardiovascular effects.

Preparations

Proprietary Preparations (details are given in Part 3)
Indon.: Cariamyl.

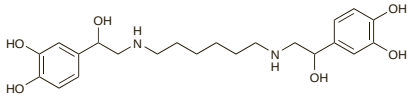
Multi-ingredient: ***Braz.:*** Sureptil; ***Spain:*** Clinadil Compositum; Diclamina.

Hexoprenaline Hydrochloride *(BANM, rINNM)* ⊗

Hexoprénaline, Chlorhydrate d'; Hexoprenalini Hydrochloridum; Hidrocloruro de hexoprenalina; ST-1512. *N,N′*-Hexamethylenebis[4-(2-amino-1-hydroxyethyl)pyrocatechol] dihydrochloride; *N,N′*-Hexamethylenebis[2-amino-1-(3,4-dihydroxyphenyl)ethanol] dihydrochloride.

Гексопреналина Гидрохлорид

$C_{22}H_{32}N_2O_6,2HCl$ = 493.4.
CAS — 3215-70-1 (hexoprenaline); 4323-43-7 (hexoprenaline dihydrochloride).
ATC — R03AC06; R03CC05.
ATC Vet — QR03AC06; QR03CC05.



(hexoprenaline)

Hexoprenaline Sulfate *(USAN, rINNM)* ⊗

Hexoprénaline, Sulfate d'; Hexoprenaline Sulphate *(BANM)*; Hexoprenalini Sulfas; Sulfato de hexoprenalina. (±)-α,α′-[Hexamethylenebis(iminomethylene)]-bis[3,4-dihydroxybenzyl alcohol] sulfate (1:1).

Гексопреналина Сульфат

$C_{22}H_{32}N_2O_6,H_2SO_4$ = 518.6.
CAS — 32266-10-7.
ATC — R03AC06; R03CC05.
ATC Vet — QR03AC06; QR03CC05.

Profile

Hexoprenaline is a direct-acting sympathomimetic with mainly beta-adrenergic activity selective to beta$_2$ receptors (a beta$_2$ agonist). It has properties similar to those of salbutamol (p.1131) and has been used as a bronchodilator in the treatment of reversible airways obstruction as occurs with asthma (p.1108) and in some patients with chronic obstructive pulmonary disease (p.1112). It has sometimes been used similarly to salbutamol in the management of premature labour (p.2003).

Hexoprenaline is usually given as the hydrochloride or sulfate.

For the relief of **bronchoconstriction**, a typical adult oral dose of the salts has been 0.5 to 1 mg three times daily. By inhalation, hexoprenaline sulfate has been given by aerosol inhaler in doses of 100 to 200 micrograms up to 6 times daily, and the hydrochloride has been given by nebulisation in doses of 250 to 500 micrograms every 4 to 6 hours to a maximum of 3 mg daily. In patients with asthma, as-required beta agonist therapy is preferable to regular use. An increased need for, or decreased duration of effect of, hexoprenaline indicates deterioration of asthma control and the need for review of therapy.

In the management of **premature labour** an intravenous infusion of hexoprenaline sulfate, diluted in glucose 5% or sodium chloride 0.9%, can be given at an initial rate of about 300 nanograms/minute. Infusion may be preceded by slow intravenous injection of 10 micrograms as a loading dose over 5 to 10 minutes. A prolonged infusion of 75 nanograms/minute has been used when there is no cervical change. Therapy may be changed from intravenous to oral once suppression of labour has been achieved for at least 24 hours.

Preparations

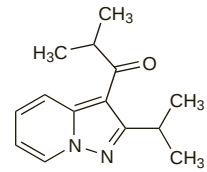
Proprietary Preparations (details are given in Part 3)
Arg.: Argocian; ***Austria:*** Gynipral; Ipradol; ***Chile:*** Gynipral†; ***Cz.:*** Gynipral; ***Hong Kong:*** Ipradol; ***Hung.:*** Gynipral†; Ipradol†; ***Rus.:*** Gynipral (Гинипрал); ***S.Afr.:*** Ipradol; ***Switz.:*** Gynipral; ***Thai.:*** Ipradol†.

Ibudilast *(rINN)*

AV-411; Ibudilastum; KC-404; MN-166. 1-(2-Isopropylpyrazolo[1,5-*a*]pyridin-3-yl)-2-methyl-1-propanone.

Ибудиласт

$C_{14}H_{18}N_2O$ = 230.3.
CAS — 50847-11-5.
ATC — R03DC04.
ATC Vet — QR03DC04.



Profile

Ibudilast is an orally active leukotriene antagonist (p.1108), phosphodiesterase inhibitor, and platelet-activating factor antagonist. It is given orally in the management of asthma (p.1108) in a dose of 10 mg twice daily.

Ibudilast is also promoted for the management of dizziness secondary to impaired cerebral circulation following cerebral infarction, in doses of 10 mg three times daily.

Ibudilast is also under investigation for the treatment of multiple sclerosis and for chronic neuropathic pain.

Preparations

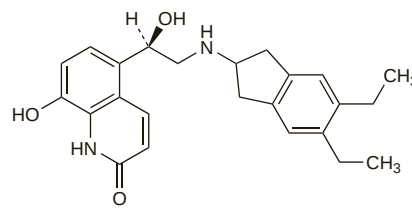
Proprietary Preparations (details are given in Part 3)
Jpn: Ketas.

Indacaterol *(rINN)* ⊗

Indacatérol; Indacaterolum; QAB-149. 5-{(1*R*)-2-[(5,6-Diethyl-2,3-dihydro-1*H*-inden-2-yl)amino]-1-hydroxyethyl}-8-hydroxyquinolin-2(1*H*)-one.

Индакатерол

$C_{24}H_{28}N_2O_3$ = 392.5.
CAS — 312753-06-3.



Profile

Indacaterol is a long-acting beta$_2$ agonist under investigation in asthma and chronic obstructive pulmonary disease.
