◊ 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†.

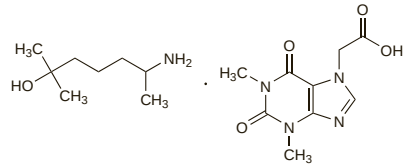
Multi-ingredient: ***Arg.:*** Neumoterol; Symbicort; ***Austral.:*** Symbicort; ***Austria:*** Symbicort; ***Belg.:*** Symbicort; ***Braz.:*** Alenia; Foraseq; Symbicort; ***Canad.:*** Symbicort; ***Chile:*** Symbicort; ***Cz.:*** Combair; Formodual; Symbicort; ***Denm.:*** Symbicort; ***Fin.:*** Symbicort; ***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.

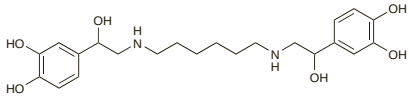
Multi-ingredient: ***Braz.:*** Sureptil; ***Spain:*** Clinadil Compositum; Diclamina.

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

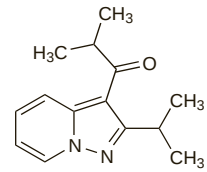
Proprietary Preparations (details are given in Part 3)
Arg.: Argocian; ***Austria:*** Gynipral; Ipradol; ***Chile:*** Gynipral†; ***Cz.:*** Gynipral; ***Hong Kong:*** Ipradol; ***Hung.:*** Gynipral†; Ipradol†; ***Rus.:*** Gynipral (Гинипрал); ***S.Afr.:*** Ipradol; ***Switz.:*** Gynipral; ***Thai.:***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

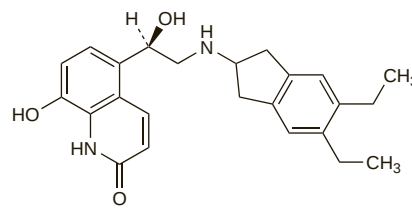
Proprietary Preparations (details are given in Part 3)
Jpn: Ketas.

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.

Ipratropium Bromide *(BAN, USAN, rINN)*

Bromuro de ipratropio; Ipratropii bromidum; Ipratropii Bromidum Monohydricum; Ipratropio bromidas; Ipratropiowy bromek; Ipratropium bromid monohydrát; Ipratropium, bromure d'; Ipratropiumbromid; Ipratropium-bromid; Ipratropiumbromidi; Ipratropyum Bromür; Sch-1000; Sch-1000-Br-monohydrate. (1*R*,3*r*,5*S*,8*r*)-8-Isopropyl-3-[(±)-tropoyloxy]tropanium bromide monohydrate.

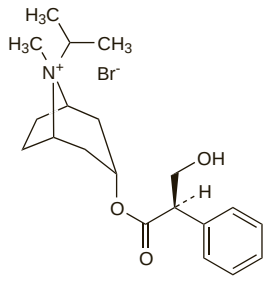
Ипратропия Бромид

$C_{20}H_{30}BrNO_3,H_2O$ = 430.4.

CAS — 22254-24-6 (anhydrous ipratropium bromide); 66985-17-9 (ipratropium bromide monohydrate).

ATC — R01AX03; R03BB01.

ATC Vet — QR01AX03; QR03BB01.



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

Ph. Eur. 6.2 (Ipratropium Bromide). White or almost white crystalline powder. Soluble in water; slightly soluble in alcohol; freely soluble in methyl alcohol. The pH of a 1% solution in water is 5.0 to 7.5.

USP 31 (Ipratropium Bromide). A white to off-white, crystalline powder. Soluble in water; slightly soluble in alcohol; freely soluble in methyl alcohol. A 10% solution has a pH of 5 to 7. Store in airtight containers.

Stability. In a study[1] of the stability of admixtures of ipratropium and salbutamol nebuliser solutions equal ratio mixtures were found to retain more than 90% of their initial concentrations after storage for 5 days at 4° or 22° in the dark or at 22° under continuous fluorescent lighting.

1. Jacobson GA, Peterson GM. Stability of ipratropium bromide and salbutamol nebuliser admixtures. *Int J Pharm Pract* 1995; **3:** 169–73.

Adverse Effects and Precautions

Ipratropium and other inhaled antimuscarinic bronchodilators commonly cause dry mouth and constipation, and rarely, urinary retention. They should be used with care in prostatic hyperplasia. Acute angle-closure glaucoma has been reported; the mist or solution should not be allowed to enter the eyes, particularly in patients susceptible to glaucoma. As with other bronchodilators, paradoxical bronchospasm has occurred. Tachycardia, palpitations, and arrhythmias have been reported with ipratropium. Hypersensitivity reactions, including urticaria, angioedema, rash, and anaphylaxis have occurred rarely. Nausea and vomiting, dyspepsia, headaches, and dizziness have also been reported.

Intranasal ipratropium has been associated with nasal dryness, irritation, and epistaxis.

For details of the adverse effects of, and precautions for, antimuscarinics in general, see Atropine, p.1219.

Buccal ulceration. A report[1] of inflammation and ulceration of the buccal mucosa associated with the use of an ipratropium bromide inhaler.

1. Spencer PA. Buccal ulceration with ipratropium bromide. *BMJ* 1986; **292:** 380.

Effects on the eyes. Ocular complications have been reported with the use of aerosolised ipratropium. A patient with a history of glaucoma developed angle-closure glaucoma after use of ipratropium from a metered dose inhaler (MDI) with nebulised salbutamol.[1] Pupillary dilatation[2] and blurred vision[3] have been reported in association with ipratropium given through a spacer device in patients also given salbutamol therapy, and a 4-year-old child who attempted to self-administer an ipratropium MDI developed anisocoria (unequal dilatation of the pupils) and ataxia.[4] Angle-closure glaucoma,[5-7] pupillary dilatation,[7-10] and anisocoria[11,12] have been reported in patients given *nebulised* ipratropium, usually with salbutamol, through a poorly fitting face mask. The antimuscarinic effects of ipratropium can lead to impaired drainage of aqueous humour in the eyes of patients predisposed to angle-closure glaucoma; use with salbutamol may intensify this problem by increasing the production of aqueous humour.[6] Studies[13,14] suggest that patients with a history of angle-closure glaucoma might be at an increased risk of developing glaucoma when nebulised ipratropium and salbutamol are used together.

1. Hall SK. Acute angle-closure glaucoma as a complication of combined β-agonist and ipratropium bromide therapy in the emergency department. *Ann Emerg Med* 1994; **23:** 884–7.
2. Weir REP, *et al.* Pupil blown by a puffer. *Lancet* 2004; **363:** 1853.
3. Kizer KM, *et al.* Blurred vision from ipratropium bromide inhalation. *Am J Health-Syst Pharm* 2000; **57:** 996–7.
4. Bond DW, *et al.* Mydriasis due to self-administered inhaled ipratropium bromide. *Eur J Pediatr* 2002; **161:** 178.
5. Packe GE, *et al.* Nebulised ipratropium bromide and salbutamol causing closed-angle glaucoma. *Lancet* 1984; **ii:** 691.
6. Shah P, *et al.* Acute angle closure glaucoma associated with nebulised ipratropium bromide and salbutamol. *BMJ* 1992; **304:** 40–1.
7. Mulpeter KM, *et al.* Ocular hazards of nebulized bronchodilators. *Postgrad Med J* 1992; **68:** 132–3.
8. Roberts TE, Pearson DJ. Wide eyed and breathless. *BMJ* 1989; **299:** 1348.
9. Woelfle J, *et al.* Unilateral fixed dilated pupil in an infant after inhalation of nebulized ipratropium bromide. *J Pediatr* 2000; **136:** 423–4.
10. Openshaw H. Unilateral mydriasis from ipratropium in transplant patients. *Neurology* 2006; **67:** 914–15.
11. Lust K, Livingstone I. Nebulizer-induced anisocoria. *Ann Intern Med* 1998; **128:** 327.
12. Iosson N. Nebulizer-associated anisocoria. *N Engl J Med* 2006; **354:** e8.
13. Watson WTA, *et al.* Effect of nebulized ipratropium bromide on intraocular pressures in children. *Chest* 1994; **105:** 1439–41.
14. Kalra L, Bone MF. The effect of nebulized bronchodilator therapy on intraocular pressures in patients with glaucoma. *Chest* 1988; **93:** 739–41.

Effects on the gastrointestinal tract. Paralytic ileus developed shortly after starting ipratropium therapy in 2 patients, apparently due to the inadvertent swallowing of the drug during inhalation.[1,2] Both patients also had other predisposing factors for paralytic ileus (cystic fibrosis,[1] spastic diplegia[2]).

1. Mulherin D, FitzGerald MX. Meconium ileus equivalent in association with nebulised ipratropium bromide in cystic fibrosis. *Lancet* 1990; **355:** 552.
2. Markus HS. Paralytic ileus associated with ipratropium. *Lancet* 1990; **355:** 1224.

Effects on the respiratory tract. Antimuscarinics typically inhibit mucociliary clearance and inhibit secretions of the nose, mouth, pharynx, and bronchi. However, inhaled ipratropium bromide has virtually no effect on sputum viscosity or volume and, in contrast to atropine, it does not affect mucociliary function in the respiratory tract.[1,2]

1. Gross NJ. Ipratropium bromide. *N Engl J Med* 1988; **319:** 486–94.
2. Mann KV, *et al.* Use of ipratropium bromide in obstructive lung disease. *Clin Pharm* 1988; **7:** 670–80.

BRONCHOSPASM. Paradoxical bronchoconstriction occurring after the use of ipratropium was reported in 3 patients.[1] A further report[2] of paradoxical bronchoconstriction after nebulised salbutamol and ipratropium suggested that this adverse effect might have been caused by benzalkonium chloride present in the nebuliser solutions. Nebuliser solutions of ipratropium in some countries contain benzalkonium chloride as a preservative. Solutions available in the UK are preservative-free but licensed product information still recommends that the first doses of ipratropium nebuliser solution should be inhaled under medical supervision.

1. Connolly CK. Adverse reaction to ipratropium bromide. *BMJ* 1982; **285:** 934–5.
2. Boucher M, *et al.* Possible associations of benzalkonium chloride in nebulizer solutions with respiratory arrest. *Ann Pharmacother* 1992; **26:** 772–4.

Effects on the urinary tract. Treatment with nebulised ipratropium bromide has resulted in urinary retention in elderly men especially those with prostatic hyperplasia.[1,2]

1. Lozewicz S. Bladder outflow obstruction induced by ipratropium bromide. *Postgrad Med J* 1989; **65:** 260–1.
2. Pras E, *et al.* Urinary retention associated with ipratropium bromide. *DICP Ann Pharmacother* 1991; **25:** 939–40.

Increased mortality. A case-control study found an unexpected association between death from asthma and treatment with ipratropium, which was not explained by co-morbidity due to chronic obstructive airways disease.[1] A retrospective cohort study[2] of elderly patients found no increase in all-cause mortality associated with the use of ipratropium for chronic obstructive pulmonary disease (COPD). In patients with asthma there was a slight increase in the risk of death, but this may have been due to the confounding effect of disease severity. A later longitudinal cohort study of 1100 patients with obstructive lung disease found an increased risk of premature death associated with ipratropium in both asthma and COPD patients.[3] After adjusting for confounding factors such as forced expiratory volume, smoking status, BMI, and presence of cor pulmonale, ipratropium was associated with a mortality risk ratio (RR) of 2.4 in asthmatic patients and 1.6 in COPD patients. Again, residual confounding by disease severity could not be ruled out.

1. Guite HF, *et al.* Risk factors for death from asthma, chronic obstructive pulmonary disease, and cardiovascular disease after a hospital admission for asthma. *Thorax* 1999; **54:** 301–7.
2. Sin DD, Tu JV. Lack of association between ipratropium bromide and mortality in elderly patients with chronic obstructive airway disease. *Thorax* 2000; **55:** 194–7.
3. Ringbæk T, Viskum K. Is there any association between inhaled ipratropium and mortality in patients with COPD and asthma? *Respir Med* 2003; **97:** 264–72.

Interactions

For interactions associated with antimuscarinics in general, see Atropine, p.1220. However, these interactions are not usually seen with antimuscarinics, such as ipratropium, given by inhalation.

Salbutamol. For reference to nebulised salbutamol exacerbating the adverse effects of nebulised ipratropium in patients predisposed to angle-closure glaucoma, see under Effects on the Eyes, above.

Pharmacokinetics

After inhalation, around 10 to 30% of a dose is deposited in the lungs where it exerts its therapeutic effect. Only a small amount of ipratropium reaches the systemic circulation. The majority of a dose is swallowed but is poorly absorbed from the gastrointestinal tract. Ipratropium and its metabolites are eliminated in the urine and faeces.

◊ References.

1. Ensing K, *et al.* Pharmacokinetics of ipratropium bromide after single dose inhalation and oral and intravenous administration. *Eur J Clin Pharmacol* 1989; **36:** 189–94.

Uses and Administration

Ipratropium bromide is a quaternary ammonium antimuscarinic (p.1108). It is used by inhalation as a bronchodilator in the treatment of reversible airways obstruction, as in asthma and chronic obstructive pulmonary disease (see below).

In the UK the dose of ipratropium bromide from the metered-dose aerosol is expressed in terms of the amount of drug released from the valve into the mouthpiece (20 micrograms) whereas in the USA it is expressed in terms of the dose emitted from the mouthpiece (17 micrograms, equivalent to 21 micrograms released from the valve); recommended doses may therefore appear lower in the USA. For **reversible airways obstruction**, the usual UK dose from a metered-dose aerosol is 1 or 2 inhalations (20 or 40 micrograms) three or four times daily; single doses of up to 4 inhalations may be required. Comparable doses are used in the USA, but it is recommended that the daily dose should not exceed 12 inhalations.

Dry powder inhalation capsules are also available; the usual dose is 40 micrograms three or four times daily, to a maximum of 320 micrograms daily.

Ipratropium bromide may be given by inhalation as a nebulised solution in doses of 250 to 500 micrograms up to 4 times daily.

Ipratropium bromide, given intranasally, is also used in the management of rhinorrhoea associated with **rhinitis**. A dose of 42 micrograms is given into each nostril by metered-dose nasal spray 2 or 3 times daily. US licensing also permits higher doses of 84 micrograms into each nostril 3 or 4 times daily, for up to 4 days when rhinorrhoea is associated with the common cold; doses of 84 micrograms may be given into each nostril 4 times daily, for up to 3 weeks when rhinorrhoea is associated with seasonal allergic rhinitis.

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

Administration in children. Children may be given ipratropium bromide via a metered dose aerosol in the treatment of **reversible airways obstruction**. UK licensed product information recommends doses by age as follows:

- under 6 years: 1 inhalation of 20 micrograms three times daily
- 6 to 12 years: 1 or 2 inhalations of 20 micrograms three times daily
- 12 years and over: adult doses, see above

Dry powder inhalation capsules are also available, and are licensed for use in children from 12 years of age using the adult dose, see above.