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.

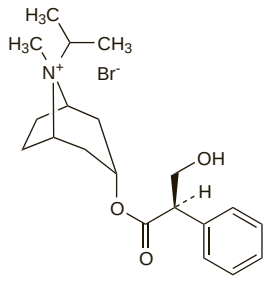
Ипратропия Бромид

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

Ipratropium bromide may also be given by inhalation as a nebulised solution. UK licensed product information recommends the following doses:

- under 6 years, for the treatment of acute asthma only: 125 to 250 micrograms, given no more often than every 6 hours up to a total daily dose of 1 mg
- 6 to 12 years, for the treatment of acute or chronic asthma: 250 micrograms, repeated if necessary up to a total daily dose of 1 mg
- 12 years and over: adult doses, see above.

Ipratropium bromide is used in the management of rhinorrhoea associated with **rhinitis**. A dose of 42 micrograms may be given into both nostrils two or three times daily. In the UK this dose may be given to children from 12 years of age, but in the USA this dose is licensed in children from 6 years of age.

US licensing also permits higher doses for up to 4 days when rhinorrhoea is associated with the common cold:

- 5 to 11 years: 84 micrograms into each nostril three times daily
- 12 years and over: adult doses, see above

Higher doses are also permitted in the USA for up to 3 weeks when rhinorrhoea is associated with seasonal allergic rhinitis. Children 5 years of age and over may be given the same dose as adults, see above.

Asthma. Ipratropium bromide is currently recommended as an adjunct to $beta_2$ agonists in the management of acute severe asthma, see p.1108. Antimuscarinic drugs, mainly ipratropium but also including oxitropium (p.1129), glycopyrronium and atropine, have been reviewed in the treatment of both acute and chronic asthma. A systematic review and meta-analysis[1] of the effectiveness of antimuscarinics in the treatment of acute asthma in children and adults, found they produced significant reductions in hospital admissions. Combined treatment with an inhaled $beta_2$ agonist also produced a significant increase in respiratory function.

Systematic reviews of antimuscarinic drugs have concluded that there is currently insufficient evidence to justify their routine use in adults[2] or children[3] with chronic asthma.

1. Rodrigo GJ, Castro-Rodriguez JA. Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with meta-analysis. *Thorax* 2005; **60:** 740–6.
2. Westby M, *et al.* Anticholinergic agents for chronic asthma in adults. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2004 (accessed 18/02/08).
3. McDonald NJ, *et al.* Anticholinergic therapy for chronic asthma in children over 2 years of age. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2003 (accessed 18/02/08).

Chronic obstructive pulmonary disease. Inhaled antimuscarinics, such as ipratropium bromide, are currently recommended as bronchodilators in chronic obstructive pulmonary disease (COPD) guidelines, see p.1112. A systematic review compared regular treatment with ipratropium (given for at least 4 weeks) with treatment using regular short-acting $beta_2$ agonists in stable COPD;[1] it found small benefits on lung function outcomes and quality of life with ipratropium compared with a short-acting $beta_2$ agonist; a reduction in the requirements for oral corticosteroids was also seen. Combination therapy with ipratropium and a short-acting $beta_2$ agonist was associated with some clinically meaningful lung function outcomes compared with the $beta_2$ agonist alone, but these were not reflected in subjective improvements or symptom scores.

A systematic review comparing ipratropium with a long-acting $beta_2$ agonist in stable COPD,[2] found that salmeterol had more effect than ipratropium on lung function, but no major differences were seen between symptom responses to ipratropium and salmeterol. Combination treatment with these two drugs was better than salmeterol alone in terms of quality of life.

1. Appleton S, *et al.* Ipratropium bromide versus short acting beta-2 agonists for stable chronic obstructive pulmonary disease. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 18/02/08).
2. Appleton S, *et al.* Ipratropium bromide versus long-acting beta-2 agonists for stable chronic obstructive pulmonary disease. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 18/02/08).

Rhinitis. Ipratropium bromide is used intranasally for the treatment of rhinorrhoea in allergic and non-allergic rhinitis (p.565). It has also relieved rhinorrhoea and sneezing associated with the common cold.

References.

1. Georgitis JW, *et al.* Ipratropium bromide nasal spray in non-allergic rhinitis: efficacy, nasal cytological response and patient evaluation on quality of life. *Clin Exp Allergy* 1994; **24:** 1049–55.
2. Hayden FG, *et al.* Effectiveness and safety of intranasal ipratropium bromide in common colds: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1996; **125:** 89–97.
3. Dockhorn R, *et al.* Ipratropium bromide nasal spray 0.03% and beclomethasone nasal spray alone and in combination for the treatment of rhinorrhea in perennial rhinitis. *Ann Allergy Asthma Immunol* 1999; **82:** 349–59.
4. Bonadonna P, *et al.* Cold-induced rhinitis in skiers—clinical aspects and treatment with ipratropium bromide nasal spray: a randomized controlled trial. *Am J Rhinol* 2001; **15:** 297–301.
5. Kim KT, *et al.* Pediatric Atrovent Nasal Spray Study Group. Use of 0.06% ipratropium bromide nasal spray in children aged 2 to 5 years with rhinorrhea due to a common cold or allergies. *Ann Allergy Asthma Immunol* 2005; **94:** 73–9.

Preparations

BP 2008: Ipratropium Nebuliser Solution; Ipratropium Powder for Inhalation; Ipratropium Pressurised Inhalation.

Proprietary Preparations (details are given in Part 3)
Arg.: Aerotrop; Atrovent; Iprabron; ***Austral.:*** Aeron; Apoven; Atrovent; Ipratrin; Ipravent; ***Austria:*** Atrovent; Itrop; ***Belg.:*** Atronase; Atrovent; ***Braz.:*** Alvent†; Ares; Atrovent; Bromovent; Iprabon; Ipraneo; ***Canad.:*** Apo-Ipravent; Atrovent; Novo-Ipramide; ***Chile:*** Atrovent; Neorinol†; ***Cz.:*** Atrovent; Itrop†; ***Denm.:*** Atrovent; ***Fin.:*** Atrovent; ***Fr.:*** Atrovent; ***Ger.:*** Atrovent; Itrop; ***Gr.:*** Atrovent; ***Hong Kong:*** Atrovent; Cyclovent; Ipravent†; ***Hung.:*** Atrovent; ***India:*** Ipranase; Ipravent; ***Indon.:*** Atrovent; ***Irl.:*** Atrovent; Rinatec; ***Israel:*** Aerovent; Apovent; Atrovent; ***Ital.:*** Atem; Rinovagos; ***Jpn:*** Atrovent; ***Malaysia:*** Atrovent; ***Mex.:*** Atrovent; ***Neth.:*** Atrovent; Ipraxa; ***Norw.:*** Atrovent; Respontin†; ***NZ:*** Apo-Ipravent; Atrovent; Ipra†; ***Philipp.:*** Atrovent; ***Pol.:*** Atrovent; ***Port.:*** Atrovent; ***Rus.:*** Atrovent (Атровент); ***S.Afr.:*** Atrovent; Ipvent; ***Singapore:*** Atrovent; ***Spain:*** Atrovent; ***Swed.:*** Atrovent; ***Switz.:*** Atrovent; Rhinovent; ***Thai.:*** Atrovent; ***Turk.:*** Atrovent; ***UAE:*** Atropulm; ***UK:*** Atrovent; Respontin; Rinatec; ***USA:*** Atrovent; ***Venez.:*** Alovent.

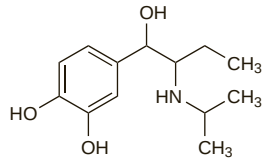
Multi-ingredient: ***Arg.:*** Berodual; Combivent; Ipradual; Iprasalb; Salbutral AC; Salbutrop†; ***Austral.:*** Combivent; ***Austria:*** Berodual; Berodualin; Combivent; Di-Promal; ***Belg.:*** Combivent; Duovent; ***Braz.:*** Combivent; Duovent; ***Canad.:*** Combivent; Duovent; ratio-Ipra Sal UDV; ***Chile:*** Berodual; Combivent; Salbutral AC; ***Cz.:*** Berodual; Combivent†; ***Denm.:*** Berodual; Combivent; ***Fin.:*** Atrodual; Atrovent Comp; ***Fr.:*** Bronchodual; Combivent; ***Ger.:*** Berodual; ***Gr.:*** Berodual; Berovent; ***Hong Kong:*** Berodual†; Combivent; ***Hung.:*** Berodual; ***India:*** Duolin; Fenovent; ***Indon.:*** Berodual; Combivent; ***Irl.:*** Combivent; Duovent; Ipramol; ***Ital.:*** Breva; Duovent; Ipraffen; ***Malaysia:*** Berodual; Combivent; Duovent; Ipramol; ***Mex.:*** Berodual; Combivent; ***Neth.:*** Berodual; Combivent; ***NZ:*** Combivent; Duolin; ***Philipp.:*** Berodual; Combipul; Combivent; Duavent; ***Pol.:*** Berodual; ***Port.:*** Berodual; Combivent; ***Rus.:*** Berodual (Бередуал); ***S.Afr.:*** Atrovent Beta; Berodual; Combivent; Duolin; Duovent; Sabax Combineb; Sabax Nebrafen; ***Singapore:*** Berodual; Combivent; Duovent; ***Spain:*** Berodual†; Combivent; Legis†; ***Swed.:*** Combivent; ***Switz.:*** Berodual; Dospir; ***Thai.:*** Berodual; Combivent; Inhalex; Punol; ***Turk.:*** Combivent; ***UK:*** Combivent; Duovent; Ipramol; ***USA:*** Combivent; DuoNeb; ***Venez.:*** Berodual; Combivent; Duolin; Duovent; Ipralin; Respidual.

Isoetarine *(BAN, rINN)* ⊗

Isoetariini; Isoetarin; Isoetarina; Isoétarine; Isoetarinum; Isoetharine *(USAN)*; Win-3406. 1-(3,4-Dihydroxyphenyl)-2-isopropylaminobutan-1-ol.

Изоэтарин

$C_{13}H_{21}NO_3$ = 239.3.
CAS — 530-08-5.
ATC — R03AC07; R03CC06.
ATC Vet — QR03AC07; QR03CC06.



Isoetarine Hydrochloride *(BANM, rINNM)* ⊗

Etyprenaline Hydrochloride; Hidrocloruro de isoetarina; Isoétarine, Chlorhydrate d'; Isoetarini Hydrochloridum; Isoetharine Hydrochloride; *N*-Isopropylethylnoradrenaline Hydrochloride.

Изоэтарина Гидрохлорид

$C_{13}H_{21}NO_3$,HCl = 275.8.
CAS — 50-96-4; 2576-92-3.
ATC — R03AC07; R03CC06.
ATC Vet — QR03AC07; QR03CC06.

Pharmacopoeias. In *US.*
USP 31 (Isoetharine Hydrochloride). A white to off-white, odourless, crystalline solid. Soluble in water; sparingly soluble in alcohol; practically insoluble in ether. A 1% solution in water has a pH of 4.0 to 5.6. Store in airtight containers.

Isoetarine Mesilate *(BANM, rINNM)* ⊗

Isoétarine, Mésilate d'; Isoetarini Mesilas; Isoetharine Mesylate; Isoetharine Methanesulphonate; *N*-Isopropylethylnoradrenaline Mesylate; Mesilato de isoetarina.

Изоэтарина Мезилат

$C_{13}H_{21}NO_3$,CH_4O_3S = 335.4.
CAS — 7279-75-6.
ATC — R03AC07; R03CC06.
ATC Vet — QR03AC07; QR03CC06.

Pharmacopoeias. In *US.*
USP 31 (Isoetharine Mesylate). White or practically white, odourless, crystals. Freely soluble in water; soluble in alcohol; practically insoluble in acetone and in ether. A 1% solution in water has a pH of 4.5 to 5.5. Store in airtight containers.

Profile
Isoetarine is a sympathomimetic with mainly beta-adrenergic activity. It has actions similar to those of salbutamol (p.1131) but is less selective for $beta_2$ adrenoceptors. Isoetarine has been used as a bronchodilator in the management of reversible airways obstruction.

Isoetarine is given by inhalation, as a nebulised solution of the hydrochloride in strengths up to 0.25%; a 1% solution can be given by a hand nebuliser.

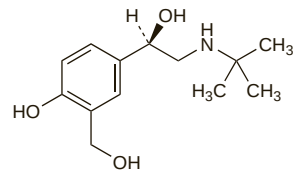
Preparations
USP 31: Isoetharine Inhalation Solution; Isoetharine Mesylate Inhalation Aerosol.

Levosalbutamol *(rINN)* ⊗

Levalbuterol; Lévosalbutamol; Levosalbutamolum. (*R*)-α^1-[(*tert*-Butylamino)methyl]-4-hydroxy-*m*-xylene-α,α′-diol.

Левосальбутамол

$C_{13}H_{21}NO_3$ = 239.3.
CAS — 34391-04-3.



Levosalbutamol Hydrochloride *(rINNM)* ⊗

Hidrocloruro de levosalbutamol; Levalbuterol Hydrochloride *(USAN)*; Lévosalbutamol, Chlorhydrate de; Levosalbutamoli Hydrochloridum. (*R*)-α^1-[(*tert*-Butylamino)methyl]-4-hydroxy-*m*-xylene-α,α′-diol hydrochloride.

Левосальбутамола Гидрохлорид

$C_{13}H_{21}NO_3$,HCl = 275.8.
CAS — 50293-90-8.

Pharmacopoeias. In *US.*
USP 31 (Levalbuterol Hydrochloride). A 1% solution has a pH of 4.5 to 5.5. Store in airtight containers at 20° to 25°, excursions permitted between 15° and 30°. Protect from light.

Levosalbutamol Sulfate *(rINNM)* ⊗

Levalbuterol Sulfate *(USAN)*; Lévosalbutamol, Sulfate de; Levosalbutamol Sulphate; Levosalbutamoli Sulfas; Sulfato de levosalbutamol. (*R*)-α^1-[(*tert*-Butylamino)methyl]-4-hydroxy-*m*-xylene-αα′-diol sulfate (2:1).

Левосальбутамола Сульфат

$(C_{13}H_{21}NO_3)_2$,H_2SO_4 = 576.7.
CAS — 148563-16-0.

Levosalbutamol Tartrate *(rINNM)* ⊗

Levalbuterol Tartrate *(USAN)*; Lévosalbutamol, Tartrate de; Levosalbutamoli Tartras; Tartrato de levosalbutamol. (α^1*R*)-α^1-{[(1,1-Dimethylethyl)amino]methyl}-4-hydroxy-1,3-benzenedimethanol (2*R*,3*R*)-2,3-dihydroxybutanedioate (2:1).

Левосальбутамола Тартрат

$2(C_{13}H_{21}NO_3)$,$C_4H_6O_6$ = 628.7.
CAS — 661464-94-4.

Adverse Effects and Precautions
As for Salbutamol, p.1131.

Incidence of adverse effects. Some studies have reported that beta-adrenergic adverse effects (e.g. nervousness and increased heart rate) are less frequent with inhaled levosalbutamol than with racemic salbutamol.[1-3] Despite preliminary evidence that the increased airway hyperresponsiveness occasionally seen with long-term racemic salbutamol (see Tolerance, p.1132) may be due to the *S*(+)-enantiomer, and therefore might not occur with levosalbutamol,[4] a small study was unable to find any favourable protective effect.[5]

1. Nelson HS, *et al.* Improved bronchodilation with levalbuterol compared with racemic albuterol in patients with asthma. *J Allergy Clin Immunol* 1998; **102:** 943–52.
2. Milgrom H, *et al.* Low-dose levalbuterol in children with asthma: safety and efficacy in comparison with placebo and racemic albuterol. *J Allergy Clin Immunol* 2001; **108:** 938–45.
3. Handley DA, *et al.* Dose-response evaluation of levalbuterol versus racemic albuterol in patients with asthma. *J Asthma* 2000; **37:** 319–27.
4. Perrin-Fayolle M. Salbutamol in the treatment of asthma. *Lancet* 1995; **346:** 1101.
5. Sjöswärd KN, *et al.* Single-isomer R-salbutamol is not superior to racemate regarding protection for bronchial hyperresponsiveness. *Respir Med* 2004; **98:** 990–9.

Interactions
As for Salbutamol, p.1132.