

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<sub>2</sub> 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<sup>1</sup> 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<sub>2</sub> 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<sup>2</sup> or children<sup>3</sup> 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<sub>2</sub> agonists in stable COPD;<sup>1</sup> it found small benefits on lung function outcomes and quality of life with ipratropium compared with a short-acting beta<sub>2</sub> agonist; a reduction in the requirements for oral corticosteroids was also seen. Combination therapy with ipratropium and a short-acting beta<sub>2</sub> agonist was associated with some clinically meaningful lung function outcomes compared with the beta<sub>2</sub> agonist alone, but these were not reflected in subjective improvements or symptom scores.

A systematic review comparing ipratropium with a long-acting beta<sub>2</sub> agonist in stable COPD,<sup>2</sup> 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 rhinorrhoea in perennial rhinitis. *Ann Allergy Asthma Immunol* 1999; **82**: 349-59.

The symbol † denotes a preparation no longer actively marketed

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 rhinorrhoea 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; Iprabron; 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; Ipratent†; **Hung.:** Atrovent; **India:** Ipranase; Atrovent; **Indon.:** Atrovent; **Irl.:** Atrovent; Rinatex; **Israel:** Aerovent; Apoven; Atrovent; **Ital.:** Atem; Rinovagos; **Jpn.:** Atrovent; **Malaysia:** Atrovent; **Mex.:** Atrovent; **Neth.:** Atrovent; Ipraxa; **Norw.:** Atrovent; Respointing†; **NZ:** Apo-Ipravent; Atrovent; Ipra†; **Philipp.:** Atrovent; **Pol.:** Atrovent; **Port.:** Atrovent; **Rus.:** Atrovent (Атропент); **S.Afr.:** Atrovent; Ipvnt; **Singapore:** Atrovent; **Spain:** Atrovent; **Swed.:** Atrovent; **Switz.:** Atrovent; Rinovent; **Thai.:** Atrovent; **Turk.:** Atrovent; **UAE:** Atropulm; **UK:** Atrovent; Respointin; Rinatex; **USA:** Atrovent; **Venez.:** Alvent.

**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; Beroint; **Hong Kong:** Berodual†; Combivent; **Hung.:** Berodual; **India:** Duolin; Fenovent; **Indon.:** Berodual; Combivent; **Irl.:** Combivent; Duovent; Ipramol; **Ital.:** Brevia; Duovent; Iprafen; **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 (Беродуал); **S.Afr.:** Atrovent Beta; Berodual; Combivent; Duolin; Duovent; Sabax Combineb; Sabax Nebrafen; **Singapore:** Berodual; Combivent; Duovent; **Spain:** Berodual†; Combivent; Legist†; **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) ⊗

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

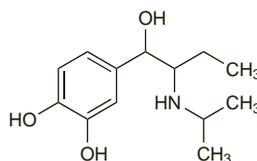
Изоэтарин

C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub> = 239.3.

CAS — 530-08-5.

ATC — R03AC07; R03CC06.

ATC Vet — QR03AC07; QR03CC06.



#### Isoetarine Hydrochloride (BANM, rINNM) ⊗

Etyrenaline Hydrochloride; Hydrochloruro de isoetarina; Isoétarine, Chlorhydrate d'; Isoetarine Hydrochloridum; Isoetharine Hydrochloride; N-Isopropylethylnoradrenaline Hydrochloride.

Изоэтарина Гидрохлорид

C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>·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'; Isoetarin Mesilas; Isoetharine Mesylate; Isoetharine Methanesulphonate; N-Isopropylethylnoradrenaline Mesylate; Mesilato de isoetarina.

Изоэтарина Мезилаат

C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>·CH<sub>3</sub>SO<sub>3</sub>S = 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<sub>2</sub> 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.

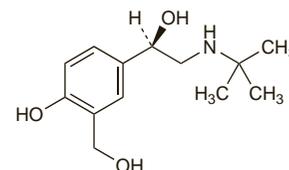
#### Levosalbutamol (rINN) ⊗

Levalbuterol; Lévosalbutamol; Levosalbutamolom. (R)-α<sup>1</sup>-[(tert-Butylamino)methyl]-4-hydroxy-m-xylene-α,α'-diol.

Левосальбутамол

C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub> = 239.3.

CAS — 34391-04-3.



#### Levosalbutamol Hydrochloride (rINNM) ⊗

Hydrocloruro de levosalbutamol; Levalbuterol Hydrochloride (USAN); Lévosalbutamol, Chlorhydrate de; Levosalbutamoli Hydrochloridum. (R)-α<sup>1</sup>-[(tert-Butylamino)methyl]-4-hydroxy-m-xylene-α,α'-diol hydrochloride.

Левосальбутамол Гидрохлорид

C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>·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; Levosalbutamoli Sulphate; Levosalbutamoli Sulfas; Sulfato de levosalbutamol. (R)-α<sup>1</sup>-[(tert-Butylamino)methyl]-4-hydroxy-m-xylene-α,α'-diol sulfate (2:1).

Левосальбутамол Сульфат

(C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>)<sub>2</sub>·H<sub>2</sub>SO<sub>4</sub> = 576.7.

CAS — 148563-16-0.

#### Levosalbutamol Tartrate (rINNM) ⊗

Levalbuterol Tartrate (USAN); Lévosalbutamol, Tartrate de; Levosalbutamoli Tartras; Tartrato de levosalbutamol. (α<sup>1</sup>R)-α<sup>1</sup>-{[(1,1-Dimethylethylamino)methyl]-4-hydroxy-1,3-benzenedimethanol (2R,3R)-2,3-dihydroxybutanedioate (2:1)}.

Левосальбутамол Тартрат

2(C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>)<sub>2</sub>·C<sub>4</sub>H<sub>4</sub>O<sub>6</sub> = 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.<sup>1-3</sup> 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,<sup>4</sup> a small study was unable to find any favourable protective effect.<sup>5</sup>

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.

The symbol ⊗ denotes a substance whose use may be restricted in certain sports (see p.vii)