A systematic review[5] of omalizumab therapy for chronic asthma found that omalizumab was more effective than placebo at reducing exacerbations and improving quality of life. Although omalizumab had an *inhaled*-corticosteroid-sparing effect, the clinical significance of the magnitude of reduction remains open to interpretation, and other factors such as cost-effectiveness and comparative efficacy compared to other add-on therapy should be considered. In patients on *oral* corticosteroids, no significant impact was seen on either exacerbations or oral corticosteroid dose.

Omalizumab has been investigated in the treatment of childhood asthma with encouraging results.[6,7]

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2. Humbert M, *et al.* Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. *Allergy* 2005; **60:** 309–16.
3. Hendeles L, Sorkness CA. Anti-immunoglobulin E therapy with omalizumab for asthma. *Ann Pharmacother* 2007; **41:** 1397–1410.
4. Price D. The use of omalizumab in asthma. *Prim Care Respir J* 2008; **17:** 62–72.
5. Walker S, *et al.* Anti-IgE for chronic asthma in adults and children. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 14/04/08).
6. Berger W, *et al.* Evaluation of long-term safety of the anti-IgE antibody, omalizumab, in children with allergic asthma. *Ann Allergy Asthma Immunol* 2003; **91:** 182–8.
7. Milgrom H, *et al.* Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). *Pediatrics* 2001; **108:** E36. Full version: http://pediatrics.aappublications.org/cgi/content/reprint/108/2/e36.pdf (accessed 14/04/08)

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Xolair; ***Austral.:*** Xolair; ***Belg.:*** Xolair; ***Canad.:*** Xolair; ***Cz.:*** Xolair; ***Fr.:*** Xolair; ***Gr.:*** Xolair; ***Hung.:*** Xolair; ***Israel:*** Xolair; ***Malaysia:*** Xolair; ***NZ:*** Xolair; ***Pol.:*** Xolair; ***Port.:*** Xolair; ***Singapore:*** Xolair; ***Swed.:*** Xolair; ***UK:*** Xolair; ***USA:*** Xolair; ***Venez.:*** Xolair.

Orciprenaline Sulfate *(rINNM)* ⊗

Metaproterenol Sulfate *(USAN)*; Metaproterenol Sulphate; Orciprenalin sulfát; Orciprénaline, sulfate d'; Orciprenaline Sulphate *(BANM)*; Orciprenalini sulfas; Orciprenalino sulfatas; Orciprenalin-sulfat; Orciprenalin-szulfát; Orcyprenaliny siarczan; Orsiprenaliini-sulfaatti; Orsiprenalin Sülfat; Sulfato de orciprenalina; Th-152. 1-(3,5-Dihydroxyphenyl)-2-isopropylaminoethanol sulphate; *N*-Isopropyl-*N*(β,3,5-trihydroxyphenethyl)ammonium sulphate.

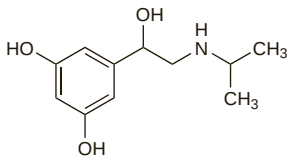
Орципреналина Сульфат

$(C_{11}H_{17}NO_3)_2,H_2SO_4$ = 520.6.

CAS — 586-06-1 (orciprenaline); 5874-97-5 (orciprenaline sulfate).

ATC — R03AB03; R03CB03.

ATC Vet — QR03AB03; QR03CB03.



(orciprenaline)

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Orciprenaline Sulphate). A white, slightly hygroscopic, crystalline powder. Freely soluble in water; slightly soluble in alcohol; practically insoluble in dichloromethane. A 10% solution in water has a pH of 4.0 to 5.5. Store in airtight containers. Protect from light.
USP 31 (Metaproterenol Sulfate). A white to off-white crystalline powder. Freely soluble in water. A 10% solution in water has a pH of 4.0 to 5.5. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Salbutamol, p.1131. Adverse effects are more common because of the non-selective beta agonist effect of orciprenaline. For the adverse effects and precautions pertaining to non-selective beta agonists see under Sympathomimetics, p.1407.

Interactions

As for Salbutamol, p.1132.

Pharmacokinetics

After oral doses orciprenaline is absorbed from the gastrointestinal tract and undergoes extensive first-pass metabolism in the liver; about 40% of an oral dose is reported to reach the circulation unchanged. It is excreted in the urine primarily as metabolites.

Uses and Administration

Orciprenaline sulfate is a direct-acting sympathomimetic with mainly beta-adrenoceptor stimulant activity. It has actions and uses similar to those of salbutamol (p.1133) but is less selective for $beta_2$ receptors.

Orciprenaline sulfate is used as a bronchodilator in the management of reversible airways obstruction, as in asthma (p.1108) and in some patients with chronic obstructive pulmonary disease (p.1112). However, more selective $beta_2$ agonists such as salbutamol or terbutaline are now preferred. On inhalation, the onset of action is usually within 30 minutes and can last from 1 to 5 hours.

A typical adult dose for the relief of acute **bronchospasm** has been 1 or 2 inhalations of orciprenaline sulfate 750 micrograms from a metered-dose aerosol, repeated as needed up to a maximum of 12 inhalations (9 mg) in 24 hours. In patients with asthma, 'as-required' beta agonist therapy is preferable to regular use. An increased need for, or decreased duration of effect of, orciprenaline indicates deterioration of asthma control and the need for review of therapy.

Orciprenaline sulfate has also been inhaled in 5% solution from a hand nebuliser, the usual adult dose being 10 inhalations. If the solution is used with any other nebulising device such as an intermittent positive-pressure breathing (IPPB) apparatus the adult dose is 0.2 to 0.3 mL of a 5% solution diluted up to about 2.5 mL with physiological saline (i.e. dilution to a 0.4 to 0.6% solution) given not more often than every 4 hours. Unit-dose vials containing a prediluted solution of orciprenaline sulfate 0.4 and 0.6% are also available for nebulisation by an IPPB device.

In the chronic management of reversible airways obstruction, orciprenaline sulfate has been given orally in a usual adult dose of 20 mg three or four times daily.

Orciprenaline sulfate has also been used similarly to isoprenaline (see p.1317) for its cardiovascular effects in the treatment of **bradycardia** of various types, notably in AV heart block and sinus bradycardia. In such cases oral doses of up to 240 mg daily in divided doses, or 250 to 500 micrograms by slow intravenous injection have been given; orciprenaline sulfate may also be given by intravenous infusion, or intramuscular or subcutaneous injection. For doses of orciprenaline used in children, see Administration in Children, below.

Administration in children. Although more selective beta agonists are generally preferred, in some countries orciprenaline sulfate is licensed for use in children via a metered-dose inhaler in similar doses to adults; in the USA, use is not recommended under 12 years of age. A metered-dose inhaler was formerly available in the UK and licensed doses in children were:

- under 6 years of age: 1 inhalation of 750 micrograms as necessary; doses should not be repeated within 30 minutes. A maximum of 4 inhalations in 24 hours was suggested
- 6 to 12 years of age: 1 or 2 inhalations of 750 micrograms as necessary; doses should not be repeated within 30 minutes. A maximum of 8 inhalations in 24 hours was suggested

In patients with asthma, 'as-required' beta agonist therapy is preferable to regular use, and chronic oral treatment with orciprenaline would generally be regarded as inappropriate in children. Nonetheless, a syrup is licensed for such use in the UK, licensed oral doses in children being:

- up to 1 year: 5 mg three times daily, increased if necessary to a maximum of 10 mg three times daily
- 1 to 3 years: 5 mg four times daily, increased if necessary to a maximum of 10 mg four times daily
- 3 to 12 years: 10 mg four times daily, increased if necessary to a maximum of 20 mg three times daily
- over 12 years: as for adults (see above)

Preparations

BP 2008: Orciprenaline Tablets;
USP 31: Metaproterenol Sulfate Inhalation Aerosol; Metaproterenol Sulfate Inhalation Solution; Metaproterenol Sulfate Syrup; Metaproterenol Sulfate Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Alupent†; ***Austria:*** Alupent; ***Canad.:*** Alupent†; ***Ger.:*** Alupent; ***Gr.:*** Alupent; ***India:*** Alupent; ***Indon.:*** Alupent; ***Irl.:*** Alupent; ***Ital.:*** Alupent; ***Jpn:*** Alotec; ***Mex.:*** Alupent; ***Pol.:*** Astmopent; ***Rus.:*** Astmopent (Астмопент); ***Thai.:*** Alupent†; ***UK:*** Alupent; ***USA:*** Alupent; ***Venez.:*** Alupent†.

Multi-ingredient: ***Chile:*** Broncodual Compuesto; Cloval Compuesto; Pulbronc; Solvanol; Tusabron; Vapoflu; ***Indon.:*** Silomat Compositum; ***Irl.:*** Alupent Expectorant; ***Mex.:*** Bisolpent Ex; ***Philipp.:*** Bisolpent; ***S.Afr.:*** Adco-Linctopent; Benylin Chesty; Bisolvon Linctus DA; Bronkese Compound; Flemeze; Silomat DA†; ***UAE:*** Orcinol; ***Venez.:*** Bisolpent†; Silomat Compositum†.

Oxitropium Bromide *(BAN, rINN)*

Ba-253; Bromuro de oxitropio; Oksitropiumbromidi; Oxitropii bromidum; Oxitropium, bromure d'; Oxitropiumbromid. 6,7-Epoxy-8-ethyl-3-[(*S*)-tropoyloxy]tropanium bromide; (3s,6*R*,7*S*,-8r)-8-Ethyl-3-[(*S*)-tropoyloxy]-6,7-epoxytropanium bromide.

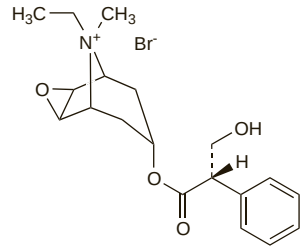
Окситропия Бромид

$C_{19}H_{26}BrNO_4$ = 412.3.

CAS — 30286-75-0.

ATC — R03BB02.

ATC Vet — QR03BB02.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Oxitropium Bromide). A white or almost white, crystalline powder. It exhibits polymorphism. Very soluble in water; sparingly soluble in alcohol; freely soluble in methyl alcohol; practically insoluble in dichloromethane.

Profile

Oxitropium bromide is a quaternary ammonium antimuscarinic with actions similar to those of ipratropium bromide (p.1124), to which it is structurally related. It is used as a bronchodilator in the treatment of reversible airways obstruction, as in asthma (p.1108) and chronic obstructive pulmonary disease (p.1112). Doses of 100 or 200 micrograms by inhalation from a metered-dose aerosol have been given 2 or 3 times daily. Oxitropium bromide may also be given as a nebulised solution in doses of 1.5 mg inhaled 2 or 3 times daily. *Animal* studies have shown reproductive toxicity with high doses of oxitropium, hence the recommendation that it should not be used during pregnancy.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Oxivent†; ***Fin.:*** Ventox†; ***Fr.:*** Tersigat†; ***Ger.:*** Ventilat†; ***Irl.:*** Oxivent†; ***Ital.:*** Oxivent; ***Jpn:*** Tersigan; ***UK:*** Oxivent†; ***Venez.:*** Tersigat†.

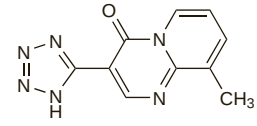
Pemirolast Potassium *(USAN, rINNM)*

BL-5617; BMY-26517; Kalii Pemirolastum; Pemirolast potásico; Pémirolast Potassique. Potassium 9-methyl-3-(1*H*-tetrazol-5-yl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one.

Калия Пемироласт

$C_{10}H_7KN_6O$ = 266.3.

CAS — 69372-19-6 (pemirolast); 100299-08-9 (pemirolast potassium).



(pemirolast)

Profile

Pemirolast potassium has mast cell stabilising properties like sodium cromoglicate (p.1136) and may also be a leukotriene inhibitor. It has been used in the treatment of chronic asthma (p.1108) and in the prophylaxis of allergic rhinitis (p.565) and conjunctivitis (p.564). Pemirolast potassium has no bronchodilator properties and should not be used for the treatment of acute asthma attacks.

For asthma, the usual dose is 10 mg orally twice daily after food. For allergic rhinitis the dose is halved. Pemirolast potassium 0.1% eye drops are instilled 4 times daily in the prophylactic management of allergic conjunctivitis. For details of doses in children, see below.

Pemirolast has also been investigated for the prevention of restenosis after coronary artery stent placement.

◊ References.

1. Tinkelman DG, Berkowitz RB. A pilot study of pemirolast in patients with seasonal allergic rhinitis. *Ann Allergy* 1991; **66:** 162–5.
2. Hasegawa T, *et al.* Kinetic interaction between theophylline and a newly developed anti-allergic drug, pemirolast potassium. *Eur J Clin Pharmacol* 1994; **46:** 55–8.
3. Anonymous. New drugs for allergic conjunctivitis. *Med Lett Drugs Ther* 2000; **42:** 39–40.
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7. Gous P, Ropo A. A comparative trial of the safety and efficacy of 0.1 percent pemirolast potassium ophthalmic solution dosed