Adverse Effects and Precautions

Inhaled nedocromil sodium may cause headache, gastrointestinal disturbances (nausea, vomiting, dyspepsia, and abdominal discomfort). An unusual or unpleasant taste is reported rarely. Paradoxical bronchospasm may occur. Eye drops may cause transient burning and stinging.

It should not be used for the treatment of acute asthma attacks. The general cautions described under sodium cromoglicate (see p.1136) also apply.

Incidence of adverse effects. A review[1] of nedocromil sodium noted that adverse effects were infrequent, mild, and short-lived. The most common effect appeared to be an unpleasant or bitter taste, which was experienced by 12 to 13% of patients, although less than 1% of patients stopped treatment because of it. Other adverse effects included cough (in 7%), headache (6%), sore throat (5.7%), nausea (4%), and vomiting (1.7%).

1. Brogden RN, Sorkin EM. Nedocromil sodium: an updated review of its pharmacological properties and therapeutic efficacy in asthma. *Drugs* 1993; **45:** 693–715.

Pharmacokinetics

Nedocromil sodium is poorly absorbed from the gastrointestinal tract; about 10% of the inhaled dose is absorbed from the lungs. Absorption is also poor after topical ophthalmic use, and occurs mainly through the nasal mucosa. Nedocromil sodium is excreted unchanged in the urine and faeces. The half-life is stated to range from about 1 to 3.3 hours.

◊ The extent of absorption or bioavailability of nedocromil sodium after inhalation in healthy subjects was 7 to 9% of the dose, including 2 to 3% oral absorption and 5 to 6% absorption from the respiratory tract.[1] After inhalation of nedocromil sodium 4 mg the mean peak plasma concentration was 3.3 nanograms/mL in healthy subjects and 2.8 nanograms/mL in asthmatic patients, with peak values being reached at about 20 and 40 minutes respectively. The mean total urinary excretion 24 hours after a single dose was 5.4% of the dose in healthy subjects and 2.3% in asthmatics.

1. Neale MG, *et al.* The pharmacokinetics of nedocromil sodium, a new drug for the treatment of reversible obstructive airways disease, in human volunteers and patients with reversible obstructive airways disease. *Br J Clin Pharmacol* 1987; **24:** 493–501.

Uses and Administration

Nedocromil sodium has a stabilising action on mast cells resembling that of sodium cromoglicate (p.1137) and is used similarly in the management of chronic asthma. It should not be used to treat an acute attack of asthma.

For **asthma**, nedocromil sodium is inhaled from a metered-dose aerosol. The usual dose for adults and children from 6 years of age is 4 mg inhaled four times daily which may be decreased to 4 mg twice daily after control of symptoms is achieved. Clinical improvement may not be obtained for 1 week or longer after beginning therapy.

Nedocromil sodium is also used topically in the treatment of **allergic conjunctivitis** and allergic **rhinitis**. For seasonal and perennial allergic conjunctivitis it is given as a 2% solution, instilled into each eye twice daily. This may be increased to 4 times daily if necessary, which is the usual dose in vernal keratoconjunctivitis. In seasonal allergic conjunctivitis, treatment is usually given for no more than 12 weeks. In allergic rhinitis nedocromil sodium is used as a 1% nasal spray: one spray is given into each nostril 4 times daily. For details of doses in children, see Administration in Children, below.

◊ General references.

1. Brogden RN, Sorkin EM. Nedocromil sodium: an updated review of its pharmacological properties and therapeutic efficacy in asthma. *Drugs* 1993; **45:** 693–715.
2. Parish RC, Miller LJ. Nedocromil sodium. *Ann Pharmacother* 1993; **27:** 599–606.

Administration in children. Nedocromil sodium is given by metered-dose aerosol inhalation for the treatment of asthma in children from 6 years of age at the adult dose, see above. Although unlicensed in the UK for younger children, the *BNFC* recommends the same dose from 5 years of age.

Similarly, for the topical treatment of seasonal allergic conjunctivitis and vernal keratoconjunctivitis, the adult dose may be given to children from 6 years of age, see above. Treatment of perennial allergic conjunctivitis with nedocromil sodium is not licensed in children in the UK, but the *BNFC* recommends adult doses from 6 years of age.

Asthma. Nedocromil sodium is generally considered to be an alternative to sodium cromoglicate in the management of asthma (p.1108). Nedocromil has been shown to improve symptoms and reduce bronchodilator intake in adults[1] and children[2] with chronic asthma. However, a systematic review[3] of nedocromil for chronic asthma in children subsequently found that although a number of small studies have shown that nedocromil improves airflow limitation, reduces symptoms, and reduces bronchial hyperresponsiveness, this has not been confirmed in a larger long-term study of children with milder asthma. Its place in relation to other asthma therapies for children is also unclear. It may be used before exercise to reduce exercise-induced bronchoconstriction,[4] and appears to be as effective as sodium cromoglicate for this indication.[5]

1. Edwards AM, Stevens MT. The clinical efficacy of inhaled nedocromil sodium (Tilade) in the treatment of asthma. *Eur Respir J* 1993; **6:** 35–41.
2. Armenio L, *et al.* Double blind, placebo controlled study of nedocromil sodium in asthma. *Arch Dis Child* 1993; **68:** 193–7.
3. Sridhar AV, McKean M. Nedocromil sodium for chronic asthma in children. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 14/04/08).
4. Spooner CH, *et al.* Nedocromil sodium for preventing exercise-induced bronchoconstriction. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 14/04/08).
5. Kelly K, *et al.* Nedocromil sodium versus sodium cromoglycate for preventing exercise-induced bronchoconstriction in asthmatics. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2000 (accessed 14/04/08).

Cough. For references indicating a positive response to sodium cromoglicate but not to nedocromil sodium in the management of cough induced by ACE inhibitor therapy, see Cough, p.1137.

Rhinitis and conjunctivitis. Nedocromil has been used in the management of allergic rhinitis (p.565) and conjunctivitis (p.564). In the management of seasonal allergic rhinitis, there is some evidence that prophylactic mometasone furoate (p.1539) reduces symptoms more effectively than nedocromil.[1] In vernal keratoconjunctivitis (see p.1138) nedocromil may be more effective than cromoglicate, but is less effective than fluorometholone.[2]

1. Pitsios C, *et al.* Efficacy and safety of mometasone furoate vs nedocromil sodium as prophylactic treatment for moderate/severe seasonal allergic rhinitis. *Ann Allergy Asthma Immunol* 2006; **96:** 673–8.
2. Tabbara KF, Al-Kharashi SA. Efficacy of nedocromil 2% versus fluorometholone 0.1%: a randomised, double masked trial comparing the effects on severe vernal keratoconjunctivitis. *Br J Ophthalmol* 1999; **83:** 180–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Tilade; ***Austria:*** Tilade; Tilarin; Tilavist; ***Braz.:*** Tilade; ***Canad.:*** Alocril; Tilade†; ***Cz.:*** Tilade; Tilarin†; Tilavist†; ***Denm.:*** Tilade; Tilavist; ***Fin.:*** Tilade; Tilarin†; Tilavist†; ***Fr.:*** Tilavist; ***Ger.:*** Halamid†; Irtan; Tilade; ***Gr.:*** Tilade; ***Hong Kong:*** Tilade†; ***Hung.:*** Tilade†; ***Irl.:*** Tilade; Tilavist†; ***Israel:*** Tilade; Tilavist; ***Ital.:*** Kovilen; Kovinal; Tilade; Tilarin; Tilavist; ***Mex.:*** Irtan; ***Neth.:*** Tilade; Tilavist; ***Norw.:*** Tilavist; ***NZ:*** Tilade; ***Port.:*** Tilavist; ***Rus.:*** Tilade (Тайлед); ***Spain:*** Brionil; Cetimil; Tilad; Tilavist; ***Swed.:*** Tilavist; ***Switz.:*** Tilade†; Tilarin; Tilavist; ***Turk.:*** Tilade; ***UK:*** Rapitil; Tilade; ***USA:*** Alocril; Tilade.

Multi-ingredient: ***Ital.:*** Zarent†.

Omalizumab *(BAN, USAN, rINN)*

CGP-51901; E-25; IGE-025; Olizumab; Omalizumabum; rhuM-Ab-E25. Immunoglobulin G, anti-(human immunoglobulin E Fc region)(human-mouse monoclonal E25 clone pSVIE26 γ-chain), disulfide with human-mouse monoclonal E25 clone pSVIE26 κ-chain, dimer.

Омализумаб

CAS — 242138-07-4.
ATC — R03DX05.
ATC Vet — QR03DX05.

Adverse Effects and Precautions

Injection site reactions are common with the use of omalizumab. Other adverse effects that have been reported include generalised pain, fatigue, arthralgia, dizziness, earache, gastrointestinal disturbances, headache, and alopecia. An increased incidence of parasitic infection has been reported in patients at high risk for helminthic infections. Viral infections, upper respiratory-tract infections, sinusitis, pharyngitis, and flu-like illness can also occur. Churg-Strauss syndrome has also been reported. Hypersensitivity reactions such as urticaria, dermatitis, and pruritus can occur. Rarely, systemic reactions, including potentially life-threatening anaphylaxis, have occurred. Anaphylactic reactions may occur up to 4 days after a dose, and as early as the first dose or more than 1 year after beginning regular treatment.

Severe thrombocytopenia has been reported with use of omalizumab.

Licensed product information notes an increased incidence of malignancies in patients given omalizumab.

Omalizumab should not be used for the treatment of acute asthma attacks, and inhaled corticosteroids should not be abruptly withdrawn on starting omalizumab therapy.

Pharmacokinetics

Omalizumab is absorbed after subcutaneous injection with a bioavailability of about 62%, reaching peak serum concentrations after 7 to 8 days. It is removed by IgG and IgE clearance processes in the liver, with a serum elimination half-life of about 26 days. During treatment with omalizumab, the serum concentration of free IgE decreases but that of total IgE increases because the omalizumab-IgE complex has a slower elimination rate than free IgE.

◊ References.

1. Hayashi N, *et al.* A mechanism-based binding model for the population pharmacokinetics and pharmacodynamics of omalizumab. *Br J Clin Pharmacol* 2007; **63:** 548–61.

Uses and Administration

Omalizumab is a recombinant humanised monoclonal antibody that selectively binds to IgE. It inhibits the binding of IgE on the surface of mast cells and basophils, thus reducing the release of mediators of the allergic response. Omalizumab is used in the prophylactic management of moderate to severe, persistent allergic asthma (p.1108). The dose depends on the patient's weight and pre-treatment serum-IgE concentrations; regimens range from 75 to 300 mg every 4 weeks to 225 to 375 mg every 2 weeks. Omalizumab is given by subcutaneous injection, and not more than 150 mg should be given at one injection site. Total IgE concentrations rise during treatment (see Pharmacokinetics, above), remaining elevated for up to 1 year after withdrawal, and cannot be used to determine continued dosage. Dose determination after treatment interruptions lasting up to 1 year should be based on pre-treatment serum-IgE concentrations.

Omalizumab is under investigation in the prophylactic management of seasonal allergic rhinitis.

◊ References.

1. Ådelroth E, *et al.* Recombinant humanized mAb-E25, an anti-IgE mAb, in birch pollen-induced seasonal allergic rhinitis. *J Allergy Clin Immunol* 2000; **106:** 253–9.
2. Easthope S, Jarvis B. Omalizumab. *Drugs* 2001; **61:** 253–60.
3. Casale TB, *et al.* Effect of omalizumab on symptoms of seasonal allergic rhinitis: a randomized controlled trial. *JAMA* 2001; **286:** 2956–67.
4. Chervinsky P, *et al.* Omalizumab, an anti-IgE antibody, in treatment of adults and adolescents with perennial allergic rhinitis. *Ann Allergy Asthma Immunol* 2003; **91:** 160–7.
5. Hanf G, *et al.* Omalizumab inhibits allergen challenge-induced nasal response. *Eur Respir J* 2004; **23:** 414–18.
6. Vignola AM, *et al.* Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with concomitant allergic asthma and persistent allergic rhinitis: SOLAR. *Allergy* 2004; **59:** 709–17.

Aspergillosis. Successful treatment of allergic bronchopulmonary aspergillosis with omalizumab has been reported in children with cystic fibrosis.[1,2] In one such report,[1] repeated improvement in symptoms and normalisation in lung function within 2 to 4 hours of giving omalizumab led to complete withdrawal of corticosteroid treatment in a 12 year old girl. Others[2] have reported similar benefits.

1. van der Ent CK, *et al.* Successful treatment of allergic bronchopulmonary aspergillosis with recombinant anti-IgE antibody. *Thorax* 2007; **62:** 276–7.
2. Zirbes JM, Milla CE. Steroid-sparing effect of omalizumab for allergic bronchopulmonary aspergillosis and cystic fibrosis. *Pediatr Pulmonol* 2008; **43:** 607–10.

Asthma. Current guidelines recommend omalizumab as an option for the treatment of severe persistent allergic (IgE mediated) asthma as an add-on therapy to optimised standard therapy in adults (see Asthma, p.1108). It has been shown to reduce exacerbations and corticosteroid requirement compared with placebo in adults with moderate-to-severe allergic asthma.[1] It also reduced exacerbation rates in patients with inadequately controlled, severe persistent asthma,[2] and is considered to be an effective therapy in difficult-to-treat, high-risk adult patients.[3,4]

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]

1. Solèr M, *et al.* The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. *Eur Respir J* 2001; **18:** 254–61.
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.

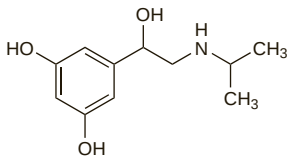
Орципреналина Сульфат

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

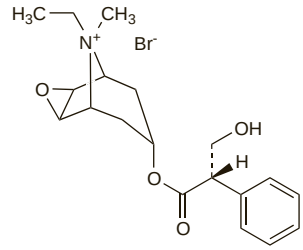
Окситропия Бромид

$C_{19}H_{26}BrNO_4$ = 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†.

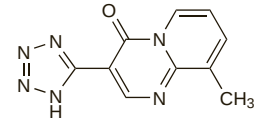
Pemirolast Potassium *(USAN, rINNM)*

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.
4. Abelson MB, *et al.* Pemirolast potassium 0.1% ophthalmic solution is an effective treatment for allergic conjunctivitis: a pooled analysis of two prospective, randomized, double-masked, placebo-controlled, phase III studies. *J Ocul Pharmacol Ther* 2002; **18:** 475–88.
5. Shulman DG. Two mast cell stabilizers, pemirolast potassium 0.1% and nedocromil sodium 2%, in the treatment of seasonal allergic conjunctivitis: a comparative study. *Adv Therapy* 2003; **20:** 31–40.
6. Ohsawa H, *et al.* Preventive effect of an antiallergic drug, pemirolast potassium, on restenosis after stent placement: quantitative coronary angiography and intravascular ultrasound studies. *J Cardiol* 2003; **42:** 13–22.
7. Gous P, Ropo A. A comparative trial of the safety and efficacy of 0.1 percent pemirolast potassium ophthalmic solution dosed