mild to moderate asthma. Significant improvements in quality of life have also been reported,[16] in association with a fall in the levels of exhaled inflammatory mediators leading the authors of this study to conclude that leukotriene receptor antagonists may provide a complementary effect to inhaled corticosteroids when suppression of inflammation is incomplete. Another study[17] has reported that the use of montelukast did permit reduction in the dose of inhaled corticosteroid; adding montelukast to an inhaled corticosteroid (budesonide) may be as effective as doubling the dose of the corticosteroid.[18]

There is some evidence that montelukast may be more effective than inhaled salmeterol for the chronic treatment of exercise-induced asthma,[19,20] and although a later study[21] found similar effects on lung function with the two drugs, a more favourable effect was seen on gas exchange during moderate exercise with the use of montelukast.

An intravenous form of montelukast is under investigation for the treatment of severe acute asthma.[22,23]

1. Anonymous. Montelukast for persistent asthma. *Med Lett Drugs Ther* 1998; **40:** 71–3.
2. Anonymous. Montelukast and zafirlukast in asthma. *Drug Ther Bull* 1998; **36:** 65–8.
3. Jarvis B, Markham A. Montelukast: a review of its therapeutic potential in persistent asthma. *Drugs* 2000; **59:** 891–928.
4. Leff JA, *et al.* Montelukast, a leukotriene-receptor antagonist, for the treatment of mild asthma and exercise-induced bronchoconstriction. *N Engl J Med* 1998; **339:** 147–52.
5. Reiss TF, *et al.* Montelukast, a once-daily leukotriene receptor antagonist, in the treatment of chronic asthma: a multicenter, randomized, double-blind trial. *Arch Intern Med* 1998; **158:** 1213–20.
6. Knorr B, *et al.* Montelukast for chronic asthma in 6- to 14-year-old children: a randomized, double-blind trial. *JAMA* 1998; **279:** 1181–6.
7. Kemp JP, *et al.* Montelukast once daily inhibits exercise-induced bronchoconstriction in 6- to 14-year-old children with asthma. *J Pediatr* 1998; **133:** 424–8.
8. Knorr B, *et al.* Montelukast, a leukotriene receptor antagonist, for the treatment of persistent asthma in children aged 2 to 5 years. Abstract: *Pediatrics* 2001; **108:** 754–5. Full version: http://pediatrics.aappublications.org/cgi/content/full/108/3/e48 (accessed 14/04/08)
9. Ducharme FM, Di Salvio F. Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 14/04/08).
10. Ostrom NK, *et al.* Comparative efficacy and safety of low-dose fluticasone propionate and montelukast in children with persistent asthma. *J Pediatr* 2005; **147:** 213–20.
11. Garcia Garcia ML, *et al.* Montelukast, compared with fluticasone, for control of asthma among 6- to 14-year-old patients with mild asthma: the MOSAIC study. *Pediatrics* 2005; **116:** 360–9.
12. Turkalj M, Plavec D. "Inferiority complex" for a reason. *Pediatrics* 2006; **117:** 588–90.
13. Vaquerizo MJ, *et al.* CASIOPEA (Capacidad de Singulair Oral en la Prevencion de Exacerbaciones Asmaticas) Study Group. Effect of montelukast added to inhaled budesonide on control of mild to moderate asthma. *Thorax* 2003; **58:** 204–10.
14. Phipatanakul W, *et al.* Montelukast improves asthma control in asthmatic children maintained on inhaled corticosteroids. *Ann Allergy Asthma Immunol* 2003; **91:** 49–54.
15. Johnston NW, *et al.* Attenuation of the September epidemic of asthma exacerbations in children: a randomized, controlled trial of montelukast added to usual therapy. *Pediatrics* 2007; **120:** e702–e712.
16. Biernacki WA, *et al.* Effect of montelukast on exhaled leukotrienes and quality of life in asthmatic patients. *Chest* 2005; **128:** 1958–63.
17. Löfdahl C-G, *et al.* Randomised, placebo controlled trial of effect of a leukotriene receptor antagonist, montelukast, on tapering inhaled corticosteroids in asthma. *BMJ* 1999; **319:** 87–90.
18. Price DB, *et al.* Clinical Outcomes with Montelukast as a Partner Agent to Corticosteroid Therapy (COMPACT) International Study Group. Randomised controlled trial of montelukast plus inhaled budesonide versus double dose inhaled budesonide in adult patients with asthma. *Thorax* 2003; **58:** 211–16.
19. Villaran C, *et al.* Montelukast versus salmeterol in patients with asthma and exercise-induced bronchoconstriction. *J Allergy Clin Immunol* 1999; **104:** 547–53.
20. Edelman JM, *et al.* Oral montelukast compared with inhaled salmeterol to prevent exercise-induced bronchoconstriction: a randomized, double-blind trial. *Ann Intern Med* 2000; **132:** 97–104.
21. Steinshamn S, *et al.* Effects of montelukast and salmeterol on physical performance and exercise economy in adult asthmatics with exercise-induced bronchoconstriction. *Chest* 2004; **126:** 1154–60.
22. Dockhorn RJ, *et al.* Comparison of the effects of intravenous and oral montelukast on airway function: a double blind, placebo controlled, three period, crossover study in asthmatic patients. *Thorax* 2000; **55:** 260–5.
23. Camargo CA, *et al.* A randomized controlled trial of intravenous montelukast in acute asthma. *Am J Respir Crit Care Med* 2003; **167:** 528–33.

Bronchiolitis. Bronchiolitis due to RSV infection is often followed by post-bronchiolitic reactive airways disease, characterised by asthma-like wheeze and other symptoms. In a pilot study,[1] montelukast 5 mg orally daily was given for 4 weeks to infants who had been admitted for moderate to severe bronchiolitis. Symptom-free days and nights were increased, daytime cough was reduced, and exacerbations were delayed compared with placebo. The benefit of montelukast over placebo was only apparent after the first 2 weeks of treatment. Although the safety and efficacy of such treatment remains to be properly established,[2] there is some interest in whether montelukast can prevent or modify more persistent asthma that has been associated with RSV.

1. Bisgaard H. Study Group on Montelukast and Respiratory Syncytial Virus. A randomized trial of montelukast in respiratory syncytial virus postbronchiolitis. *Am J Respir Crit Care Med* 2003; **167:** 379–83.
2. Szefler SJ, Simoes EAF. Montelukast for respiratory syncytial virus bronchiolitis: significant effect or provocative findings? *Am J Respir Crit Care Med* 2003; **167:** 290–1.

Cystic fibrosis. A small study in children with cystic fibrosis (p.166) found that montelukast reduced eosinophilic inflammation.[1] A later study,[2] reported improved lung function and a reduction in coughing and wheezing, and concluded that montelukast may have measurable anti-inflammatory activity in patients with cystic fibrosis. In a small group of adult patients with cystic fibrosis[3] montelukast improved symptoms, in particular exercise tolerance and peak expiratory flow rates. The patients who benefited the most had positive *Aspergillus* serology, and the authors suggested that colonisation of the airways in cystic fibrosis by *Aspergillus* stimulates T helper cell inflammation and leukotriene synthesis. A review of leukotriene receptor antagonists in cystic fibrosis[4] concluded that clinical benefit seemed likely in a subset of patients with cystic fibrosis who experience bronchial hyperresponsiveness similar to that seen in asthma.

A study into the pharmacokinetics of montelukast in cystic fibrosis[5] found that the dose of montelukast and the dosing interval do not need to be modified if the goal of therapy is to achieve similar serum concentrations as for asthma treatment; however the effectiveness of these concentrations for the inflammatory lung disease of patients with cystic fibrosis was unknown.

1. Schmitt-Grohé S, *et al.* Anti-inflammatory effects of montelukast in mild cystic fibrosis. *Ann Allergy Asthma Immunol* 2002; **89:** 599–605.
2. Stelmach I, *et al.* Effects of montelukast treatment on clinical and inflammatory variables in patients with cystic fibrosis. *Ann Allergy Asthma Immunol* 2005; **95:** 372–80.
3. Morice AH, *et al.* Montelukast sodium in cystic fibrosis. *Thorax* 2001; **56:** 244–5.
4. Schmitt-Grohé S, Zielen S. Leukotriene receptor antagonists in children with cystic fibrosis lung disease: anti-inflammatory and clinical effects. *Pediatr Drugs* 2005; **7:** 353–63.
5. Graff GR, *et al.* Montelukast pharmacokinetics in cystic fibrosis. *J Pediatr* 2003; **142:** 53–6.

Eczema. Despite early indications from some small clinical studies and case reports[1-3] that montelukast might be of benefit in eczema (p.1579) larger, more recent studies have failed to show any improvement compared with placebo.[4,5]

1. Capella GL, *et al.* A randomized trial of leukotriene receptor antagonist montelukast in moderate-to-severe atopic dermatitis of adults. *Eur J Dermatol* 2001; **11:** 209–13.
2. Hon KLE, *et al.* Brief case series: montelukast, at doses recommended for asthma treatment, reduces disease severity and increases soluble CD14 in children with atopic dermatitis. *J Dermatolog Treat* 2005; **16:** 15–18.
3. Angelova-Fischer I, Tsankov N. Successful treatment of severe atopic dermatitis with cysteinyl leukotriene receptor antagonist montelukast. *Acta Dermatovenerol Alp Panonica Adriat* 2005; **14:** 115–19.
4. Veien NK, *et al.* Montelukast treatment of moderate to severe atopic dermatitis in adults: a randomized, double-blind, placebo-controlled trial. *J Am Acad Dermatol* 2005; **53:** 147–9.
5. Friedmann PS, *et al.* A double-blind, placebo-controlled trial of montelukast in adult atopic eczema. *Clin Exp Allergy* 2007; **37:** 1536–40.

Gastrointestinal disorders. Benefit has been reported[1] with the use of montelukast in patients with eosinophilic oesophagitis, a rare condition involving eosinophilic infiltration of the oesophagus with intermittent painful dysphagia. A systematic review with recommendations for the diagnosis and treatment of eosinophilic oesophagitis[2] concluded that although leukotriene receptor antagonists had been shown to induce symptomatic relief at high doses, no significant improvements in histology were noted and their use for the treatment of eosinophilic oesophagitis is not supported by the current literature.

1. Attwood SEA, *et al.* Eosinophilic oesophagitis: a novel treatment using montelukast. *Gut* 2003; **52:** 181–5.
2. Furuta GT, *et al.* American Gastroenterological Association; North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. *Gastroenterology* 2007; **133:** 1342–63. Also available at: http://download.journals.elsevierhealth.com/pdfs/journals/0016-5085/PIIS0016508507014746.pdf (accessed 14/04/08)

Graft-versus-host disease. A pilot study in refractory, chronic graft-versus-host disease (GVHD) after allogeneic haematopoietic stem cell transplantation (p.1811),[1] saw an improvement in 15 of 19 patients after montelukast was added to their standard immunosuppressive regimens; in 4 patients signs of chronic GVHD were resolved, 2 showed significant improvement, and 9 showed moderate improvement.

1. Or R, *et al.* Sparing effect by montelukast treatment for chronic graft versus host disease: a pilot study. *Transplantation* 2007; **83:** 577–81.

Mastocytosis. Montelukast has been tried, with some success, in the treatment of systemic mastocytosis (p.1138) in an infant.[1]

1. Tolar J, *et al.* Leukotriene-receptor inhibition for the treatment of systemic mastocytosis. *N Engl J Med* 2004; **350:** 735–6.

Rhinitis. Montelukast is used in allergic rhinitis (p.565), where large placebo-controlled studies have shown it to relieve symptoms in both seasonal allergic rhinitis,[1,2] and perennial allergic rhinitis.[3] However, a meta-analysis[4] of leukotriene antagonists (mainly montelukast) for management of allergic rhinitis concluded that while leukotriene antagonists were modestly more effective than placebo and of similar efficacy to antihistamines, in reducing nasal symptoms and improving rhinoconjunctivitis, they were less effective than corticosteroids even when used with antihistamines. A later systematic review[5] commented that some studies in allergic rhinitis using a combination of montelukast and an antihistamine had produced results comparable with intranasal corticosteroids. Also, in patients with both allergic rhinitis and asthma, montelukast had resulted in significant improvements in both when compared with placebo.

1. Philip G, *et al.* Montelukast for treating seasonal allergic rhinitis: a randomized, double-blind, placebo-controlled trial performed in the spring. *Clin Exp Allergy* 2002; **32:** 1020–8.
2. van Adelsberg J, *et al.* Randomized controlled trial evaluating the clinical benefit of montelukast for treating spring seasonal allergic rhinitis. *Ann Allergy Asthma Immunol* 2003; **90:** 214–22.
3. Patel P, *et al.* Randomized, double-blind, placebo-controlled study of montelukast for treating perennial allergic rhinitis. *Ann Allergy Asthma Immunol* 2005; **95:** 551–7.
4. Wilson AM, *et al.* Leukotriene receptor antagonists for allergic rhinitis: a systematic review and meta-analysis. *Am J Med* 2004; **116:** 338–44.
5. Nayak A, Langdon RB. Montelukast in the treatment of allergic rhinitis: an evidence-based review. *Drugs* 2007; **67:** 887–901.

Sleep-disordered breathing. Montelukast with an intranasal corticosteroid has been reported to be beneficial in a small study in children with residual sleep-disordered breathing after tonsillectomy and adenoidectomy.[1]

1. Kheirandish L, *et al.* Intranasal steroids and oral leukotriene modifier therapy in residual sleep-disordered breathing after tonsillectomy and adenoidectomy in children. *Pediatrics* 2006; **117:** e61–e66.

Urticaria. Montelukast has been investigated in the treatment of urticaria (p.1584) with variable results.[1] However, urticaria has also been described as a suspected adverse effect of montelukast therapy (see above).

Montelukast has been reported to be more effective than placebo when used with the antihistamine desloratadine in the treatment of delayed pressure urticaria.[2]

1. McBayne TO, Siddall OM. Montelukast treatment of urticaria. *Ann Pharmacother* 2006; **40:** 939–42.
2. Nettis E, *et al.* Desloratadine in combination with montelukast suppresses the dermagraphometer challenge test papule, and is effective in the treatment of delayed pressure urticaria: a randomized, double-blind, placebo-controlled study. *Br J Dermatol* 2006; **155:** 1279–82.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Lukair†; Singulair; ***Austral.:*** Singulair; ***Austria:*** Singulair; ***Belg.:*** Singulair; ***Braz.:*** Singulair; ***Canad.:*** Singulair; ***Chile:*** Brondilat; Leukast†; Singulair; ***Cz.:*** Singulair; ***Denm.:*** Singulair; ***Fin.:*** Singulair; ***Fr.:*** Singulair; ***Ger.:*** Singulair; ***Gr.:*** Singulair; ***Hong Kong:*** Singulair; ***Hung.:*** Singulair; ***India:*** Montair; Montelast; ***Irl.:*** Singulair; ***Israel:*** Singulair; ***Ital.:*** Lukasm; Montegen; Singulair; ***Jpn:*** Kipres; ***Malaysia:*** Singulair; ***Mex.:*** Singulair; ***Neth.:*** Singulair; ***Norw.:*** Singulair; ***NZ:*** Singulair; ***Philipp.:*** Singulair; ***Pol.:*** Singulair; ***Port.:*** Lukair; Singulair; Singulergy; Synglarin; ***Rus.:*** Singulair (Сингуляр); ***S.Afr.:*** Singulair; ***Singapore:*** Singulair; ***Spain:*** Singulair; ***Swed.:*** Singulair; ***Switz.:*** Singulair; ***Thai.:*** Singulair; ***Turk.:*** Singulair; ***UK:*** Singulair; ***USA:*** Singulair; ***Venez.:*** Airon; Inuvic; Monukast; Singulair.

Multi-ingredient: ***India:*** Montair Plus.

Nedocromil Sodium *(BANM, USAN, rINNM)*

FPL-59002 (nedocromil); FPL-59002KC (nedocromil calcium); FPL-59002KP (nedocromil sodium); Natrii Nedocromilum; Nédocromil Sodique; Nedocromilo sódico; Nedocromilum Natricum; Nedokromiilinatrium; Nedokromil Sodyum; Nedokromilnatrium. Disodium 9-ethyl-6,9-dihydro-4,6-dioxo-10-propyl-4*H*-pyrano[3,2-*g*]quinoline-2,8-dicarboxylate.

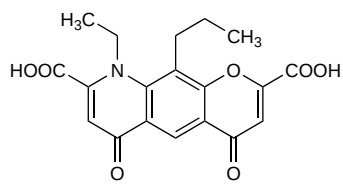
Натрий Недокромил

$C_{19}H_{15}NNa_2O_7$ = 415.3.

CAS — 69049-73-6 (nedocromil); 69049-74-7 (nedocromil sodium); 101626-68-0 (nedocromil calcium).

ATC — R01AC07; R03BC03; S01GX04.

ATC Vet — QR01AC07; QR03BC03; QS01GX04.



(nedocromil)

NOTE. Nedocromil Calcium is also *USAN*.

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]