

NEW DRUG EVALUATION

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OMALIZUMAB

Omalizumab is an anti-IgE monoclonal antibody licensed for use as an add-on to standard therapy in patients 12 years and over with severe persistent allergic asthma. It is administered as a subcutaneous injection every two to four weeks depending on body weight and baseline serum IgE level. In selected patients with severe uncontrolled asthma omalizumab treatment reduces the number of asthma exacerbations, although a significant effect on hospitalisation rates has not been demonstrated. Treatment with omalizumab should be initiated by specialists who are experienced in the diagnosis and treatment of severe asthma. If there are no improvements in symptoms and/or quality of life within 16 weeks, treatment should be stopped. At present, a clear role for anti-IgE antibodies in the stepwise treatment of asthma has not been defined.

What is it?

Omalizumab (Xolair®) is an anti-IgE monoclonal antibody licensed for the treatment of severe persistent allergic asthma in patients 12 years and over. Omalizumab binds to free immunoglobulin E (IgE) and prevents it from binding to the high affinity FCεRI receptor on mast cells and basophils. This reduces the amount of free IgE that is available to trigger the allergic cascade. It is administered as a subcutaneous injection in the deltoid region of the arm, every two to four weeks depending on body weight and baseline serum IgE level (ranging from 75mg every four weeks to 375mg every two weeks). It is licensed as add-on therapy in patients with severe asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen (with associated raised IgE levels) and reduced lung function (FEV₁<80%). Patients will also have frequent daytime symptoms or night-time awakenings, and multiple severe asthma exacerbations despite regular high-dose inhaled treatment.¹

How effective is it?

The INNOVATE trial (n=419) evaluated the effects of omalizumab (compared with placebo) on exacerbation rates of patients with more severe disease.² Patients 12-75 years of age with severe allergic asthma (mean beclometasone dose = 2330mcg/day plus regular long acting β₂ agonist use) and a history of at least two exacerbations (or ≥ 1 severe exacerbation) in the last 12 months were included. After an eight week run-in period of close monitoring and treatment optimisation, patients were treated with omalizumab or placebo. After 28 weeks of treatment, analysis of the intention-to-treat population did not show a significant reduction in exacerbation rates (rate ratio; RR=0.806, p=0.153). However, when the results were adjusted to take into account a baseline discrepancy, the reduction in exacerbations reached statistical significance (RR=0.738, 95% CI 0.55-1.00; p=0.042).

A 52 week open-label trial compared patients with poorly controlled moderate to severe persistent asthma (of more than 2 years duration) receiving omalizumab treatment (n=206) with those randomised to best standard care alone (n=106).³ Using diary data available from both treatment

groups (n=191 and 89, respectively), the rate of annualised asthma deterioration-related incidents was evaluated as the primary end-point. Treatment with omalizumab showed a significant reduction in the rate of these incidents (4.92 compared to 9.76 with placebo, relative risk reduction of 49.6%, 95%CI 27.8-64.8%, p<0.001). However, rates of emergency room visits (12.6% and 19.1%) and hospitalisations (8.4% and 9.0%) were not significantly altered.

One 32 week trial evaluated the effect of omalizumab on the dose of inhaled corticosteroid required to provide symptom control.⁴ Patients inhaling ≥ 1mg fluticasone daily reduced their steroid dose by 57.2% from baseline. Although the difference between omalizumab and placebo treatment was significant (p=0.003), the average dose reduction in the placebo group was 43.3%, suggesting that closer support and management may also be effective. Omalizumab is not licensed to facilitate inhaled corticosteroid dose reduction.

Other trials involving patients with less severe disease have been published and were used to support the licence application. However, these are not the high-risk patients for which the licence was granted.

How safe is it?

The most commonly reported adverse effects with omalizumab treatment were injection site reactions and headache.¹ Anaphylaxis, angioedema and other serious allergic conditions occurred in less than 1 in 1,000 patients who participated in all clinical trials.¹ A small increase in reported malignancies in patients treated with omalizumab (0.5% vs. 0.2% in the control patients) was not thought to be treatment-related. As the majority of the malignancies appeared within one year of treatment it was deemed likely that they were pre-existing.⁵

What other options are there?

Patients should be treated in a stepwise manner with treatment incorporating regular inhaled corticosteroids,

short and long acting inhaled β_2 agonists and finally leukotriene antagonists, theophylline, oral β_2 agonists or oral steroids depending on symptom severity.⁶

When should it be used?

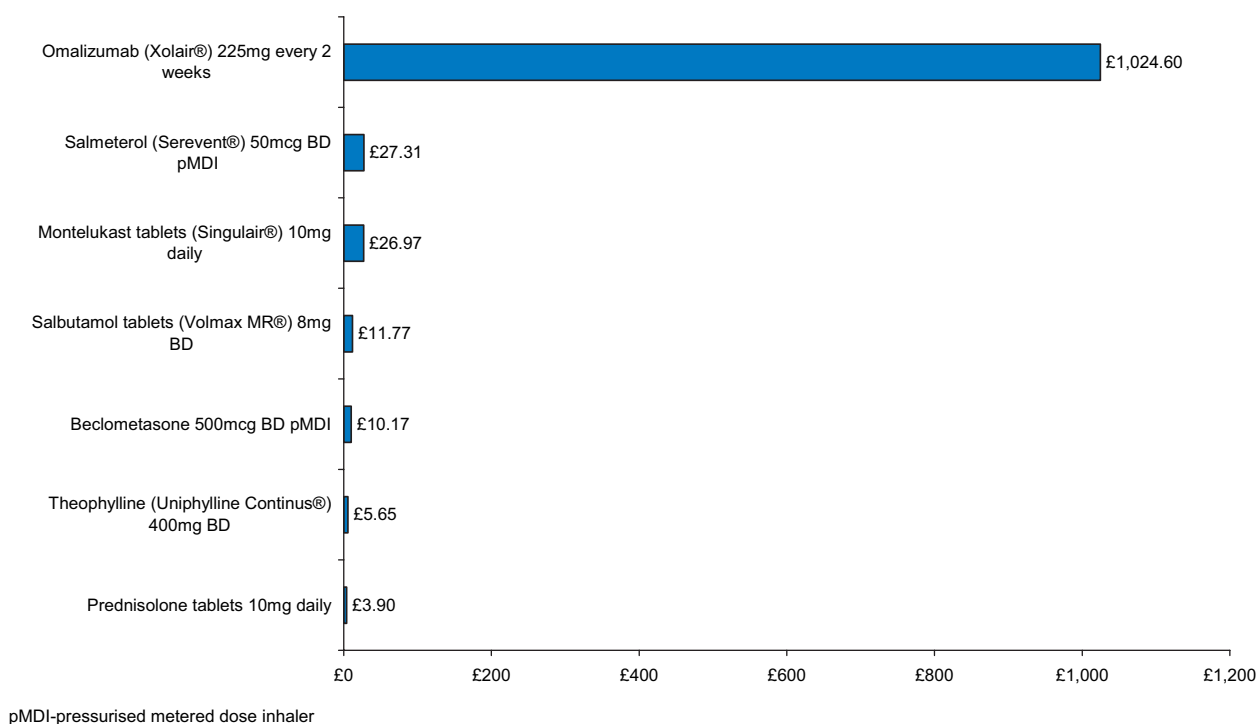
Omalizumab should only be prescribed by specialists who are experienced in diagnosing and treating severe asthma. At present it should only be used in patients with severe uncontrolled disease. Response to treatment should be evaluated at regular intervals and stopped after 16 weeks if there are no improvements in symptom control and/or quality of life.¹

Currently omalizumab can only be sourced through hospital pharmacies and cannot be prescribed in primary care. Should this situation alter then prescribing in primary care should be subject to a shared care guideline.

Placebo-treated patients involved in these clinical trials showed marked improvements in exacerbation rates, quality of life measures and ability to reduce inhaled steroid dose (from baseline). This suggests a period of close supervision and management before considering treatment with an anti-IgE antibody, may be valuable.

How much does it cost?

Cost of 28 days treatment (Drug Tariff/ eMIMS May 2006)



N.B. Doses shown are for general comparison only and do not imply therapeutic equivalence

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KEY RCT - randomised controlled trial, G-guideline, MA-meta analysis

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