NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Omalizumab for the treatment of severe persistent allergic asthma (review of TA133 and TA201)

Final Scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of omalizumab within its licensed indications for the treatment of severe persistent allergic asthma.

Background

Asthma is characterised by symptoms such as dyspnoea, chest tightness, wheezing, sputum production and cough associated with variable airflow obstruction and airway hyperresponsiveness. Asthma attacks vary in frequency and severity. Some people who have asthma are symptom-free most of the time, with only occasional episodes of shortness of breath. Other people cough and wheeze frequently and may have severe attacks after viral infections, exercise or exposure to irritants, including cigarette smoke. Asthma can have an allergic component resulting in over-production of human immunoglobulin E (IgE). Environmental allergens such as pollen or house dust mites can bind to IgE attached to cell membrane receptors resulting in the release of inflammatory mediators which lead to inflammation and swelling of the airways, resulting in asthma symptoms.

Estimates suggest that around 5.4 million people in England and Wales currently receive treatment for asthma (1.1 million children and 4.3 million adults). Asthma is the most common long-term respiratory condition in childhood. In 2008-09 there were over 67,077 emergency hospital admissions for asthma in the UK. Of these, 27,970 were for children aged 15 years or under. Asthma including IgE-mediated asthma is most prevalent in children aged between 5 and 15 years. Prevalence decreases in adulthood until the ages of 55-64 years, when it starts to rise again. Asthma is more common in boys, but this reverses in early adulthood.

People with severe asthma often have a severely impaired quality of life which can lead to fatigue, absence from school or work and psychological problems including stress, anxiety and depression. There were 1,131 deaths from asthma in the UK in 2009, twelve of which were among children aged 14 years or younger.

Current British guidelines from the British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN) recommend a stepwise approach to treatment. Control is maintained by stepping up treatment as necessary and stepping down when control is good.

Step 1 (for mild intermittent asthma) requires occasional use of inhaled short-acting beta-2 agonists and step 2 recommends the introduction of inhaled corticosteroids at doses of 200-400 micrograms per day in children and 200-800 micrograms per day in adults. Step 3 recommends the addition of an inhaled long-acting beta-2 agonist for both adults and children aged 5-12 years and the use of add-on leukotriene receptor antagonists, theophyllines or slow-release beta-2 agonists. If control remains inadequate, the dose of the inhaled steroid may be increased to 800 micrograms per day in adults and 400 micrograms per day in children, if not already on these doses. At step 4, the guidelines recommend that the dose of inhaled corticosteroids is increased up to 2000 micrograms per day in adults and up to 800 micrograms per day in children aged 5-12 years. Add-on therapies (see above) may also be considered at this stage. Prior to moving to step 5, patients whose asthma is inadequately controlled should be referred to specialist care. At step 5, patients should use daily steroid tablets at the lowest dose providing adequate control. Consideration should also be given to treatments that may minimise the use of steroid tablets including immunosuppressants (methotrexate, cyclosporin and oral gold).

NICE technology appraisal guidance 133 recommends omalizumab as an option for the treatment of severe persistent allergic (IgE mediated) asthma as add-on therapy to optimised standard therapy, only in adults and adolescents (12 years and older) who have been identified as having severe unstable disease. Technology appraisal guidance 201 does not recommend omalizumab for the treatment of severe persistent allergic asthma in children aged 6 to 11 years.

The technology

Omalizumab (Xolair, Novartis Pharmaceuticals) is a recombinant humanised anti-immunoglobulin E (anti-IgE) antibody. It binds specifically to circulating IdE thus preventing human IgE from binding to its receptor on mast cells and basophils, thus inhibiting the histamine release response normally triggered by exposure to allergens and pro-inflammatory mediators. Omalizumab is administered subcutaneously every two or four weeks by a healthcare provider.

Omalizumab has a marketing authorisation for add-on therapy to improve asthma control in adult and adolescent patients (12 years of age and above) with severe persistent allergic asthma who have all of the following:

- a positive skin test or in vitro reactivity to a perennial aeroallergen
- reduced lung function (FEV1 <80%)
- frequent daytime symptoms or night-time awakenings
- multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist.

Omalizumab also has a UK marketing authorisation as add-on therapy to improve asthma control in children aged 6 to <12 years of age with severe persistent allergic asthma who have all of the following:

- a positive skin test or in vitro reactivity to a perennial aeroallergen
- frequent daytime symptoms or night-time awakenings
- multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist.

Treatment with omalizumab should only be considered for patients with convincing IgE mediated asthma.

Intervention(s)	Omalizumab (in addition to best standard care)
Population(s)	Adults, adolescents and children (6 to <12 years of age) with severe persistent allergic (IgE mediated) asthma under the conditions specified in the marketing authorisation
Comparators	Standard therapy without omalizumab
Outcomes	The outcome measures to be considered include: • asthma symptoms • incidence of clinically significant acute exacerbations, including those which require unscheduled contact with healthcare professionals or hospitalisation • use of oral corticosteroids • mortality • time to discontinuation • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

	Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Best standard care for this population is considered to be step 4 and step 5 in the stepwise approach to treatment from the SIGN/BTS guideline. If the evidence allows, social factors affecting adherence to treatment will be considered. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal Guidance No 133. November 2007, Omalizumab for severe persistent allergic asthma. Review date August 2010. Technology Appraisal Guidance No 201. October 2010, Omalizumab for the treatment of severe persistent allergic asthma in children aged 6-11. Review date October 2010. Technology Appraisal Guidance No 10. August 2000, The use of Inhaler systems (devices) in children under the age of 5 years with chronic asthma. . Technology Appraisal Guidance No 38. March 2002, The use of inhaler systems (devices) for the routine treatment of chronic asthma in older children (aged 5-15 years). Technology Appraisal No 131. November 2007, Corticosteroids for the treatment of chronic asthma in children under the age of 12 years. Review date November 2012. Technology Appraisal No 138. March 2008, Corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and over. Review date November 2012.