NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Reslizumab for treating eosinophilic asthma inadequately controlled by inhaled corticosteroids

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of reslizumab within its marketing authorisation for treating eosinophilic asthma inadequately controlled by inhaled corticosteroids.

Background

Asthma is a chronic inflammatory disease associated with variable airflow obstruction and airway hyperresponsiveness. It is characterised by exacerbations associated with symptoms such as breathlessness, chest tightness, wheezing, sputum production and cough. Severe eosinophilic asthma is a subset of the condition that is associated with blood and sputum eosinophils and recurrent exacerbations. Eosinophilic nasal polyps may also be present. Eosinophils are thought to play a major role in airway inflammation in asthma.

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 1242 deaths from asthma in the UK in 2012.[1] Estimates suggest that around 5.4 million people in England and Wales currently receive treatment for asthma.

Current British guidelines from the British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN) recommend a stepwise approach to treatment in adults. Control is maintained by stepping up treatment as necessary and stepping down when control is good. The guideline steps are summarised as follows:

- Step 1. Inhaled short-acting beta-2 agonist as required.
- Step 2. Add inhaled corticosteroid (200–800 micrograms per day).
- Step 3. Add an inhaled long-acting beta-2 agonist. If control remains inadequate, increase the dose of the inhaled corticosteroid to 800 micrograms per day. If there is no response to the inhaled long-acting beta-2 agonist, stop this drug and increasing the inhaled corticosteroid dose 800 micrograms per day. If control is still inadequate, try a leukotriene receptor antagonist or slow-release theophylline.

- Step 4: Consider increasing the dose of inhaled corticosteroid up to 2000 micrograms per day. Consider adding a fourth drug (for example, a leukotriene receptor antagonist, slow-release theophylline or a beta-2 agonist tablet).

- Step 5: Use daily steroid tablets at the lowest dose providing adequate control. Maintain high-dose inhaled corticosteroid at 2000 micrograms per day. Consider other treatments to minimise the use of steroid tablets. Refer patients to specialist care.

NICE technology appraisal guidance 278 recommends omalizumab as an option for treating severe persistent allergic IgE-mediated asthma as add-on therapy to optimised standard therapy in people aged 6 years and older who need continuous or frequent treatment with oral corticosteroids (defined as 4 or more courses in the previous year), and only if the manufacturer makes omalizumab available with the discount agreed in the patient access scheme. Optimised standard therapy is defined in the recommendations as a full trial of and, if tolerated, documented compliance with inhaled high-dose corticosteroids, long-acting beta2 agonists, leukotriene receptor antagonists, theophyllines, oral corticosteroids, and smoking cessation if clinically appropriate.

The technology

Reslizumab (Cinquil, Teva Pharmaceuticals) is an anti-interleukin-5 monoclonal antibody. By reducing the effects of interleukin-5, reslizumab causes a reduction in circulating eosinophils, a type of white blood cell involved in allergic response and tissue inflammation. Reslizumab is administered intravenously in addition to best standard asthma care.

Reslizumab does not currently have a marketing authorisation in the UK for treating eosinophilic asthma inadequately controlled by inhaled corticosteroids. Reslizumab has been studied in clinical trials in comparison with placebo in people aged 12–75 years with eosinophilic asthma inadequately controlled by inhaled corticosteroids.

Intervention(s)	Reslizumab (in addition to best standard care)
Population(s)	People with severe eosinophilic asthma
Comparators	• Best standard care without reslizumab For people with severe persistent allergic IgE-mediated eosinophilic asthma: • Omalizumab

Outcomes	The outcome measures to be considered include: • asthma control • incidence of clinically significant exacerbations, including those which require unscheduled contact with healthcare professionals or hospitalisation • use of oral corticosteroids • patient and clinician evaluation of response • lung function • 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. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.

Other considerations	Best standard care for this population is considered to be step 4 and/or step 5 in the stepwise approach to treatment from the SIGN/BTS guideline (for example, high-dose inhaled corticosteroids and oral corticosteroids). If the evidence allows, social factors affecting adherence to treatment will be considered. If the evidence allows, the following subgroups will be considered: • People who do not adhere to treatment • People who have severe allergic IgE-mediated eosinophilic asthma • People who require maintenance oral corticosteroid treatment • People who require frequent oral corticosteroid treatment. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Omalizumab for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201)' (2013) NICE Technology Appraisal 278. Review proposal date Mar 2016. 'Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over' (2008) NICE Technology Appraisal 138. Guidance on static list. 'Mepolizumab for treating severe eosinophilic asthma'. Proposed technology appraisal ID781. Publication date to be confirmed. Related Guidelines: Clinical Guideline in Preparation, 'Asthma – diagnosis and monitoring'. Earliest anticipated date of publication: Jun 2015. Clinical Guideline in Preparation, 'Asthma management'. Anticipated publication date: TBC. Related Interventional Procedures: Interventional Procedure No. 419, Jan 2012, 'Bronchial

	thermoplasty for severe asthma'. Related Quality Standards: Quality Standard No. 25, Feb 2013, 'Asthma'. Related NICE Pathways: NICE Pathway: Asthma, Pathway created: Mar 2014.
Related National Policy	NHS England (January 2014) Adult Highly specialised respiratory services. Manual for prescribed specialised services 2013/14. NHS England (2014) Internal Medicine's Group: A14. Specialised Respiratory. Department of Health (2013) NHS Outcomes Framework 2014-2015

Questions for consultation

What is the overlap between populations with severe allergic asthma and eosinophilic asthma not controlled by inhaled corticosteroids?

Have all relevant comparators for reslizumab been included in the scope?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom reslizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Children and young people aged 12 years and older who had eosinophilic asthma not controlled by inhaled corticosteroids were included in the reslizumab clinical trials. Should the use of reslizumab for treating eosinophilic asthma in this population be included in the scope of this appraisal?

Where do you consider reslizumab will fit into the existing NICE pathway, 'Asthma'?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which reslizumab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by

making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider reslizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of reslizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) process. We welcome comments on the appropriateness of appraising this topic through this process.

References

1. Royal College of Physicians (2014) National review of asthma deaths. Accessed April 2015