APPENDIX B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Mepolizumab for treating severe eosinophilic asthma [ID798]

Final scope

Remit/appraisal objective
To appraise the clinical and cost effectiveness of mepolizumab within its marketing authorisation for treating severe eosinophilic asthma

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. 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
Mepolizumab (Nucala, GlaxoSmithKline) is an anti-interleukin-5 humanised monoclonal antibody. By reducing the effects of interleukin-5, mepolizumab causes a reduction in circulating eosinophils, a type of white blood cell involved in allergic response and tissue inflammation. Mepolizumab is administered subcutaneously in addition to best standard asthma care.

Mepolizumab does not currently have a marketing authorisation in the UK for treating severe eosinophilic asthma. Mepolizumab has been studied in clinical trials in comparison with placebo in people with severe eosinophilic asthma.

<table>
<thead>
<tr>
<th>Intervention(s)</th>
<th>Mepolizumab (in addition to best standard care)</th>
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<tr>
<td>Population(s)</td>
<td>Adults with severe eosinophilic asthma</td>
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<td>Comparators</td>
<td>- Best standard care without mepolizumab</td>
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<td></td>
<td>For people with severe persistent allergic IgE-mediated eosinophilic asthma:</td>
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<td>- Omalizumab</td>
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### 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.

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:**

Technology Appraisal No. 278, Apr 2013, ‘Omalizumab for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201)’. Review proposal date Mar 2016.


**Related Guidelines:**

Clinical Guideline in Preparation, ‘Asthma – diagnosis and monitoring’. Anticipated publication date: TBC

Clinical Guideline in Preparation, ‘Asthma management’. Earliest anticipated publication date: June 2017.

**Related Interventionsal Procedures:**

Interventional Procedure No. 419, Jan 2012, ‘Bronchial thermoplasty for severe asthma’.

**Related Quality Standards:**
### Appendix B

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<th>Related National Policy</th>
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<tr>
<td>Quality Standard No. 25, Feb 2013, 'Asthma'.</td>
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<td>Related NICE Pathways:</td>
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<tr>
<td>Related National Policy</td>
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