

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Health Technology Appraisal

Benralizumab for treating severe asthma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of benralizumab within its marketing authorisation for treating severe asthma with elevated blood eosinophils.

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 elevated 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 1,242 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.

Guidelines from the [British Thoracic Society \(BTS\) and Scottish Intercollegiate Guidelines Network \(SIGN\)](#)² recommend a stepwise approach for treating asthma. Control is maintained by stepping up treatment as necessary and stepping down when control is good. The recommendations are summarised as follows (doses and treatments may differ for children and young people):

- For all steps use an inhaled short-acting beta-2 agonist as required (consider moving up if using three doses a week or more).
- **Regular preventer:** Use an inhaled corticosteroid as a regular preventer.
- **Initial add-on therapy:** Add an inhaled long-acting beta-2 agonist to inhaled corticosteroid (normally as a combination inhaler).
- **Additional add-on therapies:** If there is no response to long-acting beta-2 agonist, stop this treatment and consider an increased dose of inhaled corticosteroid. If control is inadequate from long-acting beta-2 agonist, continue treatment and increase inhaled corticosteroid to medium dose or continue treatment and consider a trial of other

therapy (for example leukotriene receptor antagonist, slow-release theophylline or long-acting muscarinic agent).

- **High dose therapies:** Consider trials of increasing the dose of inhaled corticosteroid up to a high dose. Consider adding a fourth drug (for example, a leukotriene receptor antagonist, slow-release theophylline, a beta-2 agonist tablet or long-acting muscarinic agent). Refer patients for specialist care.
- **Continuous or frequent use of oral steroids:** Use daily steroid tablets at the lowest dose providing adequate control. Maintain high-dose inhaled corticosteroid. Consider other treatments to minimise the use of steroid tablets. Refer patients for specialist care.

[NICE technology appraisal guidance 431](#) recommends mepolizumab as an option for treating severe refractory eosinophilic asthma, as an add-on to optimised standard therapy, in adults only if the blood eosinophil count is 300 cells/microlitre or more in the previous 12 months and the person has agreed to and followed the optimised standard treatment plan and has had 4 or more asthma exacerbations needing systemic corticosteroids in the previous 12 months or has had continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months.

[NICE technology appraisal guidance 479](#) recommends reslizumab as an add-on therapy to treat severe eosinophilic asthma that is inadequately controlled in adults despite maintenance therapy with high-dose inhaled corticosteroids plus another drug, only if the blood eosinophil count has been recorded as 400 cells per microlitre or more and the person has had 3 or more severe asthma exacerbations needing systemic corticosteroids in the past 12 months.

Technology appraisals 431 and 479 define optimised standard therapy as high-dose therapies (previously step 4 in the BTS and SIGN guidelines) or continuous or frequent use of oral steroids (previously step 5).

The technology

Benralizumab (brand name unknown, Astra Zeneca) is a monoclonal antibody against anti-interleukin-5 receptor alpha. Benralizumab reduces eosinophils, a type of white blood cell involved in allergic response and tissue inflammation. Eosinophils are thought to play a major role in the pathogenesis and severity of asthma. Benralizumab is administered subcutaneously in addition to best standard asthma care.

Benralizumab does not currently have a marketing authorisation in the UK for treating severe asthma with elevated blood eosinophils. Benralizumab has been studied in clinical trials in comparison with placebo in adults with asthma that is inadequately controlled by inhaled corticosteroid and long-acting beta-2 agonist.

Intervention(s)	Benralizumab as an add-on to optimised standard therapy
Population(s)	Adults with severe asthma with elevated blood eosinophils
Comparators	<ul style="list-style-type: none"> • Optimised standard therapy • Reslizumab (in addition to optimised standard therapy) • Mepolizumab (in addition to optimised standard therapy)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • 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	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>

<p>Other considerations</p>	<p>If the evidence allows, the following subgroups will be considered:</p> <ul style="list-style-type: none"> • baseline eosinophil levels • people who require maintenance oral corticosteroid treatment • people who require frequent oral corticosteroid treatment. <p>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.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>‘Reslizumab for treating severe eosinophilic asthma’ (2017) NICE technology appraisal guidance 479. Review proposal date October 2020.</p> <p>‘Mepolizumab for treating severe eosinophilic asthma’ (2017) NICE technology appraisal guidance 431. Review proposal date January 2020.</p> <p>‘Omalizumab for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201)’ (2013) NICE technology appraisal 278. Guidance on static list.</p> <p>‘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.</p> <p>Guidelines in development:</p> <p>‘Asthma – diagnosis and monitoring’. Publication expected October 2017.</p> <p>‘Asthma management’. Publication expected October 2017.</p> <p>Related Interventional Procedures:</p> <p>‘Bronchial thermoplasty for severe asthma’ (2012). NICE interventional procedures guidance 419</p> <p>Related Quality Standards:</p> <p>‘Asthma’ (2013) NICE quality standard 25.</p> <p>Related NICE Pathways:</p> <p>Asthma (2014).</p>

	http://pathways.nice.org.uk/pathways/asthma
Related National Policy	<p>NHS England (May 2016) Adult highly specialised respiratory services and Specialist respiratory services for children. Manual for prescribed specialised services 2016/17.</p> <p>NHS England (2014) Internal Medicine's Group: A14. Specialised Respiratory.</p> <p>Department of Health (2016) The NHS Outcomes Framework 2016/167 Domains 1, 2, 3 and 4</p>

References

1. Royal College of Physicians (2014) [National review of asthma deaths](#). Accessed February 2017.
2. British Thoracic Society and Scottish Intercollegiate Guidelines Network (2016) [British guideline on the management of asthma](#). Accessed February 2017.