NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Mepolizumab for treating severe eosinophilic asthma (review of technology appraisal guidance TA431)

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 1,484 deaths from asthma in the UK in 2017.[1] . Around 4.8 million people in England and Wales currently receive treatment for asthma.[1]

NICE guideline NG80: asthma: diagnosis, monitoring and chronic asthma management and guidelines from the Global Initiative for Asthma (GINA) [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):

- Use an inhaled short-acting beta-2 agonist as reliever therapy as required (consider moving up if using three doses a week or more).
- Use a low dose inhaled corticosteroid as a regular preventer.
- Add an leukotriene receptor antagonist in addition to the low dose inhaled corticosteroid and review the response to treatment in 4 to 8 weeks. If there is no response offer a long-acting beta-2 agonist in combination with the inhaled corticosteroid with or without the leukotriene receptor antagonist..

- If control is inadequate on the above maintenance therapy, consider changing the inhaled corticosteroid and long-acting beta-2 agonist maintenance therapy to a maintenance and reliever therapy (MART) regimen with a low maintenance inhaled corticosteroid dose.

- If asthma is uncontrolled on the above MART regimen increase the inhaled corticosteroid to a moderate maintenance dose (either continuing on a MART regimen or changing to a fixed-dose inhaled corticosteroid and long-acting beta-2 agonist).

- If asthma is uncontrolled on the above regimen consider trials of high dose inhaled corticosteroid (offer as a fixed-dose regimen or trial of an additional drug (for example, slow-release theophylline, or long-acting muscarinic agent). Refer patients for specialist care where they may also receive daily steroid tablets and other treatments such as benralizumab (NICE TA565), reslizumab (NICE TA479) and mepolizumab (NICE TA431) for eospinophilic asthma and omalizumab (NICE TA278) for allergic IgE-mediated asthma to minimise the use of steroid tablets. Refer patients for specialist care.

NICE TA431 recommends mepolizumab for treating severe refractory eosinophilic asthma, in adults with a blood eosinophil count of 300 cells/microlitre or more in the previous 12 months, and have has had 4 or more asthma exacerbations needing systemic corticosteroids in the previous 12 months or has had continuous oral corticosteroids over the previous 6 months.

NICE TA479 recommends reslizumab for treating severe eosinophilic asthma that is inadequately controlled in adults with a blood eosinophil count has been recorded as 400 cells per microlitre or more and have had 3 or more severe asthma exacerbations needing systemic corticosteroids in the past 12 months.

NICE TA565 recommends benralizumab in adults for treating severe eosinophilic asthma inadequately controlled despite maintenance therapy with high-dose inhaled corticosteroids and long-acting beta-agonists. It is only recommended in people following an optimised standard treatment plan if the person is eligible for mepolizumab (blood eosinophil count of 300 cells per microlitre or more and 4 or more exacerbations needing systemic corticosteroids in the previous 12 months, or continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months) or reslizumab (blood eosinophil count of 400 cells per microlitre or more with 3 or more exacerbations needing systemic corticosteroids in the past 12 months).

.

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. Eosinophils are thought to play a major role in the pathogenesis and severity of asthma. Mepolizumab is administered subcutaneously in addition to best standard asthma care.

Mepolizumab has a marketing authorisation in the UK for treating severe refractory eosinophilic asthma in adults, adolescents and children aged 6 years and older.

Intervention(s)	Mepolizumab
Population(s)	People 6 years and older with severe refractory eosinophillic asthma
Comparators	For people with severe asthma for whom biologics are indicated and suitable according to NICE guidance: • Reslizumab • Benralizumab For people with severe asthma for whom currently available biologics are not indicated and suitable: • Optimised standard therapy without biologics
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	If the evidence allows, the following subgroups will be considered: • baseline eosinophil levels • 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: 'Benralizumab for treating severe eosinophilic asthma' (2019) NICE technology appraisal guidance 565. Review proposal date October 2022. 'Reslizumab for treating eosinophilic asthma inadequately controlled by inhaled corticosteroids' (2017) NICE technology appraisal guidance 479. Review proposal date October 2020. 'Mepolizumab for treating severe eosinophilic asthma' (2017) NICE technology appraisal guidance 431. Under review. 'Omalizumab for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201)' (2013) NICE technology appraisal 278.Guidance on static list. '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. Related Guidelines: Asthma – diagnosis, monitoring and chronic asthma management (2017) NICE guideline 80. Review proposal date November 2019.Related Interventional Procedures: Interventional Procedure No. 419, Jan 2012, 'Bronchial thermoplasty for severe asthma'.Related Quality Standards: Asthma (2013) NICE quality standard 25 (updated Sept 2018) Related NICE Pathways: Asthma (2017) NICE pathway
Related National Policy	NHS England (January 2018) Adult Highly specialised respiratory services. Manual for prescribed specialised services 2018/19. NHS England (2014) Internal Medicine's Group: A14. Specialised Respiratory. Department of Health, NHS Outcomes Framework (published May 2019): Domains1, 2, 3 and 4

References

1. Asthma UK (2020). Accessed February 2020
2. Global Initiative for Asthma (2019) Global strategy for asthma management and prevention. Accessed June 2019