NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Health Technology Appraisal

Dupilumab for treating severe asthma [ID1213]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dupilumab within its marketing authorisation for treating severe asthma inadequately controlled with optimised standard therapy .

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. 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] Estimates suggest that around 4.8 million people in England and Wales currently receive treatment for asthma.

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 TA278 recommends omalizumab for treating severe persistent confirmed allergic IgE-mediated asthma 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).

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

Dupilumab (Dupixent, Sanofi) is an anti-interleukin-4 monoclonal antibody directed against the receptor alpha subunit, which blocks signalling from both interleukin-4 and interleukin-13. Dupilumab is administered subcutaneously.

Dupilumab has received a marketing authorisation in the UK for treating severe asthma. Dupilumab has been studied as an add-on therapy in clinical trials in comparison with placebo in people aged 12 years and over with severe asthma inadequately controlled by moderate or high dose inhaled corticosteroid and long-acting beta-2 agonist or leukotriene receptor antagonist. One trial compared dupilumab with placebo in people aged 12 years and over with severe steroid dependant asthma.

Intervention(s)	Dupilumab as an add-on to optimised standard therapy
Population(s)	People 12 years and older with severe asthma inadequately controlled with optimised standard therapy (including moderate or high dose inhaled corticosteroid, and either long-acting beta-2 agonist, leukotriene receptor antagonist, slow-release theophylline or long-acting muscarinic agent)
Comparators	For people with severe asthma for whom biologics are indicated and suitable: • Reslizumab in combination with optimised standard therapy including treatment with or without oral corticosteroids for people with eosinophilic asthma (in accordance with NICE recommendations) • Mepolizumab in combination with optimised standard therapy including treatment with or without oral corticosteroids for people with eosinophilic asthma (in accordance with NICE recommendations) • Benralizumab in combination with optimised standard therapy including treatment with or without oral corticosteroids for people with eosinophilic asthma (in accordance with NICE recommendations) • Omalizumab in combination with optimised standard therapy including treatment with or without oral corticosteroids for people with allergic IgE-mediated asthma (in accordance with NICE recommendations) For people with severe asthma for whom currently available biologics are not indicated and suitable: • Optimised standard therapy including treatment with or without oral corticosteroids

Outcomes	The outcome measures to be considered include: • Objective measures of lung function (e.g. FEV1, PEF) • asthma control • incidence of clinically significant exacerbations, including those which require unscheduled contact with healthcare professionals or hospitalisation • use of oral corticosteroids • mortality • 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 of people will be considered: • People who require maintenance oral corticosteroid treatment compared with people who are not steroid dependant • People with eosinophilic asthma • People with allergic IgE- mediated asthma 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	**Related Technology Appraisals:**

and NICE Pathways	'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. Review proposal date January 2020. '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:** 'Bronchial thermoplasty for severe asthma' (2012). NICE interventional procedures guidance 419 **Related Quality Standards:** 'Asthma' (2013) NICE quality standard 25. **Related NICE Pathways:** Asthma (2014). http://pathways.nice.org.uk/pathways/asthma
Related National Policy	NHS England (May 2016) Adult highly specialised respiratory services and Specialist respiratory services for children. Manual for prescribed specialised services 2016/17. NHS England (2014) Internal Medicine's Group: A14. Specialised Respiratory. Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains1, 2, 3 and 4

References

1. Asthma UK (2017). Accessed June 2019

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