

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Dupilumab for treating severe asthma

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dupilumab within its marketing authorisation for treating severe asthma inadequately controlled with 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. 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 1,468 deaths from asthma in the UK in 2015.¹ 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):

- Use an inhaled short-acting beta-2 agonist as required (consider moving up if using three doses a week or more).
- Use an inhaled corticosteroid as a regular preventer.
- Add an inhaled long-acting beta-2 agonist to inhaled corticosteroid (normally as a combination inhaler). If there is no response, 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).
- 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.

- 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

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 does not currently have 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 (in addition to standard management)
Population(s)	People 12 years and older with severe asthma inadequately controlled with optimised standard care (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	Established clinical management without dupilumab
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • 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.

<p>Economic analysis</p>	<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>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 eosinophilic asthma inadequately controlled by inhaled corticosteroids’ (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 management’. Publication date to be confirmed.</p> <p>‘ Chronic asthma management’. Publication date to be confirmed.</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). http://pathways.nice.org.uk/pathways/asthma</p>
<p>Related National Policy</p>	<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, NHS Outcomes Framework 2016-2017 (published 2016): Domains1, 2, 3 and 4</p>

Questions for consultation

Where do you consider dupilumab will fit into the existing NICE pathway, [‘Asthma’](#)? For example would it be used in people inadequately controlled with moderate or high dose ICS? Would people have already received leukotriene receptor antagonist, slow-release theophylline or long-acting muscarinic agents or should they be comparators?

Have all relevant comparators for dupilumab been included in the scope? Could dupilumab be used in people with IgE mediated or eosinophilic asthma? Should reslizumab, mepolizumab and omalizumab be included as a comparators?
 Are the outcomes listed appropriate?

Are there any subgroups of people in whom dupilumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? Is it appropriate to consider social factors affecting adherence to treatment?

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 dupilumab 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;

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- 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 dupilumab 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 dupilumab 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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. (Information on the Institute's Technology Appraisal processes is available at <http://www.nice.org.uk/article/pmg19/chapter/1-Introduction>).

References

1. [Asthma UK](#) (2017). Accessed September 2017
2. British Thoracic Society and Scottish Intercollegiate Guidelines Network (2016) [British guideline on the management of asthma](#). Accessed September 2017.