NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Mepolizumab for treating chronic obstructive pulmonary disease

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of mepolizumab within its marketing authorisation for treating chronic obstructive pulmonary disease.

Background

Chronic obstructive pulmonary disease includes chronic bronchitis, emphysema, chronic obstructive airways disease and chronic airflow limitation. It is characterised by consistent airways obstruction, causing symptoms including persistent and progressive breathlessness, a chronic productive cough and limited exercise capacity. Chronic obstructive pulmonary disease is defined as forced expiratory volume in 1 second (FEV_1) less than 80% predicted, and forced volume capacity (FEV_1/FVC) ratio less than 70%. Severe chronic obstructive pulmonary disease is defined as FEV_1 less than 50% predicted. The impairment of lung function is usually progressive and is not fully reversible.

An estimated 1.2 million people in the UK have been diagnosed with chronic obstructive pulmonary disease, and 115,000 people are newly diagnosed each year.[1] The prevalence of this condition increases with age (it is rare before 35 years of age), and is generally higher among smokers. Chronic obstructive pulmonary disease caused nearly 30,000 deaths in the UK in 2012.[1] It is also a major cause of hospital admission.

For people with stable chronic obstructive pulmonary disease who are breathless and have limited exercise capacity, NICE clinical guideline 101 recommends initial therapy with a short-acting $beta_2$ agonist or a short-acting muscarinic antagonist. For people who remain breathless or have exacerbations despite use of short-acting bronchodilators (that, people who have severe disease), NICE clinical guideline 101 recommends using either an inhaled long-acting muscarinic antagonist alone, a fixed combination of an inhaled corticosteroid and a long-acting beta-2 agonist (dual inhaled therapy), or a combination of all these treatments (triple inhaled therapy). The choice of therapy may be influenced by the severity of disease (FEV_1 above or below 50% predicted), response to treatment and tolerability of inhaled corticosteroid.. In addition to drug therapy, NICE clinical guideline 101 recommends smoking cessation and pulmonary rehabilitation as part of the management of stable chronic obstructive pulmonary disease.

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 cells involved in allergic response and tissue inflammation. Mepolizumab is administered subcutaneously.

Mepolizumab does not currently have a marketing authorisation in the UK for treating chronic obstructive pulmonary disease. It has been studied in clinical trials, compared with placebo, as an add-on treatment in adults with chronic obstructive pulmonary disease.

Intervention(s)	Mepolizumab as an add-on to maintenance therapy.
Population(s)	Adults with chronic obstructive pulmonary disease.
Comparators	For people with FEV1 between 50–80% predicted, and FEV1/FVC ratio less than 70%: • Short-acting beta-2 agonist • Short-acting muscarinic antagonist For people with FEV1 less than 50% predicted: • Long-acting muscarinic antagonist • Dual inhaled therapy, that is, a long-acting beta-2 agonist in combination with an inhaled corticosteroid • Triple inhaled therapy, that is, a long-acting muscarinic antagonist in combination with a long-acting beta-2 agonist and an inhaled corticosteroid • Roflumilast in combination with a long-acting muscarinic antagonist, a long-acting beta-2 agonist and an inhaled corticosteroid (for people who had 2 or more exacerbations in the previous 12 months despite triple inhaled therapy)
Outcomes	The outcome measures to be considered include: • lung function • frequency of moderate/severe exacerbations • 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.
Other considerations	If the evidence allows, subgroups of people with chronic obstructive pulmonary disorder with high levels of eosinophils will be considered. 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: 'Roflimulast for the management of severe chronic obstructive pulmonary disease' (2017). NICE Technology Appraisal 461. Review date July 2020. Related Guidelines: 'Chronic obstructive pulmonary disease' (2010) NICE Clinical Guideline 101. Currently being updated. Date of publication to be confirmed. Related Quality Standards: 'Chronic obstructive pulmonary disease in adults' (2011). NICE quality standard 10. Related NICE Pathways: Chronic Obstructive Pulmonary Disease (2016) NICE pathway http://pathways.nice.org.uk/pathways/chronic-obstructive-pulmonary-disease
Related National Policy	Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1–4. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf NHS England (2014) Our ambition to reduce premature mortality [accessed June 2017]. Chapter 6: respiratory

	disease. Department of Health (2011) An outcomes strategy for chronic obstructive pulmonary disease (COPD) and asthma in England [accessed June 2017]

Questions for consultation

Have all relevant comparators for mepolizumab been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for chronic obstructive pulmonary disorder?

Are the outcomes listed appropriate?

- Are there any relevant outcomes that have not been included?

Is the subgroup suggested in 'other considerations appropriate?

- Are there any other subgroups of people in whom mepolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider mepolizumab will fit into the existing NICE pathway, Chronic Obstructive Pulmonary Disease (2016)?

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 mepolizumab 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;

- 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 mepolizumab 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 mepolizumab 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made. We welcome comments on the appropriateness and suitability of the cost comparison methodology to this topic.

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. British Lung Foundation (2016) Chronic obstructive pulmonary disease (COPD) statistics [accessed June 2017]