NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Roflumilast for treating chronic obstructive pulmonary disease (review of technology appraisal guidance 244) [ID984]

Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of roflumilast within its licensed indication for the maintenance treatment of severe chronic obstructive pulmonary disease.

Background

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

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 (rare before 35 years of age), and it is frequently associated with smoking. 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, maintenance therapy may comprise long-acting muscarinic antagonists (LAMA), long-acting $beta_2$ agonists (LABA) or inhaled corticosteroids (ICS), either individually or in combination. 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 ICS. Theophylline should only be used after a trial of short- and long-acting bronchodilators, or in people who are unable to use inhaled therapy. 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. In NICE technology appraisal 244, roflumilast was recommended for use only in the context of research. The guidance recommended that evidence should be generated on the benefits of roflumilast as an add-on to LAMA in combination with LABA and

ICS or LAMA in combination with LABA. Since TA244, the REACT trial has been published, in which roflumilast in combination with LABA and ICS, with or without LAMA, was compared with placebo.

The technology

Roflumilast (Daxas, AstraZeneca) is an orally administered long-acting selective phosphodiesterase-4 (PDE4) enzyme inhibitor which targets cells and mediators in the body believed to be important in chronic obstructive pulmonary disease.

Roflumilast has a marketing authorisation in the UK for maintenance treatment of severe chronic obstructive pulmonary disease (FEV_1 post bronchodilator less than 50% predicted) associated with chronic bronchitis in adults with a history of frequent exacerbations as an add on to bronchodilator treatment.

Intervention(s)	Roflumilast in combination with maintenance bronchodilator treatment (LABA, LABA/corticosteroid combination inhaler, LAMA, LAMA plus LABA/corticosteroid combination inhaler or LAMA plus LABA [if ICS not tolerated]).
Population(s)	Adults with severe chronic obstructive pulmonary disease (FEV_1 post bronchodilator less than 50% predicted) associated with chronic bronchitis in adult patients with a history of frequent exacerbations.
Comparators	• LAMA in combination with LABA and ICS • LAMA in combination with LABA • LAMA or LABA (with or without ICS) • Theophylline (in combination with inhaled maintenance bronchodilator treatment)
Outcomes	The outcome measures to be considered include: • lung function • incidence and severity of acute exacerbations, including hospitalisation • symptom control (e.g. shortness of breath) • 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	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: 'Roflumilast for the management of severe chronic obstructive pulmonary disease' (2012). NICE Technology Appraisal 244. To be reviewed. 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 2016]. Chapter 6: respiratory disease. Department of Health (2011) An outcomes strategy for chronic obstructive pulmonary disease (COPD) and asthma in England [accessed June 2016]

References

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