NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and over

Draft scope

Appraisal objective

To appraise the clinical and cost effectiveness of corticosteroids, including compound preparations, for the treatment of chronic asthma in adults and children aged 12 years and over and to provide guidance to the NHS in England and Wales[1].

Background

Asthma is characterised by symptoms such as dyspnoea, chest tightness, wheezing, sputum production and cough associated with variable airflow obstruction and airway hyperresponsiveness. Asthma attacks vary in frequency and severity. Some people who have asthma are symptom-free most of the time, with only occasional episodes of shortness of breath. Other people cough and wheeze most of the time and may have severe attacks after viral infections, exercise, or exposure to allergens or irritants, including cigarette smoke.

According to Asthma UK's criteria and independent analysis of large-scale surveys, there are 5.2 million people with asthma in the UK today (4.7 million in England and Wales). The total for the UK includes 590,000 teenagers with asthma.

The main mechanisms for the development and of asthma are considered to be related to inflammation and its resultant effects on airway structure and function. The role of corticosteroids in controlling inflammation is recognised as central to the pharmacological management of asthma in current guidelines.

Current British guidelines from the British Thoracic Society and Scottish Intercollegiate Guidelines Network recommend a stepwise approach to treatment. Treatment is started at the step most appropriate to the initial severity of their asthma with the aim of achieving early control of symptoms and optimisation of peak flow rates. Control is maintained by stepping up treatment as necessary and stepping down when control is good.

[1] The Department of Health and Welsh Assembly government remit to the Institute: To appraise the relative clinical and cost effectiveness of all licensed corticosteroids, including compound preparations, in the treatment of chronic asthma; and if the evidence allows, to advise on the groups of patients who are most likely to benefit from any particular corticosteroid.

Step 1 – Mild intermittent asthma

Occasional inhaled short-acting beta$_2$ agonists used as required for symptomatic relief.

Step 2 – Introduction of regular preventer therapy

Inhaled corticosteroids are the recommended preventer drugs for achieving overall treatment goals. Other, less effective preventer therapies include chromomes (sodium cromoglycate, or nedocromil sodium), leukotriene receptor antagonists (montelukast and zafirlukast) and theophyllines (aminophylline and theophylline).

Step 3 – Add-on therapy

There is no precise threshold in terms of dose of inhaled corticosteroid for the introduction of a third drug. However, the guidelines recommend a trial of add-on therapy before increasing the daily dose of inhaled corticosteroid above 800 micrograms.[2] Options for add-on therapy in adults taking inhaled corticosteroids at doses of 200-800 micrograms are as follows.

- First choice is the addition of an inhaled long-acting beta$_2$ agonist.
- Other alternatives if there is no response to the long-acting beta$_2$ agonist include leukotriene receptor antagonists or theophylline.

Step 4 – Poor control on moderate dose of inhaled steroid plus add-on therapy: addition of fourth drug.

If control remains inadequate on inhaled corticosteroids at doses of 800 micrograms plus add-on therapy the following options should be considered.

- Increasing the dose of inhaled corticosteroids up to 2000 micrograms (adults and children aged over 12 years)
- leukotriene receptor antagonists
- theophyllines
- slow release beta$_2$ agonist tablets.

Step 5: continuous or frequent use of oral corticosteroids. Before proceeding to this step, referral to specialist care should be considered especially in children.

[2] Doses refer to beclometasone dipropionate given via a pressurised metered-dose inhaler. Adjustment is necessary for fluticasone propionate and mometasone and some alternative delivery devices.

The technologies

There are five inhaled corticosteroids licensed in the UK for the treatment of asthma:

- beclometasone dipropionate (AeroBec [3M], AeroBec Forte [3M], Asmabec Clickhaler [Celltech], Beclazone Easi-Breathe [IVAX], Becloforte [Allen & Hanburys], Beclometasone Cyclocaps [APS], Becodisks [Allen & Hanburys], Becotide [Allen & Hanburys], Filair [3M], Filair Forte [3M], Qvar [3M], Pulvinal Beclometasone Dipropionate [Trinity])
- budesonide (Budesonide Cyclocaps [APS], Novoliser [Viatris], Pulmicort [AstraZeneca])
- ciclesonide (Alvesco [Altana])
- fluticasone propionate (Flixotide [Allen & Hanburys])
- mometasone furoate (Asmanex [Schering-Plough])

Beclometasone dipropionate, budesonide, and fluticasone propionate are available in both pressurised metered dose and dry powder formulations. They are also available in formulations for nebulisation. Ciclesonide is available as a pressurised metered dose aerosol only, while mometasone furoate is available in a dry powder formulation only. Ciclesonide is not licensed for use in people under the age of 18 years. All the remaining drugs listed above may be used in those over the age of 12 years.

Compound preparations are combinations of a corticosteroid and a long-acting beta$_2$ agonist in a single inhalation. There are two combinations available; budesonide with formoterol fumarate (Symbicort [AstraZeneca]) and fluticasone propionate with salmeterol xinafoate (Seretide [Allen & Hanburys])

Intervention(s)	Corticosteroids for inhalation • beclometasone dipropionate • budesonide • ciclesonide • fluticasone propionate • mometasone furoate Compound preparations containing a corticosteroid and a long-acting beta$_2$ agonist for inhalation • budesonide + formoterol fumarate • fluticasone propionate + salmeterol (as xinafoate)

Population(s)	Adults and children aged 12 years or over with asthma.
Standard comparators	For inhaled corticosteroids: • the agents will be compared with each other The compound preparations will be compared with each other and with: • inhaled corticosteroids and long-acting beta$_2$ agonists administered by separate inhalers • increased-dose inhaled corticosteroids alone • inhaled corticosteroids used in combination with oral bronchodilators
Outcomes	The outcome measures to be considered include: • objective measures of lung function (e.g. FEV_1, PEF) • symptoms (e.g. wheeze, shortness of breath) • incidence of acute exacerbations • use of systemic corticosteroids • adverse effects of treatment • health-related quality of life.
Economic analysis	Ideally, the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	The drugs will be appraised in the context of the guidelines from the British Thoracic Society and Scottish Intercollegiate Guidelines Network. That is, it is assumed that the drugs will be used in the stepwise approach recommended by these guidelines. Variation in dose-equivalence between different drugs and formulations will be taken into account as far as the evidence allows. If the evidence allows, subgroups for whom any drug or formulation may be particularly effective should be identified. The interventions will be appraised according to their licensed indications. Guidance will only be issued in accordance with the relevant marketing authorisations.

Related NICE recommendations	Related Technology Appraisals: National Institute for Clinical Excellence Guidance on the use of inhaler systems (devices) for the routine treatment of chronic asthma in older children (aged 5-15 years) Technology Appraisal Guidance No 38 London : NICE ; August 2000 Related Guidelines: None

Questions for consultation

Is it feasible and useful to compare the compound preparations with combinations of inhaled corticosteroids and *oral* bronchodilators or would it be sufficient to compare them with increased doses of corticosteroids and/or inhaled corticosteroids and long-acting beta$_2$ agonists given separately?

Would it be appropriate to make broader comparisons with other drugs such as cromones and leukotriene receptor antagonists?