ALVESCO® ▼

ciclesonide

For the treatment of persistent asthma
in adult patients aged 12 years and over

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

A Health Technology Appraisal for the
National Institute for Health and Clinical Excellence

ALTANA Pharma Limited

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1. EXECUTIVE SUMMARY

Concerted research and development efforts to improve asthma control have resulted in effective therapies with favourable safety and tolerability profiles for the maintenance treatment of asthma, and a wealth of published data has been consolidated in national and international treatment guidelines. The British Thoracic Society (BTS)/Scottish Intercollegiate Guidelines Network (SIGN) guideline for the management of asthma recommend that inhaled corticosteroids (ICS) should be used from Step 2 onwards; that is, mild persistent asthma. ICS represent the cornerstone of maintenance therapy for persistent asthma in patients of all ages and all severities. Correctly used, they can improve asthma symptoms and lung function, and reduce the need for rescue medication.

Issues surrounding current asthma therapy

Concordance with treatment plans is a significant factor in the management of asthma symptoms and subsequently has impact on the frequency and severity of induced acute exacerbations and the associated costs. However, lack of concordance in long-term conditions, such as asthma, is known to be common. This can occur for a number of reasons, including an unwillingness to take asthma medication due to issues such as side-effects, difficulty in using devices, lack of information or understanding and reduction in symptoms so that patients no longer believe that they require their regular medication.

Underuse of preventer therapy in the form of ICS remains one of the most serious concerns in asthma management. In addition to the burden posed by asthma on the lives of individual patients, inadequate asthma control is associated with high costs in terms of direct costs, such as hospital admissions and medication, and indirect costs, such as the effects of time off work and school and early death. According to the BTS, the estimated cost of corticosteroid medication in 2004 was in excess of £503 million. There is, therefore, a clear need for optimised ICS therapies to improve patients' asthma control in accordance with the treatment goals set out by the BTS/SIGN guideline.

Combination inhalers are increasingly being used at the early stages of asthma, although such treatment is not supported by the BTS/SIGN guideline for asthma management. Both inadequate asthma control and inappropriate use of asthma therapies have significant cost implications for healthcare providers in terms of hospital admissions, asthma exacerbations and high drug costs. There is a need for a more acceptable, well-tolerated ICS, to be used in accordance with the BTS/SIGN guideline before considering add-on therapy. If more appropriate single-agent inhaled corticosteroid agents were used at these stages there are savings to be made.

In clinical practice, the optimal use of ICS may be restricted by the incidence of local side-effects and concerns regarding systemic exposure. Therefore, there is a need for an additional, effective ICS with a more favourable safety and tolerability profile and a method of improving concordance.

Clinical effectiveness of ciclesonide

Ciclesonide (Alvesco®, ALTANA Pharma Ltd, UK) is a novel ICS preventer therapy characterised by prolonged anti-inflammatory activity and low oral bioavailability, which translate into a favourable clinical efficacy and safety profile compared with

other available ICS. Ciclesonide delivered by a chlorofluorocarbon (CFC)-free hydrofluoroalkane (HFA) metered-dose inhaler (MDI) is non-ozone-depleting, in accordance with the Montreal protocol, and is licensed for the treatment of persistent asthma in patients aged 12 years and over.

The recommended starting dose of ciclesonide is 160 mcg once daily, and most patients remain on this dosage as maintenance therapy. Evening dosing of ciclesonide is recommended, although the final decision on evening or morning dosing is at the discretion of the physician in consultation with the patient. Within the product licence, there is also the option to increase the dose if asthma control is not fully achieved in patients with severe asthma. Once control has been achieved, the dose should be individualised and titrated to the minimum dose (it can be halved) needed to maintain good asthma control.

A comprehensive clinical development programme in patients aged 12 years and over with persistent asthma has shown that the clinical efficacy of once-daily ciclesonide is comparable to equivalent doses of fluticasone propionate (FP; 1:1), budesonide (BUD; 1:2), and beclometasone dipropionate (BDP; 1:2) twice daily. However, the mechanism of action of ciclesonide confers a favourable systemic and local side-effect profile (for example, in clinical trials, the side-effect and tolerability profile of ciclesonide at daily doses of up to 640 mcg has been shown to be comparable to that of placebo). The convenience of once-daily administration of ciclesonide, together with the reduced burden of local adverse events and systemic exposure, may improve treatment concordance compared with other ICS.

Cost-effectiveness of ciclesonide

The acquisition cost of ciclesonide is similar to equivalent doses of FP (1:1), BDP (1:2) and BUD (1:2) in the UK. The majority of BDP and BUD products that are priced lower than ciclesonide use CFC propellants, which must be replaced by 2007. In addition, all ICS products priced lower than ciclesonide have more frequent dosing regimens, which are likely to compromise concordance and may well result in increased overall costs.

In terms of combination therapies, ciclesonide 160 mcg costs £8.40 per month, whereas comparable doses of fluticasone propionate and salmeterol (Seretide®, Allen & Hanburys Ltd, UK) 100/50 mcg costs £31.19 per month and budesonide and formoterol fumarate (Symbicort®, AstraZeneca, UK) 200/6 mcg costs £19 per month. The saving when using ciclesonide instead of a compound preparation would vary from £127–273 per patient per year. Inappropriate use of combination therapies in the management of Step 2 patients runs counter to the BTS/SIGN guideline and serves only to increase expenditure on patient management through the unnecessary use of additional medication.

Ciclesonide has a similar pattern of resource utilisation to other ICS and given that patient characteristics and preferences vary, and individual responses cannot be predicted, the once-daily dosing regimen and the reassuring adverse event profile provided by ciclesonide should be an attractive proposition for many patients and might secure improved concordance and symptom control.

In addition, the clinical development programme has produced evidence to suggest that in terms of impact on health-related quality of life (HRQoL), as measured by disease-specific and generic instruments, ciclesonide is at least equivalent to comparable doses of FP and BUD.

It is, therefore, reasonable to conclude that ciclesonide 160 mcg will secure comparable clinical benefits to FP 100 mcg twice daily, BUD 200 mcg twice daily and

BDP 200 mcg twice daily at a potentially lower overall cost to the UK NHS and Personal Social Services. The reassuring safety profile and once-daily dosing of ciclesonide may also result in improved concordance and symptom control, which would result in a potential reduction in the overall costs associated with patient management.

Treatment summary

- Treatment with ciclesonide 160 mcg once daily is consistent with the BTS/SIGN guideline that recommends maintenance therapy with ICS should be introduced from Step 2 (mild, persistent asthma) at the lowest possible dose, and that ICS therapy should be optimised before introducing other therapy, including add-on therapy.
- Once-daily ciclesonide is effective and well tolerated, and may therefore help to address some of the current issues surrounding suboptimal asthma control and management.
- The convenient one-puff, once-daily dosing, together with the reassuring local and systemic safety profile of ciclesonide, may help to improve patient concordance with therapy and thus their overall asthma control.
- Ciclesonide HFA MDI is CFC-free and thus fully compliant with the Montreal protocol.
- Combination inhalers are increasingly being used at the early stages of asthma, although such treatment is not supported by the BTS/SIGN guideline for asthma management. There is a need for a more acceptable, well-tolerated ICS, to be used in accordance with the BTS/SIGN guideline before considering add-on therapy. If more appropriate single-agent inhaled corticosteroid agents, such as ciclesonide, were used at these stages, there are savings to be made.
- It is reasonable to conclude that ciclesonide 160 mcg will secure comparable clinical benefits to FP 100 mcg twice daily, BUD 200 mcg twice daily and BDP 200 mcg twice daily at a potentially lower overall cost to the UK NHS and Personal Social Services.