Scottish Medicines Consortium

ciclesonide, 40-160 micrograms metered dose inhaler (Alvesco®)
Altana Pharma No. (249/06)

New indication: to control persistent asthma in adolescents (aged ³12 <18 years)

10 March 2006 *(Issued 5 May 2006)*

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a full submission

Ciclesonide (Alvesco®) is accepted for restricted use within NHS Scotland for treatment to control persistent asthma in adolescents (aged at least 12 years and <18 years)

It is restricted to asthma patients who require once-daily administration of an inhaled corticosteroid and whose treatment is at step 2 or step 3 of the British Guideline on the Management of Asthma. Alternative inhaled steroids are available at lower cost.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

ciclesonide, 40-160µg, inhaler (Alvesco®)

Indication

Treatment to control persistent asthma in adults and adolescents .This submission concerns use in adolescents (aged at least 12 years and <18 years).

Dosing information

For adults and adolescents, a starting dose of 160 micrograms daily is recommended. In patients with well-controlled asthma, a dose reduction to 80 micrograms once daily may be considered.

UK launch date

to be confirmed

Comparator medications

Inhaled corticosteroids (see table below)

Cost of relevant comparators

Drug	Dose	Cost per year (£)
Ciclesonide no-CFC 80 µg per dose	**80-160 µg once daily**	**£87-£102**
Budesonide (Pulmicort, aerosol) CFC	100-200 µg twice daily	£54-£76
Budesonide (Pulmicort, Turbohaler) Dry powder, 100 µg per dose	100-200 µg twice daily	£68-£135
Budesonide (Pulmicort, Turbohaler) Dry powder, 100 - 200 µg per dose	200 – 400 µg once daily	£68-£135
Beclometasone dipropionate (Becotide aerosol) CFC 100 µg per dose	200 µg twice daily	£20
Beclometasone dipropionate (generic aerosol) CFC 100 µg per dose	200 µg twice daily	£60
Fluticasone propionate (Flixotide evohaler) non-CFC 50 µg per dose	50-100µg twice daily+	£33-£66
Fluticasone propionate (Flixotide evohaler) non-CFC 250 µg per dose	250 µg twice daily++	£219

Dose ranges incorporate the starting doses of inhaled steroids and doses for well controlled adult/adolescent patients and are taken from the *British National Formulary September 2005*. Prices taken from eVadis database, NHS National Services Scotland (11/01/06)

+Dose for patients aged up to 16 years
++ Upper range of starting dose for adults and adolescents aged 16-18 years

Summary of evidence on comparative efficacy

Comparative data in adolescents aged >12 and <18 years come from sub-group analyses in trials which recruited adolescents and adults. For improvement in actual FEV_1 these showed comparable efficacy between ciclesonide 320 micrograms once daily and budesonide 400 micrograms daily (the latter given in two doses for the first four weeks and then as a single dose), n=56 and 26 respectively, and between ciclesonide 80 and 160 micrograms once daily and fluticasone propionate 100 micrograms twice daily with 40, 35 and 32 patients in each group respectively.

There were improvements in FEV_1 in adults and adolescents receiving ciclesonide in a one-year open label extension study completed by 33 patients aged 12-17 years.

Other data were also assessed but remain commercially confidential.*

Summary of evidence on comparative safety

The most common treatment-related adverse events among 676 adolescents were hoarseness and oral candidiasis (one event each). Data from placebo- and active-control trials for up to one year in 18 patients indicate a lack of effect of ciclesonide on hypothalamic-pituitary-adrenal axis function.

Summary of clinical effectiveness issues

There were no clinical effectiveness issues.

Summary of comparative health economic evidence

The manufacturer presented a simple cost-minimisation analysis, assuming equal outcomes for ciclesonide 160µg daily doses compared to equivalent doses for other frequently prescribed inhaled corticosteroid products in children aged 12-17: fluticasone propionate (FP), budesonide (BUD), and beclometasone dipropionate (BDP). The assumption of equal outcomes was based on the clinical trial evidence of non-inferiority versus the comparator products. However, a weakness of this evidence base was the trial programme did not include any evidence against BDP. Hence an assumption was made that BDP has equal outcomes with ciclesonide on the grounds that FP and BDP appear equally effective (based on the BNF). Comparison of the annual direct acquisition costs for ciclesonide and the most frequently used comparator inhaled corticosteroid products demonstrated that ciclesonide 160µg dose was less costly than the BUD 400µg per day products, similar cost to the most frequently prescribed FP 200µg per day product, but more expensive than all but one of the comparator BDP 400µg per day products.

Although ciclesonide appears more expensive than many comparator products, it has the potential advantage of once daily dosing whereas other inhaled corticosteroid products are taken twice daily. In addition, the manufacturer claims that as about 30% of BDP products contain CFC there will be a cost to primary care associated with transition to CFC free within the next 18 months, in terms of additional patient review and monitoring, which will reduce the direct cost advantage of BDP. However, the manufacturer did not quantify the impact of CFC transition costs on the cost comparisons. Also, there may be additional monitoring and review

costs associated with switching patients from CFC containing products to ciclesonide – these costs have not been covered by the economic assessment. Hence, the economic case submitted does not support ciclesonide as a cost-effective inhaled corticosteroid product for children aged 12-17.

Patient and public involvement

Patient Interest Group Submission: Asthma UK Scotland

Budget impact

Other data were also assessed but remain commercially confidential.*

Guidelines and protocols

The British Guideline on the Management of Asthma, revised in April 2004, was produced by the British Thoracic Society and the Scottish Intercollegiate Guidelines Network (SIGN). For adults and schoolchildren, Step 2 of the stepwise management of asthma recommends the use of a regular inhaled steroid when there has been an exacerbation of asthma in the last two years, or when the ß2 agonist is used more than twice weekly or when the patient is symptomatic more than twice a week or waking one night a week. The steroids recommended are beclometasone dipropionate, budesonide, fluticasone propionate and cautiously, mometasone furoate. The guideline predates the availability of ciclesonide. Options at step 3 include adding a long-acting ß2 receptor agonist and increasing the dose of inhaled steroid, at step 4 increasing the dose of inhaled steroid further, and at step 5 using an oral steroid.

Additional information

Following a full submission, ciclesonide (Alvesco®) was accepted for restricted use within NHS Scotland for the prophylactic treatment of persistent asthma in adults (18 years and older). Ciclesonide is restricted to asthma patients who require once a day administration and whose treatment is at step 2 or step 3 of the British Guideline on the Management of Asthma. Alternative inhaled steroids are available at lower costs.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

This assessment is based on data submitted by the applicant company up to and including 11 April 2006.

** Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:* http://www.scottishmedicines.org.uk/

Drug prices are those available at the time the papers were issued to SMC for consideration.

The under noted reference was supplied with the submission.

Agertoft L and Pederson S. Short-term lower-leg growth rate and urine cortisol excretion in children treated with ciclesonide. J Allergy Clin Immunol 2005;115:940-5.