ALVESCO® ▼
ciclesonide

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

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

Response to the assessment report produced by the Peninsula Technology Assessment group and Southampton Health Technology Assessments Centre

ALTANA Pharma – a Nycomed company

28 February 2007
Having had the opportunity to review the assessment report, *ICS and LABAs for the treatment of chronic asthma in adults and children aged 12 years and over: Systematic review and economic analysis*, carried out on behalf of NICE, we would like to draw the Appraisal Committee’s attention to the following points regarding Alvesco® (ciclesonide, ALTANA Pharma – a Nycomed company).

**Size of evidence base for ciclesonide**

In the assessment report, the reviewers expressed concerns regarding the size of the evidence base for newer inhaled corticosteroids (ICSs), including ciclesonide, compared with that for older compounds.

The active controlled studies showed that ciclesonide administered once daily was comparable to equivalent doses of fluticasone propionate (FP; 1:1), budesonide (BUD; 1:2) and beclometasone dipropionate (BDP; 1:2) given twice daily, for improving lung function, reducing the incidence of asthma symptoms and reducing the use of rescue medication in patients with mild-to-severe, persistent asthma.4–16 In addition, ciclesonide was shown to reduce the need for oral steroids in patients with severe steroid-dependent asthma and to be as effective as short courses of oral steroids during induced acute asthma exacerbations.17

**Comparative studies of ciclesonide versus FP, BUD and BDP**

Another concern expressed by the reviewers was the comparability between the ciclesonide and comparator doses used in the active controlled studies. We would respectfully draw your attention to section 5.2 of our original application, which summarises the results of 22 randomised, controlled studies comparing ciclesonide with FP, BUD and BDP, showing a consistent comparability of 1:1 between ciclesonide and FP, 1:2 between ciclesonide and BUD, and 1:2 between ciclesonide and BDP.

**Ciclesonide versus FP**

A safety study (Bernstein et al)25 showed that treatment of patients with moderate-to-severe asthma with ciclesonide 160 µg twice daily
or 320 µg twice daily resulted in an incidence of oropharyngeal side-effects similar to placebo and less than FP 440 µg twice daily.

**Ciclesonide versus BUD**

Ciclesonide versus BDP

In study by Adachi et al., a daily ciclesonide dose of 640 µg was found to be superior to BDP 800 µg in maintaining morning peak expiratory flow (PEF) and reducing use of rescue medication and asthma scores. In the same study, Ciclesonide 320 µg daily was as effective as BDP 800 µg.

Please note that the 80 µg, 160 µg, 320 µg, 640 µg and 1,280 µg doses of ciclesonide are ex-actuator doses delivered from the mouthpiece of the pressurised MDI (pMDI) device, in accordance with the European Union (EU) directives for inhaled formulations. These are equivalent to metered doses of 100 µg, 200 µg, 400 µg, 800 µg and 1,600 µg respectively.

**Safety and tolerability of ciclesonide**

Ciclesonide high-dose licence extension

The recommended dose of ciclesonide is 160 µg once daily, which leads to asthma control in the majority of patients. However, in light of the very favourable safety and tolerability data for ciclesonide outlined above, the European Medicines Agency (EMEA) has recently granted a licence extension for ciclesonide in the EU, under which daily doses of up to 640 µg can be administered for up to 12 weeks in patients who need increased anti-inflammatory treatment.
Once-daily administration of ciclesonide

We were surprised to note that the review did not discuss the matter of once-daily versus twice-daily administration of ICSs, since it has been shown that the complexity of a chronic treatment regimen may have a negative impact on patient adherence. Indeed, a retrospective case control study showed significant improvements in treatment compliance in a population of 222 adult asthma patients following a switch from a twice-daily ICS to a once-daily ICS. A comprehensive programme of randomised, controlled studies has demonstrated the clinical efficacy of ciclesonide administered once daily, and the current UK product licence for ciclesonide is based on this regimen. Once-daily administration of ciclesonide, either in the morning or in the evening, is likely to be more convenient for the patient than twice daily administration. This may help to improve treatment compliance – and thus overall asthma control – compared with twice-daily regimens.

Cost-effectiveness

In the assessment report, the reviewers estimated the mean annual cost per patient at £87. This, however, was based on the pack price of ciclesonide 80 µg (£0.238 per puff) as opposed to the pack price of ciclesonide 160 µg (£0.28 per puff), which results in a range of mean annual costs between £87 and £102, dependent on the dose used, as shown in the appendix to this response document.

The reviewers noted that the low cost of ciclesonide was strongly dependent on the simplistic, assumed dose-equivalence ratio of 1:2 between ciclesonide and BDP. This issue has been discussed above, along with further reference to the clinical evidence on which the justification for a cost-minimisation analysis was based. Furthermore, the reviewers’ finding that the safety profile across ICSs was essentially similar fails to appreciate the likelihood that the evidence for effectiveness of medication in everyday clinical practice may be compromised relative to findings from clinical trials.

In section 6.4.1, the reviewers highlight the nature of the research questions relating to the cost-effectiveness assessment. The ciclesonide cost-minimisation analysis clearly helps us to answer the first of these questions: ‘At low doses (200–800 µg BDP per day or equivalent), which is the most cost-effective of the five ICSs? (Step 2 of the guidelines)’ The rationale for including the cost comparison between ciclesonide and combination therapy was to highlight the cost differential of potentially inappropriate management of patients at Step 2.

References


24. 


## Appendix. Costs of inhaled corticosteroid therapies for asthma in the UK

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Generic name</th>
<th>Device name</th>
<th>Pack size</th>
<th>Price/puff</th>
<th>Daily treatment cost</th>
<th>Cost/365 days</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symbicort Budesonide/Formoterol</strong></td>
<td>Turbohaler</td>
<td>400 MIMS Dec 2006</td>
<td>120</td>
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<td>0.0414</td>
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<td>7.77</td>
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<td><strong>Becotide Beclometasone Inhaler</strong></td>
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<td>0.0463</td>
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</table>

### Notes
- **Actuation [µg]**: The amount of medication delivered per actuation.
- **Pack size** and **Price/puff** refer to the specific product and price per puff/treatment.
- **Daily treatment cost** and **Cost/365 days** are calculated based on the provided prices and pack sizes.
- **Equivalent dose** for Alvesco 160 µg is based on the table for Ciclesonide 160 µg daily.

### Additional Information
- **Brand name** and **Generic name** indicate the commercial and generic names of the medications.
- **Device name** includes the device used for delivering the medication.
- **Reference** indicates the source of the price data, such as MIMS or Drug Tariff.

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*This table summarizes the costs of inhaled corticosteroids for asthma in the UK, listing brand names, generic names, device names, pack sizes, prices per puff, and daily treatment costs. The data is sourced from various references, including MIMS and Drug Tariff.*