Pipeline Insight: Asthma/COPD/Allergic Rhinitis

As patents expire, novel combinations inspire

Coverage: US, UK, France, Germany, Italy, Spain, Pacific Rim
R3A; R3B; R3C; R3D; R3E; R3F; R3G; R3J; R3X
R1A1; R1A6; R1A7; R1B0; R6A0

Reference Code: DMHC2068

Publication Date: 4/2005
Executive Summary

- R1B0: systemic nasal preparations;
- R1A7: nasal decongestants;
- R6A: systemic antihistamines;
- R3A: beta-2 stimulants;
- R3B: xanthines;
- R3C: non-steroidal respiratory anti-inflammatories;
- R3D: inhaled corticosteroids;
- R3E: combinations of beta-2 stimulants with R3C;
- R3F: combinations of beta-2 stimulants with inhaled corticosteroids;
- R3G: antimuscarinics-plain and combinations with beta-2 stimulants;
- R3J: anti-leukotrienes;
- R3X: all other anti-asthma and COPD products.

This report focuses on those drug classes with the largest global sales according to the IMS MIDAS sales database (corticosteroids, beta-2 agonists, combinations of beta-2 agonists and corticosteroids, leukotriene modifiers, antimuscarinics and antihistamines). Within each class, the leading brands by value will be analyzed in greater depth. Throughout this report, the term “global market” is defined as the seven major pharmaceutical markets, comprising the US, Pacific Rim, France, Germany, Italy, Spain and the UK.
shows strong efficacy in both asthma and COPD and confirmed safety at high doses. This follows the publication of a Phase IIa study in November 2003, in which 210 patients with mild to moderate asthma received five single-dose treatments, with a five to 14 day washout in between. During each of these treatments, with five groups of 42 patients receiving 50µg, 100µg, 200µg, 400µg, or placebo, patients underwent 24-hour serial lung function measurements. All four doses showed significantly higher FEV1 changes from baseline when compared to placebo at one hour, with the 200µg and 400µg doses showing significant response as early as five minutes. For comparison, the onset of action of formoterol is around four minutes and for salmeterol 30 minutes (Palmqvist et al., 1997). The four doses demonstrated higher clinical response at 24 hours and beyond, with the higher doses having the greatest effect.

Initially, QAB-149 is being developed as monotherapy, with Phase III asthma and COPD studies planned to start in mid 2005, followed by regulatory submissions in 2007. According to Novartis, several options for combination products are being evaluated in parallel, which may include a QAB-149/mometasone combination product. Novartis does not have any internal inhaled corticosteroid assets, hence will need to align with a company that has a once-daily corticosteroid, the obvious choice being Schering-Plough. The future clinical development plan for QAB-149 may be confirmed at Novartis’s next pipeline update on September 20, 2005 in London, UK.

Source: Datamonitor
was similar across all groups and only one case of hoarseness (0.1%) was reported in the ciclesonide treatment group.

### Figure 10: Advantages and disadvantages of Altana’s Alvesco

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<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
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<tr>
<td>- Low incidence of local oropharyngeal side effects (thrush, hoarseness and sore throat).</td>
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<td>- Minimal propensity to suppress cortisol.</td>
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<td>- Once-daily dosing.</td>
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<td>With only the 160µg dose approved in the EU, Altana will have a number of difficulties in marketing the drug</td>
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<td>- Maximum approved dose is too low to demonstrate its safety benefit over the competition.</td>
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<td>- Lack of flexibility - physicians will be highly reluctant to initiate therapy with Alvesco, without the full range of dosage strengths offered by competitors.</td>
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<td>- Increasing use of combination therapy mean physicians may be reluctant to prescribe an ICS that is not available as a combination therapy.</td>
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Source: Datamonitor

### Ciclesonide versus budesonide (COMPASS study)

A 12-week study showed greater improvements in FEV1 and FVC with the use of once-daily ciclesonide 320µg when compared to budesonide 400µg. Ciclesonide showed earlier onset of treatment benefits than budesonide, greater improvements in FEV1, and no changes in urinary cortisol levels (Ukena et al., 2003). There was a significant increase in FEV1 (p<0.0185) and FVC (p=0.0335) in the ciclesonide group compared with budesonide-treated patients. The improvement in asthma symptoms and the use of rescue medication were similar in both groups. There were no significant changes from baseline in urine cortisol in both groups.

A second trial randomized 359 patients to either ciclesonide 80µg or 320µg once daily or budesonide 200µg twice daily for 12 weeks (Hansel et al., 2003). FEV1 and FVC increased significantly (p < 0.0001) in all treatment groups and asthma symptoms and use of bronchodilator rescue medication decreased significantly in all patients (p < 0.0001). There were no changes in 24-hour urinary cortisol excretion at 12 weeks.
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About the Respiratory & Infectious Diseases analysis team

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