Reviewer's report

**Title:** Long-Term Safety of Mometasone Furoate Administered via a Dry Powder Inhaler in Children: Results of an Open-Label Study Comparing Mometasone Furoate With Beclomethasone Dipropionate in Children With Persistent Asthma

**Version:** 1  **Date:** 10 February 2009

**Reviewer:** Eric Bateman

**Reviewer's report:**

This paper describes the safety of two high doses of mometasone furoate in children aged four to eleven years with persistent asthma. It is an open-label study comparing 200µg given either as a morning or as a split, twice daily dose compared with BDP 168µg twice daily delivered via a CFC propelled pMDI. The primary safety criteria were incidence rates and severity of AEs between groups but clinical asthma exacerbations, SAEs, morning plasma cortisol and 12 hour urinary cortisol were also assessed. A total of 233 patients were enrolled and followed for one year. Their mean duration of asthma was five years and a significant proportion were aged four or five years. The study was not powered to examine efficacy endpoints.

The rates of AEs were similar between treatment groups indicating that mometasone at twice the currently registered dose appears to be as safe as BDP in the dose administered, and whether delivered as a once daily or split dose.

The frequency of candidiasis was similar between groups but there might have been a slight excess of headaches in the mometasone 200µg morning dose group. Treatment discontinuation was similar between groups as was time to worsening of asthma, mean 8am plasma cortisol levels and 12 hourly urinary cortisol adjusted for creatinine.

The authors therefore conclude that the safety profile for MF-DPI at doses twice as high of those approved for children is satisfactory and not significantly different to that of BDP at the dose given.

**Major comments**

The study has several weaknesses.

1. It is an open study and therefore subject to bias, particularly in respect of patient-reported outcomes like adverse events.

2. The fact that it is a one year study is satisfactory as a test of the consequences of prolonged use of inhaled steroids in these children, but suffers the weakness that compliance may have fallen off during the study period. No mention is made about compliance. Was any attempt made to ensure this?

3. A third minor weakness is the fact that the comparator is the CFC-pMDI which is no longer in production. However, since this has been a reference standard for most early work with current inhaled corticosteroids, the comparison remains
valid both from the perspective of adverse events and time to first exacerbation.

4. There were significantly more children in the ages four to five years category in the BDP group. Might this have impacted the result? Was there any difference in reported AEs between the younger and older age categories specified in the demographics table?

Minor comments
The x-axis in Figure 2 stops at 180 days. Why were observations not continued to one year, or is the axis labelled incorrectly?

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

EDB has received payments for membership of advisory boards and/or lectures delivered at meetings sponsored by AstraZeneca, Boehinger Ingelheim, Glaxo SmithKline, Nycomed, Pfizer and Merck.