

# **NOVOLIZER<sup>®</sup> BUDESONIDE**

*Corticosteroids for the treatment of chronic asthma in children  
under the age of 12 years*

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

**28 February 2007**

**Meda Pharmaceuticals Ltd**



Having had the opportunity to review the assessment report, *Inhaled corticosteroids and long-acting beta<sub>2</sub>-agonists for the treatment of chronic asthma in adults and children under the age of 12 years: 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 Novolizer<sup>®</sup> Budesonide (Meda Pharmaceuticals Ltd, UK).

### **Choice of inhaler device**

The current assessment report concludes that there is no clinical difference, and very little cost difference, between the various inhaled corticosteroids (ICSs). However, it does not discuss the clinically important effects of correct use of inhaler devices; these should be considered by the report if it is to be of real use to the practising clinician and could be incorporated into Table 2 on page 19.

While we would argue with some of the cost outcomes presented in the report, we believe that simple, correct and auditable device use is the single most important discriminator between the ICSs in the absence of any efficacy differences at appropriate comparative doses. The studies currently cited will only include patients with good inhaler technique and are therefore likely to produce optimum efficacy. Poor inhaler technique is universally accepted to be associated with less than optimum efficacy, irrespective of the steroid used. On page 17, it is accepted that the choice of inhaler device is 'potentially important in the decision as to which ICS might be best suited to an individual'. This is a significant underestimate of the importance of device technique. The assessors then dismiss device technique on the grounds that 'the comparison of inhaler devices is beyond the scope of this appraisal'. However, the Novolizer is only slightly more expensive than the cheapest chlorofluorocarbon (CFC)-propelled beclometasone dipropionate (BDP) product (see Figure 10; page 166), so it ought to be stated that the advantages of such an advanced inhaler could outweigh the small additional cost over BDP and that all factors including inhaler technique, individual preference and so on should be taken into account.

Indeed, section 3.4.1.2 (page 17) clearly states that 'correct use of an inhaler is essential'. The Novolizer has a trigger mechanism that ensures that the dry powder is

not released until sufficient inhalation is generated to provide a good lung deposition. The low internal resistance of the Novolizer device makes it easier to generate this modest triggering flow, ensuring that the inhaler is used correctly. In addition, and uniquely among inhalers in current use, the Novolizer then visually confirms that the dose has been taken at the necessary inspiratory flow. This absolute confirmation of dosing can then be checked by the patient, the patient's carer/parent and the clinician.

The clinical benefits of the Novolizer device are summarised below.

### **Benefits of the Novolizer device**

Currently available inhaler devices do not fulfil the characteristics sought in an ideal inhaler. The Novolizer device has the following benefits to patients and should improve compliance.

- The Novolizer has low intrinsic airflow resistance; therefore, the elderly, children and patients with severe lung disease will be able to activate the device.
- There are multiple feedback mechanisms confirming correct dosing (visual, acoustic and taste).
- The Novolizer has one of the highest lung deposition values obtained for dry-powder inhalers (DPIs). Correct inhaler technique and good lung deposition ensure consistent maximum efficacy of an inhaled steroid.
- In randomised, controlled trials, the Novolizer has demonstrated therapeutic equivalence to established treatments for asthma.

### **No deep inhalation required**

Page 17 of the assessment report states:

*Dry powder inhalers (DPIs) require less co-ordination by an individual in order to achieve correct inhaler technique. However, lung deposition is flow-dependent requiring a forceful, deep inhalation to correctly trigger the device.*

This is not correct – a deep inhalation is not required for more advanced devices such as the Novolizer. The Novolizer can be triggered by a breath of 35 l/min and indeed has been used successfully in children as young as five years.

### **Pulmonary bioavailability**

Table 2 on page 19 should state that the pulmonary bioavailability of the Novolizer device is at least 22% of the nominal dose and can be higher depending on the depth of inhalation.

### **Once-daily administration in children**

Table 30 (page 157) is not correct. In children, 200 µg budesonide daily can be achieved with one daily dose via the Novolizer. The *British National Formulary* (BNF) does state that 200 µg should be given as 100 µg twice daily, but this is not correct for Novolizer Budesonide. Please refer to the Summary of Product Characteristics for Novolizer Budesonide (see Appendix of our submission) or the *Monthly Index of Medical Specialities* (MIMS).

Once-daily administration in children is proven to be effective compared with placebo in a study of over 1700 children<sup>1</sup> and has also been shown to be as effective as a twice-daily regimen.<sup>2</sup> Once-daily inhalation of steroids improves compliance and also has the potential to reduce healthcare costs.<sup>2-4</sup>

### **Response to the cost comparison analysis (section 6.11)**

In Figure 7 (page 162), it is claimed that the cheapest budesonide product is Pulmicort LS 50 µg at £53.50 per year. However, the cost of Novolizer 200 µg is £40.27 per year – 25% less.

This is derived from:

|                    |           |  |
|--------------------|-----------|--|
| Novolizer complete | 100 doses | £14.86                                   |
| Novolizer refill   | 265 doses | £25.41 (refill cost £9.59 per 100 doses) |
| Total              |           | £40.27                                   |

As the device is licensed for up to 20 refills, subsequent years will cost £35.00. This is 35% less than the cost of Pulmicort LS.

In Figure 8 (page 163), it is claimed that the cheapest and most expensive non-CFC-propelled budesonide product is the Pulmicort Turbohaler 100 µg at £67.50 per year. The Novolizer, at £40.27 per year (see above), costs 40% less.

As the Novolizer device is licensed for up to 20 refills, subsequent years will cost £35.00. This is 48% less than the cost of Pulmicort Turbohaler.

Novolizer should be included in the cost comparison for low-dose corticosteroids (Figures 7 and 8; pages 162–163). This will reduce the annual mean cost and budesonide (BUD) will no longer be the most expensive option.

Furthermore, the FP costs in Figures 7 and 8 appear to be incorrect. They are based on Flixotide™ Disk Refill 50 µg being equivalent to 200 µg BDP via CFC, whereas in fact Flixotide™ Disk Refill 100 µg is equivalent to 200 µg BDP via CFC. The true cost of fluticasone propionate (FP) is therefore greater than that shown in Figures 7 and 8.

### **Economic analysis**

In the Conclusion section (page 204), the assessment report states:

*The use of weighted averages to represent the cost associated with each ICS tends to conceal the wide variations in costs between the individual preparations of each drug, and the wide overlap in costs between the drugs.*

Therefore, the least expensive products in each category should be mentioned. If not, it would be useful to point the reader to the detail on the least expensive individual drugs, which can be found in section 6.11.1, beginning on page 160. In particular, the Novolizer, with its advanced inhaler technology, is only slightly more expensive than the cheapest CFC-propelled BDP product.

In Figure 10 (page 166), it should be noted that some of the cost differences between the least expensive products in the BDP, BUD and FP categories are minimal. Therefore, it is essential to consider patient preference, inhaler technique, lung deposition and so on when choosing between them. The Novolizer is less expensive than most BDP and FP products and offers the benefits of an advanced inhaler.

## **Conclusion**

In a therapeutic area where this report clearly demonstrates little difference in the efficacy of the products compared, the practical ability of the patient to use the inhaler – and that of the patient/carer/clinician to check it has been used correctly – remains the key discriminator between the products. It has long been clinically accepted that breath-actuated inhaler systems are better for patients but in the past, this usually came at a significant cost. The Novolizer is less expensive than most BDP and FP products and offers more clinically important patient benefits than any other current breath-actuated inhaler.

## **References**

1. Pauwels RA, Pedersen S, Busse WW *et al.* Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet* 2003; **361**: 1071–1076.
2. Masoli M, Weatherall M, Holt S, Beasley R. Budesonide once versus twice-daily administration: meta-analysis. *Respirology* 2004; **9**: 528–534.
3. Guest JF, Davie AM, Ruiz FJ, Greener MJ. Switching asthma patients to a once-daily inhaled steroid improves compliance and reduces healthcare costs. *Prim Care Respir J* 2005; **14**: 88–98.
4. D'Urzo A, Karpel JP, Busse WW *et al.* Efficacy and safety of mometasone furoate administered once-daily in the evening in patients with persistent asthma dependent on inhaled corticosteroids. *Curr Med Res Opin* 2005; **21**: 1281–1289.