CLENIL® MODULITE®▼

Beclometasone dipropionate (BDP)

Prophylactic management of mild, moderate or severe asthma in adults

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

A Health Technology Appraisal for the
National Institute for Health and Clinical Excellence

26 July 2006

Trinity-Chiesi Pharmaceuticals Ltd

1. EXECUTIVE SUMMARY

- Asthma is a common and potentially fatal condition, with a complex aetiology. Inhaled corticosteroids (ICSs) are a cornerstone of asthma management, as the first-choice preventer treatment at Step 2 of the current British Thoracic Society (BTS)/Scottish Intercollegiate Guidelines Network (SIGN) guideline.

- Beclometasone dipropionate (BDP) has been in clinical use for longer than any other ICS, and is the most widely prescribed ICS in the UK. This agent combines excellent efficacy with a highly favourable safety profile at licensed doses.

- Pressurised metered-dose inhalers (pMDIs) are the main inhaler devices used for asthma therapy, with equivalent effectiveness to alternative inhaler devices. However, standard pMDIs contain chlorofluorocarbons (CFCs) and must eventually be withdrawn in line with the Montreal Protocol.

- A seamless transition from CFC-containing ICS pMDIs to non-CFC-containing ICS inhalers depends on the criteria laid down in the UK transition strategy document and the availability of directly equivalent non-CFC-containing pMDI formulations of the ICS molecule that the patient is accustomed to.

- Clenil® Modulite® is the first non-CFC-containing pMDI formulation of BDP that is directly equivalent to existing CFC-containing BDP pMDIs. By enabling a seamless transition from CFC-containing to non-CFC-containing BDP inhalers, Clenil® Modulite® is likely to minimise both NHS staff time and disruption for
  the patient.

- Phase III clinical trials have demonstrated that Clenil® Modulite® is directly equivalent to a standard CFC-containing BDP pMDI (Becotide®) in the management of both mild and mild-to-moderate persistent asthma in adults.

- Clenil® Modulite® is a cost-effective option when compared with Qvar®, which is currently the only other non-CFC-containing BDP pMDI available in the UK.

- The economic benefits of Clenil® Modulite® over Qvar® include both direct drug cost savings (£370 per 1,000 patients) and reduced resource costs for nurse consultations for therapeutic reviews (£15,000 per 1,000 patients). This would mean a cost saving of around £129,000 per annum for a 300,000-population primary care organisation (PCO).
- Clenil® Modulite® offers a simple and cost-effective alternative to dry powder inhalers (DPIs) and the only non-equivalent CFC-free BDP pMDI in the transition period from CFC-containing to CFC-free BDP inhaler devices.

PULVINAL®

Beclometasone Dipropionate (BDP)

A multidose dry powder inhaler (DPI) device for the management of asthma

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

A Health Technology Appraisal for the
National Institute for Health and Clinical Excellence

26 July 2006

Trinity-Chiesi Pharmaceuticals Ltd

2. EXECUTIVE SUMMARY

This submission has been prepared to assist the National Institute for Health and Clinical Excellence (NICE) Health Technology Appraisal of the clinical and cost-effectiveness of corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and over.

This dossier presents evidence of the clinical efficacy and cost-effectiveness of Pulvinal® Beclometasone Dipropionate (BDP).

The Pulvinal device is a dry powder inhalation (DPI) device for delivery of either BDP or salbutamol (SAL) and is licensed in patients aged six years and above.

Pulvinal BDP fills an important niche in the management of asthma. The first asthma inhaler systems, pressurised metered-dose inhalers (pMDIs), are associated with a number of drawbacks.

A significant proportion of adults and children with asthma cannot use pMDIs correctly or find them unacceptable. In a large UK study 51% of patients had problems co-ordinating dose release with inspiration, and in 36% the release of aerosol into the mouth caused a halt in inspiration or an inspiration through the nose instead of the mouth despite having been instructed in correct inhaler technique. A US study found that only 15% of patients used their inhaler as often as prescribed; a further 14% actuated their inhaler more than 100 times in a three-hour interval before clinical appointments to appear to be adhering. For most non-concordant patients, Pulvinal BDP is a very practical alternative because there is no need to co-ordinate inspiration and actuation, and unpleasant effects such as cold spray in the throat and nose are avoided.

To aid both patients and doctors, Pulvinal has a transparent medication storage chamber. Patients can easily tell when the medication is running low, which helps to avoid premature disposal of the inhaler, with potential cost benefits. Patients can also be confident that they have sufficient doses available for their immediate needs.

Pulvinal is a high-resistance inhalation device that offers a consistent rate of lung deposition of drug over a wide range of inspiratory effort, even in severe asthma or obstructive disease. Even at low inspiratory flow rates, medication delivered by the

Pulvinal device penetrates the lung and achieves high levels of deposition in the lower airways. Patients who are able to generate only a slow peak flow rate still achieve good deposition and bronchodilation.

The clinical programme discussed in this submission demonstrates that the Pulvinal device delivers corticosteroid to the lungs at least as effectively as pMDIs and with at least as much clinical efficacy as other DPIs (including Turbohaler® and Diskhaler®, of which the latter will only be available up until the end of September 2006). The 2005 guideline from the British Thoracic

Society (BTS) and the Scottish Intercollegiate Guidelines Network (SIGN) specifically recognises Pulvinal BDP as an effective treatment for asthma in adults and children aged 12 years and over.

Comparison of direct acquisition costs alone show that the use of Pulvinal in place of other DPIs could save between £15 and £200 per year (depending on the type of device). In addition to its clinical benefits, Pulvinal BDP is one of the smallest DPI inhalers on the market and is one of the least costly. Considering the clinical efficacy, ease of use, patient preference and cost, Pulvinal BDP is a very cost-effective dry powder formulation of BDP.

2.1 Advantages of Pulvinal

- DPIs are not equivalent. Low-resistance devices are associated with erratic rates of lung deposition of drug, which (in these devices) is excessively dependent on inhalation rate. Pulvinal is a high-resistance device that has been shown to offer a consistent rate of lung deposition of drug, even at low inspiratory flow rates.
- Even in severe asthma and/or major obstructive disease, the vast majority of adults and children can achieve inspiratory flow rates more than adequate for good lung deposition and clinical efficacy through the Pulvinal device.
- Asthma patients (especially younger patients) are often confused by the different devices (pMDIs or DPIs) used to deliver different drugs. The Pulvinal device is used to deliver either of the two most commonly used

generic asthma medications: the corticosteroid BDP (in a brown device), and the bronchodilator salbutamol (in a blue device).

- Pulvinal is a multidose device, containing 100 doses: enough medication for up to 50 days of therapy. Some other DPIs are single-use and/or require frequent reloading of medication.
- Pulvinal is one of the smallest multidose DPI devices available and has proven ease of use, which encourages concordance, particularly in younger patients.
- Pulvinal has a transparent chamber, so patients can easily tell when the medication is running low. This aids patient confidence and avoids premature disposal.
- Pulvinal contains a carrier molecule, lactose monohydrate, which enhances the respirable fraction of the dose.
- The taste of lactose reassures patients that a successful inhalation has occurred.
- The cover of Pulvinal affords a watertight seal, which is especially relevant with active patients.
- Pulvinal is one of the lowest cost multidose DPIs on the UK market. Increased compliance and clinical efficacy will further reduce the indirect costs of Pulvinal to the NHS.
- Clinical trial evidence in adults and children aged 12 years and over has shown Pulvinal BDP to be equally as effective and well tolerated as other beclometasone DPIs currently available.
- Comparison of direct acquisition costs alone show that the use of Pulvinal BDP in place of other DPIs could save between £15 and £200 per year (depending on the type of device).
- The incidence and prevalence of asthma are increasing in the UK and will continue to increase and heighten the burden on the NHS unless doctors make use of new technologies and treatment approaches such as Pulvinal, which offer clinical benefits alongside cost-effectiveness benefits.

- The 2005 BTS/SIGN guideline specifically acknowledges that Pulvinal BDP is an effective treatment for asthma in adults and children aged 12 years and over.
- It is essential that patients be stabilised on non-chlorofluorocarbon (CFC)-containing inhalers (either pMDIs or DPIs) as soon as possible to ensure that clinically and economically serious consequences of CFC shortages are avoided. Pulvinal BDP is CFC-free.
- BDP is the most cost-effective steroid for asthma. For those patients who have difficulty or cannot use pMDIs, Pulvinal BDP is the most favourable treatment alternative.