NEW PRODUCT EVALUATION

BECLOMETASONE CFC-free

(Clenil Modulite®)[τ]

Summary

- **Chlorofluorocarbon compounds (CFCs) damage the ozone layer in the atmosphere and are being phased out of use. Hydrofluoroalkanes (HFAs) are now being used as propellant gases in most metered dose inhalers. These are known as CFC-free inhalers.**
- **There have been particular difficulties developing CFC-free beclometasone inhalers as the drug dissolves in the new propellant, in contrast to the suspension of drug in the CFC-containing products currently available.**
- **Clenil Modulite® is the second CFC-free beclometasone inhaler to become available. It provides aerosol particles of a similar size to existing CFC-containing beclometasone inhalers and can be substituted on a 1-for-1 dose basis for CFC-containing beclometasone inhaler treatment. This has been achieved by adding glycerol to the formulation.**
- **The existing CFC-free beclometasone product Qvar® delivers finer aerosol particles and the dose given needs to be halved when switching from CFC-containing beclometasone. The two CFC-free beclometasone brands, Qvar® and Clenil Modulite®, are not therefore equivalent in dose. The MHRA has written to prescribers and pharmacists indicating that brand name prescribing is essential for CFC-free beclometasone inhalers.**
- **Both Qvar® and Clenil Modulite® are currently licenced only for asthma, not for COPD. Clenil Modulite® may be used in children of any age, Qvar® is not licenced at present for children aged 12 or under.**

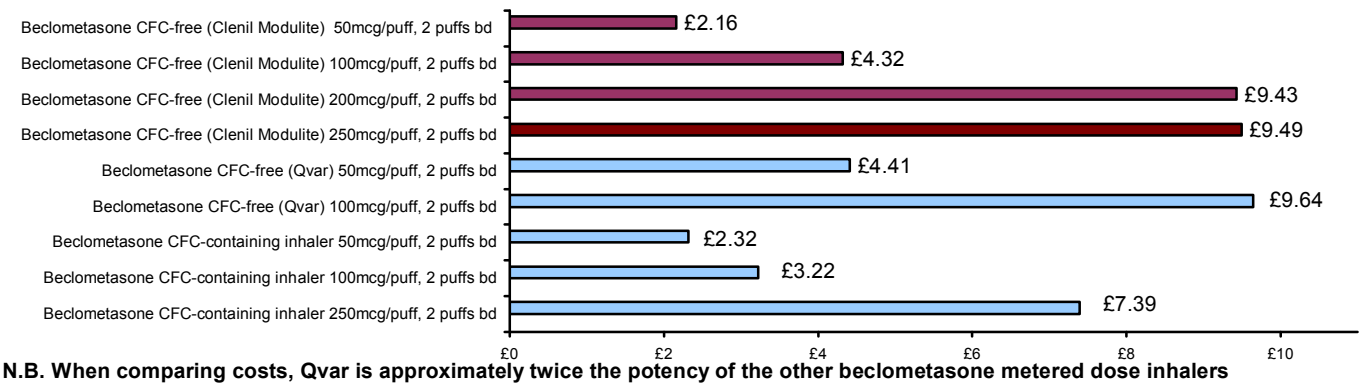
Product Metered dose inhalers, CFC-free, containing 50micrograms, 100micrograms, 200 micrograms or 250 microgams/puff, 200 doses per container. Breath-actuated devices not currently available.

Indication Asthma

Dosage Children, usually 100micrograms twice daily, increasing as needed, up to maximum of 400 micrograms daily. The SPC advises that a Volumatic spacer should be used in addition, in those aged 15 and under. Adults, 200 micrograms twice daily increasing as needed.

Date of Launch August 2006

Costs of 28 days treatment (prices from MIMS/ Drug Tariff Dec 2006)



N.B. When comparing costs, Qvar is approximately twice the potency of the other beclometasone metered dose inhalers

Produced to provide prescribers with evaluated information soon after the launch of a new product. This review is primarily intended for use within a year of publication. New information may become available and a further literature search may be appropriate. **Jan 2007**

Introduction

Clenil Modulite® is the second CFC-free beclometasone metered dose inhaler to be marketed in the UK. Unlike Qvar®, Clenil Modulite can be substituted for CFC-containing beclometasone on a 1-for-1 dose basis as the aerosol particles are larger (average 2.9 µm), compared with Qvar® (average 1.1µm).

It is not yet clear when a mandatory changeover to CFC-free beclometasone will occur, however Becotide® is due to be discontinued in the second half of 2007 and this may lead to a shortage of CFC-containing beclometasone inhalers.

Clinical Efficacy

Three clinical studies have been published comparing HFA-beclometasone (Clenil Modulite®) with CFC-beclometasone, Becotide®. All of these were double-blind double-dummy randomised controlled trials comparing the two inhaled beclometasone products. They were all designed to have sufficient patients to enable them to detect differences between the products with a power of 80% and a significance level of 5% (this is the standard required by the MHRA to compare products that will be regarded as equivalent).

In the first of these trials[1], 172 patients with mild stable persistent asthma who were already using inhaled corticosteroids were randomised to either Clenil Modulite® or Becotide® in a dose of 200 micrograms twice daily for six weeks. The two treatments had similar effects on peak expiratory flow rate (PEFR) measured in the morning and evening as well as forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) measured in clinic. Adverse effects were similar in both groups. No difference in effect was detected in other measures of control including use of rescue salbutamol, number of asthma attacks, night time awakenings or clinical symptoms recorded on a diary card. Methacholine challenge tests were carried out in 65 of the patients, no statistically significant difference was found between the two products.

In the second study, 116 adult patients with mild-moderate asthma (FEV_1 60% predicted or more) were randomised to either Clenil Modulite® or Becotide® in a dose of 500 micrograms twice daily for 12 weeks.[2] Effects of the two products were similar for the primary end point (morning PEFR) as well as evening PEFR and FEV_1.

Decreases in use of rescue salbutamol and clinical symptoms were also found during the trial in both groups, with no difference between them.

Morning cortisol levels were measured and found to be unchanged from the beginning to the end of the trial in either group. Adverse events were also similar in the two groups, occurring in 81.4% of those in the Clenil Modulite® group and 82.5% in the Becotide® group. Nine of the patients in the Clenil Modulite® group complained of taste change (HFA inhalers have a different taste and there is less of a 'cold' effect than with CFC-containing inhalers).

The third trial was in children aged 6-16 with mild-moderate stable asthma.[3] The study was carried out in primary care, 218 patients entered the trial and 181 completed it. They were required to withdraw from the trial if their asthma worsened and they needed treatment with theophylline or other similar anti-asthmatic agents. A range of pulmonary function tests were carried out at clinic visits at 2 weekly intervals during the study and patients kept a daily diary card recording morning and evening PEFR, number of daytime and nighttime asthma attacks, salbutamol use, nocturnal awakenings and clinical symptoms. A blood sample for morning serum cortisol was taken at the start and end of the 12 week trial.

Patients were randomised to one of the three treatments that delivered the same daily dose of beclometasone, either Clenil Modulite® 50mcg (4puffs twice daily) or 100mcg (2 puffs twice daily), or conventional beclometasone (Becotide®), 50mcg (4 puffs twice daily). All three treatments were found to have similar effects: no significant differences were found between the groups for PEFR, and no other significant differences were identified consistently between the groups. No significant changes were found in the morning cortisol levels, although 2 patients in the HFA-beclometasone 100mcg group had final values slightly below the lower limit of the normal range. Adverse events were similar in all three groups, two patients reported oral mycosis (in the 100mcg Clenil Modulite® group).

Adverse Effects/ Contraindications

Systemic effects of inhaled beclometasone may occur at high doses, including adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. Local candidosis of the mouth and throat, hoarseness or throat irritation may occur in some patients, using a spacer (ideally), or rinsing the mouth after administration may help. Occasional hypersensitivity reactions may occur.

The Clenil Modulite® formulation contains a tiny amount of alcohol and there is a theoretical potential for interaction with disulfiram or metronidazole.

References

1. Woodcock J et al. Aerosol Medicine 2002; 14:407-414
2. Anderson et al. J Invest Allergol Clin Immunol 2002;12:107-113.
3. Lee T et al. Pediatric Asthma Allergy & Immunol 2002; 15:133-142.