

# Fostair: new beclometasone/formoterol CFC-free combination

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## KEY POINTS

- Fostair is a CFC-free MDI containing beclometasone dipropionate 100µg and formoterol 6µg per actuation
- dosage: one or two puffs twice daily; 120 doses, £29.32
- licensed for the treatment of chronic asthma in adults and is introduced at Step 3 of the BTS/SIGN management guideline
- beclometasone is delivered as a fine aerosol that is not bioequivalent to a standard MDI: 100µg beclometasone in Fostair is equivalent to 250µg from a CFC MDI
- in two 12-week trials in patients with stable moderate to severe asthma, Fostair was not inferior to fluticasone/salmeterol (Seretide) or budesonide/formoterol (Symbicort) at equivalent doses
- the adverse effects of Fostair are typical of its component drugs
- Fostair is cheaper than alternative inhaled steroid/long-acting beta<sub>2</sub>-agonist combinations



**Fostair is the first beclometasone/formoterol combination for the treatment of asthma. Here, Steve Chaplin describes the clinical trial data relating to its efficacy and safety, and Dr Ind comments on its place in therapy.**

Current guidance on the management of chronic asthma recommends that a long-acting beta<sub>2</sub>-agonist (LABA) should be introduced for patients already treated with an inhaled steroid, for whom symptom control remains unsatisfactory (Step 3).<sup>1</sup> There is no difference in efficacy between using a fixed-dose combined inhaler or separate inhalers to administer a LABA and an inhaled steroid.<sup>1</sup>

There are now three combinations of a steroid with a LABA: Symbicort Turbohaler (budesonide/formoterol), Seretide Accuhaler and Evohaler (fluticasone/salmeterol) and Fostair (beclometasone dipropionate/formoterol).

## The technology

Fostair is a CFC-free metered-dose inhaler (MDI) containing 100µg beclometasone dipropionate and 6µg formoterol per actuation. The steroid is delivered as a fine-particle aerosol and has higher bioavailability than that of a CFC MDI: 100µg beclometasone in Fostair is equivalent to 250µg from an MDI delivering a nonfine aerosol.

Fostair is licensed for the regular treatment of asthma where use of a combination product (inhaled corticosteroid and LABA) is appropriate, *ie* patients not adequately controlled with inhaled corticosteroids and 'as-needed' inhaled short-acting beta<sub>2</sub>-agonist or patients already adequately con-

trolled on both inhaled corticosteroids and LABA.

The recommended dose is one or two actuations twice daily, to a maximum of four per day. Fostair is not recommended for people under 18.

## Clinical trials

Fostair has been compared with fluticasone/salmeterol 125/25µg (n=228)<sup>2</sup> and budesonide/formoterol 200/6µg (n=219)<sup>3</sup> in patients with moderate to severe asthma. All drugs were administered as two puffs twice daily (total daily doses are listed in Table 1).

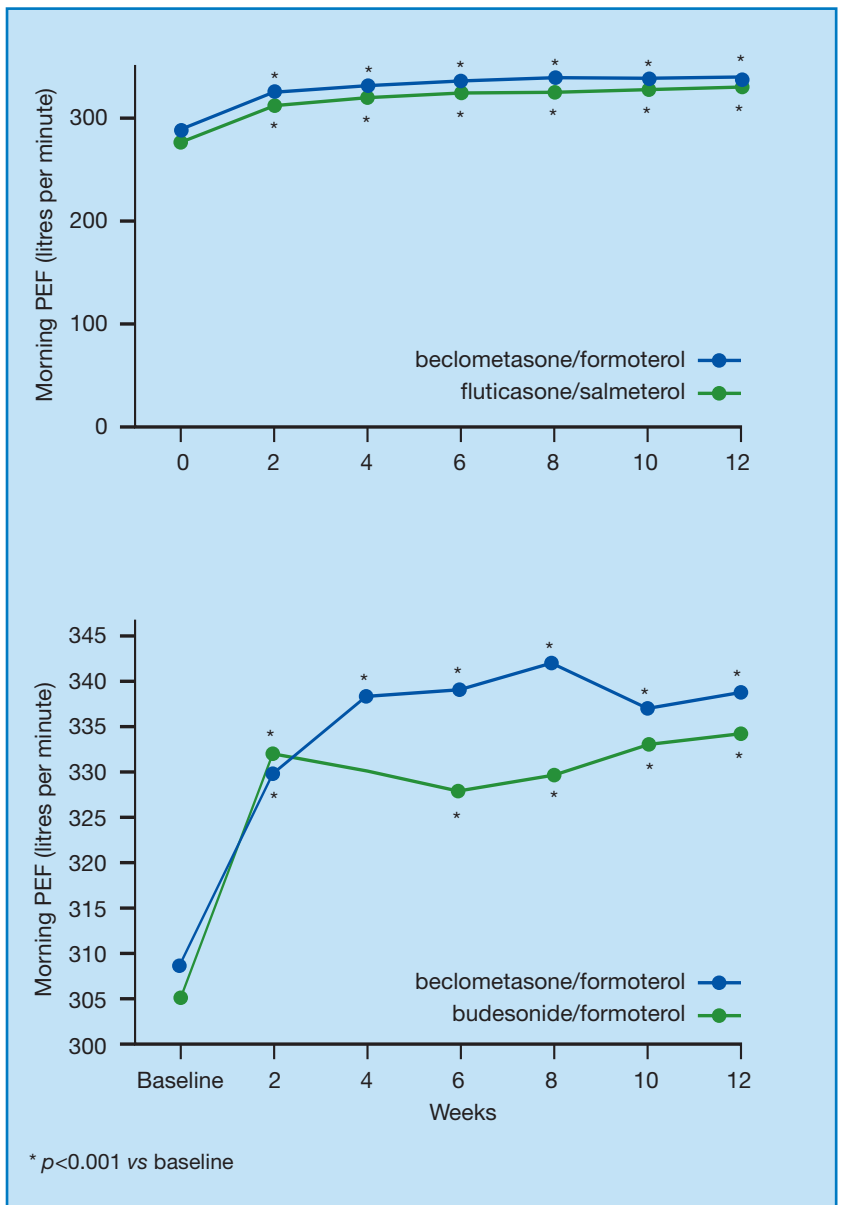
Both trials included patients with forced expiratory volume in one second (FEV<sub>1</sub>) 50-80 per cent

## New products

	Steroid	LABA
Fostair (beclometasone/formoterol)	400µg*	24µg
fluticasone/salmeterol	500µg	100µg
budesonide/formoterol	800µg	24µg

\* equivalent to 1000µg beclometasone from a non-CFC free MDI delivering a non-fine aerosol

**Table 1.** Total daily doses of inhaled steroids and LABAs in Fostair clinical trials



**Figure 1.** Mean morning PEF: Fostair vs fluticasone/salmeterol (top)<sup>2</sup> and vs budesonide/formoterol,<sup>3</sup> showing no significant difference between treatments

predicted and persistent symptoms despite treatment with up to 1000µg beclometasone dipropionate or equivalent (mean baseline dose approximately 730-810µg per day). Patients who experienced an exacerbation or increased peak expiratory flow (PEF) during a two-week run-in period were excluded.

Both studies were designed to assess the noninferiority of Fostair compared with the comparator and were of 12 weeks' duration. The primary end-point in both was the mean morning predose PEF during the last two weeks of treatment.

In both studies, Fostair was not inferior to the comparator product. Mean PEFs over 12 weeks are illustrated in Figure 1. There were

also no differences between Fostair and the comparator treatments in secondary end-points including symptom improvement, days free of symptoms and use of rescue salbutamol during the last two weeks.

There were no significant differences in the frequency of exacerbations throughout the trials.

#### Adverse effects

The adverse effects associated with Fostair are typical of its component drugs.<sup>4</sup> There were no significant differences between treatments in the two randomised trials.

#### References

1. British Thoracic Society, Scottish Intercollegiate Network. British

guideline on the management of asthma. Revised edition May 2008 ([www.sign.ac.uk/pdf/sign101.pdf](http://www.sign.ac.uk/pdf/sign101.pdf); accessed 14.05.08).

2. Papi A, Paggiaro P, Nicolini G, *et al.* Beclomethasone/formoterol vs fluticasone/salmeterol inhaled combination in moderate to severe asthma. *Allergy* 2007;62:1182-8.

3. Papi A, Paggiaro PL, Nicolini G, *et al.* Beclomethasone/formoterol versus budesonide/formoterol combination therapy in asthma. *Eur Respir J* 2007;29:682-9.

4. Trinity-Chiesi Pharmaceuticals. Fostair Summary of Product Characteristics. November 2007 ([www.trinity-chiesi.co.uk/files/SmPC\\_%20Fostair.pdf](http://www.trinity-chiesi.co.uk/files/SmPC_%20Fostair.pdf); accessed 17.1.08).

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## Place in therapy

Addition of a LABA to an inhaled steroid is probably the best evidence-based step in the asthma guidelines (step 3 of the British Thoracic Society guidelines). Combination of an inhaled steroid and a LABA in a single inhaler is logical: both components are administered twice daily, they have complementary effects, the combination prevents deliberate, or inadvertent, inhaled steroid noncompliance, it is convenient for the patient and doctor, and is cost-saving.

The launch of Fostair brings a third inhaled steroid/LABA combination product after Seretide (fluticasone/salmeterol) and Symbicort (budesonide/formoterol).

Fostair is a combination of beclometasone, the oldest (and most used world-wide) inhaled steroid, and formoterol, the rapid-onset LABA, in a CFC-free MDI. Safety is unlikely to be a major con-

cern because of the well-established track record of its constituents.

The clinical trial evidence (reviewed above) suggests that Fostair 100/6µg is equivalent to Seretide 125/25µg and Symbicort 200/6µg, all two puffs twice daily, in terms of morning PEF.<sup>1,2</sup>

A number of interesting points are raised, however:

1. How should equivalence of combination inhalers be measured?
2. Should noninferiority studies include a placebo arm?
3. What about noninferiority of other important end-points, *eg* exacerbations? Two good studies were powered for change in morning PEF but information about other measures is scant.
4. How do these findings, in a select population (patients with moderate-severe persistent asthma with a marked bronchodilator response despite inhaled steroid 800µg per day, as recruited in most LABA trials), apply in the real world?

So when should Fostair be used? Logically it should be substituted in

patients taking beclometasone and formoterol as separate inhalers. It is indicated for patients who are symptomatically uncontrolled (or with suboptimal lung function) on beclometasone, or another inhaled steroid, by MDI alone, as an alternative to CFC-free Seretide Evohaler. Fostair is also an alternative to Symbicort or Seretide Accuhaler, both dry-powder inhalers, provided the patient can use, and is happy with, an MDI. Fostair is cheaper, approximately 20 per cent less based on the comparative clinical trials, than established competitors.

Are there any potential downsides? Interestingly, in theory the microfine particles targeting small airways with beclometasone may be less appropriate for a LABA.<sup>3</sup> Fostair is not licensed for use in under-18s or COPD patients or for up-titration.

Overall, we should welcome a third, alternative, combination inhaler and hope it teaches us more about the use of these drugs in the management of asthma.

**References**

1. Papi A, Paggiaro P, Nicolini G, *et al.* Beclomethasone/formoterol vs fluticasone/salmeterol inhaled combination in moderate to severe asthma. *Allergy* 2007;62:1182-8.

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budesonide/formoterol combination therapy in asthma. *Eur Respir J* 2007; 29:682-9.

3. Usmani O, Biddiscombe MF, Barnes PJ. Regional lung deposition and bronchodilator response as a function of beta<sub>2</sub>-agonist particle size. *Am J Respir and Crit Care Med* 2005;172:1497-504.

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