

Asthma: beclometasone/formoterol (Fostair) for maintenance and reliever treatment

Evidence summary

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[nice.org.uk/guidance/esnm22](https://www.nice.org.uk/guidance/esnm22)

Key points from the evidence

The content of this evidence summary was up-to-date in June 2013. See [summaries of product characteristics](#) (SPCs), [British national formulary](#) (BNF) or the [MHRA](#) or [NICE](#) websites for up-to-date information.

Summary

A 48-week randomised controlled trial in 1714 adults found that beclometasone/formoterol (Fostair) given as maintenance and reliever treatment was more effective than beclometasone/formoterol maintenance treatment plus as-needed salbutamol for reducing exacerbations in adults with uncontrolled asthma. Both treatments were well tolerated but adverse drug reactions occurred more commonly with beclometasone/formoterol maintenance and reliever treatment.

<p>Effectiveness</p> <ul style="list-style-type: none"> • Compared with as-needed salbutamol, the time to first severe exacerbation was 75 days longer with as-needed beclometasone/formoterol (p=0.0005). • The yearly rate of severe exacerbations was reduced by a small but significant amount with as-needed beclometasone/formoterol (7.63 events per 100 patients per year; p<0.0001). • No comparisons are available with budesonide/formoterol (Symbicort) for maintenance and reliever treatment. 	<p>Safety</p> <ul style="list-style-type: none"> • Both beclometasone/formoterol and salbutamol were well tolerated. • Similar numbers of patients in both groups experienced serious adverse events (3.7% with as-needed beclometasone/formoterol and 4.8% with as-needed salbutamol; p value not reported). • Adverse drug reactions were significantly more common with as-needed beclometasone/formoterol (4.4% compared with 2.2% for as needed salbutamol; p=0.01). • The particles of beclometasone in Fostair are extra fine and more potent than in standard formulations of beclometasone; 100 micrograms of extra fine beclometasone in Fostair are equivalent to 250 micrograms of standard beclometasone.
<p>Patient factors</p> <ul style="list-style-type: none"> • Some people with uncontrolled asthma at step 3 may prefer to follow the traditional stepped model of asthma treatment. Others may prefer to change to maintenance and reliever treatment. • Fostair is a pressurised metered dose inhaler. • Symbicort is a dry powder inhaler (Turbohaler). 	<p>Resource implications</p> <ul style="list-style-type: none"> • A Fostair inhaler containing 120 doses costs £29.32. • The cost of using beclometasone/formoterol maintenance and reliever treatment is estimated to be £20.04 per month compared with £14.82 per month for beclometasone/formoterol plus as-needed salbutamol. • A Symbicort inhaler containing 120 doses costs £33.00 or £38.00, depending on the dose.

Key points

Fostair is a pressurised metered dose inhaler that contains beclometasone dipropionate (an inhaled corticosteroid [ICS]) and formoterol fumarate dihydrate (a long-acting beta-2 agonist [LABA]).

Fostair was licensed in 2007 for the maintenance therapy of asthma in adults aged 18 years or over; within this licensed indication Fostair is taken as regular maintenance treatment with a separate rapid-acting bronchodilator taken as-needed. In December 2012, the licence was extended to include maintenance and reliever therapy in adults, meaning that Fostair is taken as regular maintenance treatment and as needed in response to asthma symptoms.

This evidence review is based on a randomised controlled trial that compared the efficacy and safety of beclometasone/formoterol maintenance and reliever treatment with standard maintenance treatment using regular beclometasone/formoterol and as-needed salbutamol. The study included 1714 adults with uncontrolled asthma, the majority of whom were at step 3 or 4 of the [British guideline on the management of asthma](#) (SIGN guideline 101).

The study found that, compared with beclometasone/formoterol plus as-needed salbutamol, beclometasone/formoterol for both maintenance and reliever treatment statistically significantly increased the time to first severe exacerbation (the primary outcome) by 75 days (134 days versus 209 days respectively; hazard ratio [HR] 0.64, 95% confidence interval [CI] 0.49 to 0.82; $p=0.0005$).

A statistically significant reduction was seen in the yearly rate of severe exacerbations per patient with maintenance and reliever treatment, compared with as-needed salbutamol (14.76 events per 100 patients per year compared with 22.39 respectively; HR 0.66, 95% CI 0.55 to 0.80; $p<0.0001$).

Similar numbers of patients in the as-needed beclometasone/formoterol and salbutamol groups experienced serious adverse events (32 [3.7%] and 41 [4.8%] respectively; statistical significance of difference not reported). Adverse drug reactions occurred significantly more often in patients treated with as-needed beclometasone/formoterol compared with as-needed salbutamol (38 [4.4%] compared with 19 [2.2%] respectively; $p=0.01$).

It is not known how the efficacy and safety of beclometasone/formoterol ([Fostair](#)) compares directly with the established budesonide/formoterol ([Symbicort](#)) maintenance and reliever treatment. More data are available to support the use of budesonide/formoterol for this indication.

The [British guideline on the management of asthma](#) advises that budesonide/formoterol (Symbicort) regular maintenance and reliever treatment is an option for selected adults at step 3

whose asthma is poorly controlled, or for selected adults at step 2 whose asthma is poorly controlled and who are taking more than 400 micrograms of beclometasone dipropionate or equivalent each day. Careful education of patients about this management strategy is required. Patients taking rescue ICS/LABA once a day or more on a regular basis should have their treatment reviewed.

Based on the results of the study, beclometasone/formoterol (Fostair) may also be an option for adults at step 3 whose asthma is poorly controlled.

Some people may prefer to follow the traditional steps of the [British guideline on the management of asthma](#). For those at step 3, this involves increasing the dose of ICS in their current maintenance treatment, rather than switching to maintenance and reliever treatment.

The choice of treatment (maintenance and reliever therapy or the traditional stepped approach), product (beclometasone/formoterol or budesonide/formoterol) and inhaler device (pressurised metered dose inhaler or dry powder inhaler) may be important to individual patients.

Key evidence

Papi A, Corradi M, Pigeon-Francisco C et al. (2013) [Beclometasone–formoterol as maintenance and reliever treatment in patients with asthma: a double-blind, randomised controlled trial](#). *The Lancet Respiratory Medicine* 1: 23–31

About this evidence summary

'Evidence summaries: new medicines' provide summaries of key evidence for selected new medicines, or for existing medicines with new indications or formulations, that are considered to be of significance to the NHS. The strengths and weaknesses of the relevant evidence are critically reviewed within this summary to provide useful information for those working on the managed entry of new medicines for the NHS, **but this summary is not NICE guidance**.

Relevance to NICE guidance programmes

Use of the beclometasone/formoterol combination inhaler for maintenance and reliever therapy is not currently being considered for a NICE technology appraisal or other work programme.

[Corticosteroids for the treatment of chronic asthma in children under the age of 12 years](#) (NICE technology appraisal guidance 131) and [Corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over](#) (NICE technology appraisal guidance 138) considered

inhaled corticosteroids (ICS) for the maintenance treatment of asthma, both as a single agent and in combination with a long-acting beta-2 agonist (LABA). One of the combination treatments included in the appraisals (budesonide/formoterol) was licensed for maintenance and reliever treatment at that time. However, the focus of the technology appraisals was use of an ICS (alone or in combination with a LABA) for maintenance therapy, rather than use of a LABA/ICS combination as a replacement for ICS maintenance and short-acting bronchodilator reliever therapy.

In February 2013, technology appraisals 131 and 138 were moved to the [static list of technology appraisals](#) following a review which found that there was no new research available that would have any material effect on the current guidance. A significant change to the evidence base at any stage in the future could trigger a review proposal.

Introduction

The [British guideline on the management of asthma](#) (SIGN guideline 101), published jointly by the [Scottish Intercollegiate Guidelines Network](#) and [British Thoracic Society](#) and [accredited by NICE](#), advocates the following stepwise approach for the treatment of asthma. Inhaled corticosteroids (ICS) are the first-choice regular preventer therapy for children and adults. If asthma is not adequately controlled on an ICS alone (at step 2), add-on therapy may be needed (step 3). For children aged 5 years and over and adults, an ICS and a long-acting beta-2 agonist (LABA) should be considered. However, before starting a new drug or stepping up treatment, adherence to existing therapies, inhaler technique, and appropriate elimination of trigger factors should be confirmed.

In children aged over 12 years and adults, if poor control persists after the options at step 3 have been tried (including increasing the dose of ICS to 800 micrograms of beclometasone dipropionate [BDP] or equivalent), high-dose ICS treatment (up to 2000 micrograms of BDP or equivalent) or the addition of a fourth drug should be considered (step 4).

Cochrane reviews of regular treatment of chronic asthma with [formoterol](#) and [salmeterol](#) found that adding a LABA to an ICS can improve tests of lung function, symptoms, and reduce exacerbations. However, an increase in the risk of serious adverse events was observed with LABAs (both formoterol and salmeterol), which does not appear to be completely abolished when an ICS is used concurrently.

After an assessment of the risks and benefits of LABAs in asthma, the Medicines and Healthcare products Regulatory Agency concluded in a [Drug Safety Update](#) that the benefits of using a LABA with an ICS outweigh any apparent risks. The Commission on Human Medicines has [issued advice on the use and safety of LABAs for treating chronic asthma](#) for prescribers.

If treatment with an ICS and LABA is considered appropriate, [Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over](#) (NICE technology appraisal guidance 138) advises that using a combination inhaler within its marketing authorisation is an option. NICE recommends that the decision to use a combination inhaler or the 2 agents in separate inhalers should be made on an individual basis, taking into consideration therapeutic need and the likelihood of treatment adherence. If a combination inhaler is chosen, then the least costly device that is suitable for the individual is recommended.

When the [British guideline on the management of asthma](#) was updated in 2011, a combination inhaler containing budesonide and formoterol ([Symbicort](#)) was the only product available that was licensed for use as regular maintenance treatment and as needed in response to symptoms (as well as being licensed for regular maintenance treatment with a separate rapid-acting bronchodilator, such as a short-acting beta-2 agonist, as rescue treatment). The guideline advises that budesonide/formoterol maintenance and reliever treatment is an alternative to the traditional stepped approach to asthma treatment for some people. It may be considered in selected adults at step 3 whose asthma is poorly controlled, or in selected adults at step 2 whose asthma is poorly controlled and who are taking more than 400 micrograms of BDP or equivalent each day. Careful education of people about the specific issues around this management strategy is required.

Product overview

Drug action

[Fostair](#) is a pressurised metered dose inhaler containing beclometasone dipropionate (BDP; an inhaled corticosteroid [ICS]) and formoterol fumarate dihydrate (a long-acting beta-2 agonist [LABA]). Each metered dose contains 100 micrograms of beclometasone and 6 micrograms of formoterol.

The [summary of product characteristics](#) advises that the particles of BDP in Fostair are extra fine and more potent than in standard formulations of BDP: 100 micrograms of extra fine BDP in Fostair are equivalent to 250 micrograms of standard BDP.

Formoterol has a more rapid onset of action than salmeterol (see the [Cochrane review](#)).

New therapeutic indication

The [summary of product characteristics](#) states that Fostair is licensed for the regular treatment of asthma in adults aged 18 years or over where use of a combination ICS and LABA is appropriate in:

- people whose asthma is not adequately controlled with an ICS and as-needed inhaled rapid-acting beta-2 agonist or
- people whose asthma is already adequately controlled on both an ICS and a LABA.

Fostair is not currently recommended for children and young people under 18 years of age.

Fostair was licensed in 2007 for the maintenance therapy of asthma in adults aged 18 years or over; within this licensed indication Fostair is taken as regular maintenance treatment with a separate as-needed rapid-acting bronchodilator. In December 2012, the licence was extended to include maintenance and reliever therapy in adults, meaning that Fostair is taken as regular maintenance treatment and as needed in response to asthma symptoms.

Course and cost

The recommended maintenance dose of Fostair for maintenance and reliever treatment is 1 inhalation twice daily (in the morning and in the evening). One additional inhalation should be taken as needed in response to symptoms. If symptoms persist after a few minutes, an additional inhalation should be taken. The maximum daily dose is 8 inhalations (equivalent to 2000 micrograms of BDP). People needing frequent use of rescue inhalations daily should be strongly recommended to seek medical advice. Their asthma should be reassessed and their maintenance therapy should be reconsidered (see [summary of product characteristics](#)).

The cost of a Fostair inhaler containing 120 doses is £29.32 ([NHS electronic Drug Tariff, April 2013](#)).

Evidence review

This evidence review is based on a [randomised controlled trial](#) (RCT) that compared the efficacy and safety of as-needed treatment with beclometasone/formoterol with a short-acting beta-2 agonist (salbutamol) in adults taking beclometasone/formoterol as maintenance treatment for asthma ([Papi et al. 2013](#); see table 1).

- Design: double-[blind](#) RCT in 183 centres in 14 European countries.
- Population: 1714 adults (aged 18 years or over; mean age 48 years) with asthma (median duration 9 years) that was not fully controlled. Patients were eligible for the study if:
 - their pre-bronchodilator forced expiratory volume in 1 second (FEV1) was 60% of predicted or more (mean 74.5%)

- their FEV1 increased by at least 12% and 200 ml after inhalation of salbutamol 400 micrograms
 - they had a history of at least 1 severe exacerbation in the 12 months before study entry, but not in the past month, and
 - their asthma had been treated regularly for the previous 2 months with an inhaled corticosteroid (ICS) alone (dose of standard [not extra fine] beclometasone dipropionate [BDP] or equivalent 1000 micrograms or more per day) or in combination with a long-acting beta-2 agonist (LABA; dose of standard BDP or equivalent 500 micrograms or more per day).
- At study entry, the mean dose of standard BDP or equivalent was about 1130 micrograms per day, and around 81% of patients were using a LABA. On average, patients used 1 inhalation of their reliever inhaler per day at baseline. Asthma that was not fully controlled was defined as having at least 1 of the following:
 - use of rescue medication more than twice a week
 - any limitation of activities
 - any nocturnal symptoms or awakenings
 - daytime symptoms more than twice a week or
 - FEV1 less than 80% of predicted.
 - During a 2-week run-in period, all patients were treated with a combination inhaler containing extra fine beclometasone 100 micrograms and formoterol 6 micrograms (1 inhalation twice a day) plus salbutamol 100 micrograms as needed for the relief of symptoms.
 - Intervention and comparison: if their asthma was not fully controlled after the run-in period, patients continued to use combination maintenance treatment with beclometasone 100 micrograms and formoterol 6 micrograms (1 inhalation twice a day) and were randomised to as-needed treatment with either the fixed combination of beclometasone 100 micrograms and formoterol 6 micrograms (n=857) or salbutamol 100 micrograms (n=857). The maximum number of inhalations of as-needed treatment was 6 per day. Patients were followed up for 48 weeks.
 - Outcomes: the primary outcome was the time to the first severe exacerbation, defined as:

- deterioration in asthma needing admission to hospital or a visit to an emergency department or
- use of systemic corticosteroids for 3 consecutive days or more for asthma.
- Secondary outcomes included the rate of severe exacerbations, and the time to the first and the rate of mild exacerbations. Mild exacerbations were defined as the occurrence of 1 of the following:
 - use of 2 or more inhalations of the reliever inhaler in 24 hours
 - morning peak expiratory flow less than the baseline by 20% or more or
 - night-time awakening due to asthma.
- Further secondary outcomes included other exacerbation variables, lung function, symptom scores and asthma control.

Table 1 Summary of the study:[Papi et al. \(2013\)](#)

	Beclometasone/ formoterol	Salbutamol	Analysis
Randomised	n=857	n=857	
Efficacy^a	n=852	n=849	
Primary outcome: time to first severe exacerbation	209 days	134 days	Difference 75 days HR 0.64 95% CI 0.49 to 0.82 p=0.0005
Selected secondary outcomes:			
Percentage of patients with severe exacerbations	12% (99/852)	18% (152/ 849)	Difference 6% p=0.0003

Rate of severe exacerbations (events per 100 patients per year)	14.76	22.39	Difference 7.63 HR 0.66 95% CI 0.55 to 0.80 p<0.0001
Percentage of patients visiting the emergency department or admitted due to asthma	6% (53/852)	9% (77/849)	Difference 3% Significance not reported
Rate of visits to the emergency department or admission due to asthma (events per 100 patients per year)	6.14	9.11	Difference 2.97 HR 0.67 95% CI 0.54 to 0.84 p=0.0003
Percentage of patients using systemic corticosteroids for more than 3 days for asthma	10% (89/852)	17% (143/849)	Difference 7% Significance not reported
Rate of use of systemic corticosteroids for more than 3 days for asthma (events per 100 patients per year)	14.69	22.47	Difference 7.78 HR 0.65 95% CI 0.54 to 0.80 p<0.0001
Percentage of patients with mild exacerbations	72% (610/852)	71% (607/849)	Difference 1% Significance not reported
Time to first mild exacerbation	Not reported	Not reported	HR 0.97 95% CI 0.86 to 1.08 p=0.565 Not significant

Rate of mild exacerbations (days per patient per year)	56.04	65.11	Difference 9.07 HR 0.86 95% CI 0.76 to 0.98 p=0.021
Safety^b	n=854	n=854	
Serious treatment-emergent adverse events	3.7% (32/854)	4.8% (41/854)	Statistical significance not reported
Adverse drug reactions	4.4% (38/854)	2.2% (19/854)	p=0.010
Serious adverse events reported as asthma	0.9% (8/854)	2.2% (19/854)	Statistical significance not reported
Discontinuations due to asthma	0.1% (1/854)	1.3% (11/854)	Statistical significance not reported
Abbreviations: CI, <u>confidence interval</u> ; HR, <u>hazard ratio</u> .			
^a Efficacy analyses were by <u>intention to treat</u> . The intention-to-treat population included all randomly assigned patients who received at least 1 dose of study treatment and had at least 1 available evaluation of efficacy after baseline.			
^b The safety population consisted of all randomly assigned patients who took at least 1 dose of study medication.			

Clinical effectiveness

Beclometasone/formoterol used as maintenance and reliever treatment was statistically significantly more effective than beclometasone/formoterol used with as-needed salbutamol in reducing asthma exacerbations in adults with uncontrolled asthma.

During the 48-week study, 326 severe exacerbations were reported by 251 patients; 12% of patients in the as-needed beclometasone/formoterol group had at least 1 severe exacerbation compared with 18% of patients in the as-needed salbutamol group (p=0.0003).

Compared with beclometasone/formoterol plus as-needed salbutamol, beclometasone/formoterol for both maintenance and reliever treatment statistically significantly increased the time to first severe exacerbation (the primary outcome) by 75 days (134 days compared with 209 days respectively; hazard ratio [HR] 0.64, 95% confidence interval [CI] 0.49 to 0.82; $p=0.0005$).

A statistically significant reduction was seen in the yearly rate of severe exacerbations per patient with maintenance and reliever treatment, compared with as-needed salbutamol (14.76 events per 100 patients per year compared with 22.39 events per 100 patients per year respectively; HR 0.66, 95% CI 0.55 to 0.80; $p<0.0001$). Similar reductions were seen for the individual constituents of this composite outcome: deterioration in asthma needing visits to the emergency department or admission to hospital, and systemic corticosteroid use for more than 3 days for asthma (see table 1).

The number of days with mild asthma exacerbations was statistically significantly lower with as-needed beclometasone/formoterol compared with as-needed salbutamol (56 days per patient per year compared with 65 days per patient per year respectively; HR 0.86, 95% CI 0.76 to 0.98; $p=0.021$). No significant difference was seen between treatments in time to first mild asthma exacerbation.

Measures of lung function, asthma symptoms and asthma control (such as FEV₁, asthma symptom and control scores, reliever use and days without symptoms or reliever use) improved in both the beclometasone/formoterol and as-needed salbutamol groups. There were no significant differences between the groups.

The mean additional dose of extra fine beclometasone used by patients in the combination treatment group was 86 micrograms per day (standard BDP equivalent 215 micrograms).

Safety

Similar numbers of patients in the as-needed beclometasone/formoterol and salbutamol groups experienced serious adverse events (32 [3.7%] and 41 [4.8%] respectively; significance of difference not reported). Serious adverse events reported as asthma occurred in 8 patients (0.9%) treated with as-needed beclometasone/formoterol and 19 patients (2.2%) treated with as-needed salbutamol (significance of difference not reported). Discontinuations due to asthma also occurred more commonly in the as-needed salbutamol group (11 patients [1.3%] compared with 1 patient [0.1%] in the beclometasone/formoterol group; significance of difference not reported).

The occurrence of pharmacologically predictable adverse events related to treatment with ICS or LABA treatment (such as dysphonia, oral candidiasis, palpitation or tachycardia, and tremor) was low in both groups. However, overall, adverse drug reactions occurred significantly more often in patients treated with as-needed beclometasone/formoterol compared with as-needed salbutamol (4.4% [38] compared with 2.2% [19] respectively; $p=0.01$).

More information on the adverse effects of beclometasone and formoterol can be found in relevant [summaries of product characteristics](#).

Evidence strengths and limitations

The study was well designed and reported and the results can be considered reliable. However, it has limitations that affect its application to practice.

The study is not generalisable to all people with asthma. It included people with asthma at step 3 (ICS dose 400–800 micrograms of BDP or equivalent daily plus a LABA) or step 4 (increased ICS dose up to 2000 micrograms of BDP or equivalent daily) of the [British guideline on the management of asthma](#) who had experienced 1 or more severe exacerbation in the previous 12 months. At study entry, the mean dose of standard BDP or equivalent was about 1130 micrograms per day and around 81% of patients were using a LABA. In addition, patients' asthma was not fully controlled.

Compared with baseline, the mean daily dose of ICS was reduced in the study from 1128 micrograms to 701 micrograms of standard BDP or equivalent in the as needed beclometasone/formoterol group, and from 1139 micrograms to 489 micrograms in the as-needed salbutamol group. Measures of lung function, asthma symptoms and asthma control improved in both groups despite the reductions in the doses of ICS.

Post-hoc analyses were conducted in patients who were treated at baseline with less than 500 micrograms per day of standard BDP or equivalent ($n=281$, dose stepped up in study) and in those who were treated with 500 micrograms or more per day ($n=1420$, dose stepped down or unchanged). The results of these suggest that, in terms of reducing the risk of exacerbations, the benefits of as-needed beclometasone/formoterol over as-needed salbutamol occurred irrespective of whether the dose of ICS was stepped up, stepped down or unchanged.

The reduction in exacerbation rates seen with beclometasone/formoterol as maintenance and reliever treatment might be due to the higher dose of BDP in this group (86 micrograms of extra

fine BDP daily, equivalent to 215 micrograms of standard BDP) or the rapid onset of action of formoterol, or a combination of both mechanisms of action.

The study was undertaken in 183 centres in Europe and some centres are likely to have enrolled fewer than 10 people. Only 3 centres were in the UK.

It is unclear whether allocation was concealed in the study; unconcealed allocation is a potential source of bias.

The study was funded by Chiesi: the manufacturer of Fostair.

Context

Treatment alternatives

Beclometasone and formoterol are available in a range of separate inhaler devices.

Three other ICS/LABA combination inhalers are currently licensed in the UK:

- budesonide/formoterol (Symbicort) dry powder inhaler
- fluticasone/formoterol (Flutiform) metered dose inhaler
- fluticasone/salmeterol (Seretide) metered dose inhaler and dry powder inhaler.

Flutiform and Seretide are not licensed for maintenance and reliever treatment of asthma. Only the 2 lower strengths of Symbicort (100/6 and 200/6) are licensed for this indication.

Costs of treatment alternatives

120-dose units	Low strength	Medium strength
Fostair metered dose inhaler	Not available	100/6 micrograms ^a £29.32
Symbicort dry powder inhaler	100/6 micrograms £33.00	200/6 micrograms £38.00

^a 100 micrograms of beclometasone in Fostair is approximately equivalent to 250 micrograms of standard beclometasone dipropionate.

Prices based on [NHS electronic Drug Tariff, April 2013](#).

In the study, all patients took beclometasone 100 micrograms and formoterol 6 micrograms (1 inhalation twice a day) and were then randomised to either as-needed beclometasone/formoterol or as-needed salbutamol. During the study, the mean number of inhalations of reliever per 24 hours was 0.73 in the beclometasone/formoterol group and 0.70 in the salbutamol group. Assuming that inhalers are used at the same dosage as in the study, the cost of using beclometasone/formoterol maintenance and reliever treatment is estimated to be £20.04 per 30 days compared with £14.82 per 30 days for beclometasone/formoterol plus as-needed salbutamol. Costs are based on the [NHS electronic Drug Tariff \(April 2013\)](#).

Estimated impact for the NHS

Likely place in therapy

It is not known how the efficacy and safety of beclometasone/formoterol ([Fostair](#)) directly compares with the established budesonide/formoterol ([Symbicort](#)) maintenance and reliever treatment. There are more published data available for budesonide/formoterol (Symbicort) for this indication. However, published data for beclometasone/formoterol for the maintenance treatment of asthma suggest that its efficacy and safety is similar to other ICS/LABA combination inhalers.

Assuming that inhalers are used at the same dosage as in the study, the cost of using beclometasone/formoterol maintenance and reliever treatment is estimated to be more than beclometasone/formoterol plus as-needed salbutamol but less than budesonide/formoterol.

The [British guideline on the management of asthma](#) advises that budesonide/formoterol ([Symbicort](#)) regular maintenance and reliever treatment is an option for selected adults at step 3 whose asthma is poorly controlled, or for selected adults at step 2 whose asthma is poorly controlled and who are taking more than 400 micrograms of BDP or equivalent per day.

The place in therapy of beclometasone/formoterol ([Fostair](#)) maintenance and reliever treatment is likely to be similar to that of budesonide/formoterol. Although there is little evidence to support its use in patients at step 2 of the [British guideline on the management of asthma](#), the study by [Papi et al. \(2013\)](#) suggests that beclometasone/formoterol may be an option for selected people whose asthma is poorly controlled at step 3 or 4, and who are able to use a pressurised metered dose

inhaler. Careful education of patients about this management strategy is required. Patients taking rescue ICS/LABA once a day or more on a regular basis should have their treatment reviewed.

Some people may prefer to follow the traditional steps of the [British guideline on the management of asthma](#). For those at step 3, this involves increasing the dose of ICS in their current maintenance treatment, rather than switching to maintenance and reliever treatment.

Maintenance and reliever treatment may not be suitable for people who overuse reliever therapy (because of the potential for inadvertent use of high doses of ICS), and planned step-down therapy after a period of good asthma control is less straightforward with combination inhalers. However, it is generally agreed that in clinical practice combination inhalers aid compliance.

When considering whether to use maintenance and reliever treatment, and which licensed product to use (Symbicort or Fostair), clinicians will need to take the patient's views into account. Changing existing asthma therapy to maintenance and reliever treatment may involve switching the ICS, switching the LABA, adjusting the dose, changing the inhaler device, or any combination of these, including all of them. Prescription charges may be an important issue for some people.

The beclometasone/formoterol combination in Fostair is delivered by a pressurised metered dose inhaler, whereas the budesonide/formoterol combination in Symbicort is delivered by a dry powder inhaler (Turbohaler). If both devices are suitable and acceptable to the person, the NICE technology appraisal guidance on [ICS for asthma](#) recommends the least costly option should be chosen. However, as stated previously, these 2 options have not been compared directly.

Fostair is available in only 1 fixed-dose combination, which potentially means there is less flexibility of dosing than with Symbicort. In addition, Fostair is stored in a refrigerator before dispensing and, after dispensing, only has a shelf-life of 5 months.

Estimated usage

It is difficult to provide estimated usage for maintenance and reliever treatment based on the available data. However, in the year to February 2013, almost 600 thousand items of Fostair were prescribed in primary care in England, at a cost of nearly £20.5 million. During the same period, over 3.2 million items of Symbicort were prescribed at a cost of almost £170 million. However, it is possible that some of this prescribing was for chronic obstructive pulmonary disease.

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For information about the process used to develop this evidence summary, see [Evidence summaries: new medicines – integrated process statement](#).

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