# The cost effectiveness of chlorofluorocarbon-free beclomethasone dipropionate in the treatment of chronic asthma: a cost model based on a 1-year pragmatic, randomised clinical study

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## Record Status

This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

## Health technology

The use of hydrofluoroalkane 134a-beclomethasone dipropionate (HFA-BDP) and chlorofluorocarbon-beclomethasone dipropionate (CFC-BDP) in the treatment of patients with chronic stable asthma.

## Type of intervention

Treatment.

## Economic study type

Cost-effectiveness analysis.

## Study population

The study population comprised patients older than 12 years of age, with chronic stable asthma. The inclusion criteria considered were:

forced expiratory volume in 1 second (FEV1) of at least 60% of that predicted after withholding inhaled beta-agonist for 6 hours;

the use of inhaled corticosteroids for at least 3 months preceding the study;

maintenance on a stable dose of CFC-BDP press and breathe, pressurised metered-dose inhaler, 400 to 1,600 microg/day for the 2 weeks preceding the study;

satisfactory use of a press and breathe, pressurised metered-dose inhaler;

an increase in FEV1 or morning peak expiratory flow of at least 15% following beta-agonist inhalation, or a course of inhaled or oral corticosteroids during the past 2 years, or a positive methacholine or histamine challenge;

a morning plasma cortisol concentration at pre-study visit within the normal range, or within 10% of the lower limit of the normal range.

Several exclusion criteria, consisting of clinical conditions or drug usage that would have interfered with the study therapies, were also considered and satisfactorily reported.

## Setting

The setting was primary care. The economic study was carried out in the UK.

## Dates to which data relate

The effectiveness and resource use data were derived from a study published in 2001. The price year was 1999.

### Source of effectiveness data
The effectiveness evidence was derived from a single study, the main details of which had been published elsewhere.

### Link between effectiveness and cost data
The costing was partially carried out on the same sample of patients as that used in the effectiveness study.

### Study sample
Limited information on the methods of sample selection was provided. The study sample comprised 473 eligible patients. There were 354 patients in the HFA-BDP group and 119 in the CFC-BDP group.

### Study design
This was a pragmatic, prospective, randomised, international clinical trial, which was carried out in 57 centres in the USA (24 sites), UK (18 sites), The Netherlands (8 sites) and Belgium (7 sites). The ratio of patients randomised to HFA-BDP to those allocated to CFC-BDP was 3:1. During a 14-day run-in period, all of the patients received their usual dose (400 to 1,600 microg/day) of CFC-BDP. After randomisation, patients received the same CFC-BDP dose at their currently daily dose, or HFA-BDP at approximately half of their current daily dose. Dose titration was permitted after the second month. The length of follow-up was one year, but the outcomes were assessed from baseline to the end of the study period, which was either months 10 to 12 or last observation carried forward (LOCF).

The 12-month assessment period was completed by 83.4% (n=296) of the patients in the HFA-BDP group and 83.2% (n=99) of those in the CFC-BDP group. In both groups, about 4% of patients withdrew after the month 7-to-8 assessment, and 13% after the month 1-to-2 assessment. The reasons for withdrawal were noncompliance, lost to follow-up and personal reasons. Data from these time points were used in the analysis, as LOCF.

### Analysis of effectiveness
The clinical analysis involved all patients, but the assessment used 12-month or LOCF data. The outcome measures used were the proportion of symptom-free days (SFDs) and health-related quality of life (HRQL). SFDs were defined as the absence of all of the following symptoms, that is, wheeze, cough, shortness of breath, and chest tightness in one day (including overnight). HRQL was estimated using the Asthma Quality of Life Questionnaire (AQLQ), a well-validated asthma-specific measure. Symptoms were recorded on a diary card, both in the run-in period and in months 1 to 2, 7 to 8, and 10 to 12. The symptoms were graded on a scale of 0 (no symptoms) to 5 (severe symptoms). The AQLQs were completed on the first day of the study and at the end of 2, 4, 8 and 12 months (or upon withdrawal). A change in score of 0.5 was considered clinically relevant. The net improvement in HRQL was calculated as the number of patients in each group with improved HRQL (score improved by >0.5) minus the number of those with worsened HRQL (score decreased by >0.5). The two groups were comparable at baseline in terms of asthma duration and severity. Compliance remained comparable throughout the study period.

### Effectiveness results
At baseline, the median percentage of SFDs was 21.4% (95% confidence interval, CI: 14.3 - 28.6) with HFA-BDP and 12.7% (95% CI: 6.7 - 28.6) with CFC-BDP, (p=0.226). However, at the end of the study (12 months or LOCF), the median percentage of SFDs was 42.4% (95% CI: 32.1 - 57.9) with HFA-BDP and 20% (95% CI: 3.8 - 37.9) with CFC-BDP, (p=0.006).

The corresponding mean values were 34% (95% CI: 30.4 - 37.6) with HFA-BDP and 30.4% (95% CI: 24.2 - 36.5) with CFC-BDP at baseline, and 45.6% (95% CI: 41.6 - 49.6) and 35% (95% CI: 28.2 - 41.8), respectively, at the end of the study (12 months or LOCF).

On average, there were 3 SFDs per week in the HFA-BDP group and 1.4 per week in the CFC-BDP group.

The proportion of patients with clinically significant net improvements in HRQL was 35.3% in the HFA-BDP group and 16.1% in the CFC-BDP group. The difference was statistically significant.

### Clinical conclusions
The effectiveness analysis showed that HFA-BDP was more effective than CFC-BDP in terms of both SFDs and improvements in quality of life.

### Measure of benefits used in the economic analysis
The summary benefit measures were the proportion of SFDs and improvements in HRQL. These were derived directly from the effectiveness analysis. Mean rather than median values were used.

### Direct costs
Discounting was not relevant since the costs per patient were incurred during a short time. The unit costs were presented separately from the average resource use data. The health services included in the economic evaluation were study drugs, other prescribed respiratory drugs, scheduled and unscheduled primary care visits, hospitalisation, and accident or emergency attendance. The cost/resource boundary of the health care provider was used. Resource use was estimated using from trial data and a number of assumptions, based mainly on current guidelines and UK recommendations. The costs came from the British National Formulary for drugs and from the Personal Social Services Research Unit for other items. The price year was 1999.

### Statistical analysis of costs
No statistical analyses were conducted to test the statistical significance of differences in the estimated costs. The costs were presented as mean values, despite a non-normal distribution.

### Indirect Costs
The indirect costs were not considered.

### Currency
UK pounds sterling ().

### Sensitivity analysis
To address the issue of variability in the data, six alternative scenarios were considered in the sensitivity analysis:

lower 95% CI estimate for SFDs with HFA-BDP and upper 95% CI estimate for SFDs with CFC-BDP (scenario 1);

upper 95% CI estimate for SFDs with HFA-BDP and lower 95% CI estimate for SFDs with CFC-BDP (scenario 2);

upper 95% CI estimate for total health care costs with HFA-BDP and lower 95% CI estimate for total health care costs with CFC-BDP (scenario 3);

lower 95% CI estimate for total health care costs with HFA-BDP and upper 95% CI estimate for total health care costs with CFC-BDP (scenario 4);

scenarios 1 and 3 combined (scenario 5); and

scenarios 2 and 4 combined (scenario 6).

Therefore, one- and two-way sensitivity analyses were conducted.

### Estimated benefits used in the economic analysis

The mean SFDs per patient per year was 166.31 with HFA-BDP and 127.78 with CFC-BDP. The difference was 38.53 days.

The number of patients with a net clinically significant improvement in HRQL was 116 out of 329 patients with HFA-BDP, and 18 out of 112 patients with CFC-BDP.

### Cost results

The average total costs per patient per year were 225.62 (95% CI: 210.15 - 241.08) with HFA-BDP and 231.07 (95% CI: 208.86 - 253.29) with CFC-BDP.

Drug costs accounted for about two thirds of the total costs.

### Synthesis of costs and benefits

The average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the two alternative treatment strategies.

The average cost per SFD per patient was 1.36 with HFA-BDP and 1.81 with CFC-BDP.

The incremental analysis revealed that HFA-BDP dominated CFC-BDP since the former was more effective and less costly. Similar results were achieved when only drug costs were considered.

The weekly cost to achieve a clinically significant improvement in HRQL was 13.24 with HFA-BDP and 29.38 with CFC-BDP.

As the costs were generally comparable, the advantage of HFA-BDP was generally due to the better efficacy and safety profile.

The results of the sensitivity analysis showed that HFA-BDP dominated CFC-BDP in three scenarios (2, 4, and 6). In addition, CFC-BDP dominated in scenario 5 (the worst case for HFA-BDP). CFC-BDP had an incremental cost per SFD gained of 6.20 in scenario 1, while HFA-BDP had an incremental cost per SFD gained of 0.84 in scenario 3.

Overall, the results favoured HFA-BDP, except in very unfavourable scenarios.

### Authors' conclusions

Hydrofluoroalkane 134a-beclomethasone dipropionate (HFA-BDP) was a cost-effective treatment for patients with chronic stable asthma in comparison with standard chlorofluorocarbon-beclomethasone dipropionate (CFC-BDP). The HFA-BDP patients showed improvements in both quality of life and symptom-free days at a cost comparable to that associated with CFC-BDP.

### CRD COMMENTARY - Selection of comparators

The authors stated that CFC-BDP represented a common therapy for patients with chronic stable asthma and that HFA-BDP had been launched in the UK market as a CFC-free alternative treatment. Therefore, a comparison between the two treatments was warranted. However, it should be noted that other CFC-free treatments were available, but were not considered in the analysis. You should decide whether they are valid comparators in your own setting.

### Validity of estimate of measure of effectiveness

The analysis of effectiveness was based on a randomised clinical trial, which was appropriate for the study question. Limited information on the design and methods of the trial were reported, as the study had been published elsewhere. Therefore, it was difficult to assess the robustness of the study although, from some of the details reported in the current paper, the internal validity of the analysis appears to have been high. The authors stated that a larger sample size

(leading to narrower CIs) would have been required to assess the statistical significance of differences between the two therapies in terms of cost-effectiveness. Very strict inclusion criteria were used to select the study sample, thus caution is needed when extrapolating the results of the analysis to patient populations different from that considered in the analysis (i.e. patients with poorly controlled asthma).

### Validity of estimate of measure of benefit

The summary benefit measures were derived directly from the effectiveness analysis and were specific to the disease considered in the study. Therefore, it would be difficult to compare them with the benefits of other health care interventions. However, the choice of the benefit measures appears to have been appropriate and was supported by a panel of experts.

### Validity of estimate of costs

The authors stated explicitly the perspective that was adopted in the study. As such, it appears that all the relevant categories of costs have been included in the analysis. Information on the cost analysis, such as the price year, unit costs, quantities of resources used, data source and use of assumptions, was satisfactorily reported. This enhances the possibility of replicating the cost analysis and conducting reflation exercises in other settings. Sensitivity analyses, in which the total costs were varied over reasonable ranges (CIs), were conducted to assess worst- and best-case scenarios. The arithmetic mean, as recommended for the economic evaluations of pragmatic trials, was used to present the costs, although this is a somewhat debatable issue given the skewed distribution of the costs. Overall, the cost analysis was well conducted.

### Other issues

The authors highlighted the difficulties in making comparisons with other studies assessing asthma therapies, owing to differences in the study populations, outcome measures and follow-up. In fact, it was stated that this was the first economic evaluation assessing both SFDs and HRQL simultaneously. However, even when considering some limitations in the comparisons, it appears that the cost-effectiveness ratio of HFA-BDP compared well with the cost-effectiveness estimates calculated in other studies. The issue of generalisability of the study results to other settings was addressed through the sensitivity analysis and HFA-BDP appears to have remained the most cost-effective strategy across several scenarios. The authors discussed the reasons for the choice of a pragmatic trial as the source of the efficacy evidence, and noted that this will reflect real-world treatment patterns.

### Implications of the study

The study results suggested that HFA-BDP has a high probability of being the most cost-effective strategy for treating patients with chronic stable asthma in the UK.

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### Bibliographic details

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### Other publications of related interest

Fireman P, Prenner BM, Vincken W, et al. Long-term safety and efficacy of a CFC-free beclomethasone dipropionate extrafine aerosol. Annals of Allergy, Asthma and Immunology 2001;86:557-65.

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