# Common Drug Review
## *Pharmacoeconomic Review Report*

**February 2016**

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|---|---|
| **Drug** | Fluticasone furoate/vilanterol (Breo Ellipta) |
| **Indication** | Once-daily maintenance treatment of asthma in patients aged 18 years and older with reversible obstructive airways disease |
| **Listing request** | As per indication |
| **Dosage form(s)** | Dry powder for oral inhalation, 100/25 and 200/25 mcg |
| **NOC date** | August 5, 2015 |
| **Manufacturer** | GlaxoSmithKline |

**Redactions:** Confidential information in this document has been redacted at the request of the manufacturer in accordance with the *CADTH Common Drug Review Confidentiality Guidelines.*

**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

# TABLE OF CONTENTS



**Tables**

# ABBREVIATIONS

| | |
|---|---|
| **BUD** | budesonide |
| **CDR** | CADTH Common Drug Review |
| **F** | formoterol fumarate |
| **FF** | fluticasone furoate |
| **$FEV_1$** | forced expiratory volume in one second |
| **FF** | fluticasone furoate |
| **FP** | fluticasone propionate |
| **ICS** | inhaled corticosteroid |
| **LABA** | long-acting beta2-agonist |
| **MOM** | mometasone furoate |
| **NMA** | network meta-analysis |
| **PBAC** | Pharmaceutical Benefits Advisory Committee |
| **SMC** | Scottish Medicines Consortium |
| **S** | salmeterol |
| **VI** | vilanterol |

# SUMMARY

## Background

Fluticasone furoate/vilanterol (FF/VI; Breo Ellipta) is a fixed-dose combination of an inhaled corticosteroid (ICS; FF) and a long-acting beta2-agonist (LABA; VI). It is indicated for once-daily maintenance treatment of asthma in patients aged 18 years and older with reversible obstructive airways disease.[1] The recommended dose is 100/25 mcg (FF/VI 100/25 mcg) or 200/25 mcg (FF/VI 200/25 mcg) once daily. It is available as a 30-dose inhaler providing dry powder for inhalation, at a confidential submitted price of $[redacted] per 100/25 mcg and $[redacted] per 200/25 mcg inhaler.[2] At the recommended daily dose, the cost of FF/VI 100/25 mcg is $[redacted] daily or $[redacted] annually per patient, and the cost of FF/VI 200/25 mcg is $[redacted] daily or [redacted] annually per patient.[2]

FF/VI is also indicated for the maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, and to reduce exacerbations of COPD in patients with a history of exacerbations.[1] The 100/25 mcg dose was previously reviewed for this indication and received a "list with clinical criteria" recommendation by the CADTH Canadian Drug Expert Committee (CDEC) in July 2014.[3]

## Summary of the Economic Analysis Submitted by the Manufacturer

The manufacturer submitted a cost analysis comparing the drug costs of FF/VI 100/25 mcg and FF/VI 200/25 mcg with ICS/LABA combination products currently available and indicated in Canada for the same population. These included budesonide/formoterol fumarate dihydrate (BUD/F), fluticasone propionate/salmeterol (FP/S), and mometasone furoate/formoterol fumarate dihydrate (MOM/F). (See Table 3 for details on strengths and dosages.[2]) In the manufacturer's base-case analysis, FF/VI 100/25 mcg was compared with a claims-based weighted average cost of low- and medium-dose available ICS/LABA combination therapies, and FF/VI 200/25 mcg was compared with a claim-weighted average cost of high-dose available ICS/LABA combination therapies.[2] Additionally, the manufacturer compared FF/VI overall to a claims-based weighted average cost of all ICS/LABA combination therapies (combining low, medium, and high doses), assuming that 75.8% of patients are treated with low to medium doses and 24.2% of patients are treated with high-dose ICS/LABA combination therapies.[2] Utilization data were obtained from IMS Rx Dynamics using an asthma diagnostic algorithm (data for Ontario from December 2013 to November 2014).

The analysis was conducted from the perspective of the publicly funded health care system, based on daily and one-year time horizons.[2] Only drug costs were considered; it was assumed that other resource use components were equal between comparators. Drug costs were obtained from the Ontario Drug Benefit Formulary (cited April 2015). All prices excluded mark-up and dispensing fees.

The assumption of similar efficacy and safety of FF/VI and other ICS/LABA combination products was based on direct trial evidence and a manufacturer-submitted network meta-analysis (NMA).[2] The manufacturer claimed that study HZA-091, a phase 3 randomized controlled trial (RCT), reported similar efficacy of FF/VI 100/25 mcg once daily to FP/S 250/50 mcg for the primary outcome of weighted mean serial forced expiratory volume in 1 second ($FEV_1$) over zero hours to 24 hours post-dose.[2] Additionally, the manufacturer's interpretation of the NMA — which compared FF/VI 100/25 mcg and FF/VI 200/25 mcg to FP/S, BUD/F, beclomethasone dipropionate/formoterol fumarate dihydrate (BDP/F), fluticasone propionate/formoterol fumarate dihydrate (FP/F), and MOM/F — was that FF/VI is similar to these comparators across the following outcomes: lung function (peak expiratory flow [PEF] and $FEV_1$), asthma

exacerbation rate, and health status (asthma quality of life questionnaire [AQLQ]).[2] The NMA did not assess comparative safety and tolerability.

### Key Limitations

- **Unclear clinical significance of FF/VI versus single-drug ICS**: Overall, FF/VI was determined to be statistically significantly superior to ICS monotherapy (FF 100 mcg, FF 200 mcg, FP 500 mcg) for the following outcomes: rate of asthma exacerbation and improvement in lung function ($FEV_1$ and PEF) (see CADTH Common Drug Review [CDR] Clinical Review report). However, as stated in the Clinical Review report, the overall evidence to support these findings may lack robustness, and there is uncertainty in their clinical significance. This leads to some uncertainty in the relative health economic benefit of adding a LABA to ICS monotherapy, and calls for prudence when doing so (as in this case), especially considering the higher price of combination therapies.
- **Uncertain comparative efficacy and safety of FF/VI versus other ICS/LABA combination therapies:** As noted in the CDR Clinical Review report, the study that compared FF/VI 100/25 mcg once daily to FP/S 250/50 mcg twice daily (HZA-091) was a superiority trial. The results from this study did not demonstrate statistical superiority of FF/VI to FP/S for its primary outcome, mean serial $FEV_1$ over zero hours to 24 hours post-dose at 24 weeks. In this context, care is needed when interpreting this evidence as showing equal efficacy. Additionally, the manufacturer-submitted NMA, from which the manufacturer assumed similar efficacy and safety of FF/VI to other ICS/LABA combination therapies, had a number of methodological and analytical limitations that hinder the ability to draw any firm conclusions (see CDR Clinical Review report). As such, the relative efficacy and safety of FF/VI versus other ICS/LABA combination therapies is unclear.
- **Limitations of using claims-based utilization data:** As noted previously, the manufacturer used claims-based (Ontario-specific) utilization data from IMS Rx Dynamics to calculate market shares for each of the ICS/LABA combination therapies and determine weighted average costs. There are limitations in this approach. First, there is uncertainty regarding how the database optimally differentiated between different respiratory conditions, especially given the range of doses that can be used for this condition. Secondly, as FF/VI is indicated in adults, and many of the combination therapies are also indicated in children and/or adolescents in addition to adults, it is not clear from the manufacturer's submission whether claims for children or adolescents were excluded in the calculation of the market shares. Finally, considering there are differences in the number of daily doses for the different ICS/LABA combination therapies and the number of doses per inhalant options, the percentage of claims is likely different from actual market shares for each combination therapy. Given the limitations in this case regarding using claims-based utilization data, it would be more appropriate to compare FF/VI with individual ICS/LABA combination therapies.
- **Inappropriate comparison of FF/VI 100/25 mcg to low-dose ICS/LABA combination therapies:** In the manufacturer's analysis, FF/VI 100/25 mcg was compared with low- and medium-dose ICS/LABA combination therapies. As indicated by the CDR clinical expert and noted in the cost comparison table (Table 1), FF/VI 100/25 mcg is considered to be of medium-dosage strength, and as such, should appropriately be compared with other medium-dose ICS/LABA combination therapies.

## Issues for Consideration

- As noted by the CDR clinical expert, compared with other ICS/LABA combination therapies, there is less flexibility when treating patients with FF/VI because there is no low-dose strength available, and it is dosed only once a day (as opposed to all other options). A lower dosage is often used as part of step-down therapy when patients respond well to higher dosages.
- In its submission, the manufacturer stated that FF/VI would have better treatment compliance because of once-daily dosing. However, FF/VI did not demonstrate better compliance versus other ICS/LABA combination therapies, as noted in the CDR Clinical Review report. Better treatment compliance may generally have a beneficial impact on the use of health care resources.
- The CDR clinical expert noted that there is potential for FF/VI to be misused in clinical practice. In general practice (compared with specialist care), where treatment for asthma is often prescribed, there is potential for FF/VI to be prescribed to patients for whom ICS monotherapies would be more appropriate (i.e., mild asthmatic patients). This would result in greater costs to public drug plans.

## Results and Conclusions

At a daily cost of $[redacted], FF/VI 100/25 mcg is less costly than other medium-dose ICS/LABA combination therapies ($2.80 to $3.25). Additionally, at a daily cost of $[redacted], FF/VI 200/25 mcg is less costly than all other high-dose ICS/LABA combination therapies ($3.62 to $5.59). However, the comparative cost-effectiveness of FF/VI versus the other ICS/LABA combination therapies cannot be fully assessed due to the clinical uncertainty in comparative efficacy and safety. Finally, the unclear clinical significance of FF/VI versus single-drug ICS leads to some uncertainty in the relative health economic benefit of adding a LABA to ICS monotherapy, and calls for prudence when doing so (as in this case), especially considering the higher price of combination therapies.

## Cost Comparison Table

The comparators presented in Table 1 have been deemed appropriate by clinical experts. Comparators may be recommended (appropriate) practice versus actual practice. Comparators are not restricted to drugs, but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified. Existing product listing agreements are not reflected in the table; as such, they may not represent the actual costs to public drug plans.

It should be noted that FF/VI (Breo Ellipta) is available only in medium- and high-dose strengths for the maintenance treatment of asthma in patients aged 18 years and older with reversible obstructive airways disease. Thus, the only relevant comparators for the purposes of this analysis are the medium- and high-dose strengths of these drugs. Low-dosage strengths were included for more information.

**TABLE 1: COST COMPARISON TABLE FOR THE MAINTENANCE TREATMENT OF ASTHMA IN PATIENTS AGED 18 YEARS AND OLDER — INHALED CORTICOSTEROID/LONG-ACTING BETA2-AGONIST COMBINATION THERAPIES**

| Drug/Comparator | Strength | Dosage Form | Price ($)[a] | Price/ Dose ($) | Recommended Daily Use[b] | | Daily Drug Cost ($) | Annual Drug Cost ($) |
|---|---|---|---|---|---|---|---|---|
| Fluticasone furoate/vilanterol (Breo Ellipta) | 100/25 mcg 200/25 mcg | Inhalant pwd (30 doses) | [redacted][c] | [redacted] | Low | NA | NA | NA |
| | | | | | Medium | 100/25 mcg, 1 inhalation once daily | [redacted] | [redacted] |
| | | | | | High | 200/25 mcg, 1 inhalation once daily | [redacted] | [redacted] |
| **ICS/LABA Combinations** | | | | | | | | |
| Budesonide/ formoterol fumarate dihydrate (Symbicort Turbuhaler) | 100/6 mcg 200/6 mcg | Inhalant pwd (120 doses) | 64.5600 83.8800 | 0.5380 0.6990 | Low | 100/6 mcg, 2 inhalations twice daily | 2.15 | 785.48 |
| | | | | | Medium | 200/6 mcg, 1 to 2 inhalations twice daily[d] | 1.40 to 2.80 | 510.27 to 1,020.54 |
| | | | | | High | 200/6 mcg, 4 inhalations twice daily[e] | 5.59 | 2,041.08 |
| Fluticasone propionate/ salmeterol (Advair) | 125/25 mcg 250/25 mcg | MDI (120 doses) | 97.4299 138.3141 | 0.8119 1.1526 | Low | 125/25 mcg, 1 inhalation twice daily | 1.62 | 592.70 |
| | | | | | Medium | 125/25 mcg, 2 inhalations twice daily | 3.25 | 1,185.40 |
| | | | | | High | 250/25 mcg, 2 inhalations twice daily | 4.61 | 1,682.82 |
| Fluticasone propionate/ salmeterol (Advair Diskus) | 100/50 mcg 250/50 mcg 500/50 mcg | Inhalant pwd (60 doses) | 81.3929 97.4299 138.3141 | 1.3565 1.6238 2.3052 | Low | 100/50 mcg, 1 inhalation twice daily | 2.71 | 990.28 |
| | | | | | Medium | 250/50 mcg, 1 inhalation twice daily | 3.25 | 1,185.40 |
| | | | | | High | 500/50 mcg, 1 inhalation twice daily | 4.61 | 1,682.82 |
| Mometasone furoate/ formoterol fumarate dihydrate (Zenhale) | 50/5 mcg 100/5 mcg 200/5 mcg | MDI (120 doses) | 70.5600 89.5560 108.5400 | 0.5880 0.7463 0.9045 | Low | 50/5 mcg, 2 inhalations twice daily | 2.35 | 858.48 |
| | | | | | Medium | 100/5 mcg, 2 inhalations twice daily | 2.99 | 1,089.60 |
| | | | | | High | 200/5 mcg, 2 inhalations twice daily | 3.62 | 1,320.57 |

ICS = inhaled corticosteroid; LABA = long-acting beta2-agonist; MDI = metered dose inhaler; NA = not applicable; pwd = powder.

[a] There is a small price difference between some of the public drug plans. However, this difference is negligible.

[b] The recommended daily use for the comparator agents was determined based on a combination of respective product monographs, the Canadian Thoracic Society guidelines (*Diagnosis and management of asthma in preschoolers, children and adults*, 2012),[5] and feedback from the clinical expert. FF/VI 100/25 mcg was determined to be equivalent to a medium-dosage strength, while FF/VI 200/25 mcg was determined to be equivalent to a high-dosage strength.[6]

[c] Manufacturer's confidential submitted price. Of note, the current list price of the 100/25 mcg formulation on the Ontario Drug Benefit Formulary is $120, or $4.00 per day.

[d] As indicated by the clinical expert, patients receiving the medium-dosage strength of the ICS/LABA budesonide/formoterol fumarate dihydrate would likely receive 200/6 mcg two inhalations twice daily; however, in certain situations, they may receive one inhalation twice daily.

[e] Will be given only to severe asthmatic patients, as mentioned by the clinical expert.

Source: Ontario Drug Benefit Formulary (accessed November 2015) unless otherwise indicated.[4]

# APPENDIX 1: REVIEW OF OTHER HEALTH TECHNOLOGY ASSESSMENT AGENCY REPORTS

Three technology appraisals were identified that assessed the fluticasone furoate/vilanterol (FF/VI) combination therapy. These included appraisals from the Scottish Medicines Consortium (SMC, Scotland), the Pharmaceutical Benefits Advisory Committee (PBAC, Australia), and the Pharmaceutical Management Agency (PHARMAC, New Zealand).[7-9]

The appraisal by the SMC was based on a cost-minimization analysis submitted by the manufacturer, which compared FF/VI 92/22 mcg and FF/VI 182/22 mcg to fluticasone propionate/salmeterol (FP/S), budesonide/formoterol fumarate dihydrate (BUD/F), fluticasone propionate/ formoterol fumarate dihydrate (FP/F), and beclomethasone dipropionate/ formoterol fumarate dihydrate (BDP/F) for the regular treatment of asthma in adults and adolescents aged 12 years and older where the use of a combination medicinal product (inhaled corticosteroid [ICS] with long-acting beta2-agonist [LABA]) is appropriate in patients not adequately controlled with ICS and "as needed" inhaled short-acting beta2-agonists. Equal efficacy was assumed primarily on the basis of a manufacturer-submitted mixed treatment comparison (MTC) that assessed the probability of non-inferiority of FF/VI versus each of the comparators. The SMC identified some minor limitations with the indirect evidence; however, overall it considered the MTC to be acceptable. Only drug costs were included in the analysis. The results indicated that FF/VI 92/22 mcg is cost saving versus low- or medium-dose FP/S and BUD/F (costs savings of £18 to £96 per patient per year) and high-dose FP/S and BUD/F (costs savings of £25 to £452 per patient, per year). SMC accepted the use of FF/VI within the National Health Service Scotland.[7]

The PBAC appraisal was also based on a cost-minimization analysis submitted by the manufacturer, which compared FF/VI 100/25 mcg and FF/VI 200/25 mcg to FP/S for the same indication noted in the SMC review. Equal efficacy was assumed on the basis of one head-to-head randomized controlled trial (RCT) that compared FF/VI 100/25 mcg once daily to FP/S 250/50 mcg twice daily and an indirect comparison that compared FF/VI 200/25 mcg once daily to FP/S 500/50 mcg twice daily. PBAC noted that the results from the direct trial were reliable and applicable to the specific population. Additionally, they noted that there were some concerns with the indirect comparison, but that on the basis of all the evidence presented, non-inferiority between the higher strengths was established. The manufacturer's submission used a market- based approach assuming that FF/VI will substitute market shares from FP/S and BUD/F. From this, the manufacturer proposed that FF/VI was cost savings. No costs were publicly available. PBAC recommended that FF/VI 100/25 mcg and 200/25 mcg be listed.[8]

No details on the economic analysis submitted to PHARMAC were available publicly. The committee noted that it considered there to be no difference in effectiveness between FF/VI and FP/S, an opinion that aligned with the manufacturer's submission. The committee recommended listing FF/VI 100/25 mcg on the pharmaceutical schedule with a low priority; however, it declined the listing of FF/VI 200/25 mcg.[9]

# APPENDIX 2: REVIEWER WORKSHEETS

## Manufacturer Submission

### TABLE 2: SUMMARY OF MANUFACTURER'S SUBMISSION

| | |
|---|---|
| **Drug Product** | Fluticasone furoate/vilanterol (Breo Ellipta) 100/25 mcg and 200/25 mcg dry powder for inhalation |
| **Treatment** | 100/25 mcg or 200/25 mcg once daily |
| **Comparators** | Low to medium dose:<br>• FP/S 100/50 mcg (1 inhalation twice daily)<br>• FP/S 250/50 mcg (1 inhalation twice daily)<br>• FP/S 125/25 mcg (2 inhalations twice daily)<br>• BUD/F 100/6 mcg (2 inhalations twice daily)<br>• BUD/F 200/6 mcg (2 inhalations twice daily)<br>• MOM/F 50/5 mcg (2 inhalations twice daily)<br>• MOM/F 100/5 mcg (2 inhalations twice daily)<br>High dose:<br>• FP/S 500/50 mcg (1 inhalation twice daily)<br>• FP/S 250/25 mcg (2 inhalations twice daily)<br>• MOM/F 200/5 mcg (2 inhalations twice daily) |
| **Study question** | From the manufacturer's submission:<br>1) "Does the pharmacoeconomic value of FF/VI 100/25 mcg and 200/25 mcg differ from that of usual care with ICS/LABA fixed-dose combination therapy?"<br>2) "Does the pharmacoeconomic value of FF/VI 100/25 mcg, a low- to medium-dose, once-daily ICS LABA, differ from that of usual care with low- and medium-dose ICS/LABA fixed-dose combination therapy?"<br>3) "Does the pharmacoeconomic value of FF/VI 200/25 mcg, a high-dose, once-daily ICS LABA, differ from that of usual care with high-dose ICS/LABA fixed-dose combination therapy?" |
| **Type of economic evaluation** | Cost comparison (drug costs only) |
| **Target population** | Patients aged 18 years and older with asthma who require regular maintenance treatment with an ICS/LABA combination |
| **Perspective** | Publicly funded health care system |
| **Outcomes considered (in the NMA)** | • Lung function (PEF and $FEV_1$)<br>• Asthma exacerbation rate<br>• Health status as measured by the AQLQ |
| **Key data sources** | |
| **Cost** | Ontario Drug Benefit Formulary (April 2015) |
| **Market share** | IMS Brogan Rx Dynamics (December 2013 to November 2014) |
| **Clinical efficacy** | To assess the comparative efficacy and safety of FF/VI versus other ICS/LABA combination options:<br>Manufacturer conducted clinical trials: HZA-091<br>Manufacturer-submitted indirect comparison |
| **Harms** | Not considered |
| **Time horizon** | Daily and one year |
| **Results for base case** | • FF/VI 100/25 mcg resulted in cost savings of $[redacted] per patient daily (or $[redacted] annually) versus a claims-based weighted average cost of low- to medium-dose ICS/LABA combination therapies. |

| | |
|---|---|
| | • FF/VI 200/25 mcg resulted in cost savings of $[redacted] per patient daily (or $[redacted] annually) versus a claims-based weighted average cost of high-dose ICS/LABA combination therapies.<br>• Overall, FF/VI resulted in a cost savings of $[redacted] per patient daily (or $[redacted] annually) versus a claims-based weighted average cost of ICS/LABA comparators (assuming 75.8% of patients are treated with low to medium dose and 24.2% of patients are treated with high-dose ICS/LABA combination therapies).<br>See Table 3 for more details on the manufacturer's analysis. |
| **Results from the sensitivity analysis** | The manufacturer also conducted various scenario analyses. These included the following:<br>1) Alternate source for the utilization data (Canadian Disease and Therapeutic Index, 2014)<br>2) Assuming FP/S is the main comparator<br>3) Assuming BUD/F is the main comparator<br>4) Addition of higher dosages for MOM/F 200/5 mcg (two inhalations twice daily as a medium dose) and BUD/F 200/6 mcg (four inhalations twice daily as a high dose)<br>5) The use of open duals (i.e., the use of ICS and LABA products in separate inhaler devices)<br>The results did not differ from the base-case analysis. FF/VI 100/25 mcg and 200/25 mcg still produced cost savings. |

AQLQ = Asthma Quality of Life Questionnaire; BUD = budesonide formoterol; $FEV_1$ = forced expiratory volume in 1 second; F = formoterol fumarate dihydrate; FF = fluticasone furoate; FP = fluticasone propionate; ICS = inhaled corticosteroid; LABA = long-acting beta2-agonist; MOM = mometasone furoate; NMA = network meta-analysis; PEF = peak expiratory flow; S = salmeterol; VI = vilanterol.

The manufacturer's base-case results summarized in Table 2 are shown in more detail in Table 3.

**TABLE 3: MANUFACTURER'S BASE-CASE ANALYSIS RESULTS**

| Drug/ Comparator | Strength, Dosage | Total Daily Dose | Daily Cost ($) | Incremental Cost, Daily ($) | Annual Cost[a] ($) | Incremental Cost, Annual[a] ($) | Utilization |
|---|---|---|---|---|---|---|---|
| Low to medium dose | | | | | | | |
| **Fluticasone furoate/vilanterol (Breo Ellipta)** | **100/25 mcg, 1 inhalation** | **100/25 mcg** | [redacted] | **Reference** | [redacted] | **Reference** | **100.0%** |
| Budesonide/ formoterol fumarate dihydrate (Symbicort Turbuhaler) | 100/6 mcg, 2 inhalations twice daily[b] | 400/24 mcg | 2.15 | [redacted] | 785.48 | [redacted] | 2.7% |
| | 200/6 mcg, 2 inhalations twice daily[c] | 800/24 mcg | 2.80 | [redacted] | 1,020.54 | [redacted] | 55.0% |
| Fluticasone propionate/salmeterol (Advair) | 125/25 mcg, 2 inhalations twice daily[c] | 500/100 mcg | 3.25 | [redacted] | 1,185.40 | [redacted] | 7.7% |
| Fluticasone propionate/salmeterol (Advair Diskus) | 100/50 mcg, 1 inhalation twice daily[b] | 200/100 mcg | 2.71 | [redacted] | 990.28 | [redacted] | 1.3% |
| | 250/50 mcg, 1 inhalation twice daily[c] | 500/100 mcg | 3.25 | [redacted] | 1,185.40 | [redacted] | 29.5% |
| Mometasone furoate/ | 50/5 mcg, 2 | 200/20 mcg | 2.35 | [redacted] | 858.48 | [redacted] | 0.1% |

| Drug/ Comparator | Strength, Dosage | Total Daily Dose | Daily Cost ($) | Incremental Cost, Daily ($) | Annual Cost[a] ($) | Incremental Cost, Annual[a] ($) | Utilization |
|---|---|---|---|---|---|---|---|
| formoterol fumarate dihydrate | inhalations twice daily[b] | | | | | | |
| | 100/5 mcg, 2 inhalations twice daily[c] | 400/20 mcg | 2.99 | [redacted] | 1,089.60 | [redacted] | 3.7% |
| Utilization-weighted comparison | | | 2.95 | [redacted] | 1,077.52 | [redacted] | |
| High dose[d] | | | | | | | |
| **Fluticasone furoate/vilanterol (Breo Ellipta)** | **200/25 mcg, 1 inhalation** | **200/25 mcg** | [redacted] | **Reference** | [redacted] | **Reference** | **100.0%** |
| Fluticasone propionate/salmeterol (Advair) | 250/25 mcg, 2 inhalations twice daily | 1,000/100 mcg | 4.61 | [redacted] | 1,682.82 | [redacted] | 55.3% |
| Fluticasone propionate/salmeterol (Advair Diskus) | 500/50 mcg, 1 inhalation twice daily | 1,000/100 mcg | 4.61 | [redacted] | 1,682.82 | [redacted] | 31.5% |
| Mometasone furoate/ formoterol fumarate dihydrate | 200/5 mcg, 2 inhalations twice daily | 800/20 mcg | 3.62 | [redacted] | 1,320.57 | [redacted] | 13.2% |
| Utilization-weighted comparison | | | 4.48 | [redacted] | 1,635.00 | [redacted] | |
| Net utilization-weighted comparison[d] | | | 3.32 | [redacted] | 1,212.43 | [redacted] | |

CDR = CADTH Common Drug Review; ICS = inhaled corticosteroid; LABA = long-acting beta2-agonist.
[a] Note that CDR recalculated the total and incremental costs in order to align with the manufacturer's base-case analysis. It was determined that several of the costs were slightly off due to differences in rounding.
[b] Low-dose strength.
[c] Medium-dose strength.
[d] The manufacturer assumed that 75.8% of patients use a low to medium dose and 24.2% of patients use a high dose (based on claims-based data).
Source: Adapted from the manufacturer's pharmacoeconomic submission.[2]

## CADTH Common Drug Review Results

CDR compared fluticasone furoate/vilanterol (FF/VI) to other inhaled corticosteroid/long-acting beta2-agonist (ICS/LABA) combination therapies by dose level, reported as total costs per patient per year (Table 4). When comparing medium-dose ICS/LABA combination therapies, FF/VI 100/25 mcg is less costly than fluticasone propionate/salmeterol (FP/S) 125/25 mcg, FP/S 250/50 mcg, and mometasone furoate/formoterol fumarate dihydrate (MOM/F) 100/5 mcg (costs savings ranging from $[redacted]-$[redacted]). [redacted] When comparing high-dose ICS/LABA combination therapies, FF/VI 200/25 mcg is less costly than budesonide/formoterol fumarate dihydrate (BUD/F) 200/6 mcg, FP/S 250/25 mcg, FP/S 500/50 mcg, and MOM/F 200/5 mcg (costs savings ranging from $[redacted]-$[redacted]).

**TABLE 4: CADTH COMMON DRUG REVIEW COST COMPARISON ANALYSIS**

| Drug/Comparator | Strength, Dosage | Total Daily Dose | Daily Drug Cost ($) | Annual Drug Cost ($) | Incremental Cost ($) |
|---|---|---|---|---|---|
| **Medium-dose ICS/LABA combination therapies** | | | | | |
| **Fluticasone furoate/vilanterol (Breo Ellipta)** | **100/25 mcg, 1 inhalation once daily** | **100/25 mcg** | [redacted] | [redacted] | **Reference** |
| Budesonide/formoterol fumarate dihydrate (Symbicort Turbuhaler) | 200/6 mcg, 1 inhalation twice daily | 400/12 mcg | 1.40 | 510.27 | [redacted] |
| | 200/6 mcg, 2 inhalations twice daily | 800/24 mcg | 2.80 | 1,020.54 | [redacted] |
| Fluticasone propionate/ salmeterol (Advair) | 125/25 mcg, 2 inhalations twice daily | 500/100 mcg | 3.25 | 1,185.40 | [redacted] |
| Fluticasone propionate/ salmeterol (Advair Diskus) | 250/50 mcg, 1 inhalation twice daily | 500/100 mcg | 3.25 | 1,185.40 | [redacted] |
| Mometasone furoate/ formoterol fumarate dihydrate | 100/5 mcg, 2 inhalations twice daily | 400/20 mcg | 2.99 | 1,089.60 | [redacted] |
| **High-dose ICS/LABA combination therapies** | | | | | |
| **Fluticasone furoate/vilanterol (Breo Ellipta)** | **200/25 mcg, 1 inhalation once daily** | **200/25 mcg** | [redacted] | [redacted] | **Reference** |
| Budesonide/formoterol fumarate dihydrate (Symbicort Turbuhaler) | 200/6 mcg, 4 inhalations twice daily | 1,600/48 mcg | 5.59 | 2,041.08 | [redacted] |
| Fluticasone propionate/ salmeterol (Advair) | 250/25 mcg, 2 inhalations twice daily | 1,000/100 mcg | 4.61 | 1,682.82 | [redacted] |
| Fluticasone propionate/ salmeterol (Advair Diskus) | 500/50 mcg, 1 inhalation twice daily | 100/100 mcg | 4.61 | 1,682.82 | [redacted] |
| Mometasone furoate/ formoterol fumarate dihydrate | 200/5 mcg, 2 inhalations twice daily | 800/20 mcg | 3.62 | 1,320.57 | [redacted] |

ICS = inhaled corticosteroid; LABA = long-acting beta2-agonist.

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