

## Product Summary for *Breo Ellipta*

This information is provided in response to your request for information about Breo® Ellipta™ (fluticasone furoate/vilanterol 100 mcg/25 mcg).

### DISEASE BACKGROUND

- For patients with chronic obstructive lung disease (COPD), the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) committee recommends an inhaled corticosteroid (ICS) plus a long-acting beta<sub>2</sub>-adrenergic agonist (LABA) as a first choice therapy for patients with severe airflow limitation, frequent exacerbations (≥2 exacerbations/year), and/or 1 or more COPD-related hospitalization.<sup>(1)</sup>

### DESCRIPTION

- Breo Ellipta* is a new, once-daily, combination ICS/LABA delivered from a dry powder breath-actuated device. The dry powder inhaler contains two double-foil blister strips of powder formulation for oral inhalation, one strip containing fluticasone furoate 100 mcg per blister and the other containing vilanterol 25 mcg per blister.<sup>(2)</sup>

### INDICATION

- Breo Ellipta* is a combination ICS/LABA indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema. *Breo Ellipta* is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations.<sup>(2)</sup>
- Important Limitations of Use: *Breo Ellipta* is NOT indicated for the relief of acute bronchospasm or for the treatment of asthma.

### DOSING

- Breo Ellipta* 100/25 mcg should be administered as 1 inhalation once daily by the orally inhaled route only. After inhalation, the patient should rinse his/her mouth with water without swallowing to help reduce the risk of oropharyngeal candidiasis.<sup>(2)</sup>
- Breo Ellipta* should be taken at the same time every day. Do not use *Breo Ellipta* more than 1 time every 24 hours.

### BOXED WARNING

- WARNING: ASTHMA-RELATED DEATH:** Long-acting beta<sub>2</sub>-adrenergic agonists (LABA) increase the risk of asthma-related death. Data from a large placebo-controlled US trial that compared the safety of another LABA (salmeterol) with placebo added to usual asthma therapy showed an increase in asthma-related deaths in subjects receiving salmeterol. This finding with salmeterol is considered a class effect of LABA, including vilanterol, an active ingredient in *Breo Ellipta* [see Warnings and Precautions (5.1)].<sup>(2)</sup>
- The safety and efficacy of *Breo Ellipta* in patients with asthma have not been established. *Breo Ellipta* is not indicated for the treatment of asthma.

### EFFICACY DATA

- Two 24-week, randomized, double-blind, placebo-controlled trials (N=2,254) assessed different strengths of fluticasone furoate/vilanterol (FF/VI) in improving lung function as measured by weighted mean forced expiratory volume in one second (FEV<sub>1</sub>) (0-4 hour) on day 168 and change from baseline in trough FEV<sub>1</sub> on day 169.<sup>(3,4)</sup>
- In the first trial the FF/VI doses tested were 100/25 mcg and 200/25 mcg. The difference in the weighted mean FEV<sub>1</sub> (0-4 hours) between FF/VI 100/25 mcg and placebo was 214 mL (95% CI: 161, 266) and between FF/VI 100/25 mcg and FF 100 mcg was 168 mL (95% CI: 116, 220).<sup>(4)</sup> The difference between FF/VI 100/25 mcg and VI 25 mcg for the change from baseline in trough FEV<sub>1</sub> was 45 mL (95% CI: -8, 97). In this trial, the statistical significance of the primary endpoints for FF/VI 100/25 mcg could not be inferred because of the pre-specified statistical hierarchy that was imposed to account for the multiple statistical tests that were conducted across treatment comparisons and endpoints.
- In the second trial, the FF/VI doses tested were 100/25 mcg and 50/25 mcg. FF/VI 100/25 mcg significantly improved weighted mean FEV<sub>1</sub> (0-4 hours) compared to placebo (difference of 173 mL [95% CI: 123, 224 mL], *P* < 0.001) and compared with FF 100 mcg (difference of 120 mL [95% CI: 70, 170], *P* < 0.001); however no significant difference was seen between FF/VI 100/25 mcg and VI 25 mcg in trough FEV<sub>1</sub> (48 mL [95% CI: -6, 102 mL], *P* = 0.082).<sup>(3)</sup>
- Two 52-week, randomized, double-blind, controlled trials assessed the efficacy of 3 different strengths of FF/VI (50/25 mcg, 100/25 mcg, and 200/25 mcg) measured by the annual rate of moderate/severe exacerbations in 3,255 patients with COPD.<sup>(5)</sup> The difference in annual rate of moderate/severe exacerbations in FF/VI 100/25 mcg compared to VI 25 mcg was statistically significant in the first trial (21% reduction, [95% CI: 3, 36], *P* = 0.024), but statistical significance in the second trial (34% reduction [95% CI: 19, 46]) could not be inferred because of the pre-specified statistical hierarchy that was imposed to account for the multiple statistical tests that were conducted across treatment comparisons and endpoints.

### CONTRAINDICATIONS

- The use of *Breo Ellipta* is contraindicated in patients with severe hypersensitivity to milk proteins or who have demonstrated hypersensitivity to either fluticasone furoate, vilanterol, or any of the excipients.<sup>(2)</sup>

### WARNINGS AND PRECAUTIONS

- LABA increase the risk of asthma-related death.<sup>(2)</sup>
- Breo Ellipta* should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD. *Breo Ellipta* should not be used for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm.
- Breo Ellipta* should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medications containing LABAs, as an overdose may result.
- In clinical trials, the development of localized infections of the mouth and pharynx with *Candida albicans* has occurred in subjects treated with *Breo Ellipta*. Patients should be advised to rinse his/her mouth without swallowing following inhalation to help reduce the risk of oropharyngeal candidiasis.
- An increase in the incidence of pneumonia has been observed in patients with COPD receiving FF/VI in clinical trials. In replicate 12-month trials in subjects with COPD, the incidence of pneumonia was 6% with FF/VI 50/25 mcg, 6% with 100/25 mcg, and 7% with 200/25 mcg. There was a fatal pneumonia in 1 subject receiving FF/VI 100/25 mcg and in 7 subjects receiving FF/VI 200/25 mcg (less

than 1% for each treatment group). Physicians should remain vigilant for the possible development of pneumonia in patients with COPD, as the clinical features of such infections overlap with the symptoms of COPD exacerbations.

- Persons who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals. More serious or even fatal course of chickenpox or measles can occur in susceptible patients. Inhaled corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract; systemic fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex.
- Deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids. Taper patients slowly from systemic corticosteroids if transferring to *Breo Ellipta*.
- Hypercorticism and adrenal suppression may occur with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue *Breo Ellipta* slowly.
- If paradoxical bronchospasm occurs, discontinue *Breo Ellipta* and institute alternative therapy.
- Vilanterol, like other beta<sub>2</sub>-agonists, can produce a clinically significant cardiovascular effect in some patients. If such effects occur, *Breo Ellipta* may need to be discontinued. Use *Breo Ellipta* with caution in patients with cardiovascular disorders because of beta-adrenergic stimulation.
- Decreases in bone mineral density (BMD) have been observed with long-term administration of products containing ICS. In replicate 12-month trials in subjects with COPD, bone fractures were reported by 2% of subjects receiving FF/VI 50/25 mcg, 100/25 mcg, and 200/25 mcg compared with <1% of subjects receiving vilanterol 25 mcg alone. Assessment of BMD is recommended prior to initiating *Breo Ellipta* and periodically thereafter.
- Glaucoma, increased intraocular pressure, and cataracts have been reported in patients with COPD following the long-term administration of ICS. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma, and/or cataracts. In replicate 12-month trials in subjects with COPD, similar incidences of ocular effects (including glaucoma and cataracts) were reported in subjects receiving the fluticasone furoate/vilanterol combination as those receiving vilanterol 25 mcg alone.
- Use with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, and ketoacidosis.
- Be alert to hypokalemia and hyperglycemia.
- The most common adverse reactions (≥3% and more common than placebo) reported in two 6-month clinical trials with *Breo Ellipta* (and placebo) were nasopharyngitis, 9% (8%); upper respiratory tract infection, 7% (3%); headache, 7% (5%); and oral candidiasis, 5% (2%).

**Please refer to the Prescribing Information and Medication Guide for *Breo Ellipta*.**

**This information is provided in response to your request. GSK requests that the recipient of this information only share the contents with the Pharmacy & Therapeutics (P & T) Committee members for the purposes of making evidence-based decisions regarding formulary inclusion.**

#### REFERENCE(S)

1. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2014. Available from <http://www.goldcopd.org>. Accessed January 28, 2014. \*
2. GlaxoSmithKline Local Label. \*
3. Kerwin EM, Scott-Wilson C, Sanford L, et al. A randomised trial of fluticasone furoate/vilanterol (50/25 µg; 100/25 µg) on lung function in COPD. *Respir Med* 2013;107:560–569.\*
4. Martinez FJ, Boscia J, Feldman G, et al. Fluticasone furoate/vilanterol (100/25; 200/25 µg) improves lung function in COPD: A randomised trial. *Respir Med* 2013;107:550–559.\*
5. Dransfield MT, Bourbeau J, Jones PW, et al. Once-daily fluticasone furoate and vilanterol versus vilanterol only for prevention of exacerbations of COPD: two replicate double-blind, parallel-group, randomised controlled trials. *Lancet Respir Med* 2013;1:210–223.\*