

COPD maintenance with dosing both day and night

## BREZTRI AEROSPHERE: TWICE-DAILY ADMINISTRATION WITH A SINGLE pMDI DEVICE<sup>1</sup>

 **2** inhalations  
in the morning +  **2** inhalations  
in the evening

## PHARMACODYNAMICS: BREZTRI AEROSPHERE ACHIEVED RAPID ONSET OF ACTION<sup>1\*</sup>



Improvement in FEV<sub>1</sub> within 5 minutes of the first dose on Day 1 (median time to  $\geq 100$  mL)



\* Clinical significance has not been established.

Please see the Product Monograph for full dosing information.

COPD: chronic obstructive pulmonary disease; FEV<sub>1</sub>: forced expiratory volume in 1 second; pMDI: pressurized metered-dose inhaler.

## CHOOSE BREZTRI AEROSPHERE FOR YOUR COPD PATIENTS: DEMONSTRATED POWERFUL EFFICACY AND SAFETY<sup>1</sup>

BREZTRI AEROSPHERE offers:



Demonstrated reduction in moderate and severe COPD exacerbations, regardless of patients' recent exacerbation history



Significant improvements observed in quality of life and breathlessness



Demonstrated consistent safety profile with the known pharmacologic class effects of ICSs, LAMAs, and/or LABAs

### Clinical use:

BREZTRI AEROSPHERE is not indicated for:

- Treatment of acute episodes of bronchospasm or asthma.
- Use in pediatric patients <18 years of age.

### Relevant warnings & precautions:

- Risk of serious asthma-related events, including hospitalization, intubations, and death
- Should not be used in patients with deteriorating COPD
- Excessive use with other LAMA and LABA products
- Anticholinergic activity: Use with caution in patients with symptomatic prostatic hyperplasia, urinary retention, or narrow-angle glaucoma
- Cardiovascular effects, including arrhythmias, and changes in pulse and blood pressure, or QTc prolongation
- Driving and operating machinery
- Candidiasis
- Risk of systemic effects, including Cushing's syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, hypokalemia and hyperglycemia, cataract, intraocular pressure, and glaucoma

**References:** 1. BREZTRI AEROSPHERE Product Monograph. AstraZeneca Canada Inc. 2. Ferguson GT, et al. Triple therapy with budesonide / glycopyrrolate / formoterol fumarate with co-suspension delivery technology versus dual therapies in chronic obstructive pulmonary disease (KRONOS): a double-blind, parallel-group, multicentre, phase 3 randomised controlled trial. *Lancet Respir Med.* 2018(6):747-758. 3. Rabe KF, et al. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. *NEJM.* 2020;383(1):35-48. 4. AstraZeneca Canada Inc. *Data on file - ETHOS trial Table 2.14.1.* 2022. 5. Rabe KF, et al. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD - Supplementary Appendix. *NEJM.* 2020;383(1):35-48. 6. Martinez FJ, et al. Benefits of budesonide/glycopyrrolate/formoterol fumarate (BGF) on symptoms and quality of life in patients with COPD in the ETHOS trial. *Respir Med.* 185(106509). 7. Chronic Obstructive Pulmonary Disease: Use of the St. George's Respiratory Questionnaire as a PRO Assessment Tool. Food and Drug Administration. March 2018. Available at: [www.fda.gov/files/drugs/published/Chronic-Obstructive-Pulmonary-Disease--Use-of-the-St.-George%E2%80%99s-Respiratory-Questionnaire-as-a-PRO-Assessment-Tool-Guidance-for-Industry.pdf](http://www.fda.gov/files/drugs/published/Chronic-Obstructive-Pulmonary-Disease--Use-of-the-St.-George%E2%80%99s-Respiratory-Questionnaire-as-a-PRO-Assessment-Tool-Guidance-for-Industry.pdf). Retrieved November 30, 2023.

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## CHOOSE BREZTRI<sup>®</sup> AEROSPHERE<sup>®</sup> FOR ITS POWER TO REDUCE EXACERBATIONS IN COPD<sup>1</sup>



## BUDESONIDE (ICS), GLYCOPYRRONIUM (LAMA), AND FORMOTEROL (LABA) IN 1 pMDI DEVICE<sup>1</sup>

BREZTRI AEROSPHERE is indicated for the long-term maintenance treatment to reduce exacerbations of COPD and treat airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema, who are not adequately treated by a combination of an ICS/LABA or a combination of LAMA/LABA.<sup>1</sup>

\* Clinical significance has not been established.

COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; LABA: long-acting beta<sub>2</sub>-adrenergic agonist; LAMA: long-acting muscarinic antagonist; pMDI: pressurized metered-dose inhaler.



## CHOOSE POWERFUL DEMONSTRATED EFFICACY AGAINST MODERATE TO SEVERE COPD EXACERBATIONS (INCLUDING THOSE RESULTING IN HOSPITALIZATIONS OR DEATH)<sup>1</sup>

### KRONOS\*



Reduction in rate of **MODERATE OR SEVERE EXACERBATIONS<sup>†</sup>** vs. a LAMA/LABA (GFF MDI)

0.46 vs. 0.95, respectively (HR: 0.48; 95% CI: 0.37, 0.64;  $p < 0.0001$ ; 2° endpoint)<sup>1</sup>

**18% numerical reduction in rate of moderate or severe exacerbations vs. an ICS/LABA (BFF MDI) (HR: 0.82; 95% CI: 0.58, 1.17;  $p = 0.2792$ )<sup>1,2</sup>**

### ETHOS<sup>‡</sup>



Reduction in rate of **SEVERE EXACERBATIONS (resulting in hospitalization or death)** vs. an ICS/LABA (BFF MDI)

0.13 vs. 0.16 respectively (HR: 0.80; 95% CI: 0.66, 0.97;  $p = 0.0221$ )<sup>1,3†</sup>

**16% numerical reduction in rate of severe exacerbations vs. a LAMA/LABA (GFF MDI) (HR: 0.84; 95% CI: 0.69, 1.03;  $p = 0.0944$ )<sup>1</sup>**

\* KRONOS: 24-week randomized, double-blind, multi-centre, chronic-dosing, parallel-group study in 1,896 patients with moderate to very severe COPD with or without exacerbations in the year prior to screening. Patients were allocated BREZTRI AEROSPHERE (320/14.4/10 mcg), GFF MDI (14.4/10 mcg), BFF MDI (320/10 mcg), or open-label budesonide/formoterol fumarate dihydrate dry powder for inhalation (400/12 mcg), all administered twice daily. The two primary endpoints were FEV<sub>1</sub> area under the curve from 0-4 hours and change from baseline in morning pre-dose trough FEV<sub>1</sub> over 24 weeks.

† Moderate exacerbation was defined as: treatment with systemic corticosteroids and/or antibiotics for 3 or more days required. Severe exacerbation was defined as: resulting in hospitalization or death.

‡ ETHOS: 52-week randomized, double-blind, multi-centre, parallel-group study in 8,509 patients with moderate to very severe COPD with a history of 1 or more moderate or severe COPD exacerbation(s) in the year prior to screening. Patients were allocated BREZTRI AEROSPHERE (320/14.4/10 mcg), BGF MDI (160/14.4/10 mcg), GFF MDI (14.4/10 mcg), or BFF MDI (320/10 mcg), all administered twice daily. The primary endpoint was the rate of moderate or severe COPD exacerbations.

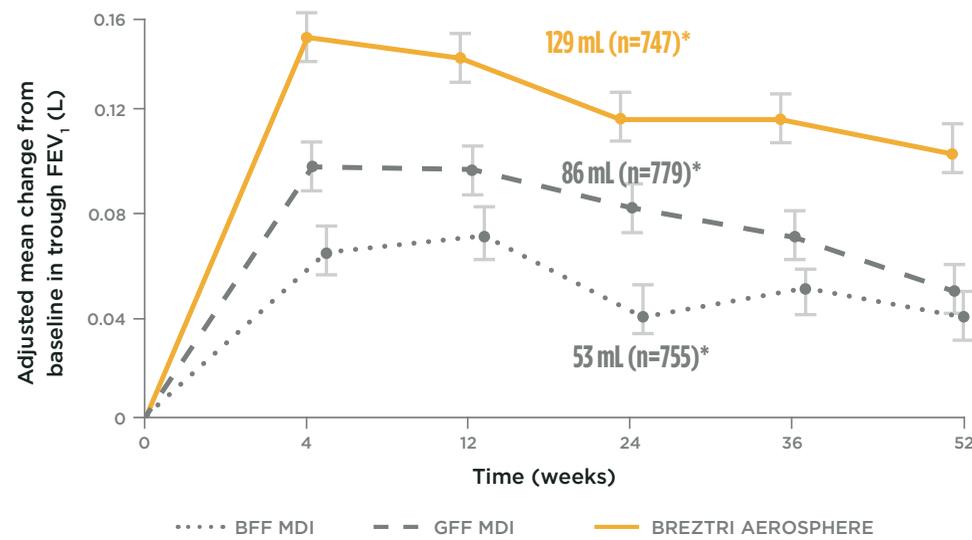
BFF: budesonide/formoterol fumarate dihydrate; BGF: budesonide/glycopyrronium/formoterol fumarate dihydrate; CI: confidence interval; COPD: chronic obstructive pulmonary disease; HR: hazard ratio; GFF: glycopyrronium/formoterol fumarate dihydrate; ICS: inhaled corticosteroid; LABA: long-acting beta<sub>2</sub>-adrenergic agonist; LAMA: long-acting muscarinic antagonist; MDI: metered-dose inhaler.

### ETHOS trial

## POWERFUL AND SUSTAINED IMPROVEMENTS OBSERVED IN LUNG FUNCTION (FEV<sub>1</sub>) OVER 24 WEEKS VS. A LAMA/LABA (GFF MDI) AND AN ICS/LABA (BFF MDI) (SUB-STUDY; 1° ENDPOINT)<sup>1,4</sup>

BREZTRI AEROSPHERE provided statistically significant improvements in trough FEV<sub>1</sub> vs. a LAMA/LABA (GFF MDI) and an ICS/LABA (BFF MDI).

• The improvements in lung function were sustained up to 52 weeks



Adapted from the BREZTRI AEROSPHERE Product Monograph and data on file.

**43 mL improvement vs. a LAMA/LABA (GFF MDI) (95% CI: 25, 60;  $p < 0.0001$ )<sup>†</sup>**

**76 mL improvement vs. an ICS/LABA (BFF MDI) (95% CI: 58, 94;  $p < 0.0001$ )<sup>†</sup>**

FEV <sub>1</sub> AUC <sub>0-4</sub> over 24 weeks, LS mean change from baseline (SE)	BREZTRI AEROSPHERE (n=747)*	GFF MDI (n=779)*	BFF MDI (n=755)*
	294 mL (6.3)	245 mL (6.3)	194 mL (6.3)
		49 mL improvement vs. a LAMA/LABA (GFF MDI) (95% CI: 31, 66; $p < 0.0001$ ) <sup>†</sup>	99 mL improvement vs. an ICS/LABA (BFF MDI) (95% CI: 82, 117; $p < 0.0001$ ) <sup>†</sup>

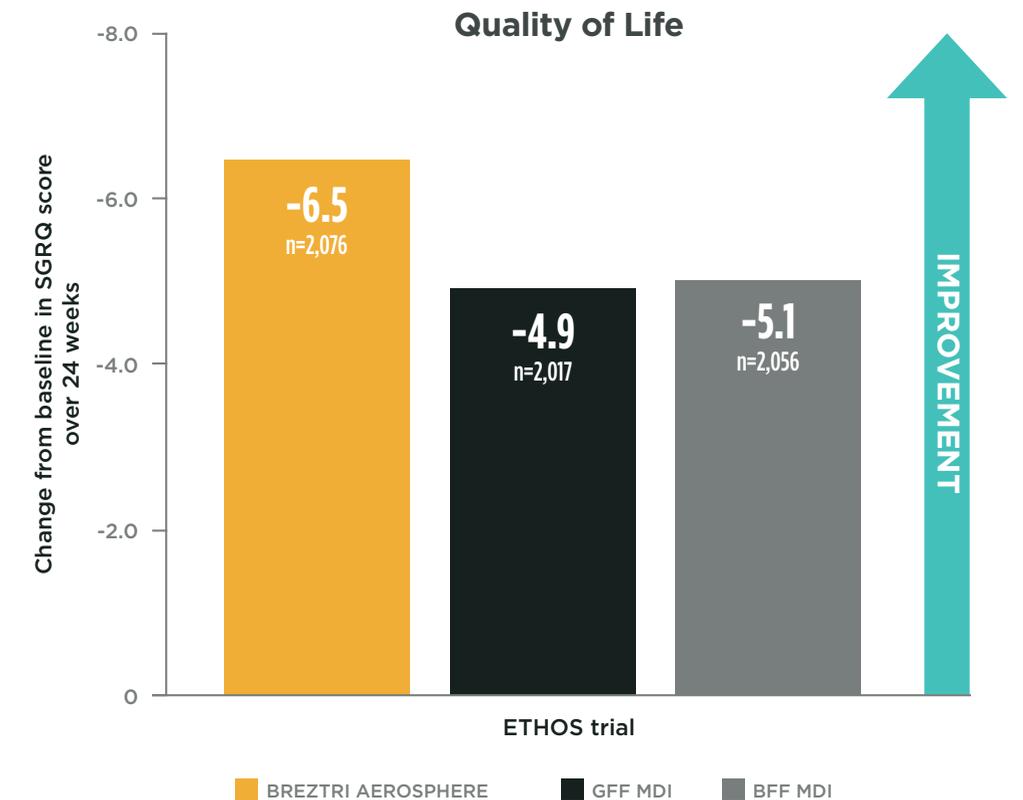
\* Administered orally as two inhalations of BREZTRI AEROSPHERE 160/7.2/5 mcg, GFF MDI 7.2/5 mcg, BFF MDI 160/5 mcg, BID.

† Statistically significant.

AUC<sub>0-4</sub>: area under the curve from 0-4 hours; BFF: budesonide/formoterol fumarate dihydrate; CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; GFF: glycopyrronium/formoterol fumarate dihydrate; ICS: inhaled corticosteroid; LABA: long-acting beta<sub>2</sub>-adrenergic agonist; LAMA: long-acting muscarinic antagonist; LS: least squares; MDI: metered-dose inhaler; SE: standard error.

## POWERFUL IMPROVEMENTS IN QUALITY OF LIFE (SGRQ) (2° ENDPOINT)<sup>1,5†</sup>

Statistically significant improvements in patient quality of life were observed over 24 weeks vs. a LAMA/LABA (GFF MDI) and vs. an ICS/LABA (BFF MDI) in the ETHOS trial.



Adapted from the BREZTRI AEROSPHERE Product Monograph, Rabe et al. (suppl.) and Ferguson et al.

**36% increase in likelihood of clinically important improvement\*\* in SGRQ for BREZTRI AEROSPHERE vs. a LAMA/LABA (GFF MDI) at week 24 (OR: 1.358; 95% CI: 1.199, 1.539;  $p < 0.0001$ ).<sup>6</sup>**

**A ≥4-unit change in the SGRQ score is clinically important.<sup>7</sup>**

† Quality of life assessed by the SGRQ score.

\*\* Clinically important improvement defined as achieving an MCID decrease of ≥4 units.<sup>7</sup>

BFF: budesonide/formoterol fumarate dihydrate; CI: confidence interval; GFF: glycopyrronium/formoterol fumarate dihydrate; ICS: inhaled corticosteroid; LABA: long-acting beta<sub>2</sub>-adrenergic agonist; LAMA: long-acting muscarinic antagonist; MCID: minimal clinically important difference; MDI: metered-dose inhaler; OR: odds ratio; SGRQ: St. George's Respiratory Questionnaire.