

ETHOS PIVOTAL TRIAL



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.¹

Study design¹

- 52 weeks
- Randomized, double-blind, multicentre, parallel-group design

Patient population^{1,2}

Key inclusion criteria

- Patients with moderate to very severe COPD
- History of ≥ 1 exacerbation(s) in the previous 12 months
- Baseline FEV₁ $\geq 25\%$ to $< 65\%$ of predicted normal
- Symptomatic COPD while receiving ≥ 2 inhaled maintenance therapies for COPD at the time of screening

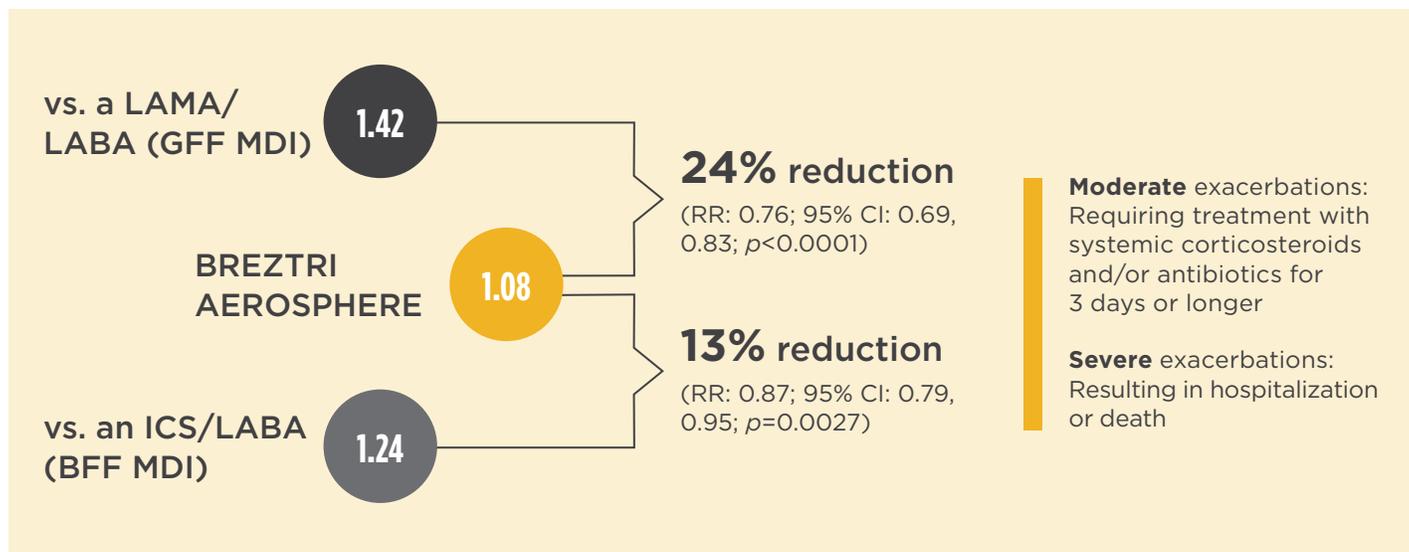
	BREZTRI AEROSPHERE budesonide 320 mcg / glycopyrronium 14.4 mcg / formoterol fumarate dihydrate 10 mcg, BID (ICS/LAMA/LABA)	Budesonide 160 mcg / glycopyrronium 14.4 mcg / formoterol fumarate dihydrate 10 mcg, BID (BGF MDI; ICS/LAMA/LABA)*	Glycopyrronium 14.4 mcg / formoterol fumarate dihydrate 10 mcg, BID (GFF MDI; LAMA/LABA)	Budesonide 320 mcg / formoterol fumarate dihydrate 10 mcg, BID (BFF MDI; ICS/LABA)
8,509 patients randomized	n=2,137	n=2,121	n=2,120	n=2,131

* Not an available dose. Results are not presented.

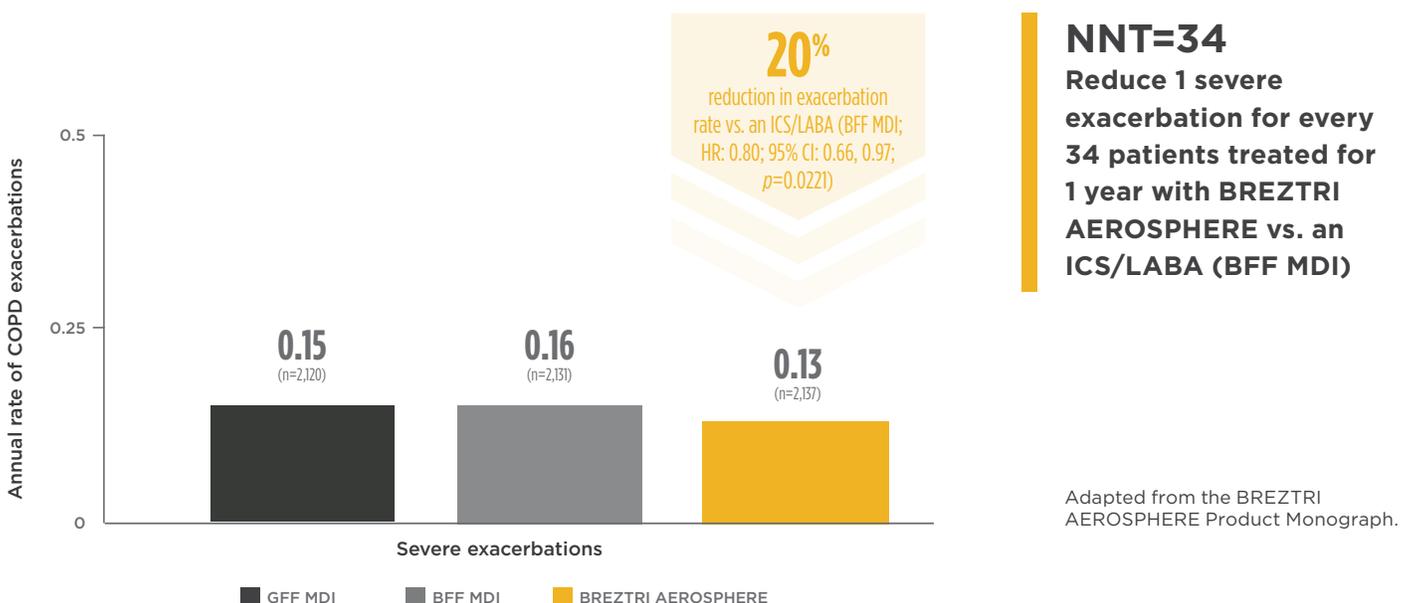
BID: twice daily; BFF: budesonide/formoterol fumarate dihydrate; BGF: budesonide/glycopyrronium/formoterol fumarate dihydrate; COPD: chronic obstructive pulmonary disease; FEV₁: forced expiratory volume in 1 second; GFF: glycopyrronium/formoterol fumarate dihydrate; ICS: inhaled corticosteroid; LABA: long-acting beta₂-agonist; LAMA: long-acting muscarinic antagonist; MDI: metered-dose inhaler.

POWERFUL REDUCTION OBSERVED IN MODERATE AND SEVERE EXACERBATIONS (RESULTING IN HOSPITALIZATION OR DEATH) VS. AN ICS/LABA (BFF MDI)^{1,2}

Primary endpoint: Annual rate of moderate or severe COPD exacerbations¹



Secondary endpoint: Annual rate of severe COPD exacerbations (resulting in hospitalization or death)^{1,2}



BFF: budesonide/formoterol fumarate dihydrate; CI: confidence interval; COPD: chronic obstructive pulmonary disease; GFF: glycopyrronium/formoterol fumarate dihydrate; HR: hazard ratio; ICS: inhaled corticosteroid; LABA: long-acting beta₂-agonist; LAMA: long-acting muscarinic antagonist; MDI: metered-dose inhaler; NNT: number needed to treat; RR: rate ratio.

STATISTICALLY SIGNIFICANT IMPROVEMENTS IN BREATHLESSNESS (TDI FOCAL SCORE) AND PATIENT QUALITY OF LIFE (SGRQ) WERE OBSERVED OVER 24 WEEKS VS. A LAMA/LABA (GFF MDI) AND VS. AN ICS/LABA (BFF MDI) (2° ENDPOINT)^{1,3}



Breathlessness

(change from baseline in TDI focal score over 24 weeks)

1.3

BREZTRI
AEROSPHERE

0.9

GFF MDI

1.0

BFF MDI

A ≥ 1 -unit change in the TDI focal score is clinically important.⁴

31% improvement vs. a LAMA/LABA (GFF MDI; mean change 0.40; 95% CI: 0.24, 0.55)

24% improvement vs. an ICS/LABA (BFF MDI; mean change 0.31; 95% CI: 0.15, 0.46)



Quality of life

(change from baseline in SGRQ score over 24 weeks)

-6.5

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-4.9

GFF MDI

-5.1

BFF MDI

A decrease in the SGRQ score represents improvement.

A ≥ 4 -unit change in the SGRQ score is clinically important.⁵

25% improvement vs. a LAMA/LABA (GFF MDI; mean change -1.62; 95% CI: -2.27, -0.97)

21% improvement vs. an ICS/LABA (BFF MDI; mean change -1.38; 95% CI: -2.02, -0.73)



POWERFUL and SUSTAINED IMPROVEMENTS observed in trough FEV₁ (sub-study; 1° endpoint)¹

BREZTRI AEROSPHERE provided statistically significant improvements in trough FEV₁ over 24 weeks vs. a LAMA/LABA (GFF MDI) and an ICS/LABA (BFF MDI)

- The improvements in trough FEV₁ were sustained over 52 weeks

Trough FEV₁ (mL) over 24 weeks, LS mean change from baseline (SE)

**129 mL
(6.5)**

BREZTRI
AEROSPHERE
(n=747)*

**86 mL
(6.6)**

GFF MDI
(n=779)*

**53 mL
(6.5)**

BFF MDI
(n=755)*

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

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

* 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.

CHOOSE THE POWERFUL DEMONSTRATED EFFICACY OF BREZTRI AEROSPHERE IN COPD¹

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, 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
- Hypercorticism, adrenal suppression
- Adrenal insufficiency in patients transferred from systemic steroid
- Patients with symptomatic prostatic hyperplasia, glaucoma, convulsive disorders, thyrotoxicosis, sensitivity to sympathomimetic amines, severe hepatic impairment/hepatic disease, or urinary retention



- In rare cases, eosinophilic conditions
- Susceptibility or decreased resistance to infections
- Monitoring of hypokalemia, hyperglycemia, bone and ocular effects, and corticosteroid effects in patients with hepatic impairment
- Paradoxical bronchospasm
- Increased risk of pneumonia
- Pregnant and nursing women
- Geriatrics (≥65 years of age)

For more information:

Consult the Product Monograph at breztri-en.azpm.ca for important information regarding adverse reactions, drug interactions, and dosing. The Product Monograph is also available by calling AstraZeneca Canada at **1-800-668-6000**.

COPD: chronic obstructive pulmonary disease; LABA: long-acting beta₂-agonist; LAMA: long-acting muscarinic antagonist.

References:

1. BREZTRI AEROSPHERE Product Monograph. AstraZeneca Canada Inc. **2.** Rabe KF, et al. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. *NEJM*. 2020;383(1):35-48. **3.** 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. **4.** Witek TJ, et al. Minimal important difference of the transition dyspnoea index in a multinational clinical trial. *Eur Respir J*. 2003(21):267-272. **5.** 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. Retrieved November 30, 2023.

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