Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol) – New drug approval

- On July 24, 2020, AstraZeneca announced the FDA approval of Breztri Aerosphere (budesonide/glycopyrrolate/formoterol), for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
    - Breztri Aerosphere is not indicated for the relief of acute bronchospasm or for the treatment of asthma.
- Breztri Aerosphere is a single-inhaler, fixed dose triple-combination of budesonide, an inhaled corticosteroid, with glycopyrrolate, a long-acting muscarinic antagonist, and formoterol fumarate, a long-acting beta$_2$-agonist, delivered in a pressurized metered-dose inhaler (MDI).
- The clinical efficacy of Breztri Aerosphere was demonstrated in two parallel-group studies of 10,484 patients with moderate to very severe COPD. In study 1, patients were randomized to Breztri Aerosphere, BGF MDI (same ingredients as Breztri, but different strengths), GFF MDI (glycopyrrolate/formoterol) or BFF MDI (budesonide/formoterol) for a total of 52 weeks. The primary endpoint was the rate of moderate to severe COPD exacerbations of Breztri vs. GFF MDI and BFF MDI.
    - Breztri Aerosphere demonstrated a 24% reduction in exacerbation rate vs. GFF MDI ($p < 0.0001$).
    - Breztri Aerosphere demonstrated a 13% reduction in exacerbation rate vs. BFF MDI ($P = 0.0027$)
- In study 2, patients were randomized to Breztri Aerosphere, GFF MDI, BFF MDI, or open-label active comparator for a total of 24 weeks. The primary endpoints were first second of forced expiration area under the curve from 0 – 4 hours (FEV_1 AUC_{0-4}) for Breztri vs. BFF MDI and change in baseline for morning pre-dose trough FEV_1 for Breztri vs. GFF MDI.
    - The difference in FEV_1 AUC_{0-4} was 116 mL (95% CI: 80, 152) for Breztri Aerosphere vs. BFF MDI.
    - The change in baseline for morning pre-dose trough FEV_1 was 13 mL (95% CI: -9, 36) for Breztri Aerosphere vs. GFF MDI (this change was not statistically significant).
- Warnings and precautions of Breztri Aerosphere include serious asthma-related events – hospitalizations, intubations, death; deterioration of disease and acute episodes; avoid excessive use of Breztri Aerosphere and avoid use with other long-acting beta$_2$-agonists; oropharyngeal candidiasis; pneumonia, immunosuppression and risk of infections; transferring patients from systemic corticosteroid therapy; hypercorticism and adrenal suppression; drug interactions with strong cytochrome P450 3A4 inhibitors; paradoxical bronchospasm; hypersensitivity reactions including anaphylaxis; cardiovascular effects; reduction in bone mineral density; glaucoma and cataracts, worsening of narrow-angle glaucoma; worsening of urinary retention; coexisting conditions; and hypokalemia and hyperglycemia.
- The most common adverse reactions (≥ 2%) with Breztri Aerosphere use were upper respiratory tract infection, pneumonia, back pain, oral candidiasis, influenza, muscle spasm, urinary tract infection, cough, sinusitis and diarrhea.
- The recommended dose of Breztri Aerosphere is twice daily in the morning and in the evening by oral inhalation. Do not take more than two inhalations twice daily.

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- AstraZeneca's launch plans for Breztri Aerosphere are pending. Breztri Aerosphere will be available as a metered dose inhaler that delivers a combination of 160 mcg budesonide, 9 mcg glycopyrrolate, and 4.8 mcg formoterol fumarate per inhalation.

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