Symbicort Aerosphere® (budesonide/formoterol) – New formulation approval

- On April 28, 2023, the FDA approved AstraZeneca's Symbicort Aerosphere (budesonide/formoterol), for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
    - Symbicort Aerosphere is not indicated for the relief of acute bronchospasm or for the treatment of asthma.
- This is a new Symbicort formulation that uses the Aerosphere inhalation device. The original Symbicort inhalation device is approved for:
    - Treatment of asthma in patients 6 years of age and older.
    - Maintenance treatment of airflow obstruction and reducing exacerbations in patients with COPD including chronic bronchitis and/or emphysema.
- The efficacy of Symbicort Aerosphere was established in two randomized, double-blind studies (TELOS and SOPHOS) in patients with COPD who remained symptomatic despite maintenance treatment for COPD. TELOS was conducted over 24 weeks in a total of 2,389 patients randomized to receive Symbicort Aerosphere 320 mcg/9.6 mcg, budesonide and formoterol fumarate 160 mcg/9.6 mcg, formoterol fumarate 9.6 mcg (FF MDI), budesonide 320 mcg (BD MDI), or open label budesonide and formoterol fumarate 320 mcg/9 mcg (inhalation powder). The primary endpoints were FEV_1 area under the curve from 0 to 4 hours (FEV_1 AUC_{0-4}) for Symbicort Aerosphere compared to BD MDI and change from baseline in morning pre-dose trough FEV_1 for Symbicort Aerosphere compared to FF MDI at week 24.
    - Treatment with Symbicort Aerosphere resulted in a statistically significant increase in FEV_1 AUC_{0-4} relative to BD MDI and trough FEV_1 relative to FF MDI at week 24. The effects on lung function (mean change from baseline in morning pre-dose trough FEV_1) of Symbicort Aerosphere compared with FF MDI were observed at all timepoints over the course of the study.
    - Additionally, treatment with Symbicort Aerosphere resulted in an improvement in time to first moderate or severe COPD exacerbation compared with FF MDI (hazard ratio [HR] 0.70; 95% CI: 0.55, 0.90).
- SOPHOS was conducted over 12 to 52 weeks in a total of 1,876 patients randomized to receive Symbicort Aerosphere 320 mcg/9.6 mcg, budesonide and formoterol fumarate 160 mcg/9.6 mcg, or FF MDI. The primary endpoint was change from baseline in morning pre-dose trough FEV_1 for Symbicort Aerosphere compared to FF MDI at week 12.
    - Treatment with Symbicort Aerosphere resulted in a numerical increase in morning pre-dose trough FEV_1 at week 12 compared with FF MDI.
    - Additionally, treatment with Symbicort Aerosphere resulted in an improvement in time to first moderate or severe COPD exacerbation compared with FF MDI (HR 0.82; 95% CI: 0.69, 0.98).
- Warnings and precautions for Symbicort Aerosphere include serious asthma-related events - hospitalizations, intubations and death; deterioration of disease and acute episodes; risk associated with excessive use of long-acting $beta_2$-agonists, including Symbicort Aerosphere; oropharyngeal candidiasis; risk of 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

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including anaphylaxis; cardiovascular effects; reduction in bone mineral density; glaucoma and cataracts; risks of using sympathomimetic amines in certain coexisting conditions; and hypokalemia and hyperglycemia.

- The most common adverse reactions (≥ 2%) with Symbicort Aerosphere use were upper respiratory tract infection, COPD, back pain, headache, bronchitis, oral candidiasis, dysphonia, and muscle spasm.

- The recommended dose of Symbicort Aerosphere is 2 actuations (containing total dose of budesonide 320 mcg and formoterol fumarate 9.6 mcg) twice daily in the morning and in the evening (approximately 12 hours apart) by oral inhalation.

- AstraZeneca's launch plans for Symbicort Aerosphere are pending. Symbicort Aerosphere will be available as a pressurized metered dose inhaler that delivers a combination of budesonide (160 mcg), and formoterol fumarate (4.8 mcg) per actuation.

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