## Bronchitol® (mannitol) – New drug approval

- On November 2, 2020, Chiesi announced the FDA approval of Bronchitol (mannitol), as add-on maintenance therapy to improve pulmonary function in adult patients 18 years and older with cystic fibrosis (CF).
    - Bronchitol should only be used in adults who have passed the Bronchitol Tolerance Test.
- The efficacy of Bronchitol was established in three randomized, double-blind, controlled trials in CF patients. Trial 1 included 423 patients 18 years of age or older. Trial 2 and 3 included 600 patients 6 years of age or older. Patients were randomized to receive either Bronchitol 400 mg or control (50 mg inhaled mannitol) twice daily. The primary efficacy endpoint in all three studies was improvement in lung function as determined by the mean change from baseline in pre-dose $FEV_1$ (mL) over 26 weeks of treatment.
    - In trial 1, the treatment difference between Bronchitol and control for the adjusted mean change in $FEV_1$ from baseline over 26 weeks was 51 mL (95% CI: 6, 97; p = 0.028).
    - In trial 2 and 3, the adjusted mean treatment difference in the change from baseline in $FEV_1$ over 26 weeks between Bronchitol and control was 68 mL (95% CI: 24, 113) and 52 mL (95% CI: -3, 107), respectively. In a post-hoc analysis of the adult subgroup, the adjusted mean treatment difference in the change from baseline in $FEV_1$ over 26 weeks between Bronchitol and control was 78 mL (95% CI: 21, 135) in trial 2 and 78 mL (95% CI: 2, 153) in trial 3.
    - While CF patients aged 6 to 17 years were included in trials 2 and 3, Bronchitol is not indicated for use in this age group.
- Bronchitol is contraindicated in patients with hypersensitivity to mannitol or to any of the capsule components and in patients with failure to pass the Bronchitol Tolerance Test.
- Warnings and precautions for Bronchitol include bronchospasm and hemoptysis.
- The most common adverse reactions (≥ 3%) with Bronchitol use were cough, hemoptysis, oropharyngeal pain, vomiting, bacteria sputum identified, pyrexia, and arthralgia.
- The recommended dose of Bronchitol is 400 mg twice a day by oral inhalation (the contents of 10 capsules administered individually) via the inhaler. Bronchitol should be taken once in the morning and once in the evening, with the later dose taken at least 2-3 hours before bedtime.
    - A short-acting bronchodilator should be administered by oral inhalation, 5 to 15 minutes before every dose of Bronchitol.
    - Prior to prescribing Bronchitol for treatment of CF, the Bronchitol Tolerance Test must be administered and performed under the supervision of a healthcare practitioner who is able to manage acute bronchospasm, to identify patients who are suitable candidates for Bronchitol maintenance therapy.

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- Chiesi plans to launch Bronchitol in March 2021. Bronchitol will be available as a 40 mg per capsule inhalation powder.

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