Clinical Policy: Mannitol (Bronchitol)

Reference Number: PA.CP.PHAR.518
Effective Date: 01/2021
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Revision Log

Description
Inhaled dry powder mannitol (Bronchitol®) is a sugar alcohol used as an osmotic agent.

FDA Approved Indication(s)
Bronchitol is indicated as add-on maintenance therapy to improve pulmonary function in adult patients 18 years of age and older with cystic fibrosis (CF).

Bronchitol should only be used in adults who have passed the Bronchitol tolerance test (BTT) to identify patients who are suitable candidates for Bronchitol maintenance therapy.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Bronchitol is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cystic Fibrosis (must meet all)**:**

1. Diagnosis of CF;
2. Prescribed by or in consultation with a pulmonologist;
3. Age ≥ 18 years;
4. Documentation of inadequate response to hypertonic saline and Pulmozyme®, unless both are contraindicated or clinically significant adverse events are experienced;
   **Prior authorization may be required for Pulmozyme*
5. If request is for the 7-day or 4-week treatment pack, member meets both of the following (a and b):
   a. Documentation that member has successfully completed the BTT (*see Appendix D*);
   b. Bronchitol is prescribed concurrently with a short-acting bronchodilator (*see Appendix D*);
6. Dose does not exceed one of the following (a or b):
   a. For BTT (both i and ii):
      i. 400 mg once;
      ii. 10 capsules once;
   b. For 7-day or 4-week treatment pack (both i and ii):
      i. 800 mg per day;
      20 capsules per day.

Approval duration:
BTT: 4 weeks
7-day/4-week treatment pack: 6 months

B. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Cystic Fibrosis (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for BTT, re-authorization is not permitted;
4. If this is the first authorization for the 7-day or 4-week treatment pack, member meets both of the following (a and b):
   a. Documentation that member has successfully completed the BTT (*see Appendix D*);
   b. Bronchitol is prescribed concurrently with a short-acting bronchodilator (*see Appendix D*);
5. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 800 mg per day;
   b. 20 capsules per day.
6. **Approval duration: 12 months**

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 for specialty months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53;

B. Members < 18 years of age (*see Appendix D*).

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
BTT: Bronchitol tolerance test
CF: cystic fibrosis
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Pulmozyme® (dornase alfa)	2.5 mg once daily or 2.5 mg twice daily administration via nebulization	5 mg/day
hypertonic saline (HyperSal®, NebuSal®, PulmoSal™)	4 mL vial via oral inhalation twice daily through a nebulizer	8 mL/day

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to mannitol or to any of the capsule components, and failure to pass the BTT
- Boxed warning(s): none reported

Appendix D: General Information

- Short-acting bronchodilator: albuterol (Accuneb®, Proventil®, Ventolin®, ProAir®, ProAir RespiClick®), levalbuterol (Xopenex®, Xopenex® nebulizer solution), ipratropium bromide/albuterol (Combivent®, Duoneb®)
- Prior to a mannitol dose, administer a bronchodilator 5 to 15 minutes before.
- The three main types of mucus thinners are hypertonic saline, mannitol (Bronchitol), and dornase alfa (Pulmozyme).
- BTT is used to identify patients who are suitable candidates for inhaled mannitol use. BTT must be administered under the supervision of healthcare practitioner who can treat severe bronchospasm. If a patient does not experience bronchospasm, a decrease in FEV1, or a decrease in oxygen saturation during BTT, the patient has passed the BTT and is a candidate for Bronchitol therapy.
- Cystic Fibrosis Foundation guidelines recommend hypertonic saline use in all CF patients regardless of disease severity as maintenance therapy. Dornase alfa is also recommended for all levels of lung disease severity with a strong recommendation in moderate-to-severe lung disease.
- Bronchitol is not indicated for use in children and adolescents. In clinical trials evaluating the use of Bronchitol in patients with CF 6 years and older, patients treated with mannitol had a higher occurrence of hemoptysis, particularly in pediatric patients. Improvements in FEV1 compared to control in relative change in ppFEV1 were not statistically significant in children and adolescents.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Mannitol (Bronchitol)	400 mg (10 capsules) twice a day by oral inhalation, in the morning and evening, with the later dose taken 2-3 hours before bedtime	800 mg/day
Mannitol (Bronchitol Tolerance Test)	400 mg (10 capsules) once by oral inhalation under supervision of a healthcare practitioner who is able to manage acute bronchospasm	400 mg/day

VI. Product Availability

- 4-week treatment pack (4 x 7-day treatment packs): 4 inhalers, 560 capsules
- 7-day treatment pack: 1 inhaler, 140 capsules
- Tolerance test: 1 inhaler, 10 capsules

VII. References

1. Bronchitol Prescribing Information. Cary, NC: Chiesi USA, Inc.; October 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/202049s000lbl.pdf. Accessed October 7, 2022.
2. National Institute for Health and Care Excellence. Mannitol dry powder for inhalation for treating cystic fibrosis. NICE Technology appraisal guidance; November 2012. Available at: https://www.nice.org.uk/guidance/ta266/resources/mannitol-dry-powder-for-inhalation-for-treating-cystic-fibrosis-pdf-82600555351237. Accessed October 7, 2022.
3. Cystic Fibrosis Foundation: Clinical Care Guidelines. Available at: https://www.cff.org/medical-professionals/clinical-care-guidelines. Accessed October 6, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01/2021	
1Q 2022 annual review: references reviewed and updated.	01/2022	
1Q 2023 annual review: no significant changes; updated Appendix D; references reviewed and updated.	01/2023	