Clinical Policy: Mannitol (Bronchitol)

Reference Number: ERX.SPA.423
Effective Date: 03.01.21
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Inhaled dry power 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).

Limitation(s) of use: 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 effects 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: 400 mg (10 capsules) once;
   b. For 7-day or 4-week treatment pack: 800 mg (20 capsules) per day.

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

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

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 800 mg (20 capsules) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents;

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 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®)
- 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 the BTT 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 the supervision of a health 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 22, 2021.
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 22, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.08.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	10.22.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.