Clinical Policy: Mannitol (Bronchitol)

Reference Number: CP.PHAR.518
Effective Date: 03.01.21
Last Review Date: 08.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

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 health plans affiliated with Centene Corporation® 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, *see Appendix D*):
   a. Documentation that member has successfully completed the BTT;
   b. Bronchitol is prescribed concurrently with a short-acting bronchodilator;
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;
      ii. 20 capsules per day.

Approval duration:

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

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Cystic Fibrosis (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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, *see Appendix D*):
   a. Documentation that member has successfully completed the BTT;
   b. Bronchitol is prescribed concurrently with a short-acting bronchodilator;
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.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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 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 forced expiratory volume in one second (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 percent predicted forced expiratory volume in one second (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 May 9, 2024.
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 May 20, 2024.

3. Cystic Fibrosis Foundation: Clinical Care Guidelines. Available at: https://www.cff.org/medical-professionals/clinical-care-guidelines. Accessed May 17, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created; references to HIM.PHAR.21 revised to HIM.PA.154.	12.08.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	10.22.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.03.22	
1Q 2023 annual review: no significant changes; updated Appendix D; references reviewed and updated.	10.07.22	02.23
3Q 2023 annual review: no significant changes; references reviewed and updated.	05.08.23	08.23
3Q 2024 annual review: no significant changes; for Appendix D, defined FEV1 and ppFEV1; references reviewed and updated.	05.09.24	08.24

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.