BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

BRONCHITOL® (mannitol) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for BRONCHITOL (mannitol)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a Pulmonologist or in consultation with a Pulmonologist

Indication
- Used as add on maintenance therapy to improve pulmonary function in individual with confirmed diagnosis of cystic fibrosis

ORIGINAL EFFECTIVE DATE: 05/202021 | ARCHIVE DATE: | LAST REVIEW DATE: 05/21/2026 | LAST CRITERIA REVISION DATE: 05/15/2025

PHARMACY COVERAGE GUIDELINE

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Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Has taken and passed the Bronchitol Tolerance Test
- FEV1 is greater than 40 percent and less than 90 percent predicted

Alternative Therapies
- Failure (trial for at least three months duration), contraindication, intolerance to **BOTH** of the following:
  - Inhaled Pulmozyme (dornase alpha)
  - Inhaled hypertonic (7 percent) saline

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No concomitant use with hypertonic saline
- No history of hemoptysis (episode of 60 milliliters or more) within the previous 3 months
- No FDA labeled contraindications such as:
  - Failure to pass the Bronchitol Tolerance Test
  - Hypersensitivity to mannitol

Additional Requirements
- Will continue other cystic fibrosis therapies
- Prescription for short acting bronchodilator therapy to use with each dose

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (FEV1 values)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications
- Continues to be seen by a physician specializing in or is in consultation with a Pulmonologist

PHARMACY COVERAGE GUIDELINE

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Clinical Response
- **ONE** of the following:
  - Improvement in FEV1 over baseline of at least 100 mL
  - Improvement in FEV1 over baseline of at least 10 percent

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No new contraindications or significant adverse drug effects such as:
  - Severe bronchospasms
  - Hemoptysis
  - Hypersensitivity to mannitol

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in cystic fibrosis
- Lab values that confirm safe use (FEV1 values)

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Bronchitol (mannitol) is indicated as add-on maintenance therapy to improve pulmonary function in adult patients 18 years and older with cystic fibrosis (CF). Use Bronchitol (mannitol) only for adults who have passed the Bronchitol Tolerance Test (BTT). The BTT 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 (mannitol) maintenance therapy.

An individual who experiences any of the following: bronchospasm, a decrease in FEV1, or a decrease in oxygen saturation with administration of Bronchitol (mannitol) is deemed to have failed the BTT. Bronchitol (mannitol) must not be prescribed. Individual who passes the BTT is a candidate for Bronchitol (mannitol) and must have inhaled short-acting bronchodilator therapy before each use of Bronchitol (mannitol).

Difficulty clearing purulent secretions from the airways is a common complaint among CF patients who have moderate to severe lung disease. Airway clearance is accomplished by a combination of inhaled drugs such as dornase alfa and/or hypertonic saline to loosen and liquefy the mucus along with physical means to dislodge and help the patient clear the secretions. It has been shown that dornase alfa reduces pulmonary exacerbations and improves lung function. Regular treatment with hypertonic saline leads to only modest improvements in lung function in adults and children, but there are substantial reductions in pulmonary exacerbations. There is little evidence that N-acetylcysteine has any beneficial effect. Use of inhaled N-acetylcysteine is no longer recommended within the guidance from the Cystic Fibrosis Foundation (CFF). This agent can liquefy CF sputum, but it has the potential to induce airway inflammation and/or bronchospasm in a subgroup of patients and to inhibit ciliary function which has led to a reduction in its use.

In a published guideline in 2013 the CFF supported the use of inhaled dornase alpha to improve lung function and reduce exacerbations for individuals 6-years of age and older with mild disease and for individuals 6-years of age and older with moderate to severe disease. It also supported the use of inhaled hypertonic saline in individuals 6-years of age and older to improve lung function, quality of life, and reduce exacerbations. Severity of lung disease was defined by FEV1% predicted as follows: normal, > 90% predicted; mildly impaired, 70–89% predicted; moderately impaired, 40–69% predicted; and severely impaired, < 40% predicted. The CFF recommended the following order of inhaled medications: bronchodilator; hypertonic saline; dornase alfa; airway clearance; and aerosolized antibiotic.

Dornase alfa is an endonuclease that decreases the viscosity of purulent CF sputum by cleaving long strands of denatured DNA that are released by degenerating neutrophils, which helps to liquefy CF sputum. Inhaled hypertonic saline or inhaled mannitol helps to hydrate the mucus that is present in the airways of patients with CF. Guidelines from the CFF recommend that most patients with CF use both dornase alfa and hypertonic saline, without assigning priority of one over the other. Inhaled mannitol is considered a second-line option to replace hypertonic saline for adult patients with CF who fail the combination of dornase alfa and hypertonic saline for airway clearance.

In 2020 a Cochrane Database Systematic Review of inhaled mannitol indicated that moderate-quality evidence showed that treatment with mannitol over a six-month period was associated with an improvement in some measures of lung function in people with CF compared to various controls (very low dose of mannitol, non-respirable mannitol, and dornase alpha). It also concluded that mannitol could be considered as a treatment in CF; but further research is required in order to establish who may benefit most and whether this benefit is sustained in the longer term. The review noted that studies comparing its efficacy against other (established) mucolytic therapies need to be undertaken before it can be considered for mainstream practice.

All patients should have an airway clearance regimen with the following: 1) children of any age who have chronic daily cough or FEV1 below the normal range, chronic treatment with dornase alfa is recommended. It is also recommended that dornase alfa treatment be used for patients with mild or asymptomatic lung disease. 2) chronic treatment with inhaled hypertonic saline for patients ≥ 2 years is also recommended. It is also suggested as therapy for younger children and infants. Typical dosing regimen is 4 mL of 7% saline via nebulizer twice daily.

PHARMACY COVERAGE GUIDELINE

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Because inhaled hypertonic saline can trigger acute bronchospasm, bronchodilator therapy (e.g., with a short-acting beta-adrenergic agonist) is given as a pretreatment. 3) all patients who produce sputum should be encouraged to adhere to a regular regimen of chest physiotherapy for secretion clearance. 4) respiratory therapies should be performed twice daily in the following order: inhaled short-acting beta-adrenergic agonist, then inhaled hypertonic saline, then inhaled dornase alfa (given only once daily) and chest physiotherapy in either order, followed by any other inhaled treatments such as aerosolized antibiotics.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Bronchitol (mannitol) powder for oral inhalation use product information, revised by Arna Pharma Pty Ltd. 10-2024, at DailyMed http://dailymed.nlm.nih.gov. Accessed February 12, 2026.

Simon RH. Cystic fibrosis: Overview of the treatment of lung disease. In: UpToDate, Chmiel JF, Hoppin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through March 2026. Topic last updated September 11, 2025. Accessed May 01, 2026.