**Effective Date** ..... **10/15/2023**
**Next Review Date** ..... **10/15/2024**
**Coverage Policy Number** ..... **IP0483**

# Dornase Alfa

## Table of Contents

Overview ..... 1
Medical Necessity Criteria ..... 1
Reauthorization Criteria ..... 2
Authorization Duration ..... 2
Conditions Not Covered ..... 2
Background ..... 2
References ..... 3
Supplemental References ..... 3

## Related Coverage Resources

***INSTRUCTIONS FOR USE***
*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

## Overview

This policy supports medical necessity review for dornase alfa inhalation solution (**Pulmozyme**®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

## Medical Necessity Criteria

**Dornase Alfa inhalation solution (Pulmozyme) is considered medically necessary when ONE of the following is met (1 or 2):**

1. **Cystic Fibrosis.** Individual meets **BOTH** of the following criteria (A and B):
   A. Used to improve pulmonary function in cystic fibrosis (CF)
   B. The medication is prescribed by, or in consultation with, a pulmonologist or a physician who specializes in the treatment of cystic fibrosis

2. **Treatment of Complicated Pleural Effusion(s).** Individual meets ALL of the following criteria (A, B and C):
    A. Documented diagnosis of pleural effusion(s) confirmed by imaging (for example, x-ray, CT scan)
    B. Individual has inadequate response to **BOTH** of the following concomitantly:
        i. Empiric trial of antibiotic therapy
        ii. Drainage via chest tube or catheter thoracostomy
    C. The medication is prescribed by, or in consultation with, a pulmonologist or thoracic surgeon

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

## Reauthorization Criteria

Dornase Alfa inhalation solution (Pulmozyme) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

## Authorization Duration

Initial approval duration:

- Cystic Fibrosis: up to 12 months
- Treatment of Complicated Pleural Effusion: up to 30 days

Reauthorization approval duration:

- Cystic Fibrosis: up to 12 months
- Treatment of Complicated Pleural Effusion: not applicable

## Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

1. **Asthma**
   Mucus hypersecretion may be mediated by a variety of causes, including inflammation, irritation, stimulation, or mucus-producing tumors.[7] However, efficacy of Pulmozyme is not established for conditions other than cystic fibrosis. In a pilot study of patients with severe acute asthma (n = 50), there was no significant difference in forced expiratory volume in 1 second ($FEV_1$) with Pulmozyme use vs. placebo.[8]

2. **Bronchiectasis, Idiopathic**
   A multicenter, double-blind, randomized, placebo-controlled 24-week trial (n = 349) examined the effect of Pulmozyme vs. placebo on patients with idiopathic bronchiectasis (i.e., bronchiectasis not related to cystic fibrosis).[9] Patients in the Pulmozyme arm experienced worsened lung function and more frequent pulmonary exacerbations vs. placebo. The authors concluded that Pulmozyme should not be used in this population.

## Background

**OVERVIEW**
Pulmozyme, a recombinant human deoxyribonuclease I, is indicated in conjunction with standard therapies for the management of patients with **cystic fibrosis** to improve pulmonary function.[1]

**Guidelines**

According to Patient Registry data compiled by the Cystic Fibrosis Foundation (2021), Pulmozyme is used by the vast majority of patients with cystic fibrosis.[2] Guidelines from the Cystic Fibrosis Foundation (2007, updated in 2013) address the chronic use of medications for management of lung health in cystic fibrosis patients 6 years of age and older.[3,4] These guidelines recommend Pulmozyme use for cystic fibrosis patients regardless of disease severity to improve lung function and reduce exacerbations. Separate guidelines have addressed Pulmozyme use in younger patients.[5,6] Although efficacy data are lacking in patients under 5 years of age, safety and tolerability have been established in patients as young as 3 months.[1,6] Cystic Fibrosis Foundation guidelines for infants under 2 years of age (2009) and children between 2 and 5 years of age (2016) support Pulmozyme use in these populations based on individual circumstances.[5,6]

**Additional Clinical Information**

*Treatment of Complicated Pleural Effusion*

Complicated pleural effusions are associated with large free-flowing or loculated effusions and bacterial presence in the pleural space. Evolution to empyema is characterized by pus in the pleural space, culture, or Gram stain–confirmed bacterial presence, and proliferation of fibroblasts resulting in thick fibrous pleural peel and loculations.[10] Pleural infection is usually managed by antibiotics alone or with drainage, depending on size and severity of the effusions. Surgical intervention is usually held in reserve for cases non-responsive to antibiotics and drainage but may be used when urgent treatment is needed. In more complicated loculated effusions and empyemas, intrapleural fibrinolytics have been used to reduce fibrin load and disrupt septations, thus enhancing the evacuation of fluid. Monotherapy with fibrinolytics has demonstrated conflicting results in adults.[11,12] Whereas, the combination of fibrinolytics with deoxyribonuclease (for example, dornase alfa) has been suggested as an additional method to reduce pleural fluid viscosity and improve pleural drainage.[13]

## References


1. Pulmozyme inhalation solution [prescribing information]. South San Francisco, CA: Genentech/Roche; July 2021.
2. Cystic Fibrosis Foundation. Patient Registry: 2021 Annual Data Report. Available at: https://www.cff.org/medical-professionals/patient-registry. Accessed on May 9, 2023.
3. Flume PA, O'Sullivan BP, Robinson KA, et al. Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health. *Am J Respir Crit Care Med.* 2007;176:957-969.
4. Mogayzel PJ Jr, Naureckas ET, Robinson KA, et al, Pulmonary Clinical Practice Guidelines Committee. Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health. *Am J Respir Crit Care Med.* 2013;187(7):680-689.
5. Borowitz D, Robinson KA, Rosenfeld M, et al, Cystic Fibrosis Foundation. Cystic Fibrosis Foundation evidence-based guidelines for management of infants with cystic fibrosis. *J Pediatr.* 2009;155(6 Suppl):S73-93.
6. Lahiri T, Hempstead SE, Brady C, et al. Clinical practice guidelines from the Cystic Fibrosis Foundation for preschoolers with cystic fibrosis. *Pediatrics.* 2016;137(4): e20151784.
7. Rubin BK. Aerosol medications for treatment of mucus clearance disorders. *Respiratory Care.* 2015;60(6):825-832.
8. Silverman RA, Foley F, Dalipi R, et al. The use of rhDNase in severely ill, non-intubated adult asthmatics refractory to bronchodilators: a pilot study. *Respir Med.* 2012; 106(8):1096-1102.
9. O'Donnell AE, Barker AF, Ilowite JS, Fick RB. Treatment of idiopathic bronchiectasis with aerosolized recombinant human DNase I. rhDNase Study Group. *Chest.* 1998;113(5):1329-1334.


## Supplemental References


10. Hamblin SE, Furmanek DL. Intrapleural tissue plasminogen activator for the treatment of parapneumonic effusion. Pharmacotherapy. 2010;30(8):855-862.[PubMed 20653362].
11. Janda S, Swiston J. Intrapleural fibrinolytic therapy for treatment of adult parapneumonic effusions and empyemas: a systematic review and meta-analysis. Chest. 2012;142(2):401-411.[PubMed 22459772].
12. Nie W, Liu Y, Ye J, et al. Efficacy of intrapleural instillation of fibrinolytics for treating pleural empyema and parapneumonic effusion: a meta-analysis of randomized control trials. Clin Respir J. 2014;8(3):281-291.[PubMed 24428897].
13. Psallidas I, Corcoran JP, Rahman NM. Management of parapneumonic effusions and empyema. Semin Respir Crit Care Med. 2014;35(6):715-722.[PubMed 25463162].