Pharmacy Policy Bulletin: J-0430 Cystic Fibrosis Inhaled Medications – Commercial and Healthcare Reform	
Number: J-0430	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Other Managed Prior Authorization = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0430-021	**Original Date:** 06/03/2015
Effective Date: 04/25/2025	**Review Date:** 04/09/2025

Drugs Product(s):	• Bethkis (tobramycin inhalation solution) 300 mg/4 mL • Bronchitol (mannitol inhalation powder) • Cayston (aztreonam inhalation solution) • Kitabis Pak (tobramycin inhalation solution) • Pulmozyme (dornase alfa) • Tobi (tobramycin inhalation solution) 300 mg/5 mL ○ Generic formulation – **Applies only to Commercial Plans** • Tobi Podhaler (tobramycin inhalation powder)

FDA-Approved Indication(s):	• Bethkis 300 mg/4 mL
	  ○ Management of cystic fibrosis (CF) patients with *Pseudomonas aeruginosa*
	• Bronchitol
	  ○ Add-on maintenance therapy to improve pulmonary function in adult patients 18 years of age and older with CF
	• Cayston
	  ○ Improve respiratory symptoms in CF patients with *Pseudomonas aeruginosa*
	• Kitabis Pak
	  ○ Management of CF in adults and pediatric patients 6 years of age and older with *Pseudomonas aeruginosa*
	• Pulmozyme
	  ○ Management of CF patients to improve pulmonary function in conjunction with standard therapies
	• Tobi (tobramycin inhalation solution) 300 mg/5 mL
	  ○ Management of CF in adults and pediatric patients 6 years of age and older with *Pseudomonas aeruginosa*
	• Tobi Podhaler
	  ○ Management of CF patients with *Pseudomonas aeruginosa*

Background:	• Bethkis, Kitabis Pak, Tobi, and Tobi Podhaler are aminoglycosides that act primarily by disrupting protein synthesis in the bacterial cell and leads to death of

	the cell. Tobramycin has activity against a wide range of gram-negative bacteria including *P. aeruginosa*. • Bronchitol is used as a mucolytic agent for which the precise mechanism of action is unknown. Prior to prescribing, the member needs to pass a Bronchitol Tolerance Test (BTT). Bronchitol can cause bronchospasm, which can be severe in susceptible patients. The BTT must be administered under the supervision of a healthcare practitioner who can treat severe bronchospasm. • Cayston binds to penicillin-binding proteins of susceptible bacteria, which leads to inhibition of bacterial cell wall synthesis and death of the cell. Cayston exhibits activity *in vitro* against gram-negative aerobic pathogens including *P. aeruginosa* and its activity is not decreased in the presence of CF lung secretions. • Pulmozyme is a recombinant human deoxyribonuclease I (rhDNase), an enzyme that selectively cleaves DNA. In CF patients, retention of viscous purulent secretions in the airways contributes both to reduced pulmonary function and to exacerbations of infection. Purulent pulmonary secretions contain very high concentrations of extracellular DNA released by degenerating leukocytes that accumulate in response to infection. • According to the Centers of Disease Control and Prevention, *Burkholderia cepacia*, also known simply as *B. cepacia*, is the name for a group or "complex" of opportunistic bacteria that can be found in soil and water. The Cystic Fibrosis Foundation states that there are almost 20 different *B. cepacia* complex species, though the most common species found in patients with cystic fibrosis are: *B. cenocepacia, B. multivorans, B. vitenamiensis,* and *B. dolosa.* • Standard therapies for CF include a variety of therapies including bronchodilators, hypertonic saline, anti-inflammatory treatments (for example corticosteroids, azithromycin, ibuprofen), antibiotics (oral, intravenous, or inhaled), pancreatic enzyme replacement therapy, and cystic fibrosis transmembrane conductance regulator (CFTR) modulators. • Prescribing Considerations: ○ Safety and efficacy of Bethkis have not been demonstrated in patients under the age of six years, patients with a forced expiratory volume in one second (FEV1) < 40% or > 80% predicted, or patients colonized with *B. cepacia.* ○ Safety and effectiveness of Cayston have not been established in pediatric patients below the age of 7 years, patients with FEV1 < 25% or > 75% predicted, or patients colonized with *B. cepacia*. ○ Safety and efficacy of Kitabis Pak have not been demonstrated in patients under the age of 6 years, patients with FEV1 < 25% or > 75% predicted, or patients colonized with *B. cepacia.* ○ Safety and efficacy of Tobi have not been demonstrated in patients under the age of 6 years, patients with FEV1 < 25% or > 75% predicted, or patients colonized with *B. cepacia*. ○ Safety and efficacy of Tobi Podhaler have not been demonstrated in patients under the age of 6 years, patients with an FEV1 < 25% or > 80%, or patients colonized with *B. cepacia*.

Approval Criteria

I. Initial Authorization

A. Bethkis 300 mg/4 mL (tobramycin inhalation solution), Kitabis Pak, Tobi (tobramycin inhalation solution) 300 mg/5 mL, and Tobi Podhaler

When a benefit, coverage of a tobramycin product may be approved when all of the following criteria are met **(1., 2., and 3.):**

1. The member has a diagnosis of CF. (ICD-10: E84)
2. The member is colonized with *Pseudomonas aeruginosa*.
3. The member meets one (1) of the following **(a. or b.)**:
   a. If the request is for brand Tobi inhalation solution, the member has experienced therapeutic failure or intolerance to generic tobramycin inhalation solution.
   b. If the request is for brand Bethkis 300 mg/4 mL inhalation solution, Kitabis Pak, or Tobi Podhaler, the member has experienced therapeutic failure or intolerance to plan-preferred, generic tobramycin inhalation solution.

B. Bronchitol

When a benefit, coverage of Bronchitol may be approved when all of the following criteria are met **(1. through 5.)**:

1. The member is 18 years of age or older.
2. The member has a diagnosis of CF. (ICD-10: E84)
3. The prescriber attests that the member has passed a Bronchitol Tolerance Test.
4. The prescriber attests that Bronchitol will be used in conjunction with standard therapies (for example, bronchodilators, hypertonic saline, antibiotics, anti-inflammatory therapy, CFTR modulators, pancreatic enzymes).
5. The member has experienced therapeutic failure, contraindication, or intolerance to hypertonic saline solution for inhalation.

C. Cayston

When a benefit, coverage of Cayston may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of CF. (ICD-10: E84)
2. The member is colonized with *Pseudomonas aeruginosa*.

D. Pulmozyme

When a benefit, coverage of Pulmozyme may be approved when all of the following criteria are met (**1. and 2.**):

1. The member has a diagnosis of CF. (ICD-10: E84)
2. The prescriber attests that Pulmozyme will be used in conjunction with standard therapies (for example, bronchodilators, hypertonic saline, antibiotics, anti-inflammatory therapy, CFTR modulators, pancreatic enzymes).

II. Reauthorization

A. Bethkis 300 mg/4 mL, Cayston, Kitabis Pak, Tobi (tobramycin inhalation solution) 300 mg/5 mL, and Tobi Podhaler

When a benefit, reauthorization of a tobramycin product may be approved when one (1) of the following criteria is met **(1. through 4.)**:

1. The prescriber attests that the member experienced a decrease in sputum density of *Pseudomonas aeruginosa.*
2. The prescriber attests that the member experienced an increase in $FEV_{1.}$
3. The prescriber attests that the member experienced a decrease in the number of hospitalizations.
4. The prescriber attests that the member experienced a decrease in the number of pulmonary exacerbations.

B. Bronchitol

When a benefit, reauthorization of Bronchitol may be approved when the following criterion is met **(1.)**:

1. The prescriber attests that the member experienced an increase in $FEV_{1.}$

C. Pulmozyme

When a benefit, reauthorization of Pulmozyme may be approved when one (1) of the following criteria is met **(1., 2., or 3.)**:

1. The prescriber attests that the member experienced an increase in FEV_1.
2. The prescriber attests that the member experienced a decrease in the number of hospitalizations.
3. The prescriber attests that the member experienced a decrease in the number of pulmonary exacerbations.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 24 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Bethkis [package insert]. Woodstock, IL: Chiesi USA, Inc.; February 2023.
2. Bronchitol [package insert]. Cary, NC: Chiesi USA, Inc; October 2020.
3. Cayston [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2019.
4. Kitabis Pak [package insert]. Woodstock, IL: Catalent Pharma Solutions; April 2023.
5. Pulmozyme [package insert]. South San Francisco, CA: Genentech, Inc.; Febryary 2024.
6. Tobi [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2023.
7. Tobi Podhaler [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2023.
8. Tobramycin Inhalation Solution [package insert]. Princeton, NJ: Dr. Reddy's Laboratories, Inc.; July 2021.
9. *DRUGDEX System* (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2024.
10. Cystic Fibrosis Foundation. Clinical Care Guidelines. Available at: https://www.cff.org/medical-professionals/clinical-care-guidelines. Accessed March 6, 2025.
11. CDC. About Burkholderia cepacia complex. Available at: https://www.cdc.gov/b-cepacia/about/?CDC_AAref_Val=https://www.cdc.gov/hai/organisms/bcepacia.html. Accessed August 13, 2024.
12. Cystic Fibrosis Foundation. Burkholderia Cepacia Complex (B. cepacia). Available at: https://www.cff.org/Life-With-CF/Daily-Life/Germs-and-Staying-Healthy/What-Are-Germs/Burkholderia-Cepacia-Complex/. Accessed August 13, 2024.