PRIOR AUTHORIZATION POLICY

POLICY: Antibiotics (Inhaled) – TOBI Podhaler Prior Authorization Policy
- TOBI® Podhaler (tobramycin inhalation powder – Novartis Pharmaceuticals)

REVIEW DATE: 04/07/2021

OVERVIEW

TOBI Podhaler, an aminoglycoside antibiotic, is indicated for the management of **cystic fibrosis** (CF) patients with *Pseudomonas aeruginosa*.[1] Safety and efficacy have not been demonstrated in patients < 6 years of age, patients with forced expiratory volume in 1 second (FEV1) < 25% or > 80% predicted, or patients colonized with *Burkholderia cepacia*.

Disease Overview

CF is a complex, chronic, multi-organ, inherited disorder.[2] Lung disease accounts for nearly 85% of mortality in patients with CF. Lung destruction in CF is caused by obstruction of the airways due to dehydrated and thickened secretions, resultant endobronchial infection, and an exaggerated inflammatory response leading to development of bronchiectasis and progressive obstructive airway diseases. In patients with CF, there are a number of maintenance treatments that may be prescribed, including inhaled antibiotics.

Aerosolized delivery of antimicrobial agents for pulmonary infections provides an ideal method for achieving high local drug concentration in the lungs while minimizing systemic exposure.[3] It has been estimated that by 18 years of age, 80% of patients with CF have *P. aeruginosa* infection. Once *P. aeruginosa* is established in the respiratory tract of a patient with CF, the clinical course of the disease can worsen. Although many organisms can be found in the lower respiratory tract of patients who have CF, infection with mucoid *P. aeruginosa* is common and is associated with poorer outcomes.[4] Infection with chronic mucoid *P. aeruginosa* is associated with poor growth, more rapid decline in lung function, increased need for antibiotic treatment and hospitalization, and earlier death. In addition, mucoid *P. aeruginosa* (characterized by its biofilm) is more resistant to antibiotics than non-mucoid *P. aeruginosa*. Therefore, effective antimicrobial therapies targeting *P. aeruginosa* are central to the management of CF.

Guidelines

The Cystic Fibrosis Foundation (CFF) established a Pulmonary Therapeutics Committee which provided recommendations, based on available evidence (2007) for the use of medications intended to maintain lung health.[2] In 2013, the Committee published updated recommendations for the use of chronic medications in the management of CF lung disease.[5] In patients ≥ 6 years of age with CF and moderate-to-severe lung disease with *P. aeruginosa* persistently present in cultures of the airways, the chronic use of inhaled tobramycin is strongly recommended to improve lung function, quality of life, and reduce exacerbations. For mild disease, the Committee recommends chronic use of inhaled tobramycin for patients with CF ≥ 6 years of age with *P. aeruginosa* persistently present in cultures of the airways, to reduce exacerbations.

The CFF published a systematic review of the literature regarding eradication of initial *P. aeruginosa* infections to develop guidelines for effective prevention (2014).[6] The recommendations pertaining to inhaled antibiotics are as follows: 1) Inhaled antibiotic therapy is recommended for the treatment of initial or new growth of *P. aeruginosa* (the favored antibiotic regimen is tobramycin [300 mg BID] for 28 days); and 2) Prophylactic antipseudomonal antibiotics to prevent the acquisition of *P. aeruginosa* are not recommended.

The American Thoracic Society (ATS) published a clinical review (2013) of non-cystic fibrosis bronchiectasis on their webpage.[7] The review lists nebulized antibiotics (e.g., colistin, gentamicin, tobramycin) as treatment options for the eradication or suppression of *P. aeruginosa*. The European Respiratory Society (ERS) have published guidelines (2017) for the management of adult bronchiectasis and recommend patients with a new isolate of *P. aeruginosa* be offered eradication antibiotic treatment which includes nebulized antibiotics (e.g., colistin, gentamicin, tobramycin).[8] Neither the ATS or the ERS guidelines include Tobi Podhaler® (tobramycin inhalation powder) as a treatment option for bronchiectasis and no clinical trials have been published with Tobi Podhaler for treatment of non-cystic fibrosis bronchiectasis.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of TOBI Podhaler. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with TOBI Podhaler as well as the monitoring required for adverse events and long-term efficacy, approval requires TOBI Podhaler to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of TOBI Podhaler is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Cystic Fibrosis.** Approve for 1 year if the patient meets the following criteria (A, B and C):
   - **A)** Patient is ≥ 6 years of age; AND
   - **B)** Patient has *Pseudomonas aeruginosa* in culture of the airway (e.g., sputum culture, oropharyngeal culture, bronchoalveolar lavage culture); AND
   - **C)** TOBI Podhaler is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of cystic fibrosis.

Other Uses with Supportive Evidence

2. **Continuation of TOBI Podhaler**. Approve for 1 month if the patient was started on TOBI Podhaler and is continuing course of therapy.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of TOBI Podhaler is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. TOBI® Podhaler inhalation powder [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
2. Flume PK, 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.

3. Le J, Ashley ED, Neuhauser MM, et al and the Society of Infectious Diseases Pharmacists Aerosolized Antimicrobials Task Force. Consensus summary of aerosolized antimicrobial agents: application of guideline criteria. Insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy*. 2010;30(6):562-584.
4. Geller DE. Aerosol antibiotics in cystic fibrosis. *Respir Care*. 2009;54(5):658-669.
5. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic Fibrosis Pulmonary Guidelines. Chronic Medications for Maintenance of Lung Health. *Am J Respir Crit Care Med*. 2013;187:680-689.
6. Mogayzel PJ, Naureckas ET, Robinson KA, et al; and the Cystic Fibrosis Foundation Pulmonary Clinical Practice Guidelines Committee. Pharmacologic approaches to prevention and eradication of initial *Pseudomonas aeruginosa* infection. *Ann Am Thorac Soc*. 2014;11(10):1640-1650.
7. McShane PJ, Naureckas ET, Tino G, Strek ME. Non-cystic fibrosis bronchiectasis. *Am J Respir Crit Care Med*. 2013;188:647-656.
8. Polverino E, Goeminne PC, McDonnell, et al. European Respiratory Society guidelines for the management of adult bronchiectasis. *Eur Respir J*. 2017;50:1700629.