Original Effective Date: 11/01/2016
Current Effective Date: 11/23/2023
Last P&T Approval/Version: 10/25/2023
Next Review Due By: 10/2024
Policy Number: C8665-A

Tobramycin for Inhalation

PRODUCTS AFFECTED

Bethkis (tobramycin neb solution), Kitabis (tobramycin neb solution), Tobi (tobramycin neb solution), Tobi Podhaler (tobramycin inhal caps), tobramycin nebulized solution

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Cystic fibrosis, Bronchiectasis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. CYSTIC FIBROSIS:
   1. Documented diagnosis of cystic fibrosis
      AND
   2. Documentation of pseudomonas aeruginosa in at least one airway [DOCUMENTATION

REQUIRED]
AND

3. FOR BETHKIS: Documentation that member has a forced expiratory volume in one second (FEV1) between 40% and 80% predicted [DOCUMENTATION REQUIRED]
   OR
   FOR KITABIS, TOBI INHALATION SOLUTION, TOBRAMYCIN INHALATION SOLUTION: Documentation that member has a forced expiratory volume in one second (FEV1) between 25% and 75% predicted [DOCUMENTATION REQUIRED]
   OR
   FOR TOBI PODHALER: Documentation that member has a forced expiratory volume in one second (FEV1) between 25% and 80% predicted [DOCUMENTATION REQUIRED
   AND
4. Prescriber attests (or the clinical reviewer has found) that the member is not colonized with Burkholderia cepacia
   AND
5. (a) Documentation that therapeutic plan does NOT include concurrent or alternating use of Cayston with TOBI/TOBI Podhaler or tobramycin inhalation
   OR
   (b) If concurrent therapy is requested: Member has tried and failed monotherapy with Cayston (aztreonam) AND tobramycin separately prior to using concurrent alternating therapy [DOCUMENTATION REQUIRED]
   AND
6. Documentation member has tried, failed or has medical necessity for using any product other than preferred formulary agent (tobramycin nebulized solution)
   AND
7. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to inhaled tobramycin include: patients with a known hypersensitivity to any aminoglycoside]

B. NON-CYSTIC FIBROSIS BRONCHIECTASIS:
   1. Documented diagnosis of non-cystic fibrosis bronchiectasis
      AND
   2. Documentation member has had three or more exacerbations per year OR significant morbidity from fewer exacerbations
      AND
   3. Documentation that member has tobramycin sensitive pseudomonas aeruginosa present in the respiratory secretions
      AND
   4. Documentation of baseline forced expiratory volume in one second (FEV1) for assessment of efficacy
      AND
   5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to inhaled tobramycin include: patients with a known hypersensitivity to any aminoglycoside]

CONTINUATION OF THERAPY:

A. CYSTIC FIBROSIS:
   1. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms
      AND
   2. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
      AND

3. If inhaled tobramycin (Bethkis, Kitabis Pak, TOBI, TOBI Podhaler) is prescribed concurrently (or for alternating use) with Cayston, documentation supports inadequate response to both agents alone (e.g., deteriorating pulmonary status, recurrent pulmonary exacerbations) [DOCUMENTATION REQUIRED]
   AND
4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

B. NON-CYSTIC FIBROSIS BRONCHIECTASIS:
1. Documentation showing the benefit of therapy including reduced sputum Pseudomonas density, improved forced expiratory volume in one second (FEV1), and decreased hospitalizations
   AND
2. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a pulmonologist, infectious disease specialist, cystic fibrosis specialist or physician from a CF center accredited by the Cystic Fibrosis Foundation. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
6 years of age and older

QUANTITY:
CYSTIC FIBROSIS: 28 day supply every 56 days (28 days on, 28 days off)
NON-CYSTIC FIBROSIS BRONCHIECTASIS: 160 mg or 300 mg twice daily (28 days on, 28 days off)

PLACE OF ADMINISTRATION:
The recommendation is that inhalation medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Inhalation

DRUG CLASS:
Aminoglycoside

FDA-APPROVED USES:
Indicated for the management of cystic fibrosis patients with Pseudomonas aeruginosa
Safety and efficacy have not been demonstrated in patients under the age of 6 years, patients with a forced expiratory volume in one second (FEV1) less than 40% or greater than 80% predicted [BETHKIS], FEV1 less than 25% or greater than 75% predicted [KITABIS, TOBI INHALATION SOLUTION, TOBRAMYCIN INHALATION SOLUTION], FEV1 less than 25% or greater than 80% predicted [TOBI PODHALER], or patients colonized with Burkholderia cepacia.

COMPENDIAL APPROVED OFF-LABELED USES:
Pseudomonas aeruginosa lower respiratory tract infection in patients with non-cystic fibrosis bronchiectasis

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Tobramycin for inhalation are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Tobramycin for inhalation include: patients with a known hypersensitivity to any aminoglycoside.

OTHER SPECIAL CONSIDERATIONS:
The use of continuous alternating therapy (i.e., alternating different inhaled antibiotics in order to provide continuous therapy) lacks sufficient evidence. The efficacy of this practice was evaluated in a randomized, double-blind, phase 3 trial. 90 patients received 28-days inhaled tobramycin alternating with either 28- days inhaled aztreonam or placebo. Although the study found reduced exacerbation and respiratory hospitalization rates with the alternating tobramycin/aztreonam regimen compared to tobramycin/placebo, it was underpowered, and these results were not statistically significant.
Administer Bethkis using a hand-held PARI LC PLUS Reusable Nebulizer with a PARI Vios Air compressor.
Administer Kitabis, TOBI, Tobramycin inhalation solution using the PARI LC PLUS Reusable Nebulizer and DeVilbiss Pulmo-Aide compressor.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	N/A

AVAILABLE DOSAGE FORMS:
Bethkis NEBU 300MG/4ML
Kitabis Pak NEBU 300MG/5ML
Tobi NEBU 300MG/5ML
Tobi Podhaler CAPS 28MG
Tobramycin NEBU 300MG/4ML
Tobramycin NEBU 300MG/5ML

REFERENCES

1. Kitabis Pak (tobramycin inhalation solution) [prescribing information]. Woodstock, IL: Catalent Pharma Solutions, LLC; April 2023.

2. Bethkis (tobramycin) [prescribing information]. Woodstock, IL: Chiesi USA Inc; February 2023.
3. Tobi Podhaler (tobramycin) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2023.
4. Tobi (tobramycin) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; February 2023.
5. Flume PA, Clancy JP, Retsch-Bogart GZ, et al. Continuous alternating inhaled antibiotics for chronic pseudomonal infection in cystic fibrosis. J Cyst Fibrosis. 2016; 15(6): 809-815
6. Shaw PK, Braun TL, Liebergen A, et al, “Aerosolized Tobramycin Pharmacokinetics in Cystic Fibrosis Patients,” J Pediatr Pharm Pract, 1997, 2(1):23-6.
7. Ramsey BW, Pepe MS, Quan JM, et al, "Intermittent Administration of Inhaled Tobramycin in Patients With Cystic Fibrosis. Cystic Fibrosis Inhaled Tobramycin Study Group," N Engl J Med, 1999, 340(1):23-30
8. MacLusky IB, Gold R, Corey M, Levison H. Long-term effects of inhaled tobramycin in patients with cystic fibrosis colonized with Pseudomonas aeruginosa. Pediatr Pulmonol.1989;7(1):42-48.
9. Le J, Ashley ED, Neuhauser MM, et al; 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.
10. Brodt AM, Stovold E, Zhang L. Inhaled antibiotics for stable non-cystic fibrosis bronchiectasis: a systematic review. Eur Respir J 2014; 44:382.
11. Mogayzel, P., Naureckas, E., Robinson, K., Brady, C., Guill, M., & Lahiri, T. et al. (2014). Cystic Fibrosis Foundation Pulmonary Guideline. Pharmacologic Approaches to Prevention and Eradication of Initial Pseudomonas aeruginosa Infection. Annals Of The American Thoracic Society, 11(10), 1640-1650. doi: 10.1513/annalsats.201404-166oc
12. Polverino, E., Goeminne, P., McDonnell, M., Aliberti, S., Marshall, S., & Loebinger, M. et al. (2017). European Respiratory Society guidelines for the management of adult bronchiectasis. European Respiratory Journal, 50(3), 1700629. doi: 10.1183/13993003.00629-2017

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Age Restrictions FDA-Approved Uses Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms References	Q4 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q4 2022
Q2 2022 Established tracking in new format	Historical changes on file