Clinical Policy: Tobramycin (Bethkis, Kitabis Pak, TOBI, TOBI Podhaler)

Reference Number: NH.PHAR.211
Effective Date: 10.25
Last Review Date: 10.25
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder **at the end of this policy for important regulatory and legal information.**

Description

Tobramycin (Bethkis®, Kitabis® Pak, TOBI®, TOBI® Podhaler®) is an aminoglycoside antibacterial drug.

FDA Approved Indication(s)

Bethkis, Kitabis Pak, TOBI, and TOBI Podhaler are indicated for the management of cystic fibrosis (CF) in patients with *Pseudomonas aeruginosa*. Kitabis Pak and TOBI are specifically indicated for patients 6 years of age and older.

Limitations(s) of use: Safety and efficacy have not been demonstrated in patients under the age of 6 years, patients colonized with *Burkholderia cepacia*, or patients with forced expiratory volume in one second (FEV_1):

- < 25% or > 75% predicted for Kitabis Pak and TOBI
- < 25% or > 80% predicted for TOBI Podhaler
- < 40% or > 80% predicted for Bethkis

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that members have met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Bethkis, Kitabis Pak, TOBI, and TOBI Podhaler are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cystic Fibrosis (must meet all)**:**

1. Diagnosis of CF;
2. Prescribed by or in consultation with a pulmonologist, an infection disease specialist, or an expert in treatment of cystic fibrosis;
3. Age ≥ 6 years;
4. *Pseudomonas aeruginosa* is present in at least one airway culture;
5. **If request is for Bethkis, Kitabis Pak**, member must use **brand name**, unless contraindicated or clinically significant adverse effects are experienced;
6. If tobramycin is prescribed concurrently (or for alternating use) with Cayston®, documentation supports inadequate response to either agent alone (e.g., deteriorating pulmonary status, recurrent pulmonary exacerbations);
7. Dose does not exceed one of the following (a or b):

a. Inhalation solution (Bethkis, Kitabis Pak, TOBI): 600 mg per day administered on a 28 days on/28 days off cycle;
b. Inhalation powder (TOBI Podhaler): 224 mg per day administered on a 28 days on/28 days off cycle.

Approval duration:
Medicaid – 6 months ***(Bethkis and Kitabis Pak approvals must be approved for brand name only unless generic specifically requested and contraindication or clinically significant adverse effects are experienced)**

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL, the no coverage criteria policy: CP.PMN.255; or
   b. For drugs NOT on the PDL, the non-formulary policy: CP.PMN.16; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy: CP.PMN.53.

II. Continued Therapy

A. Cystic Fibrosis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by reduction in respiratory symptoms (e.g., cough, wheezing, sputum production, or pulmonary exacerbations due to *Pseudomonas aeruginosa*);
3. If request is for **Bethkis, Kitabis Pak**, member must use **brand name**, unless contraindicated or clinically significant adverse effects are experienced;
4. If tobramycin is prescribed concurrently (or for alternating use) with Cayston, documentation supports inadequate response to either agent alone (e.g., deteriorating pulmonary status, recurrent pulmonary exacerbations);
5. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Inhalation solution (Bethkis, Kitabis Pak, TOBI): 600 mg per day administered on a 28 days on/28 days off cycle;
   b. Inhalation powder (TOBI Podhaler): 224 mg per day administered on a 28 days on/28 days off cycle.

Approval duration:
Medicaid – 12 months ***(Bethkis and Kitabis Pak approvals must be approved for brand name only unless generic specifically requested and contraindication or clinically significant adverse effects are experienced)**

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL, the no coverage criteria policy: CP.PMN.255; or
   b. For drugs NOT on the PDL, the non-formulary policy: CP.PMN.16; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy: CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CF: cystic fibrosis
FDA: Food and Drug Administration
FEV_1: forced expiratory volume in one second

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): known hypersensitivity to any aminoglycoside
- Boxed warning(s): none reported

Appendix D: General Information
- Tobramycin is recommended for chronic use in both mild and moderate-to-severe disease per the American Thoracic Society 2013 CF guidelines. Severity of lung disease is defined by FEV_1 predicted as follows: normal, > 90% predicted; mildly impaired, 70-89% predicted; moderately impaired, 40-69% predicted; and severely impaired, < 40% predicted.
- 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. A total of 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.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Tobramycin inhalation solution (Bethkis, Kitabis Pak, TOBI)	300 mg inhaled BID for 28 days (followed by 28 days off tobramycin therapy)	600 mg/day
Tobramycin inhalation powder (TOBI Podhaler)	112 mg (4 capsules) inhaled BID for 28 days (followed by 28 days off tobramycin therapy)	224 mg/day

VI. Product Availability

Drug Name	Availability
Tobramycin inhalation solution (Bethkis)	4 mL single-dose ampule: 300 mg
Tobramycin inhalation solution (Kitabis Pak)	5 mL single-dose ampule: 300 mg Co-packaged with a PARI LC PLUS Reusable Nebulizer
Tobramycin inhalation solution (TOBI)	5 mL single-dose ampule: 300 mg
Tobramycin inhalation powder (TOBI Podhaler)	Capsule: 28 mg

VII. References

1. Bethkis Prescribing Information. Woodstock, IL: Catalent Pharm Solutions, LLC; February 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/201820s006lbl.pdf. Accessed April 14, 2025.
2. Kitabis Pak Prescribing Information. Woodstock, IL: Catalent Pharm Solutions, LLC; August 2023. Available at: https://kitabis.com/HealthcareProviders/prescribing-information. Accessed April 14, 2025.
3. TOBI Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/050753s028lbl.pdf. Accessed April 14, 2025.
4. TOBI Podhaler Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2023. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/201688s019lbl.pdf. Accessed April 14, 2025.
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.* April 1, 2013; 187 (7): 680-689.
6. 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.
7. Kapnadak SG, Dimango E, Hadjiliadis D, et al. Cystic Fibrosis Foundation consensus guidelines for the care of individuals with advanced cystic fibrosis lung disease. *J Cyst Fibros* 2020 May;19(3):344-354. doi: 10.1016/j.jcf.2020.02.015.
8. Cystic Fibrosis Foundation: Clinical Care Guidelines. Available at: https://www.cff.org/medical-professionals/clinical-care-guidelines. Accessed April 15, 2025.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7682	Tobramycin, inhalation solution, FDA-approved final product, non-compounded, unit dose form, administered through DME, per 300 mg
J7685	Tobramycin, inhalation solution, compounded product, administered through DME, unit dose form, per 300 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.25	10.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.