Clinical Policy: Infectious Disease Agents: Antibiotics - Inhaled

Reference Number: OH.PHAR.PPA.68
Effective Date: 01/01/2020
Last Review Date: N/A
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description:

INFECTIOUS DISEASE AGENTS: ANTIBIOTICS - INHALED

CLINICAL PA REQUIRED "PREFERRED"	PA REQUIRED "NON-PREFERRED"
KITABIS® PAK (tobramycin inhalation solution with nebulizer) TOBRAMYCIN inhalation solution- (generic of TOBI™)	BETHKIS® inhalation solution (tobramycin) CAYSTON® inhalation solution (aztreonam) TOBI™ Podhaler™ (tobramycin inhalation powder)

INFECTIOUS DISEASE AGENTS: ANTIBIOTICS – INHALED AMIKACIN

CLINICAL PA REQUIRED "PREFERRED"	PA REQUIRED "NON-PREFERRED"
ARIKAYCE® (amikacin)	

FDA Approved Indication(s):

- Kitabis Pak, Tobi, Bethkis, TOBI Podhaler, and Cayston are indicated for the management of cystic fibrosis patients with Pseudomonas aeruginosa.
- Arikayce is indicated for the treatment of Mycobacterium avium complex infection (MAC).

Policy/Criteria

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

It is the policy of Buckeye Health Plan, an affiliate of Centene Corporation®, that Kitabis Pak, Tobi, Bethkis, TOBI Podhaler, Cayston, and Arikayce are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. For Kitabis Pak, Tobi, Bethkis, TOBI Podhaler, Cayston (must meet all)**:**

1. Diagnosis of cystic fibrosis with pseudomonas-related infection;
2. Age ≥ 6 years for tobramycin products;
3. Age ≥ 7 years for aztreonam (Cayston);
4. "Pulse" dosing cycles of 28 days on drug, followed by 28 days off drug;

5. 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);
6. No less than a 28-day trial of at least one preferred medication UNLESS there is a reason the member cannot be changed to a preferred medication. Acceptable reasons include:
   - Allergies to all medications that are preferred.
   - Contraindication to or drug-to-drug interaction with medications that are preferred.
   - History of unacceptable/toxic side effects to medications that are preferred.
7. Dose does not exceed the FDA-approved maximum recommended dose for the relevant drug.

NOTE: Kitabis Pak and Tobramycin inhalation solution are preferred.

Approval duration: 28 days, reauthorized through electronic PA if history of product in previous 120 days.

B. For Arikayce (must meet all)**:**

1. Diagnosis of *Mycobacterium avium* complex (MAC) lung disease;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an infectious disease specialist or pulmonologist;
4. Member has not achieved negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy (e.g., macrolide, rifampin, & ethambutol);
5. Dose does not exceed 1 dose per day.

Approval duration: Initial authorization 180 days.

C. Other diagnoses/indications:

1. There are no pharmacy and therapeutic committee approved off-label use criteria for the diagnosis;
2. Use is supported by one of the following (a, b, or c):
   a. The National Comprehensive Cancer Network (NCCN) Drug Information and Biologics Compendium level of evidence 1 or 2A;
   b. Evidence from at least two high-quality, published studies in reputable peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i – iv):
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
      iii. Clinically meaningful outcomes as a result of the drug therapy in question;
      iv. Appropriate experimental design and method to address research questions;
   c. Micromedex DrugDex® with strength of recommendation Class I, IIa, or IIb;
3. Prescribed by or in consultation with an appropriate specialist for the diagnosis;
4. Failure of an adequate trial of at least two FDA-approved drugs for the indication and/or drugs that are considered the standard of care, when such agents exist for the same indication at maximum indicated doses, unless no such drugs exist, at maximum

indicated doses, unless contraindicated or clinically significant adverse effect are experienced;
5. Dosing regimen and duration are within dosing guidelines recommended by clinical practice guidelines and/or medical literature.

Approval duration: Initial authorization 180 days.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. For Kitabis Pak, Tobi, Bethkis, TOBI Podhaler, Cayston: Member is responding positively to therapy.
2. For Arikayce: Evidence of culture conversion (negative sputum culture).

Approval duration: Subsequent authorizations 12 months.

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

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 policy – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MAC: Mycobacterium Avium Complex
PA: Prior Authorization

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
tobramycin inhalation solution (Kitabis Pak)	**Cystic fibrosis patients with Pseudomonas aeruginosa** 300 mg (one ampule) via inhalation twice daily for 28 days. Administer in alternating 28-day periods (i.e., administer for 28 days, then 28 days off therapy).	600 mg/day
tobramycin inhalation solution (Tobi)	**Cystic fibrosis patients with Pseudomonas aeruginosa** 300 mg (one ampule) via inhalation twice daily for 28 days. Administer in alternating 28-day periods (i.e., administer for 28 days, then 28 days off therapy).	600 mg/day
Arikayce (amikacin)	**Mycobacterium avium complex infection (MAC)** 590 mg inhalation by nebulizer once daily as part of combination therapy.	590 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Aminoglycoside Hypersensitivity
- Boxed warning(s):
  - Neonates
  - Nephrotoxicity
  - Neuromuscular blockade
  - Neurotoxicity
  - Ototoxicity
  - Pregnancy
  - Premature neonates
  - Pulmonary disease
  - Renal impairment

V. Dosage and Administration

Indication: Adults, Adolescents, and Children 6 years and older with cystic fibrosis			
Medication	**Dosing Regimen**	**Maximum Dose**	**Reference**
Tobramycin 300 mg/5 mL inhalation solution (Kitabis Pak)	300 mg (one ampule) via inhalation twice daily for 28 days. Administer in alternating 28-day periods (i.e., administer for 28 days, then 28 days off therapy). Administer the twice daily dose as close to 12 hours apart as possible. Safety and efficacy have not been demonstrated in patients with FEV1 less than 25% or more than 75% predicted (for TOBI), or in patients colonized with Burkholderia cepacia.	600 mg/day (two ampules)	FDA-approved labeling
Tobramycin 300 mg/5 mL inhalation solution (Tobi)	300 mg (one ampule) via inhalation twice daily for 28 days. Administer in alternating 28-day periods (i.e., administer for 28 days, then 28 days off therapy). Administer the twice daily dose as close to 12 hours apart as possible. Safety and efficacy have not been demonstrated in patients with FEV1 less than 25% or more than 75% predicted (for TOBI), or in patients colonized with Burkholderia cepacia.	600 mg/day (two ampules)	FDA-approved labeling

Indication: Adults, Adolescents, and Children 6 years and older with cystic fibrosis			
Medication	**Dosing Regimen**	**Maximum Dose**	**Reference**
Bethkis 300 mg/4 mL inhalation solution	300 mg (one ampule) via inhalation twice daily for 28 days. Administer in alternating 28-day periods (i.e., administer for 28 days, then 28 days off therapy). Administer the twice daily dose as close to 12 hours apart as possible. Safety and efficacy have not been demonstrated in patients with FEV1 less than 40% or more than 80% predicted (for Bethkis), or in patients colonized with Burkholderia cepacia.	600 mg/day (two ampules)	FDA-approved labeling
TOBI Podhaler 28mg inhalation powder	112 mg (four 28 mg capsules) via oral inhalation twice daily for 28 days. Administer in alternating 28-day periods (i.e., administer for 28 days, then 28 days off therapy). Administer the twice daily dose as close to 12 hours apart as possible. Safety and efficacy have not been demonstrated in patients with FEV1 less than 25% or more than 80% predicted, or in patients colonized with Burkholderia cepacia.	224 mg/day (eight capsules)	FDA-approved labeling

Indication: Adults, children, and adolescents 7 to 17 years with cystic fibrosis			
Medication	**Dosing Regimen**	**Maximum Dose**	**Reference**
Cayston 75mg powder for inhalation solution	75 mg nebulized 3 times daily for 28 days, then 28 days off aztreonam. Doses should be administered at least 4 hours apart. Safety and efficacy have not been demonstrated in patients colonized with Burkholderia cepacia.	225 mg/day nebulized	FDA-approved labeling

Indication: Adults with mycobacterium avium complex infection (MAC)			
Medication	**Dosing Regimen**	**Maximum Dose**	**Reference**
Arikayce 590mg/8.4mL inhalation suspension	590 mg inhalation by nebulizer once daily as part of combo therapy in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy.	590 mg/day	FDA-approved labeling

VI. Product Availability

Drug Name	Availability
Arikayce	Inhalation suspension: 590 mg/8.4 mL
Bethkis	Inhalation solution: 300 mg/4 mL
Cayston	Powder for inhalation solution: 75 mg
Kitabis	Inhalation solution: 300 mg/5 mL
TOBI Podhaler	Inhalation powder (capsule): 28 mg
Tobramycin	Inhalation solution: 300 mg/5 mL

VII. References

- Arikayce (amikacin). [package insert]. Bridgewater, NJ; Insmed Inc.; Revised 2018.
- Tobramycin. Clinical Pharmacology. Elsevier. Tampa, FL. Available at https://www.clinicalpharmacology-ip.com. Accessed November 15, 2019.
- Cayston (aztreonam). [package insert]. Foster City, CA; Gilead Sciences Inc.; Revised 02/2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created.	10.19	N/A

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.

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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.