Clinical Policy: Aztreonam (Cayston)

Reference Number: ERX.SPA.27
Effective Date: 07.01.16
Last Review Date: 02.21
Line of Business: Commercial, Medicaid

Revision Log

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

Description
Aztreonam (Cayston®) is a monobactam antibacterial.

FDA Approved Indication(s)
Cayston is indicated to improve respiratory symptoms in cystic fibrosis (CF) patients with *Pseudomonas aeruginosa*.

Limitation(s) of use:
- Safety and effectiveness have not been established in pediatric patients below the age of 7 years, patients with forced expiratory volume in one second (FEV_1) < 25% or > 75% predicted, or patients colonized with *Burkholderia cepacia*.
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cayston and other antibacterial drugs, Cayston should be used only to treat patients with CF known to have *Pseudomonas aeruginosa* in the lungs.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Cayston is **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 or infection disease specialist;
3. Age ≥ 6 years;
4. Pseudomonas aeruginosa is present in at least one airway culture;
5. Member meets one of the following (a or b):
   a. Failure of inhaled tobramycin, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for inhaled tobramycin*
   b. Antibiotic susceptibility testing indicates that aztreonam would be more effective than tobramycin;
6. If Cayston is prescribed concurrently (or for alternating use) with inhaled tobramycin (Bethkis®, Kitabis® Pak, TOBI®, TOBI® Podhaler), documentation supports inadequate response to either agent alone (e.g., deteriorating pulmonary status, recurrent pulmonary exacerbations);
7. Dose does not exceed 225 mg per day administered on a 28 days on/28 days off cycle.

Approval duration: 6 months

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Cystic Fibrosis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 Cayston is prescribed concurrently (or for alternating use) with inhaled tobramycin (Bethkis, Kitabis Pak, TOBI, TOBI Podhaler), documentation supports inadequate response to either agent alone (e.g., deteriorating pulmonary status, recurrent pulmonary exacerbations);
4. If request is for a dose increase, new dose does not exceed 225 mg per day administered on a 28 days on/28 days off cycle.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
inhaled tobramycin (Bethkis, Kitabis Pak, TOBI, TOBI Podhaler)	Inhalation solution (Bethkis, Kitabis Pak, TOBI): 300 mg inhaled BID for 28 days (followed by 28 days off tobramycin therapy) Inhalation powder (TOBI Podhaler): 112 mg (4 capsules) inhaled BID for 28 days (followed by 28 days off tobramycin therapy)	Solution: 600 mg/day Powder: 224 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): known allergy
- Boxed warning(s): none reported

Appendix D: General Information

- Aztreonam 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. 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

Indication	Dosing Regimen	Maximum Dose
CF	One dose (one single use vial and ampule of diluent) inhaled TID for 28 days (followed by 28 days off Cayston therapy)	225 mg/day

VI. Product Availability

Vial: 75 mg

VII. References

1. Cayston Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; November 2019. Available at www.cayston.com. Accessed December 2, 2020.
2. Flume PA, Mogayzel PJ, Robinson KA, et al. Cystic fibrosis pulmonary guidelines: treatment of pulmonary exacerbations. Am J Respir Crit Care Med. 2009; 180: 802-808.
3. 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(7): 680-689.
4. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.16	06.16
Annual review completed- no changes	04.17	05.17
1Q18 annual review: Modified age restriction from ≥ 7 to ≥ 6 years per ATS guideline recommendations. Added allowance for concurrent/alternating use with tobramycin pending supportive documentation of inadequate response to either agent alone. Added Appendix C: General Information.	10.26.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	10.17.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	10.28.19	02.20
1Q 2021 annual review: added prescriber restriction of pulmonologist or infection disease specialist to initial criteria; added positive response to therapy examples: reduction in respiratory symptoms (e.g., cough, wheezing, sputum production, or pulmonary exacerbations due to Pseudomonas aeruginosa) in continuation criteria; references reviewed and updated.	12.02.20	02.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.