Clinical Policy Title:	amikacin
Policy Number:	RxA.17
Drug(s) Applied:	Arikayce®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Amikacin (Arikayce®) is a liposomal formulation of amikacin – an aminoglycoside antibiotic active against aerobic gram-negative rods.

Arikayce® is indicated in adults who have limited or no alternative treatment options, for the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. As only limited clinical safety and effectiveness data for Arikayce® are currently available, reserve Arikayce® for use in adults who have limited or no alternative treatment options. This drug is indicated for use in a limited and specific population of patients.

This indication is approved under accelerated approval based on achieving sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by Month 6. Clinical benefit has not yet been established.

Limitation(s) of use: Arikayce® has only been studied in patients with refractory MAC lung disease defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. The use of Arikayce® is not recommended for patients with non-refractory MAC lung disease.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
amikacin (Arikayce®)	MAC	Inhalation of the contents of one 590 mg/8.4 mL Arikayce® vial once daily	590 mg/8.4 mL per day

Dosage Forms

- Solution for inhalation: 590 mg/8.4 mL

Clinical Policy

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

I. Initial Approval Criteria

A. Mycobacterium Avium Complex (MAC) (must meet all)**:**

1. Diagnosis of MAC;
2. Prescribed by or in consultation with an infectious disease specialist or pulmonologist;
3. Age ≥ 18 years;
4. Failure, as evidenced by positive sputum culture, of at least a 6-month trial of a multidrug background regimen therapy at up to maximally indicated doses *(see Appendix B)*, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed one vial (590 mg/8.4 mL) per day.

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Mycobacterium Avium Complex (MAC) (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Documentation of at least 3 consecutive negative monthly sputum cultures in the first 6 months of therapy or at least 2 consecutive negative monthly sputum cultures in the last 2 months of therapy;
3. If request is for a dose increase, new dose does not exceed one vial (590 mg/8.4 mL) per day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MAC: mycobacterium avium complex

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
clarithromycin (Biaxin®) or azithromycin (Zmax®) + ethambutol (Myambutol®) + rifampin (Rifadin®)	Variable dosing	Combo used for initial therapy for nodular/ bronchiectatic disease
clarithromycin (Biaxin®) or azithromycin (Zmax®) + ethambutol (Myambutol®) + rifampin (Rifadin®) + streptomycin or amikacin (Amikin®) or none.	Variable dosing	Combo used for initial therapy for cavitary disease

clarithromycin (Biaxin®) or azithromycin (Zmax®) + ethambutol (Myambutol®) + rifampin (Rifadin®) or rifabutin (Mycobutin®) + streptomycin or amikacin (Amikin®)	Variable dosing	Combo used for advanced (severe) or previously treated disease

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):
  - Arikayce® is contraindicated in patients with a known hypersensitivity to any aminoglycoside.

- Boxed Warning(s):
  - Arikayce® has been associated with a risk of increased respiratory adverse reactions, including, hypersensitivity pneumonitis, hemoptysis, bronchospasm, and exacerbation of underlying pulmonary disease that have led to hospitalization in some cases.

APPENDIX D: General Information

- Most common adverse reactions (incidence ≥10% and higher than control) in the patients with refractory MAC lung disease were dysphonia, cough, bronchospasm, hemoptysis, musculoskeletal pain, upper airway irritation, ototoxicity, fatigue/asthenia, exacerbation of underlying pulmonary disease, diarrhea, nausea, and headache.

References

1. Arikayce® Prescribing Information. Bridgewater, NJ: Insmed; October 2020. Available at: https://www.arikayce.com/pdf/full-prescribing-information.pdf. Accessed February 1, 2021.
2. Olivier KN, et al. Randomized Trial of Liposomal Amikacin for Inhalation in Nontuberculous Lung Disease. American Journal of Respiratory and Critical Care Medicine. 195;6. March 15, 2017: 814-823.
3. Griffith DE, et al. Amikacin Liposome Suspension for Treatment-Refractory Lung Disease Caused by Mycobacterium Avium Complex (CONVERT): A Prospective, Open-Label, Randomized Study. American Journal of Respiratory and Critical Care Medicine. September 2018. doi: 10.1164/rccm.201807-1318OC.
4. Arikayce® Drug Monograph. Clinical Pharmacology. http://www.clinicalpharmacology-ip.com. Accessed February 1, 2021.
5. Griffith DE, et al. An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases. American Journal of Respiratory and Critical Care Medicine. 2007; 175:367-416.
6. Daley CL, Iaccarino JM, Lange C, Cambau E, et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. Eur Respir J. 2020 Jul 7;56(1):2000535. doi: 10.1183/13993003.00535-2020. PMID: 32636299. Accessed February 1, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
References updated. No policy changes.	05/2020	05/20/2020
Policy was reviewed: 1. Clinical policy title table was	02/01/2021	03/09/2021

updated. 2. Initial therapy criteria I.A.5 and continued therapy criteria II.A.3 were updated to include vial size for maximum dosing. 3. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4. Appendix B standard verbiage was updated. 5. References were updated.		