Arikayce (amikacin liposome inhalation suspension) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
03-01-2025

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Arikayce® (amikacin liposome inhalation suspension) Oral inhalation	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 Limitations of Use: Arikayce has been studied only 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.		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Nontuberculous Mycobacteria (NTM) Lung Disease	Nontuberculous mycobacteria (NTM) species are mycobacterial organisms other than those belonging to the *Mycobacterium tuberculosis* complex. NTM are free-living organisms, ubiquitous in soil and water worldwide. The most common species of NTM is *Mycobacterium avium* complex (MAC) which causes pulmonary disease. MAC lung disease causes progressive inflammatory lung damage which often occurs in the context of preexisting lung disease (e.g., chronic obstructive pulmonary disease [COPD], bronchiectasis, cystic fibrosis, previous tuberculosis). As a result, the clinical manifestations of NTM lung disease (e.g., cough, fatigue, malaise, fever, weight loss, dyspnea, hemoptysis, chest discomfort) are often similar to those of the underlying disease and complicate evaluation and diagnosis of NTM pulmonary disease.(3,4)
	
	Diagnosis of NTM lung disease, jointly established by the American Thoracic Society (ATS) and Infectious Disease Society of America (IDSA), includes the following:(3,4,8)
	
	• Clinical findings (ALL required)
	  ○ Pulmonary or systemic symptoms AND
	  ○ Nodular or cavitary opacities on chest radiograph OR a high-resolution computed tomography scan that shows multifocal bronchiectasis with multiple small nodules AND
	  ○ Appropriate exclusion of other diagnoses
	• Microbiologic findings (only ONE is required)
	  ○ Positive culture results from at least two separate expectorated sputum samples
	  ○ Positive culture result from at least one bronchial wash or lavage

	○ Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or acid-fast bacilli [AFB]) and positive culture for NTM; OR biopsy showing mycobacterial histopathologic features (granulomatous inflammation or AFB) and one or more sputum or bronchial washings that are culture positive for NTM Drug therapy for MAC disease involves multiple drugs; therefore, the risk of adverse drug reactions and/or toxicities is relatively high. In addition, the choice of therapeutic regimen for a specific patient depends on (but is not limited to) the goals of therapy, comorbidities, and whether the patient has failed prior drug therapy. For these reasons, the treatment of MAC disease is best accomplished by physicians experienced in the treatment of mycobacterial diseases.(3,4) Initial treatment regimen for MAC contains a three-drug regimen consisting of a macrolide (azithromycin or clarithromycin), a rifamycin (rifampin, rifabutin), and ethambutol. For patients who have severe nodular bronchiectatic disease or fibrocavitary disease, rapidly growing mycobacteria, or have failed conventional treatments, a parenteral aminoglycoside (streptomycin or amikacin) is also often used as a 4th agent for 2-4 months.(2,3,4,6,8) Nebulized amikacin may be considered in place of an injectable aminoglycoside when parenteral administration is impractical or contraindicated.(2,4,6) If sputum cultures have not converted to negative after 6 months of guideline-based treatment, nebulized amikacin should be used as part of the continuation treatment regimen.(3) For patients with less severe disease, or those who are intolerant to the three-drug regimen, a two-drug regimen with a macrolide and ethambutol may be appropriate. However, there are concerns that a two-drug regimen might promote the emergence of macrolide-resistant MAC isolates.(2,3) The goals of therapy include symptomatic, radiographic, and microbiologic improvement. The primary microbiologic treatment endpoint for MAC lung disease is the conversion of sputum cultures to negative. Therefore, AFB smears and cultures of sputum should be obtained every 1-2 months during therapy to assess patient response; once sustained conversion (repeat negative cultures) has been documented, sputum cultures can be obtained less frequently.(2,3,8) Patients should show clinical improvement within 3 to 6 months and should convert their sputum to negative within 12 months on macrolide-containing regimens.(2,3,4) Studies suggest that culture-negative status for 12 months consecutively while receiving a clarithromycin- or azithromycin-containing regimen is adequate for most patients.(3,4,8) However, the optimal duration of therapy for treatment of macrolide-susceptible MAC pulmonary disease (beyond 12 months after culture conversion) is not currently known.(3) Less emphasis is placed on symptomatic and radiographic improvement because, while important, underlying concomitant disease progression or exacerbation may complicate assessment.(2,3) There is no currently widely accepted definition for treatment failure, although most experts define is as the failure to achieve culture conversion after 6 to 12 months of therapy.(2,3,4) Patients with treatment failure warrant evaluation for adherence to the drug regimen, assessment of serum drug concentrations, and susceptibility testing to macrolides and other drugs that may be needed for treatment. Once treatment failure has occurred, other interventions that should be considered include administration of an inhaled aminoglycoside and/or resectional surgery.(2,4) For patients with colonization by more than one organism, for example a cystic fibrosis patient with a Pseudomonal infection as well as MAC, 2007 ATS/IDSA guidelines state that it is important that nonmycobacterial pathogens be maximally treated before initiating specific antimycobacterial treatment, given the overlapping spectrum of antimycobacterial drugs for common CF pathogens, to facilitate assessment of the clinical response to antimycobacterial treatment.(10)
Efficacy	In an open-label, randomized, multi-center trial in patients with refractory MAC lung disease [as confirmed by at least 2 positive sputum culture results after a minimum duration of 6 consecutive months of guidelines-based background regimen therapy (GBT)], patients were randomized to either Arikayce plus background regimen (ALIS +

	GBT) or background regimen alone (GBT). The primary endpoint was culture conversion, defined as three consecutive monthly MAC-negative sputum cultures by Month 6. Culture conversion was achieved by 65 of 224 patients (29.0%) with ALIS + GBT and 10 of 112 (8.9%) with GBT alone (odds ratio, 4.22; 95% confidence interval, 2.08–8.57; p less than 0.001).(1,7) Patients with culture conversion by month 6 continued treatment for 12 months after the time of conversion. Of the 65 enrolled patients on ALIS + GBT therapy, 63% (41/65) remained culture negative after 12 months of subsequent treatment; 63% (41/65) of patients also remained culture negative 3 months off all antibiotics.(9)
Safety	Arikayce has a boxed warning due to an increased risk of respiratory adverse reactions including hypersensitivity pneumonitis, hemoptysis, bronchospasm, exacerbation of underlying pulmonary disease that have led to hospitalizations in some cases.(1)

REFERENCES

Number	Reference
1	Arikayce prescribing information. Insmed Incorporated. February 2023.
2	Akram SM, Attia FN. Mycobacterium Avium Complex. [Updated 2023 Feb 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK431110/.
3	Daley CL, Iaccarino JM, Lange C, et al. Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline. Clin Infect Dis. 2020;71(4):e1-e36.
4	Haworth CS, Banks J, Capstick T, et al. British Thoracic Society Guidelines for the Management of Non-Tuberculous Mycobacterial Pulmonary Disease (NTM-PD). Thorax. 2017;72:ii1-ii64.
5	Reference no longer used.
6	Olivier KN, Shaw PA, Glaser TS, et al. Inhaled Amikacin for Treatment of Refractory Pulmonary Nontuberculous Mycobacterial Disease. Ann Am Thorac Soc. 2014;11(1):30-35.
7	Griffith DE, Eagle G, Thomson R, et al. Amikacin Liposome Inhalation Suspension for Treatment-Refractory Lung Disease Caused by Mycobacterium Avium Complex (CONVERT): A Prospective, Open-Label, Randomized Study. Am J Respir Crit Care Med. 2018;198(12).
8	Floto RA, Olivier KN, Saiman L, et al. US Cystic Fibrosis Foundation and European Cystic Fibrosis Society Consensus Recommendations for the Management of Non-Tuberculous Mycobacteria in Individuals with Cystic Fibrosis. Thorax. 2016;71:i1-i22.
9	Griffith DE, Thomson R, Addrizzo-Harris DJ, et al. Durability of Culture Conversion in Patients Receiving Amikacin Liposome Inhalation Suspension (ALIS) for Treatment-Refractory Mycobacterium Avium Complex Lung Disease (MAC-LD) in the CONVERT Study. Eur Respir J. 2019;54(63):OA4951.
10	Griffith DE, Aksamit T, Brown-Elliott BA, et al. Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases: An Official ATS/IDSA Statement. Am J Respir Crit Care Med. 2007;175:367-416.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Arikayce	amikacin sulfate liposome inhal susp	590 MG/8.4ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Arikayce	Amikacin Sulfate Liposome Inhal Susp 590 MG/8.4ML (Base Eq)	590 MG/8.4 ML	28	Vials	28	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Arikayce	amikacin sulfate liposome inhal susp	590 MG/8.4ML	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Arikayce	Amikacin Sulfate Liposome Inhal Susp 590 MG/8.4ML (Base Eq)	590 MG/8.4ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of *Mycobacterium avium* complex (MAC) lung disease as confirmed by BOTH of the following: A. The patient has at least ONE of the following clinical findings: pulmonary or systemic symptoms; nodular or cavitary opacities on chest radiograph; a high-resolution computed tomography scan that shows multifocal bronchiectasis with multiple small nodules **AND** B. The patient has at least ONE of the following microbiological findings: positive culture results from at least two separate expectorated sputum samples; positive culture result from at least one bronchial wash or lavage; transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or acid-fast bacilli [AFB]) AND positive culture for nontuberculous mycobacteria (NTM); biopsy showing mycobacterial histopathologic features (granulomatous inflammation or AFB) AND one or more sputum or bronchial washings that are culture positive for NTM **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. The patient has positive sputum cultures despite at least 6 consecutive months of treatment with guideline-based combination antibiotic therapy for MAC lung disease (e.g., standard combination may include a macrolide [clarithromycin, azithromycin], a rifamycin [rifampin, rifabutin], and ethambutol) **AND** 4. The patient will continue treatment with guideline-based combination antibiotic therapy for MAC lung disease with the requested agent (e.g., combination may include a

Module	Clinical Criteria for Approval
	macrolide [clarithromycin, azithromycin], a rifamycin [rifampin, rifabutin], and ethambutol) **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., infectious disease, immunologist, pulmonologist, thoracic specialist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 6. ONE of the following: A. The patient is NOT currently being treated with another inhaled antibiotic (e.g., aztreonam for inhalation, tobramycin for inhalation) **OR** B. The patient is currently being treated with another inhaled antibiotic AND ONE of the following: 1. The patient will discontinue the other inhaled antibiotic prior to starting the requested agent **OR** 2. There is support for the use of another inhaled antibiotic concurrently with the requested agent **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient will continue treatment with guideline-based combination antibiotic therapy for *Mycobacterium avium* complex (MAC) lung disease with the requested agent (e.g., combination may include a macrolide [clarithromycin, azithromycin], a rifamycin [rifampin, rifabutin], and ethambutol) **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., infectious disease, immunologist, pulmonologist, thoracic specialist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. ONE of the following: A. The patient is NOT currently being treated with another inhaled antibiotic (e.g., aztreonam for inhalation, tobramycin for inhalation) **OR** B. The patient is currently being treated with another inhaled antibiotic AND ONE of the following: 1. The patient will discontinue the other inhaled antibiotic prior to starting the requested agent **OR** 2. There is support for the use of another inhaled antibiotic concurrently with the requested agent **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Universal QL	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following:

Module	Clinical Criteria for Approval
	A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: A. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** B. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of Approval:** up to 12 months