BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ARIKAYCE® (amikacin sulfate liposome) inhalation suspension Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**

Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for ARIKAYCE (amikacin sulfate liposome)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by or in consultation with a Pulmonologist or an Infectious Disease Specialist

Indication
- Diagnosis of refractory *Mycobacterium avium* complex (MAC) lung disease with **ALL** of the following:
  - Limited or no alternative treatment options

- Has not achieved three consecutive negative monthly sputum cultures after 6-months of multidrug background regimen therapy (culture report must be submitted)
- Mycobacterium avium complex isolate is susceptible to amikacin

Age Requirement
- 18 years or older

Alternative Therapies
- Failure (trial for at least three months duration), contraindication, intolerance to **BOTH** of the following:
  - Parenteral amikacin
  - Parenteral streptomycin

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No previous hypersensitivity reaction to **any** aminoglycoside
- Not currently using ethacrynic acid, furosemide, urea, or intravenous mannitol
- Does not have a pre-existing neuromuscular disorder such as myasthenia gravis

Additional Requirements:
- Does **NOT** have non-refractory MAC lung disease
- Will continue to use multidrug background regimen for MAC that consists of ethambutol, a macrolide (clarithromycin or azithromycin), and a rifamycin/rifampicin (rifampin or rifabutin), as clinically appropriate for the individual

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (including culture report and susceptibility to amikacin)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:
- 28 unit-dose vials per 28-days for 6 months OR end of plan year
- Arikayce to be given by nebulization only with the Lamira™ Nebulizer System

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

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Prescriber Qualification

- Continues to be seen by or in consultation with a Pulmonologist or an Infectious Disease Specialist

Clinical Response

- **ONE** of the following:
  - Achieved sputum culture conversion (3 consecutive negative monthly sputum cultures) by month 4 of initial treatment (culture report must be submitted)
  - Sustained sputum culture conversion by month 6 (no positive culture on solid media or no more than 2 consecutive positive cultures in liquid media) following initial conversion (culture report must be submitted) and needs to continue treatment to complete a total of 12 months

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No new contraindications or significant adverse drug effects, including:
  - Hypersensitivity pneumonitis (allergic alveolitis, pneumonitis, interstitial lung disease, allergic reaction)
  - Ototoxicity (deafness, dizziness, presyncope, tinnitus, vertigo)
  - No previous hypersensitivity reaction to **any** aminoglycoside
- Does not have a pre-existing neuromuscular disorder such as myasthenia gravis
- Is not currently using ethacrynic acid, furosemide, urea, or intravenous mannitol

Additional Requirements:

- Does **NOT** have non-refractory MAC lung disease
- Will continue to use multidrug background regimen for MAC that consists of ethambutol, a macrolide (clarithromycin or azithromycin), and a rifamycin/rifampicin (rifampin or rifabutin), as clinically appropriate for the individual

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in MAC lung disease
- Lab values confirming safe use

Continuation Therapy Criteria Approval Duration:

- 28 unit-dose vials per 28-days for 12 months OR end of plan year
- Arikayce to be given by nebulization only with the Lamira™ Nebulizer System

ORIGINAL EFFECTIVE DATE: 11/15/2018 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 05/15/2025

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Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Arikayce (amikacin sulfate liposome) 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 monthly sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. Approval of Arikayce was based on achieving sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by month 6 of treatment. Clinical benefit has not yet been established.

Arikayce (amikacin sulfate liposome) should be reserved for use in adults who have limited or no alternative treatment options and is intended for use in a limited and specific patient population. Use of Arikayce (amikacin sulfate liposome) is not recommended for patients with non-refractory MAC lung disease.

Amikacin is a polycationic, semisynthetic, bactericidal aminoglycoside. Amikacin enters the bacterial cell by binding to negatively charged components of the bacterial cell wall disrupting the overall architecture of the cell wall. The primary mechanism of action is the disruption and inhibition of protein synthesis in the target bacteria by binding to the 30S ribosomal subunit.

Traditionally, *MAC* was thought to include two species, *M. avium* and *Mycobacterium intracellulare*. Due to advances in molecular identification, MAC is actually composed of several different species including *M. avium*, *M. intracellulare*, *Mycobacterium indicus pranii*, *Mycobacterium chimaera*, *Mycobacterium arosiense*, *Mycobacterium vulneris*, *Mycobacterium bouchedurhonense*, *Mycobacterium colombiense*, *Mycobacterium marseillense*, *Mycobacterium yongonense*, and *Mycobacterium timonense.* There are four subspecies of *M. avium*: *hominissuis, avium, paratuberculosis,* and *silvaticum*. *M. avium* subsp. *hominissuis* causes human infections.

MAC infection is contracted through exposure to soil, water, or infected tissues. Entry into the body can be through the respiratory, oral, and cutaneous routes.

There are three major disease syndromes produced by MAC infections in humans: pulmonary disease (usually in adults whose systemic immunity is intact); disseminated disease (usually in patients with advanced human immunodeficiency virus (HIV) infection); and cervical lymphadenitis. Rarely, MAC can cause disease in other sites, such as cutaneous disease.

Treatment of all MAC infections is through use of a combination two or more antimicrobial agents. Regimen selection depends, in part, on susceptibility to macrolides; most MAC isolates, particularly in patients who have

not been treated before, are macrolide susceptible. For initial treatment of patients with MAC lung disease, a three-drug regimen containing a macrolide (usually azithromycin), a rifamycin (usually rifampin), and ethambutol is used. For patients who have severe or fibrocavitary disease, a parenteral aminoglycoside (amikacin or streptomycin) is also often used in the initial phase of treatment. For patients who cannot use parenteral aminoglycosides, inhaled amikacin three to five days a week, depending on the extent of disease and drug tolerance may be used.

Treatment should be continued until sputum cultures are consecutively negative for at least 12 months. Since sputum conversion usually requires 3-6 months of treatment, a typical patient will be treated for 15-18 months.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Arikayce (amikacin liposome oral inhalation suspension) product information, revised by manufacturer Insmed Incorporated. 02-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Griffith DE. Overview of nontuberculosis mycobacteria infections. In: UpToDate, von Reyn CF, Bloom A (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025. Topic last updated November 08, 2024. Accessed February 21, 2025.

Kasperbauer S, Daley CL. Treatment of *Mycobacterium avium* complex pulmonary infection in adults. In: UpToDate, von Reyn CF, Winthrop KL, Bloom A (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025. Topic last updated October 08, 2024. Accessed February 21, 2025.