BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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ARIKAYCE® (amikacin sulfate liposome) inhalation suspension

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

ARIKAYCE® (amikacin sulfate liposome) inhalation suspension

Criteria:

- **Criteria for initial therapy:** Arikayce (amikacin sulfate liposome) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Pulmonologist or an Infectious Disease Specialist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of refractory *Mycobacterium avium* complex (MAC) lung disease and **ALL** of the following:
     a. Individual has limited or no alternative treatment options
     b. Individual has not achieved three consecutive negative monthly sputum cultures by month 6 of a multidrug background regimen therapy (*culture report must be sent*)

  4. Individual 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

  5. **NOT** being used for the treatment of non-refractory MAC lung disease

  6. Individual has failure, contraindication or intolerance to **ALL** the following preferred step therapy agents:
     a. Parenteral amikacin
     b. Parenteral streptomycin

  7. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Comprehensive metabolic for assessment of renal function

  8. Does not have a pre-existing neuromuscular disorder such as myasthenia gravis

  Initial approval duration: 28 unit-dose vials per 28-days for 6 months
  Arikayce to be given by nebulization only with the Lamira™ Nebulizer System

- **Criteria for continuation of coverage (renewal request):** Arikayce (amikacin sulfate liposome) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Pulmonologist or an Infectious Disease Specialist

  2. Individual's condition has responded while on therapy
     a. Response is defined as **ONE** of the following:

i. Achieved sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by month 6 with initial treatment (*culture report must be sent*)
ii. Sustained sputum culture conversion through month 6 (defined as no positive culture on solid media or no more than 2 consecutive positive cultures in liquid media) following achieving initial culture conversion (*culture report must be sent*)

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
   a. Significant adverse effect such as:
      i. Hypersensitivity pneumonitis reported as allergic alveolitis, pneumonitis, interstitial lung disease, or allergic reaction
      ii. Severe hemoptysis, despite medical treatment
      iii. Severe bronchospasms reported as asthma, bronchial hyper-reactivity, dyspnea, dyspnea on exertion, prolonged expiration, throat tightness, wheezing, despite medical treatment
      iv. Severe exacerbation of underlying pulmonary disease reported as COPD, infective exacerbation of COPD, infective exacerbation of bronchiectasis, despite medical treatment
      v. Ototoxicity reported as deafness, dizziness, presyncope, tinnitus, and vertigo
      vi. Nephrotoxicity
      vii. Neuromuscular blockade reported as muscle weakness

5. Individual continues 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

6. **NOT** being used for the treatment of non-refractory MAC lung disease

7. There are no significant interacting drugs

Renewal duration: 28 unit-dose vials per 28-days for 12 months
Arikayce to be given by nebulization only with the Lamira™ Nebulizer System

- 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 a Non-Cancer Medications**

  2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

ARIKAYCE® (amikacin sulfate liposome) inhalation suspension

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.

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Resources:

Arikayce (amikacin) product information, revised by manufacturer Insmed 03-2020, at https://www.arikayce.com/pdf/full-prescribing-information.pdf accessed September 13, 2020

Griffith DE. Microbiology of non-tuberculosis mycobacteria. In: UpToDate, von Reyn CF, Bloom A (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on September 13, 2020.

Kasperbauer S, Daley C. Treatment of Mycobacterium avium complex lung infection in adults. In: UpToDate, von Reyn CF, Bloom A (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on September 13, 2020.