amikacin suspension (Arikayce®)

Policy # 00663
Original Effective Date: 06/19/2019
Current Effective Date: 07/12/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider amikacin suspension (Arikayce®)‡ for the treatment of *Mycobacterium avium* complex (MAC) lung disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for amikacin suspension (Arikayce) will be considered when the below patient selection criteria are met:

- Initial (12 months):
  - Patient has a diagnosis of *Mycobacterium avium* complex (MAC) lung disease based on prescriber attestation to the presence of nodular or cavitary opacities on chest radiograph or a high-resolution CT scan that shows bronchiectasis with multiple small nodules; AND
  - Patient has been adherent to an appropriate multi-drug treatment regimen for at least 6 months; AND
  - Patient's sputum cultures continue to be positive for MAC; AND
  - Arikayce will be used in combination with the appropriate multi-drug treatment regimen.
- Continuation (12 months):
  - Patient has previously met the initial criteria for Arikayce; AND
  - Patient continues to be adherent to an appropriate multi-drug treatment regimen; AND
  - Patient meets ONE of the following:

- Patient's sputum cultures continue to be positive for MAC; OR
- Patient's sputum cultures have converted to negative for MAC AND requested drug will be discontinued ≤12 months after culture conversion. *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the continued use of amikacin suspension (Arikayce) for greater than 12 months after sputum cultures have converted to negative to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of amikacin suspension (Arikayce) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Arikayce is a liposomal formulation of amikacin that is approved for inhalation in patients with *Mycobacterium avium* complex (MAC) lung disease who have not achieved negative sputum cultures after at least 6 consecutive months of a multidrug background regimen therapy. It was approved by the FDA via the limited population pathway for antibacterial and antifungal drugs as well as the accelerated approval pathway. Additional post-market studies with this drug are still ongoing. In patients who meet the criteria for treatment, one vial (590 mg) of Arikayce should be administered daily via the Lamira™‡ nebulizer system. Pre-treatment with a short acting beta agonist should be considered for patients with known hyperreactive airway disease, COPD, asthma, or bronchospasm. Arikayce also has a black box warning for increased risk of respiratory conditions including hypersensitivity pneumonitis, bronchospasm, exacerbation of underlying lung disease, and hemoptysis.

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MAC is the most common non-tuberculous mycobacterial (NTM) organism and causes pulmonary and extra-pulmonary disease in susceptible people. The estimated annual prevalence of pulmonary NTM infection ranged from 1.4-13.9 per 100,000 persons in the contiguous US, up to 44 per 100,000 in Hawaii and 47 per 100,000 in persons >65 years of age. The primary risk factor for the development of pulmonary NTM infection is underlying pulmonary disease. It typically presents in one of two common patterns. The first is an upper lobe fibrocavitary disease, usually occurring in older males with COPD or other structural lung disease. The onset of disease is insidious and symptoms include a chronic cough, hemoptysis, weight loss, and a low-grade fever. The disease is typically slowly progressive and patients usually die from other underlying illnesses. The second pattern of NTM infections occurs in patients without any known underlying pulmonary disease (except bronchiectasis). The majority of patients with this pattern are nonsmoking, elderly females with a long-standing indolent cough as the only symptom. The disease is slowly progressive.

Treatment recommendations for MAC lung disease are based on disease severity and previous therapies received; almost all are three-drug regimens. For those with nodular/bronchiectatic disease or with fibrocavitary disease who cannot tolerate daily treatment, a three times weekly, three-drug regimen consisting of azithromycin 500 mg to 600 mg or clarithromycin 1000 mg, ethambutol 25 mg/kg, and rifampin 600 mg is recommended. For patients with fibrocavitary disease or severe nodular/bronchiectatic disease, daily administration of azithromycin or clarithromycin, ethambutol, and rifampin is recommended. Treatment recommendations for patients with severe or previously-treated disease include azithromycin 250 mg to 300 mg or clarithromycin 500 mg to 1000 mg, ethambutol 15 mg/kg, and rifabutin 150 to 300 mg or rifampin 600 mg daily. Intermittent IV amikacin or streptomycin are recommended for the first 2 to 3 months in patients with cavitary disease or previous treatment failure. Patients should be treated for 12 months beyond the time that the sputum cultures convert to negative. For most patients, conversion occurs within 6 months of initiation of treatment. According to the American Thoracic Society (ATS) and the Infectious Disease Society of America (IDSA) guidelines for NTM, amikacin liposomal inhalation suspension should be added in patients who experience treatment failure after at least 6 months on standard treatment.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Arikayce is approved for 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.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Arikayce was established in an open-label, randomized (2:1), multicenter trial in patients with refractory MAC lung disease as confirmed by at least 2 sputum culture results. Patients were considered to have refractory MAC lung disease if they did not achieve negative sputum cultures after a minimum duration of 6 consecutive months of background regimen therapy that was either ongoing or stopped no more than 12 months before the screening visit. Patients were randomized to either Arikayce plus a background regimen or background regimen alone. The surrogate endpoint for assessing efficacy was based on achieving culture conversion (3 consecutive monthly negative sputum cultures) by month 6. The date of conversion was defined as the date of the first of the 3 negative monthly cultures, which had to be achieved by month 4 in order to meet the endpoint by month 6.

A total of 336 patients were randomized with a mean age of 64.7 years and 69.3% of females. At the time of enrollment, of the 336 subjects in the population, 302 were either on a guideline-based regimen for MAC or off guideline-based therapy for MAC in less than 3 months while 34 were off treatment for 3 to 12 months prior to enrollment. AT screening, patients were stratified by smoking status and by whether patients were on treatment or off treatment for at least 3 months.

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The proportion of patients achieving culture conversion was significantly ($p<0.0001$) greater for Arikayce plus background regimen (65/224, 29%) compared to background regimen alone (10/112, 8.9%). An analysis of sustained sputum culture conversion through month 6 showed that 3 subjects in each treatment arm who initially achieved culture conversion did not have sustained sputum culture conversion through month 6. Thus, 27.7% of Arikayce plus background regimen patients and 6.8% of background regimen alone patients had sustained sputum culture conversion through Month 6. Thus, 27.7% (62/244) of Arikayce plus background regimen patients and 6.3% (7/112) of background regimen alone patients had sustained sputum culture conversion through month 6.

References

1. Arikayce [package insert]. Insmed Incorporated. Bridgewater, NJ. April 2021.
2. Arikayce Drug Evaluation. Express Scripts. October 2018.
3. Daley CL, Iaccarino JM, Lang C, et al. Treatment of Nontuburculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline. *Clin Infect Dis.* 2020;71(4):e1-36.

Policy History

Original Effective Date: 06/19/2019
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06/06/2019	Medical Policy Committee review
06/19/2019	Medical Policy Implementation Committee approval. New policy.
06/04/2020	Medical Policy Committee review
06/10/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/03/2021	Medical Policy Committee review
06/09/2021	Medical Policy Implementation Committee approval. Added continuation criteria. Updated diagnostic criteria requirement and updated background information to reflect guideline updates.

Next Scheduled Review Date: 06/2022

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into

standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.