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Coverage Policy Number **IP0383**

Amikacin Liposome

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Related Coverage Resources

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Overview

This policy supports medical necessity review for amikacin liposome inhalation suspension for oral inhalation (**Arikayce**®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Amikacin liposome (Arikayce) is considered medically necessary when ONE of the following is met:

1. ***Mycobacterium avium* complex (MAC) Lung Disease.** Individual meets **ALL** of the following criteria:
   A. Age 18 years or older
   B. Has refractory MAC lung disease defined as not achieving negative sputum cultures after a minimum of 6 consecutive months of a background multidrug regimen
   C. The *Mycobacterium avium* complex isolate is susceptible to amikacin
   D. Arikayce will be used in conjunction with a background multidrug regimen

E. Medication is prescribed by a pulmonologist, infectious diseases physician, or a physician who specializes in the treatment of *Mycobacterium avium* complex lung infections.

2. **Cystic Fibrosis.** Individual meets **BOTH** of the following criteria:
   A. Has *Pseudomonas aeruginosa* in culture of the airway
   B. Medication is prescribed by, or in consultation with, a pulmonologist or a physician who specializes in the treatment of cystic fibrosis.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of Amikacin liposome (Arikayce) is considered medically necessary when **ONE** of the following is met:

1. ***Mycobacterium avium* complex (MAC) Lung Disease.** Individual meets **BOTH** of the following criteria:
   A. Arikayce will be used in conjunction with a background multidrug regimen
   B. **ONE** of the following:
      i. Has not achieved negative sputum cultures for *Mycobacterium avium* complex
      ii. Has achieved negative sputum cultures for *Mycobacterium avium* complex for less than 12 months and will be continuing Arikayce in order to complete 12 months of therapy following the negative sputum culture

2. **Cystic Fibrosis.** Individual meets the above medical necessity criteria AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months.
Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Arikayce is indicated for the treatment of ***Mycobacterium avium* complex (MAC) lung disease**, in adults who have limited or no alternative treatment options, as part of a combination antibacterial regimen in patients who do not achieve negative sputum cultures after at least 6 consecutive months of a background multidrug regimen (MDR) therapy.[1] As only limited clinical safety and efficacy data are available, reserve Arikayce for adults with limited or no other treatment options.

This indication was approved under accelerated approval based on achieving sputum culture conversion (defined as three consecutive negative monthly sputum cultures) by Month 6.[1]

Limitation of Use: Arikayce has only been studied in patients with refractory MAC lung disease defined as not achieving culture negativity after at least 6 months of background MDR treatment.[1] Arikayce is not recommended in patients with non-refractory MAC lung disease.

Efficacy
The efficacy of Arikayce was established in one open-label, randomized (2:1), multi-center trial in patients with refractory MAC lung disease as confirmed by at least 2 sputum culture results (n = 336).[7] 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 ≤ 12 months before the screening visit. The surrogate efficacy endpoint was based on achieving culture conversion (3 consecutive monthly negative sputum cultures) by Month 6. Patients who achieved culture conversion by Month 6 were continued on Arikayce plus background multidrug regimen or background multidrug regimen alone based on their randomization for a total of 12 months after the first negative sputum culture. At baseline, 329 patients were on a multidrug background regimen that included a macrolide (93.3%), a rifamycin (86.3%), or ethambutol (81.4%). The proportion of patients achieving culture conversion by Month 6 was significantly greater with Arikayce plus background multidrug regimen vs. background multidrug regimen alone (29% vs. 8.9%, respectively; P < 0.0001). Among patients who achieved culture conversion by Month 6, 55.4% of patients in the Arikayce group vs. no patients in the background multidrug regimen only group had sustained and durable conversion (P = 0.0017).[8] Relapse rates through 3 months after treatment were 9.2% in the Arikayce group vs. 30.0% in the background therapy only group.

Guidelines
The American Thoracic Society, the European Respiratory Society, the European Society of Clinical Microbiology and Infectious Disease, and the Infectious Disease Society of America developed clinical practice guidelines for the treatment of nontuberculous mycobacterial (NTM) pulmonary disease (2020).[2] Treatment recommendations for MAC lung disease are based on disease severity and previous therapies received and almost all are three drug regimens. Typical regimens involve azithromycin or clarithromycin; ethambutol; and rifampin. For select patients, a two-drug regimen consisting of azithromycin or clarithromycin plus ethambutol daily is acceptable. Liposomal amikacin is not recommended for the initial treatment of MAC pulmonary disease. The guidelines recommend the addition of liposomal amikacin to guideline-based therapy in patients with MAC pulmonary disease who have failed treatment (failure to convert sputum culture) after ≥ 6 months of treatment with guideline-based therapy. Patients should be treated for ≥12 months after culture conversion. The breakpoint for resistance to amikacin is ≥ 64 mcg/mL for parenteral amikacin and ≥ 128 mcg/mL for amikacin liposome inhalation suspension and finding these MICs would lead to cessation of therapy. In patients with MAC pulmonary disease, guidelines suggest susceptibility-based treatment for macrolides and amikacin over empiric therapy (conditional recommendation, very low certainty in estimates of effect).

The US Cystic Fibrosis Foundation and the European Cystic Fibrosis Society (2016 version) developed consensus recommendations on the treatment of NTM lung disease in which nebulized amikacin is listed as a treatment option for MAC and *M. abscessus* lung disease in cystic fibrosis (CF) patients.[3] The guidelines recommend that inhaled amikacin be used in conjunction with other NTM antibiotics.

Other Uses with Supportive Evidence
The efficacy of Arikayce in the treatment of *Pseudomonas aeruginosa* infection in patients with CF has been assessed in three studies.[4] In a Phase III, randomized, open-label, non-inferiority study, patients with CF were randomized to Arikayce 590 mg once daily (QD) or tobramycin inhalation solution (TIS) 300 mg twice daily (n = 302). Patients received three cycles of treatment which consisted of 28 days on treatment followed by 28 days off treatment. The primary endpoint of the study was the relative change from baseline to the end of the 24-week study in forced expiratory volume in 1 second (FEV_1). FEV_1 improvement at Day 168 with Arikayce was non-inferior to TIS (mean difference -1.31%). More patients receiving Arikayce experienced pulmonary exacerbations compared with TIS; however, fewer patients required all-cause hospitalization. Change in CF Questionnaire Revised was similar between groups at the end of each treatment course. Mean reductions in *P. aeruginosa* $\log_{10}$ CFU was similar for Arikayce and TIS at Day 28 and at Day 140.

A pooled report included 24 patients with CF and chronic *P. aeruginosa* infection from two Phase Ib/IIa pharmacokinetic/pharmacodynamic studies.[5] Patients received liposomal amikacin 500 mg QD by inhalation for 14 days. Statistically significant changes from baseline to Days 7 and 14 were seen in FEV_1, FEV_1 % predicted, and forced expiratory flow between 25% and 75% of forced vital capacity. Another report included pooled data from two dose-ranging studies (one Phase Ib/IIa and one Phase IIa) in patients with CF (n = 105) chronically

infected with *P. aeruginosa*.[6] Patients received 70-, 140-, 280- or 560-mg of liposomal amikacin or placebo QD for 28 days and were followed for an additional 28 days. In repeated-measures mixed-effect models, the 560 mg dose was associated with statistically significant improvements in FEV_1, and FEV_1 % predicted and a reduction in log_{10} CFUs.

References

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