ARIKAYCE®
(amikacin liposome inhalation suspension)
590 mg/8.4 mL

Limited Population

Counseling your patients on the ARIKAYCE treatment journey

A guide for healthcare professionals and staff

INDICATION

LIMITED POPULATION: ARIKAYCE® 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 sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. As only limited clinical safety and effectiveness data for ARIKAYCE are currently available, reserve ARIKAYCE for use in adults who have limited or no alternative treatment options. This drug is indicated for use in a limited and specific population of patients.

This indication is approved under accelerated approval based on achieving sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by Month 6. Clinical benefit has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitation of Use: ARIKAYCE has only been studied 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.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF INCREASED RESPIRATORY ADVERSE REACTIONS
ARIKAYCE has been associated with an increased risk of respiratory adverse reactions, including hypersensitivity pneumonitis, hemoptysis, bronchospasm, and exacerbation of underlying pulmonary disease that have led to hospitalizations in some cases.

Please see additional Important Safety Information throughout and enclosed full Prescribing information.

Counseling patients for what's ahead

This is a guide for healthcare professionals like you who are counseling refractory MAC patients for ARIKAYCE + standard therapy.[1] It is meant to serve as a reference when fielding questions that patients are likely to have around adding ARIKAYCE and the journey to getting and staying culture negative—questions best answered in the office.

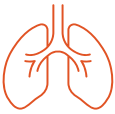
Patients, frustrated when initial therapy fails, will be looking for guidance from you on next steps. They may take comfort in knowing they are not alone:

- **Nearly one-third of patients** with refractory MAC lung disease fail to achieve culture conversion when assessed at Month 6 and Month 12 on standard therapy[2-4]

With a better understanding of what to expect when starting ARIKAYCE, your patients may be better prepared for the treatment journey ahead.[5,6]

- **The 2020 NTM Treatment Guidelines** recommend remaining on therapy for 12 months after initial conversion to culture negative[6]

ARIKAYCE is the first and only FDA-approved treatment for refractory MAC lung disease[1]



- Adding ARIKAYCE to standard therapy may increase the chances of becoming and staying MAC-negative[1]
  - In the clinical trial, 29% of patients on ARIKAYCE + standard therapy (n=65/224) culture converted vs 8.9% on standard therapy alone (n=10/112)
  - 18.3% of patients on ARIKAYCE + standard therapy (41/224) remained culture negative 12 months after initial conversion vs 2.7% on standard therapy alone (3/112)
  - Only patients on ARIKAYCE + standard therapy (n=36/224) remained culture converted 3 months after treatment ended vs standard therapy alone (n=0/112)
  - During the trial, the endpoints of the change from baseline in 6MWT distance and SGRQ did not demonstrate clinical benefit at Month 6

For more information about culture conversion results for ARIKAYCE, scan here or visit ARIKAYCEhcp.com.

IMPORTANT SAFETY INFORMATION (cont'd)

Hypersensitivity Pneumonitis has been reported with the use of ARIKAYCE in the clinical trials. Hypersensitivity pneumonitis (reported as allergic alveolitis, pneumonitis, interstitial lung disease, allergic reaction to ARIKAYCE) was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (3.1%) compared to patients treated with background regimen alone (0%). Most patients with hypersensitivity pneumonitis discontinued treatment with ARIKAYCE and received treatment with corticosteroids. If hypersensitivity pneumonitis occurs, discontinue ARIKAYCE and manage patients as medically appropriate.

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Getting patients started on ARIKAYCE

ARIKAYCE is a once-daily oral inhalation with at-home administration. ARIKAYCE should be taken as part of a multidrug antibacterial regimen.[1,7] The entire healthcare team can play a role in helping patients establish a routine for taking ARIKAYCE by answering their questions and sharing information.

- The following self-administration tips may be helpful to patients:
  - ✓ Establish a regular time of day to take ARIKAYCE
  - ✓ Establish a regular place to take ARIKAYCE, where patient can sit upright by a clean, flat surface with proximity to a power outlet for plugging in the Lamira® Nebulizer System[7]
  - ✓ Prior to first use, and subsequently after each use, the Nebulizer Handset must be cleaned and disinfected[7]
  - ✓ Patients who use a bronchodilator should use it prior to taking ARIKAYCE[1]

A basic understanding of the time frame required for taking ARIKAYCE—including cleaning and disinfecting the Nebulizer Handset after each use—can help patients successfully establish a routine. Self-administering treatment takes **14-20 minutes**.[7]

6MWT=6-minute walk test; MAC=*Mycobacterium avium* complex; NTM=nontuberculous mycobacteria; SGRQ=St George's Respiratory Questionnaire.

For more information on how to take ARIKAYCE, including a video with step-by-step instructions, scan here or visit ARIKAYCEhcp.com.

IMPORTANT SAFETY INFORMATION (cont'd)

Hemoptysis has been reported with the use of ARIKAYCE in the clinical trials. Hemoptysis was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (18.4%) compared to patients treated with background regimen alone (13.4%). If hemoptysis occurs, manage patients as medically appropriate.

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Discussing common side effects and possible management strategies

As patients may have questions for you as side effects arise, an upfront conversation can inform patients on what they may experience during treatment.

- To facilitate an ongoing conversation, ask patients to keep track of their side effects so you can share further information as needed

There are potential techniques and management strategies to help manage certain respiratory-related adverse events that can be found online via the QR code below.[5] A downloadable **Patient Adverse Event Tear Pad**—a guide that will help patients know what to expect from treatment with ARIKAYCE—is available at **www.ARIKAYCEhcp.com/resources.**

- When patients have a plan for dealing with side effects, they may have a better chance of taking treatment as prescribed[5,6]
- The most common adverse events (≥10%) experienced with ARIKAYCE + standard therapy were dysphonia, cough, bronchospasm, hemoptysis, musculoskeletal pain, upper airway irritation, ototoxicity, fatigue/asthenia, exacerbation of underlying pulmonary disease, diarrhea, nausea, and headache[1]
  - The emergence of most adverse events in the ARIKAYCE + standard therapy group were reported during the first month of treatment[8]

For more information about ARIKAYCE safety—including management strategies for common side effects—scan here or visit ARIKAYCEhcp.com.

IMPORTANT SAFETY INFORMATION (cont'd)

Bronchospasm has been reported with the use of ARIKAYCE in the clinical trials. Bronchospasm (reported as asthma, bronchial hyperreactivity, bronchospasm, dyspnea, dyspnea exertional, prolonged expiration, throat tightness, wheezing) was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (28.7%) compared to patients treated with background regimen alone (10.7%). If bronchospasm occurs during the use of ARIKAYCE, treat patients as medically appropriate.

Exacerbations of underlying pulmonary disease have been reported with the use of ARIKAYCE in the clinical trials. Exacerbations of underlying pulmonary disease (reported as chronic obstructive pulmonary disease (COPD), infective exacerbation of COPD, infective exacerbation of bronchiectasis) have been reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (15.2%) compared to patients treated with background regimen alone (9.8%). If exacerbations of underlying pulmonary disease occur during the use of ARIKAYCE, treat patients as medically appropriate.

Please see additional Important Safety Information throughout and enclosed full Prescribing information.

The *Arikares*® *Support Program* offers ongoing support and information

Once your patient is prescribed ARIKAYCE, the *Arikares Support Program* is available. Your patient will receive a welcome pack and a call from an *Arikares Coordinator* to discuss next steps and answer questions.

- It is important to encourage patients to answer the phone when receiving calls from any number as it may be *Arikares*
- The *Arikares Support Program* can be reached at **1-833-ARIKARE (1-833-274-5273)** or **1-973-437-2376**
- An *Arikares Coordinator* is available for 1:1 support, Monday through Friday, 8 AM to 8 PM ET

The *Arikares Coordinator* and the specialty pharmacy will work with the patient to coordinate the shipment of medication. Once the order is placed, patients will receive their first shipment of ARIKAYCE, which will arrive in 2 separate boxes.

- The first contains the 28-day supply of medicine; the second delivers the **Lamira Nebulizer System** and **Getting Started Kit**

The *Arikares Support Program* can provide patients with live or virtual voluntary training on how to set up and use the Lamira Nebulizer System.

To assist patients in enrolling in the *Arikares Support Program*, scan here or visit ARIKAYCEhcp.com.

IMPORTANT SAFETY INFORMATION (cont'd)

Anaphylaxis and Hypersensitivity Reactions: Serious and potentially life-threatening hypersensitivity reactions, including anaphylaxis, have been reported in patients taking ARIKAYCE. Signs and symptoms include acute onset of skin and mucosal tissue hypersensitivity reactions (hives, itching, flushing, swollen lips/tongue/uvula), respiratory difficulty (shortness of breath, wheezing, stridor, cough), gastrointestinal symptoms (nausea, vomiting, diarrhea, crampy abdominal pain), and cardiovascular signs and symptoms of anaphylaxis (tachycardia, low blood pressure, syncope, incontinence, dizziness). Before therapy with ARIKAYCE is instituted, evaluate for previous hypersensitivity reactions to aminoglycosides. If anaphylaxis or a hypersensitivity reaction occurs, discontinue ARIKAYCE and institute appropriate supportive measures.

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IMPORTANT SAFETY INFORMATION (cont'd)

Ototoxicity has been reported with the use of ARIKAYCE in the clinical trials. Ototoxicity (including deafness, dizziness, presyncope, tinnitus, and vertigo) were reported with a higher frequency in patients treated with ARIKAYCE plus background regimen (17%) compared to patients treated with background regimen alone (9.8%). This was primarily driven by tinnitus (8.1% in ARIKAYCE plus background regimen vs 0.9% in the background regimen alone arm) and dizziness (6.3% in ARIKAYCE plus background regimen vs 2.7% in the background regimen alone arm). Closely monitor patients with known or suspected auditory or vestibular dysfunction during treatment with ARIKAYCE. If ototoxicity occurs, manage patients as medically appropriate, including potentially discontinuing ARIKAYCE.

Nephrotoxicity was observed during the clinical trials of ARIKAYCE in patients with MAC lung disease but not at a higher frequency than background regimen alone. Nephrotoxicity has been associated with the aminoglycosides. Close monitoring of patients with known or suspected renal dysfunction may be needed when prescribing ARIKAYCE.

Neuromuscular Blockade: Patients with neuromuscular disorders were not enrolled in ARIKAYCE clinical trials. Aminoglycosides may aggravate muscle weakness by blocking the release of acetylcholine at neuromuscular junctions. Closely monitor patients with known or suspected neuromuscular disorders, such as myasthenia gravis. If neuromuscular blockade occurs, it may be reversed by the administration of calcium salts but mechanical respiratory assistance may be necessary.

Embryo-Fetal Toxicity: Aminoglycosides can cause fetal harm when administered to a pregnant woman. Aminoglycosides, including ARIKAYCE, may be associated with total, irreversible, bilateral congenital deafness in pediatric patients exposed *in utero*. Patients who use ARIKAYCE during pregnancy, or become pregnant while taking ARIKAYCE should be apprised of the potential hazard to the fetus.

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IMPORTANT SAFETY INFORMATION (cont'd)

Contraindications: ARIKAYCE is contraindicated in patients with known hypersensitivity to any aminoglycoside.

Most Common Adverse Reactions: The most common adverse reactions in Trial 1 at an incidence ≥5% for patients using ARIKAYCE plus background regimen compared to patients treated with background regimen alone were dysphonia (48% vs 2%), cough (40% vs 17%), bronchospasm (29% vs 11%), hemoptysis (18% vs 13%), musculoskeletal pain (18% vs 9%), upper airway irritation (18% vs 2%), ototoxicity (17% vs 10%), fatigue and asthenia (16% vs 10%), exacerbation of underlying pulmonary disease (15% vs 10%), diarrhea (13% vs 5%), nausea (12% vs 4%), headache (10% vs 5%), pneumonia (9% vs 9%), pyrexia (8% vs 5%), decreased weight (7% vs 1%), vomiting (7% vs 4%), rash (6% vs 1%), change in sputum (6% vs 1%), and chest discomfort (5% vs 3%).

Drug Interactions: Avoid concomitant use of ARIKAYCE with medications associated with neurotoxicity, nephrotoxicity, and ototoxicity. Some diuretics can enhance aminoglycoside toxicity by altering aminoglycoside concentrations in serum and tissue. Avoid concomitant use of ARIKAYCE with ethacrynic acid, furosemide, urea, or intravenous mannitol.

Overdosage: Adverse reactions specifically associated with overdose of ARIKAYCE have not been identified. Acute toxicity should be treated with immediate withdrawal of ARIKAYCE, and baseline tests of renal function should be undertaken. Hemodialysis may be helpful in removing amikacin from the body. In all cases of suspected overdosage, physicians should contact the Regional Poison Control Center for information about effective treatment.

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Before starting treatment with ARIKAYCE, your patients may want to better understand:

- Reasons for adding ARIKAYCE and what to expect
- How to administer at home using the nebulizer
- Common side effects and partnering on how to manage them
- Support available through the *Arikares Support Program*
- ARIKAYCE is covered by most insurance plans and financial support options may be available†

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†Source: Managed Markets Insights & Technology, LLC, database as of June 2021. All information includes applicable public and private payers. The information available here is compiled from a source believed to be accurate, but Insmed makes no representation that it is accurate. This information is subject to change. Payer requirements may vary or change over time, so it is important to regularly check with each payer as to payer-specific requirements. The use of this information does not guarantee payment or that any payment received will cover your costs.

References: 1. ARIKAYCE [package insert]. Bridgewater, NJ: Insmed Incorporated; 2020. **2.** Jeong BH, et al. *Am J Respir Crit Care Med*. 2015;191(1):96-103. **3.** Moon SM, et al. *Eur Respir J*. 2019;53(5). doi:10.1183/13993003.01636-2018. **4.** Diel R, et al. *Chest*. 2018;153(4):888-921. **5.** Swenson C, et al. *Open Forum Infect Dis*. 2020:7(4). doi:10.1093/ofid/ofaa079. **6.** Daley CL, et al. *Clin Infect Dis*. 2020;71(4):e1-e36. **7.** Lamira Nebulizer System instructions for use. Midlothian, VA: PARI Respiratory Equipment, Inc; 2018. **8.** Griffith DE, et al. *Am J Respir Crit Care Med*. 2018;198(12):1559-1569.

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