Arikayce® (amikacin liposome inhalation suspension) – New orphan drug approval

- On September 28, 2018, the FDA announced the approval of Insmed's Arikayce (amikacin liposome inhalation suspension) 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.
    - As only limited clinical safety and effectiveness data for Arikayce are currently available, Arikayce should be reserved 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.
    - 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.

- MAC lung disease is a rare and serious disorder that can significantly increase morbidity and mortality. Symptoms of MAC lung disease include chronic cough, dyspnea, fatigue, fever, weight loss, and chest pain. In some cases, it can cause severe, even permanent damage to the lungs, and can be fatal.
    - MAC lung disease is an emerging public health concern worldwide with significant unmet needs. Current guideline-based treatment involves the use of multi-drug regimens that are not specifically approved for MAC lung disease. The course of treatment is often two years or more and is inadequate in treating the disease in many patients.

- Arikayce is a novel, inhaled, once-daily formulation of amikacin, an established antibiotic that was historically administered intravenously and associated with severe toxicity to hearing, balance, and kidney function.
    - The liposomal technology enables the delivery of amikacin directly to the lungs, where it is taken up by lung macrophages where the infection resides. This approach prolongs the release of amikacin in the lungs while limiting systemic exposure.

- The safety and efficacy of Arikayce was demonstrated in a clinical trial of 336 patients randomized to Arikayce plus a background multidrug antibacterial regimen, or a background multidrug antibacterial regimen alone. The surrogate endpoint for assessing efficacy was based on achieving culture conversion (3 consecutive monthly negative sputum cultures) by month 6.
    - By month 6, 29.0% of patients treated with Arikayce achieved culture conversion vs. 8.9% of patients who were treated with background therapy alone ($p < 0.0001$).

- Arikayce carries a boxed warning for risk of increased respiratory adverse reactions.

- Warnings and precautions of Arikayce include hypersensitivity pneumonitis, hemoptysis, bronchospasm, exacerbation of underlying pulmonary disease, ototoxicity, nephrotoxicity, neuromuscular blockade, and embryo-fetal toxicity.

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- The most common adverse reactions (≥ 10% and higher than control) with Arikayce use were dysphonia, cough, bronchospasm, hemoptysis, ototoxicity, upper airway irritation, musculoskeletal pain, fatigue/asthenia and exacerbation of underlying pulmonary disease, diarrhea, and nausea.

- The recommended dosage of Arikayce is a once daily inhalation of the contents of one 590 mg/8.4 mL Arikayce vial (590 mg of amikacin) using the Lamira™ Nebulizer System.

    — Arikayce should be administered by nebulization only with the Lamira Nebulizer System.
    — Pre-treatment with short-acting selective beta-2 agonists should be considered for patients with known hyperreactive airway disease, chronic obstructive pulmonary disease, asthma, or bronchospasm.
    — Refer to the Arikayce drug label for further instructions.

- Insmed has launched the Arikares Support Program, which provides dedicated coordinators to help patients navigate the reimbursement process and trainers who can familiarize patients with how to use Arikayce.

- Insmed plans to launch Arikayce early in the fourth quarter of 2018. Arikayce will be available as a sterile, aqueous, liposome suspension for oral inhalation in a unit-dose glass vial containing amikacin 590 mg/8.4 mL. The product will be dispensed in a 28-vial kit that also contains one Lamira Nebulizer Handset and four Lamira aerosol heads.