NDA 207356/S-003

ACCELERATED APPROVAL
LPAD PATHWAY APPPROVAL

Insmed Incorporated
Attention: Diane C. Fiorenza, BS
Vice President, Regulatory Affairs
700 U.S. Highway 202/206
Bridgewater, NJ 08807-1704

Dear Ms. Fiorenza:

Please refer to your supplemental new drug application (sNDA) dated December 19, 2019, received December 19, 2019, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ARIKAYCE (amikacin liposome inhalation suspension), 590 mg.

This "Prior Approval" sNDA provides updates to the prescribing information based on the final data from clinical trials INS-212 and INS-312 that were ongoing at the time of NDA approval. Revisions were made to the **HIGHLIGHTS OF PRESCRIBING INFORMATION (PI)** and to the following sections of the **FULL PI: WARNINGS AND PRECAUTIONS (5)**, **ADVERSE REACTIONS (6)**, **Clinical Trials Experience (6.1)** subsection, **USE IN SPECIFIC POPULATIONS (8)**, **Geriatric Use (8.5)** subsection, and **CLINICAL STUDIES (14)**. Additionally, minor editorial revisions have been made throughout the PI.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.500), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

LPAD PATHWAY APPROVAL

This supplemental application is furthermore approved under section 506(h) of the FDCA and marketing of this drug product is subject to the requirements for labeling and promotional materials described therein.

Under section 506(h)(7), FDA may terminate the limitations associated with the LPAD pathway when FDA has determined that the product is safe and effective for a broader

population. The additional data supporting approval for the broader population should demonstrate that the conditions of the LPAD pathway are no longer necessary for the drug product. If you decide to conduct clinical trials to support termination of limitations, submit final reports to this NDA as a supplemental application. For administrative purposes, designate this submission "**LPAD Pathway Termination Request**."

ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies/clinical trials to verify and describe clinical benefit. You are required to conduct such studies/clinical trials with due diligence. If postmarketing studies/clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 314.530, withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated September 26, 2018. This requirement, along with required completion dates, is listed below.

3480-1 Conduct a randomized, double-blind, placebo-controlled clinical trial to assess and describe the clinical benefit of ARIKAYCE in patients with nontuberculous mycobacterial (NTM) lung disease caused by MAC. The trial will evaluate the effect of ARIKAYCE on a clinically meaningful endpoint, as compared to an appropriate control in the intended patient population of patients with MAC infection.

Final Protocol Submission:	06/2019
Trial Completion:	06/2023
Final Report Submission:	06/2024

Submit clinical protocols to your **IND 108674** for this product. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each requirement in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial.

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this post marketing requirement must be clearly designated "**Subpart H Postmarketing Requirement(s)**."

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

PROMOTIONAL MATERIALS

Under 21 CFR 314.550, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 314.550, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable). We note that meeting the requirements under 21 CFR 314.550 described above will also satisfy the requirements in section 506(h)(3)(B) of the FDCA for the submission of promotional materials for drugs approved under the LPAD Pathway.

For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.[3]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

If you have questions, call Deborah Kim, PharmD, RAC, Regulatory Project Manager, at (301) 796-9053.

Sincerely,

{See appended electronic signature page}

Sumathi Nambiar, MD, MPH
Director
Division of Anti-Infectives
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - ARIKAYCE Patient Instructions for Use
  - LAMIRA Nebulizer System Instructions for Use
- Quick Start Guide

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SUMATHI NAMBIAR
10/19/2020 07:30:15 PM