

NDA 207356/S-012

## SUPPLEMENT APPROVAL

Insmed Incorporated  
Attention: Brian Martin, MBA, RAC  
Director, Regulatory Affairs  
700 U.S. Highway 202/206  
Bridgewater, NJ 08807-1704

Dear Mr. Martin:

Please refer to your supplemental new drug application (sNDA), dated and received October 24, 2022, and your amendment, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Arikayce (amikacin liposome inhalation suspension), 590 mg.

We also refer to our letter dated, September 28, 2022, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we have determined should be included in the labeling for aminoglycosides. This information pertains to the higher risk for ototoxicity in patients receiving aminoglycosides who have mitochondrial DNA variants, particularly the nucleotide 1555 A to G substitution in the 12S rRNA gene (*MT-RNR1*).

This supplemental new drug application provides for revisions to the labeling for Arikayce (amikacin liposome inhalation suspension).

The agreed upon changes to the language included in our September 28, 2022, letter are as follows (additions are noted by underline).

### Medication Guide

**Before using ARIKAYCE, tell your healthcare provider about all of your medical conditions, including if you**

- have been told you have certain gene variants (a change in the gene) related to hearing abnormalities inherited from your mother.

### APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

## **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.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effectuated” (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*.<sup>2</sup>

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).

## **PROMOTIONAL MATERIALS**

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety-related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

## **PATENT LISTING REQUIREMENTS**

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> 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>.

314.53(c)(2)(ii). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

### **REPORTING REQUIREMENTS**

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

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

Sincerely,

*{See appended electronic signature page}*

Peter Kim, MD, MS  
Director  
Division of Anti-Infectives  
Office of Infectious Diseases  
Center for Drug Evaluation and Research

### **ENCLOSURES:**

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use

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**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.**  
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/s/  
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PETER W KIM  
02/10/2023 08:56:43 AM