BLA 022472/S-029

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

MannKind Corporation
Attention: Sree Tummala, PharmD, M.S.
Associate Director, CMC Regulatory Affairs
One Casper Street
Danbury, CT 06810

Dear Dr. Tummala:

Please refer to your supplemental biologics license application (sBLA) received July 29, 2025, and your amendments, submitted under section 351(a) of the Public Health Service Act for Afrezza (insulin human) inhalation powder.

This Prior Approval sBLA provides for expanding the indication of Afrezza to include pediatric patients 6 years of age and older based on the results of study MKC-TI-155 INHALE-1. This study was conducted to address the following postmarketing requirement (PMR) listed originally in the June 27, 2014, approval letter and reissued in the December 1, 2022, new postmarketing requirement letter:

2166-6 An open-label pharmacokinetic (PK), and multiple-dose safety and tolerability dose-titration study of Afrezza in pediatric patients ages 8 to 17 years (inclusive) with type 1 diabetes (Part 1), followed by a prospective, multicenter, open-label, randomized, controlled study comparing the efficacy and safety of prandial Afrezza to prandial subcutaneous rapid-acting insulin used in combination with subcutaneous basal insulin in pediatric patients 4 to 17 years old (inclusive) with type 1 or type 2 diabetes (Part 2). Part 2 of the study should include a run-in phase, a 26-week randomized intervention phase, and a 26-week extension phase.

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, via the FDA automated drug registration and listing system (eLIST), the content of labeling

[21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your supplemental application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

This submission contains the final report for PMR 2166-6, cited above. We have reviewed the submission and conclude that the above requirement has been fulfilled.

This closes all of your postmarketing requirements acknowledged in our June 27, 2014, letter. You are not required to report on the status of closed (released or fulfilled) PMRs in your annual report required under 21 CFR 601.70.

[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

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 601.12(f)(4)]. Form FDA 2253 is available at FDA.gov.[3] Information and Instructions for completing the form can be found at FDA.gov.[4]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

If you have any questions, contact Shiva Salartash, Regulatory Project Manager, at Shiva.Salartash@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Raymond E. Soccio, MD, PhD
Supervisory Physician (Acting)
Division of Diabetes, Lipid Disorders, and Obesity
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

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

[3] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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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.

/s/

MAHTAB NIYYATI
05/29/2026 10:34:32 AM
On behalf of Raymond Soccio