NDA 215866/S-034

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Teresa Berg
Senior Director, Global Regulatory Affairs - Regional Regulatory – Americas
Lilly Corporate Center, Drop Code 2543
Indianapolis, IN 46285

Dear Teresa Berg:

Please refer to your supplemental new drug application (sNDA) dated and received March 31, 2025, and your amendments, submitted under section 505(b) the Federal Food, Drug, and Cosmetic Act (FDCA) for Mounjaro (tirzepatide) injection.

This Prior Approval sNDA provides for revisions to subsection 8.2, Lactation, of the Prescribing Information and revisions to the Medication Guide for Mounjaro and Zepbound based on data obtained from study I8F-MC-GPIN entitled "A Study to Evaluate Tirzepatide Concentrations in Breastmilk Following Administration of Single Dose of Tirzepatide by Subcutaneous Injection in Healthy Lactating Females." This study was conducted to address the following Postmarketing Requirement (PMR) listed in the May 13, 2022, approval letter for Mounjaro (NDA 215866):

PMR 4272-2	Conduct a milk-only lactation study in lactating women who have received a dose of tirzepatide to assess concentrations of tirzepatide in breast milk using a validated assay.

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.[1] 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 Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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

FULFILLMENT OF POSTMARKETING REQUIREMENT

This submission contained the final report for PMR 4272-2, cited above. We have reviewed the submission and conclude that the above requirement has been fulfilled.

We remind you that there are postmarketing requirements listed in the May 13, 2022, NDA Approval letter and the November 29, 2024, New Postmarketing Requirement letter that are still open.

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

[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.

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 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).

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.[3]

If you have any questions, contact Lindsey Kelly, PharmD, Regulatory Project Manager, at (301) 837-7654 or Lindsey.Kelly@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

John Sharretts, MD
Director
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- single dose vial (version previously approved July 28, 2023)
  - Instructions for Use- single-dose pen (version previously approved May 13, 2022)
  - Quick Reference Guide (version previously approved May 13, 2022)

[3] https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products

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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/

JOHN M SHARRETTS
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