



NDA 215866/S-039

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
REQUIREMENT**

Eli Lilly and Company
Attention: Michael P. Roesner
Director-Global Regulatory Affairs-Americas
Lilly Corporate Center
Drop Code: 2543
Indianapolis, IN 46285

Dear Michael P. Roesner:

Please refer to your supplemental new drug application (sNDA) received June 20, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Mounjaro (tirzepatide) injection.

This Prior Approval supplemental new drug application provides for updates to the Prescribing Information (PI) and Medication Guide (MG) based on the results of trial I8F-MC-GPGV, titled, *A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study With an Open-Label Extension Assessing the Efficacy, Safety, and Pharmacokinetics/ Pharmacodynamics of Tirzepatide in Pediatric and Adolescent Participants With Type 2 Diabetes Mellitus Inadequately Controlled With Metformin, or Basal Insulin, or Both*, including expansion of the currently approved indication to include pediatric patients aged 10 years and older with type 2 diabetes mellitus. Trial GPGV was conducted to address the following Postmarketing Requirement (PMR) listed in the May 13, 2022, approval letter for Mounjaro:

PMR 4271-1	Conduct a 30-week, randomized, double-blind, placebo-controlled, multicenter, parallel-arm study of the safety and efficacy of Mounjaro (tirzepatide) for the treatment of type 2 diabetes mellitus in pediatric patients ages 10 to 17 years (inclusive), followed by a 22-week open-label extension.
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This supplement provides for pediatric information pursuant to both the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Act (PREA).

Updates were also made to the following sections in the PI to align with recent changes to the labeling for other glucagon-like peptide-1 receptor agonists: Warnings and Precautions for Acute Pancreatitis (5.2), Acute Kidney Injury Due to Volume Depletion (5.5), and Severe Gastrointestinal Adverse Reactions (5.6).

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 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*.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.

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>.

FULFILLMENT OF POSTMARKETING REQUIREMENT

This submission contained the final report for PMR 4271-1, 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.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. 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

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 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

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 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).

³ For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/media/128163/download>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

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.⁶

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

Sincerely,

{See appended electronic signature page}

John Sharretts, M.D.
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)

⁶ <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

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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