

NDA 215866/S-044
NDA 215866/S-045

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Jacob Monroe, PhD and Asavari Wagle
Associate Director – Global Regulatory Affairs – Regulatory Regional - Americas
Lilly Corporate Center, Drop Code 2543
Indianapolis, IN 46285

Dear Dr. Monroe and Asavari Wagle:

Please refer to your supplemental new drug applications (sNDAs) received October 27 and November 5, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Mounjaro (tirzepatide) injection.

These Prior Approval sNDAs provide for the following:

S-044: Updates to the Prescribing Information (PI) and Medication Guide (MG) based on results of trial I8F-MC-GPGN, titled, *The Effect of Tirzepatide versus Dulaglutide on Major Adverse Cardiovascular Events in Patients with Type 2 Diabetes* (SURPASS-CVOT), including the addition of a new indication as a treatment to reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who are at high risk for these events. Changes to the WARNINGS AND PRECAUTIONS, Diabetic Retinopathy Complications in Patients with a History of Diabetic Retinopathy, were also made based on the SURPASS-CVOT.

S-045: Updates the Mounjaro PI to indicate that the 2.5 mg dose of tirzepatide can be used for ongoing glycemic control in patients with type 2 diabetes mellitus.

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 with minor editorial revisions listed below and reflected in the enclosed labeling:

- Revision to the DOSAGE FORMS AND STRENGTHS section of the Highlights of the Prescribing Information.

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 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 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.

We are waiving the pediatric study(ies) requirement for the S-044 application because the necessary studies are impossible or highly impracticable, as the condition rarely or never occurs in pediatric populations.

Because none of these criteria apply to the S-045 supplemental application, you are exempt from this requirement for S-045.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see

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>.

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

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 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.⁵

³ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁵ <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

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

Sincerely,

{See appended electronic signature page}

Mahtab Niyyati, MD
Associate Director of Therapeutic Review (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 – KwikPen (version previously approved January 20, 2026)
 - Instructions for Use- multi dose vial (version previously approved January 7, 2026)
 - Instructions for Use- single dose vial (version previously approved April 22, 2026)
 - Instructions for Use- single dose pen (version previously approved April 22, 2026)
 - Quick Reference Guide (version previously approved May 13, 2022)

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
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