



BLA 125469/S-036

## SUPPLEMENT APPROVAL

Eli Lilly and Company  
Attention: Susan D. Sutton, PhD  
Advisor, Global Regulatory Affairs - US Lilly Corporate Center  
Drop Code 2543  
Indianapolis, IN 46285

Dear Dr. Sutton:

Please refer to your supplemental biologics license application (sBLA), dated and received November 4, 2019, and your amendments, submitted under section 351(a) of the Public Health Service Act for Trulicity (dulaglutide) injection.

This Prior Approval supplemental biologics application provides for the use of additional doses of Trulicity, 3.0 mg and 4.5 mg once weekly, as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM).

### **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,<sup>1</sup> 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 the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible via publicly available labeling repositories.

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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>.

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).

### **CARTON AND CONTAINER LABELING**

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved BLA 125469/S-036.**” Approval of this submission by FDA is not required before the labeling is used.

### **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.

We are waiving the pediatric study requirement for ages 0 to 9 years because necessary studies are impossible or highly impracticable. This is because the prevalence of children with T2DM in this age range is too low to study.

We are deferring submission of your pediatric study for ages 10 to <18 years for this application because pediatric studies should be delayed until additional safety or effectiveness data have been collected in both pediatrics (for dulaglutide 0.75 mg and 1.5 mg), and adults (for dulaglutide 3.0 mg and 4.5 mg).

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(B) of the FDCA. This required study is listed below.

- 3931-1 Conduct a Phase 3, open-label, multicenter, single-arm study to evaluate the safety and PK of dulaglutide (3.0 mg and/or 4.5 mg) in pediatric patients 10 to <18 years of age with T2DM of at least 26 weeks duration.

Draft Protocol Submission:	June 2024
Final Protocol Submission:	December 2024
Study Completion:	December 2027
Final Report Submission:	June 2028

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.<sup>3</sup>

Submit the protocols to your IND 070930, with a cross-reference letter to this BLA. Reports of this required pediatric postmarketing study must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from this study. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

### **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*.<sup>4</sup>

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.<sup>5</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>6</sup>

### **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).

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<sup>3</sup> See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019)*.

<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

<sup>4</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>6</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

If you have any questions, call Peter Franks, Regulatory Project Manager, at (240) 402-4197.

Sincerely,

*{See appended electronic signature page}*

Lisa B. Yanoff, M.D.  
Director (Acting)  
Division of Diabetes, Lipid Disorders, and Obesity  
Office of Cardiology, Hematology, Endocrinology,  
and Nephrology  
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use (3.0 and 4.5 mg doses)
  - Instruction for Use (0.75 and 1.5 mg doses; versions approved September 21, 2018)
- Carton and Container Labeling

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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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LISA B YANOFF  
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