



NDA 018780/S-172

**SUPPLEMENT APPROVAL**

Eli Lilly and Company  
Attention: Ingrid Hensley  
Advisor, Global Regulatory Affairs- U.S. Diabetes  
Lilly Corporate Center  
Indianapolis, IN 46285

Dear Dr. Hensley:

Please refer to your supplemental new drug application (sNDA) dated February 20, 2019, received February 21, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Humulin R (insulin human injection).

This Prior Approval supplemental new drug application provides for an update to the Humulin R U-500 prescribing information (PI) for compliance with the pregnancy and lactation labeling rule (PLLR). The patient package insert (PPI) as well as the KwikPen instructions for use (IFU) were modified for consistency with the PI. In addition, changes were made to the carton and container labeling.

**APPROVAL & LABELING**

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, with minor editorial revisions listed below and reflected in the enclosed labeling.

Revision dates added to the PI, PPI, and KwikPen IFU.

**WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of 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.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Instructions for Use), 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*.<sup>2</sup>

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).

## **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 NDA 018780/S-172.**” 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

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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>.

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 application, you are exempt from this requirement.

## **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Callie Cappel-Lynch, Regulatory Project Manager, at (301) 796-8436.

Sincerely,

*{See appended electronic signature page}*

Lisa B. Yanoff, M.D.  
Director (Acting)  
Division of Metabolism and Endocrinology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

## **ENCLOSURES:**

- Content of Labeling
  - Prescribing Information U-100 (previously approved May 25, 2018)
  - Patient Package Insert U-100 (previously approved May 25, 2018)
  - Instructions for Use Vial U-100 (previously approved May 25, 2018)
  - Prescribing Information U-500
  - Patient Package Insert U-500
  - Instructions for Use KwikPen U-500
  - Instructions for Use Vial U-500 (previously approved July 8, 2016)
  - Carton and Container labeling U-500

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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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