BLA 761109/S-004

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Katherin M. Ruiz
Director, Global Regulatory Affairs- North America, Diabetes
Lilly Corporate Center
Indianapolis, IN 46285

Dear Ms. Ruiz:

Please refer to your supplemental biologics license application (sBLA), dated and received December 14, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for Lyumjev (insulin lispro-aabc) injection.

This Prior Approval sBLA provides for an expansion of the indication to pediatric patients with diabetes mellitus and addition of continuous subcutaneous insulin infusion as a condition of use in the pediatric population.

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 date added to Patient Package Insert (PPI)

WAIVER OF HIGHLIGHTS 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, 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,[1] that is identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Instructions for Use) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

[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 via publicly available labeling repositories.

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).

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 studies requirement for type 1 diabetes mellitus in ages 0 to < 1 year and type 2 diabetes mellitus in ages 0 to < 10 years because necessary studies are impossible or highly impracticable. This is because there are too few children in this age range with diabetes mellitus to study.

We note that you have fulfilled the pediatric study requirement for patients with diabetes ages 1 to 17 years (inclusive) for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT

This sBLA contained the final report for the following postmarketing requirement listed in the June 15, 2020, approval letter:

3874-1 Conduct a 26-week, randomized, controlled efficacy and safety study comparing Lyumjev (insulin lispro-aabc) administered at mealtime and Lyumjev (insulin lispro-aabc) administered 20 minutes postmeal to Humalog administered at mealtime, in combination with long acting insulin, in pediatric patients with type 1 diabetes ages 1 to 17 years (inclusive).

[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.

We have reviewed your submission and conclude that the above requirement was fulfilled.

This completes all of your postmarketing requirements acknowledged in our June 15, 2020, letter.

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]

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.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

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).

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.

If you have any questions, call Callie Cappel-Lynch, Chief Project Management Staff, at (301) 796-8436.

Sincerely,

{See appended electronic signature page}

Patrick Archdeacon, M.D.
Deputy Director
Division of Diabetes, Lipid Disorders, and Obesity

[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

Office of Cardiology, Hematology, Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - Vial Instructions for Use (previously approved August 13, 2021)
  - KwikPen Instructions for Use (previously approved June 15, 2020)
  - Tempo Pen Instructions for Use (previously approved June 15, 2020)
  - Junior KwikPen Instructions for Use (previously approved June 15, 2020)
  - U-200 KwikPen Instructions for Use (previously approved June 15, 2020)

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/

PATRICK ARCHDEACON
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