DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125469/S-004

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Kenneth Mace, PhD
Advisor, Global Regulatory Affairs-US
Lilly Corporate Center, DC 2543
Indianapolis, IN 46285

Dear Dr. Mace:

Please refer to your supplemental Biologics License Application (sBLA), dated and received May 29, 2015, submitted under section 351(a) of the Public Health Service Act for Trulicity (dulaglutide) Injection.

We acknowledge receipt of your amendments dated July 21 and 23, 2015.

This supplemental new drug application provides for proposed modifications to the approved Trulicity risk evaluation and mitigation strategy (REMS). This supplement is in response to our April 29, 2015, REMS Modification Notification letter.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Trulicity (dulaglutide) was originally approved on September 18, 2014. The REMS consists of a communication plan and a timetable for submission of assessments of the REMS. In order to ensure the benefits of Trulicity outweigh its risks, we determined that you were required to submit a REMS modification to conform the REMS to the safety labeling changes approved on March 9, 2015, in sBLA No.001. The required modifications included a revised REMS document and changes to the following REMS appended materials: REMS Letters, REMS Factsheet, and REMS webpage.

Your proposed modified REMS, submitted on July 23, 2015, and appended to this letter, is approved. We acknowledge receipt of your updated REMS supporting document that includes a description of all proposed modifications.

The timetable for submission of assessments of the REMS may remain the same as that approved on September 18, 2014.

The REMS assessment plan must include, but is not limited to, the following:

I. REMS Communication Plan Activities

a. Date when REMS website went live and number of total and unique site visits during the assessment period.

The 18-month REMS assessment will also report:

b. Number of Health care providers (HCPs) and professional societies targeted by the REMS.

c. Number of REMS Letters sent to HCPs and Professional Societies via e-mail, standard mail, and facsimile, and the dates the letters were sent.

d. Number of letters sent via standard mail because the HCP did not have an e-mail address, and the number sent because the e-mail was undeliverable. For letters sent via e-mail, include the number of letters successfully delivered, and the number of e-mail letters opened by the recipients.

e. Number of REMS Factsheets distributed to HCPs during the 12 months after product launch.

II. Evaluation of HCPs' Understanding of:

a. The potential risk of medullary thyroid carcinoma (MTC)

b. The risk of pancreatitis

c. The need for prompt evaluation of patients who develop symptoms suggestive of pancreatitis

d. The need to discontinue Trulicity if pancreatitis is suspected and not restart Trulicity if pancreatitis is confirmed

e. Appropriate Trulicity patients

III. Safety Surveillance

a. Trulicity utilization information including, but not limited to, indication and type of HCP (that is, endocrinologist, general practitioner, internist, etc.)

b. Evaluation and post-marketing case reports of pancreatitis

c. Evaluation and post-marketing case reports of MTC

d. Any other relevant data and analysis employed to assess if the Trulicity REMS is meeting its goals

e. The evaluation shall include, with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any of goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A). This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of that the last assessment and if any modifications of the REMS have been proposed since that assessment.
e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

BLA 125469 REMS CORRESPONDENCE
insert concise description of content in bold capital letters, e.g.,

UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 125469 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 125469/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 125469/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 125469/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES
SUBMITTED IN SUPPLEMENT S-XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 125469/S-000
< other supplement identification >
PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR BLA 125469

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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).

If you have any questions, call Marisa Petruccelli, Regulatory Project Manager, at (240) 402-6147.

Sincerely,

{See appended electronic signature page}

Jennifer Rodriguez Pippins, M.D., M.P.H.
Deputy Director for Safety
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JENNIFER R PIPPINS
07/27/2015