DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22307/S-012

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Anindita Sen, M.S., Ph.D.
Director, Global Regulatory Affairs – US
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Sen:

Please refer to your Supplemental New Drug Application (sNDA) dated 24 March 2015, received 24 March 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Effient (prasugrel hydrochloride) 5 mg and 10 mg Tablets.

This Prior Approval supplemental new drug application provides for language to be included in labeling describing the data from the ACCOAST trial.

APPROVAL & LABELING
We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with the minor editorial revisions. These changes are as follows:

Changes made to the Full Prescribing Information and Highlights

- To Section 1, **INDICATIONS AND USAGE**, the following was deleted:

(b) (4)

- The following language was added to Section 2, **DOSAGE AND ADMINISTRATION**:

  Timing of Loading Dose
  In the clinical trial that established the efficacy and safety of Effient, the loading dose of Effient was not administered until coronary anatomy was established in UA/NSTEMI patients and in STEMI patients presenting more than 12 hours after symptom onset. In STEMI patients presenting within 12 hours of symptom onset, the loading dose of Effient was administered at the time of diagnosis, although most received Effient at the time of PCI *[see Clinical Studies (14)]*. For the small fraction of patients that required urgent CABG after treatment with Effient, the risk of significant bleeding was substantial.

  Although it is generally recommended that antiplatelet therapy be administered promptly in the management of ACS because many cardiovascular events occur within hours of initial presentation, in a trial of 4033 NSTEMI patients, no clear benefit was observed when Effient loading dose was administered prior to diagnostic coronary angiography compared to at the time of PCI; however, risk of bleeding was increased with early administration in patients undergoing PCI or early CABG.

- The following section was deleted from Section 11, **DESCRIPTION**:

(b) (4)

Changes to the Medication Guide

- The following information was deleted:

(b) (4)

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert 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 the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications 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 MS Word format, that includes the changes with the revisions listed approved in this supplemental application, as well as annual reportable changes, and annotate each change. To facilitate review of your submission, 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).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

You must submit final promotional materials and package insert(s), 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 http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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, please call:

Alison Blaus, RAC
Senior Regulatory Project Manager
(301) 796-1138

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD
Deputy Director for Safety
Division of Cardiovascular & Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling

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

/s/

MARY R SOUTHWORTH
07/07/2015