



NDA 22307/S-008

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attention: Peter Morrow, MS
Director, Global Regulatory Affairs - US
Lilly Corporate Center
Indianapolis, IN 46285

Dear Mr. Morrow:

Please refer to your Supplemental New Drug Application (sNDA) dated December 14, 2012, received December 17, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Effient (prasugrel hydrochloride) 5 mg and 10 mg Tablets.

We acknowledge receipt of your amendments dated January 31, February 5, 8, and 18, March 19, April 1, 23, and 26, May 3, 10, 17, and 31, June 28, July 9, September 25, and October 11, 2013.

This Prior Approval efficacy supplemental new drug application contained effectiveness, safety, and clinical pharmacology data from Study H7T-MC-TABY (“A Comparison of Prasugrel and Clopidogrel in Acute Coronary Syndrome (ACS) Subjects with Unstable Angina/Non-ST-Elevation Myocardial Infarction (UA/NSTEMI) Who are Medically Managed—The TRILOGY ACS Study”). This application did not seek any new indication [REDACTED] (b) (4)

[REDACTED] this application proposed changes to the labeling based on results from four completed pharmacokinetic/pharmacodynamic studies. Lastly, the submission contained final reports for Postmarketing Requirement #2 (95-2) and Postmarketing Commitment #6 (95-6).

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. [REDACTED] (b) (4)

[REDACTED] we have updated the label in Section 12 with new pharmacokinetic/pharmacodynamic data.

We note that your October 11, 2013, submission includes final printed labeling (FPL) for your package insert and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

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 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 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 from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes 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 MS Word format, that includes the changes 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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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.

Given the limited number of children with acute coronary syndrome, we are waiving the pediatric study requirement for this application because studies would be impossible or highly impracticable.

POSTMARKETING REQUIREMENTS UNDER 505(o)

We remind you of your post-marketing requirements listed in our action letter dated July 10, 2009. These requirements are listed below:

- 95-2 You will gather baseline cancer history and cancer adverse event data from the ongoing trial TRILOGY, a 10,300-subject trial being conducted in patients with acute coronary syndrome who are being managed medically (without coronary revascularization). The final report on cancers in this trial is to be submitted to IND 63,449.

The timetable you submitted on July 8, 2009 states that you will conduct this trial according to the following timetable:

Protocol Submission: Received 06/20/2008
Trial Completion Date: 12/2012
Final Report Submission: 01/2013

POSTMARKETING COMMITMENTS REPORTABLE UNDER SECTION 506B

We also remind you of your post-marketing commitment listed in our action letter dated July 10, 2009. This commitment is listed below:

- 95-6 You commit to the collection of samples at baseline for genotyping CYP450 enzymes in TRILOGY subjects, to allow a comparison of effectiveness and bleeding in prasugrel and clopidogrel subgroups by metabolizer status. These data will be submitted with the final study report of TRILOGY. The periodic reports will include the fraction of subjects who consented to genetic testing.

We understand that the protocols for these trials have been submitted.

Final Protocol Submission: Received 06/20/2008
Trial Completion Date: 12/2012
Final Report Submission: 01/2013

Submit clinical protocols to your IND (63,449) for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “**Postmarketing Commitment Protocol**,” “**Postmarketing Commitment Final Report**,” or “**Postmarketing Commitment Correspondence**.”

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:

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

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/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. 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>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package

labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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
Regulatory Project Manager
(301) 796-1138

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular & Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
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/

NORMAN L STOCKBRIDGE
10/16/2013