DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-307

Eli Lilly and Company
Attention: Elizabeth Bearby, PharmD
Sr. Scientific Director, US Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Bearby:

Please refer to your supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Effient™ (prasugrel hydrochloride) Tablets.

Upon review of the data submitted in the December 18, 2008 and March 5, 2009 amendments to the NDA, the Agency recommends revising the following acceptance criteria in the prasugrel drug product specification to ensure consistent product quality:

1. Tablet form conversion for both 5 and 10 mg prasugrel tablets as measured by XRPD to be Not More Than — This recommendation is based on review of the stability data of batches manufactured with the proposed commercial controls that show form conversion did not exceed — even during storage at accelerated conditions for 6 months for most batches Moreover, the current limit of NMT — was set prior to the implementation of the recent stringent controls which allow manufacturing of prasugrel tablets with limited batch to batch variability in form conversion —

b(4)

2. Dissolution to be Q= — at 30 minutes. The rationale for this recommendation is based on data from the new dissolution method as provided in the December 18th, 2008 amendment. This acceptance criterion will minimize the probability of the release of batches with markedly different release characteristics that might result in bioinequivalent lots.

An expiration dating period of 12 months for prasugrel hydrochloride tablets packaged in both bottles and blisters can be granted considering the limited bottle data provided.

If you have questions, call Rebecca McKnight, Regulatory Project Manager, at (301) 796-1765.

Sincerely,

{See appended electronic signature page}

Christine Moore, Ph.D.
Acting Director, Division of Pre-Marketing Assessment I
Acting Deputy Director
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Christine Moore
4/3/2009 11:45:41 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

REQUEST FOR METHODS VALIDATION MATERIALS

NDA 22-307

Joerg Pfeifer
Eli Lilly
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Pfeifer:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Effient (Prasugrel) Tablets, 5 and 10 mg.

We will be performing methods validation studies on Effient Tablets, 5 and 10 mg using method B11714, Analysis of Prasugrel Hydrochloride Tablets by Quantitative X-ray Powder Diffraction (XRPD), as described in NDA 22-307.

In order to perform the necessary testing, we request the following sample materials and equipments:

Materials

b(4)

Equipment

X-ray Powder Diffraction sample cell

Forward these materials via express or overnight mail to:

Food and Drug Administration
Division of Pharmaceutical Analysis

Attn: James Allgire
1114 Market Street, Room 1002
St. Louis, MO 63101

Please notify me upon receipt of this letter. If you have questions, you may contact me by telephone (314-539-3813), FAX (314-539-2113), or email (james.allgire@fda.hhs.gov).

Sincerely,

{See appended electronic signature page}

James Allgire
Team Leader
Division of Pharmaceutical Analysis, HFD-920
Office of Testing and Research
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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/s/

James F Allgire
3/16/2009 04:39:19 PM

DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS
FOOD AND DRUG ADMINISTRATION

WHITE OAK COMPLEX
10903 NEW HAMPSHIRE AVE
BLDG. 22
SILVER SPRING, MD 20993

US Mail address:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardiovascular and Renal Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Transmitted via e-mail to:	Elizabeth Bearby
Company Name:	Eli Lilly and Daiichi-Sankyo
Phone:	317.276.1203
Subject:	**Minutes for the teleconference with FDA on 02.27.2009 N22-307**
Date:	March 16, 2009
Pages including this sheet:	4

From:	**Meg Pease-Fye, M.S.**
Phone:	**301-796-1130**
Fax:	**301-796-9838**
E-mail:	**meg.peasefye@fda.hhs.gov**

Please note that you are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

Teleconference with Eli Lilly and Daiichi-Sankyo

Sponsor:	Eli Lilly and Daiichi-Sankyo
Drug:	prasugrel
Meeting/Teleconference Date:	February 27, 2009
Meeting Chair:	John Jenkins, M.D.
Recorder:	Meg Pease-Fye, M.S.

LIST OF ATTENDEES

Food and Drug Administration

John Jenkins, M.D.	Director, Office of New Drugs
Norman Stockbridge, M.D., Ph.D.	Director, Division of Cardiovascular and Renal Products
Ellis Unger, M.D.	Deputy Director (acting), ODE-I
Meg Pease-Fye, M.S., R.A.C.	Regulatory Health Project Manager

Eli Lilly

Jennifer Stotka, M.D.	Vice President, Global Regulatory Affairs

Daiichi-Sankyo

James Molt, Ph.D.	Vice President, Global Regulatory

BACKGROUND

On February 27, 2009 Lilly requested a teleconference with Dr. Jenkins to discuss the status of their pending application for prasugrel. Lilly stated that the purpose of the meeting would be limited to a discussion of the internal regulatory briefings that FDA was planning.

Summary of the conversation

The Sponsors noted they were aware that one, or possibly two, internal meetings were planned to discuss issues relating to the prasugrel NDA prior to the Agency's action on the application. The Sponsors noted that they were aware that in one of these meetings the review staff might meet with Dr. Sanjay Kaul, a member of the Cardiovascular and Renal Advisory Committee who did not participate in the February 3, 2009, meeting on prasugrel. Dr. Jenkins clarified that the objective of these meetings will be to discuss the status of the review of the application, the planned action, and to ensure that all issues and concerns have been voiced and addressed prior to the Agency's action on the application.

The sponsors asked if these Center briefings were going to be a regular part of the review process in the future. Dr. Jenkins noted that the planned internal meeting(s) were not a typical CDER regulatory briefing, and briefings such as the one(s) planned for prasugrel were not planned as part of the regular review process for all applications. Review of the prasugrel application has raised many complex issues across multiple disciplines and the planned briefing for Dr. Woodcock is a follow up to an internal meeting that she attended earlier in the review cycle. Dr. Woodcock wants to be certain that all the complex issues and any differing perspectives of members of the review team have been well considered and adequately addressed.

The sponsors asked if Prasugrel's regulatory action would be taken at the Office level. Dr. Jenkins declined to discuss any change in signatory authority.

Lilly and Sankyo asked to have an opportunity to weigh in on the scientific issues that would be discussed at the internal meetings. Dr. Jenkins noted that the meeting was internal and that any issues that required involvement of the sponsors would be raised with them as appropriate.

Dr. Jenkins stated that the Agency believes the process by which Dr Kaul was disinvited from the Advisory Committee meeting was a mistake caused by FDA not following its own procedures in making such determinations. Dr. Jenkins noted that it is known publicly that the sponsors contacted the Division on January 30, 2009, to voice their concerns about Dr. Kaul's participation in the Advisory Committee meeting, and that that contact initiated the process that led the Agency to disinvite him from the meeting. Dr. Stotka opined that the public advisory committee meeting on February 3 was comprehensive in scope, all issues were vetted, and the deliberations were wide-ranging. Dr. Jenkins agreed that the discussion was robust, but noted that the Agency's decision to disinvite Dr. Kaul presented the appearance that the sponsors may have "stacked the deck" by trying to eliminate an adversarial opinion. Dr. Jenkins noted that it would have been preferable had Dr. Kaul participated in the meeting so that his opinions could have been discussed publicly and considered by the committee as a whole in offering their advice on the application. The sponsors stated that they would not have done anything differently and that their concerns were still valid; they disclosed pre-formed opinions and conclusions that should have been made public, or appeared through the vetting process done by Advisors and Consultants.

Dr. Stotka stated that, given what has been in the news and the impact of prasugrel on public health, they would like the Agency to get to decision on approvability as soon as possible. They noted that patients that could benefit are waiting. Dr. Jenkins explained that the Division has already missed the PDUFA goal date and has set a new internal timeline. Dr. Jenkins noted that he could not give the sponsors assurances or a definitive answer on the action or the timeline for the action. There are many uncertainties and perspectives, and the Agency needs to be comfortable when taking a regulatory action. The Agency will need to be able to explain and defend whatever action it takes.

Date Minutes Drafted: March 9, 2009
Date Minutes Finalized: March 16, 2006

Recorder: *{See appended electronic signature page}*
Meg Pease-Fye, M.S., R.A.C.

Chair Concurrence: *{See appended electronic signature page}*
John Jenkins, M.D.

Reviewed:
E. Unger 03.10.2009/03.12.09
N. Stockbridge 03.11.2009, 3/13/09
J. Jenkins 03.12.2009, 03.13.2009

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/s/

Margaret Pease-Fye
3/16/2009 12:52:48 PM
CSO

These are the minutes for the 02.27.2009 teleconfernce for parsugrel

John Jenkins
3/16/2009 01:06:30 PM
MEDICAL OFFICER

MEMORANDUM

To: **Meg Pease-Fye, MS**
Division of Cardiovascular and Renal Products

From: **Iris Masucci, PharmD, BCPS**
for Study Endpoints and Label Development (SEALD) Team, OND

Date: **March 10, 2009**

Re: **Comments on draft labeling for Effient (prasugrel)**
NDA 22-307

We have reviewed the proposed label for Effient (FDA version dated 3/3/09) and offer the following comments. These comments are based on Title 21 of the Code of Federal Regulations (201.56 and 201.57), the preamble to the Final Rule, labeling Guidances, and FDA recommendations to provide for labeling quality and consistency across review divisions. We recognize that final labeling decisions rest with the Division after a full review of the submitted data.

Please see attached label for recommended changes.

13 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

X Draft Labeling (b4)

X Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

Iris Masucci
3/10/2009 10:56:40 AM
DDMAC PROFESSIONAL REVIEWER

Laurie Burke
3/11/2009 12:36:01 PM
INTERDISCIPLINARY