DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-863/S-007

Otsuka America Pharmaceutical, Inc.
Attention: Gerald Young, Ph.D.
2440 Research Blvd.
Rockville, MD 20850

Dear Dr. Young:

Please refer to your supplemental new drug application dated March 20, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pletal (cilostazol) 50 and 100 mg Tablets.

We acknowledge receipt of your submissions dated April 10, and November 7, 2003, and January 21, 2004.

Your submission of January 21, 2004 constituted a complete response to our March 20, 2003 action letter.

This supplemental new drug application provides for changes in the labeling; the package insert revisions include changes in the **Clinical Pharmacology, Pharmacokinetics**, **Dosage and Administration**, **Adverse Events, Post Marketing Experience**, and **Clinical Efficacy** sections. Also, this supplement provides for changes in the patient package insert.

We have completed our review of this supplemental new drug application, as amended. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on November 7, 2003, and January 21, 2004. In addition, we note the word "Omeprazole" under **CLINICAL PHARMACOLOGY, Pharmacokinetics,** *Pharmacokinetic and Pharmacodynamic Drug-Drug Interactions, Inhibitors of CYP2C19*, should not be in bold print. Change this to normal font at the time of the next printing.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We also refer to your submission dated May 16, 2001, that contained the final report on the following post-marketing study commitment:

1. Study 1: A single-center, randomized, three-period cross-over, single-dose study of the effects of ketoconazole or grapefruit juice on cilostazol (OPC-13013) pharmacokinetics.

This report culminated, in part, to labeling changes included in this supplement. As such, we conclude that the above commitment has been fulfilled.

We note that the following commitment acknowledged in our January 15, 1999 letter is still pending:

1. Study 2: A study to understand better the risk, if any, of long-term use of cilostazol. This trial will compare the effects of cilostazol with those of pentoxifylline and placebo in about 1800 intermittant claudication patients of any severity (including patients on clopidogrel). Efficacy will be monitored for a total of 12 months.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Meg Pease-Fye, Regulatory Project Manager, at (301) 594-5312.

Sincerely,

{See appended electronic signature page}

Douglas C. Throckmorton, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Doug Throckmorton

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