CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: NDA 20-863

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CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 20-863

Trade Name: PLETAL 50 and 100 mg Tablets

Generic Name:(cilostazol)

Sponsor: Otsuka Pharmaceutical Company, Ltd.

Approval Date: January 15, 1999

Indication:Provides for the use of Pletal (cilostazol) 50 and 100 mg Tablets for the reduction of symptoms of intermittent claudication.

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20-863

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-863

JAN 15 1999

Otsuka Pharmaceutical Company, Ltd
c/o Otsuka America Pharmaceutical, Inc.
Attention: Tanveer Ahmad, Ph.D.
2440 Research Boulevard
Rockville, MD 20850

Dear Dr. Ahmad:

Please refer to your new drug application (NDA) dated September 19, 1997, received September 19, 1997, 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 September 24, 29, and 30, October 2, 14, and 19, November 9 (two), 10, 16, and 30, and December 8, 11, and 22, 1998.

This new drug application provides for the use of Pletal (cilostazol) 50 and 100 mg Tablets for the reduction of symptoms of intermittent claudication.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed package insert and patient package insert must be identical to the enclosed marked-up drafts. The final printed immediate container and carton labels submitted November 30, 1998 are acceptable and need not be resubmitted. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the final printed package insert and patient package insert as soon as they are available, in no case more than 30 days after they are printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-863." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated November 9, 1998. These commitments, along with any completion dates agreed upon, are listed below.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug product when it is available.

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, please contact:

Mr. Gary Buehler
Regulatory Health Project Manager
(301) 594-5332

Sincerely yours,

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

FINAL PRINTED LABELING HAS NOT BEEN SUBMITTED TO THE FDA

DRAFT LABELING IS **NO LONGER** BEING SUPPLIED SO AS TO ENSURE ONLY CORRECT AND CURRENT INFORMATION IS DISSEMINATED TO THE PUBLIC.

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

21 pages

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APPLICATION NUMBER: NDA 20-863

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

G. Buehler

NDA 20-863

SEP 18 1998

Otsuka America Pharmaceutical, Inc.
Attention: Tanveer Ahmad, Ph.D.
2440 Research Boulevard
Rockville, MD 20850

Dear Dr. Ahmad:

Please refer to your September 19, 1997 new drug application (NDA) 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 October 2, 6, 10, 15 and 22, November 7, 12, 14 and 25, 1997; January 29, February 17, 19, 20, 23 and 26, March 3, 11, 18, 19 and 20, April 6, 13, 14, 21, 24 (two) and 30, May 4, 6, 8 (two), 13 (two), 15 (two), 22 (two), 26 (two), and 29 (two), June 1 (two), 3 (two), 4, 5, 8, 9, 11 (two), 12 and 26, July 2 (two), 6 (two), 7, 14, 17, 21, 24 (two), 27 (two), 28, 29 and 30, August 3, 4, 5 (two), 11, 14, 17, 19 and 26 and September 2 and 3, 1998.

The user fee goal date for this application is September 19, 1998.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for the drug. The labeling should be identical in content to the enclosed draft.

In addition, we have the following requests that need to be addressed prior to approval of this application:

Please submit 20 copies of the final printed labeling, ten of which are individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available before we receive the final printed labeling, revision of that labeling may be required.

Please note that we have determined the dissolution method, medium and specifications to be:

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to the Division of Cardio-Renal Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, please contact:

Mr. Gary Buehler
Regulatory Health Project Manager
(301) 594-5332

Sincerely yours,

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

cc:
Archival NDA 20-863
HFD-110/Div. Files
HFD-002/ORM
HFD-101/ADRA
HFD-95/DDMS
HFD-40/DDMAC (with labeling)
HFD-810/DNDC Division Director
~~DISTRICT~~ OFFICE
HFD-110/G.Buehler/7/27/98
sb/7/28/98;~~8/4/98;8/14~~/98
Initialed by: F Zielinski/8/12/98
S Rodin/8/10/98
A Karkowsky/8/10/98
K Mahjoob for K Jin/8/10/98
P Marroum for R Uppoor/8/10/98
X Joseph/8/12/98
C Resnick/8/12/98
N Morgenstern/8/13/98
filename: 20863ae.doc

APPROVABLE (AE)