CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20931

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

OCT 1 1999

NDA 20-931

Pfizer Pharmaceutical Production Limited
c/o Pfizer Inc.
Attention: William R. Murphy, Ph.D.
Eastern Point Road
Groton, CT 06340

Dear Dr. Murphy:

Please refer to your new drug application (NDA) dated March 9, 1998, received March 9, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tikosyn (dofetilide) Capsules.

We acknowledge receipt of your submissions dated March 11 and 19, April 9, 23 and 29, May 3, 21 and 28, June 24, July 7, September 8 and 15, 1999. Your submission of September 15, 1999 constituted a complete response to our March 5, 1999 action letter.

This new drug application provides for the use of Tikosyn (dofetilide) Capsules for the maintenance of normal sinus rhythm (delay in time to recurrence of atrial fibrillation/atrial flutter [AF/AFl]) in patients with atrial fibrillation /atrial flutter of greater than one week duration who have been converted to normal sinus rhythm. Because Tikosyn can cause life threatening ventricular arrhythmias, it should be reserved for patients in whom atrial fibrillation /atrial flutter is highly symptomatic. Tikosyn is also indicated for the conversion of atrial fibrillation and atrial flutter to normal sinus rhythm. Tikosyn has not been shown to be effective in patients with paroxysmal atrial fibrillation.

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 submitted final printed labeling (package insert and immediate carton and container labels in your submission dated September 8, 1999) and the agreed upon patient package insert text with minor editorial revisions indicated in the enclosed labeling. Accordingly, the application is approved effective on the date of this letter.

The final printed patient package insert must be identical to the enclosed text, including the minor editorial revisions. These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as requested, in the product's printed patient package insert may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the final printed patient package insert as soon as it is available, in no case more than 30 days after it is printed. Individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for NDA 20-931." Approval of this submission by FDA is not required before the labeling is used.

We have determined the approved interim dissolution method, medium, and specification to be: USP Apparatus I (basket) at 100 rpm in 0.001 M hydrochloric acid; Q= [redacted] at 30 minutes.

We remind you of your Phase 4 commitment specified in your submission dated September 8, 1999.

> You have agreed to submit (after NDA approval) an experimental protocol to evaluate alternative dissolution test methods and/or criteria. After agreement is reached on the protocol, this experimental work will be conducted and the results submitted to the FDA within one year after NDA approval, at which point final dissolution methods for Tikosyn will be determined.

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 this commitment in your annual report to this NDA. For administrative purposes, all submissions relating to this Phase 4 commitment 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.

As of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632)(21 CFR 314.55 (or 601.27)). The Agency has not made a determination if a health benefit would be gained by studying dofetilide in pediatric patients for its approved indications. FDA is deferring submission of the pediatric assessments of safety and effectiveness that may be required under these regulations until additional data have been collected and reviewed. FDA will inform you on or before two years from the date of this letter whether pediatric studies are required under the rule. If FDA determines at that time that pediatric studies are necessary, FDA will also set a specific time at which you must submit the required assessments.

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. David Roeder
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

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

Enclosure