
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020974

MEDICAL REVIEW(S)

MEMORANDUM

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

DATE: March 8, 1999

FROM: Thomas P. Laughren, M.D. */S/*
Team Leader, Psychiatric Drug Products
Division of Neuropharmacological Drug Products
HFD-120

SUBJECT: Recommendation for Approval Action for Prozac (fluoxetine) 10 mg and 20 mg
Tablets

TO: File NDA 20-974
[Note: This memo should be filed with the 3-19-98 original submission.]

This NDA for a new tablet formulation of Prozac in 10 and 20 mg strengths was submitted 3-19-98. It included CMC information, the results of a bioequivalence study, and draft labeling (changes in the Description & How Supplied sections).

The bioequivalence study compared the 10 and 20 mg tablets with the marketed 10 and 20 mg capsules. The results from this study were reviewed by Rae Yuan, Ph.D. from OCPB who concluded that bioequivalence had been established. However, she disagreed with the proposed dissolution specs and proposed alternative specs. These will be conveyed in the approval letter.

The CMC information, including labeling, was reviewed by Donald Klein, Ph.D. Several minor issues were resolved over the course of the review cycle and ONDC has recommended that this NDA can now be approved.

I agree that this NDA can now be approved.

cc:
Orig NDA 20-974
HFD-120/DivFile
HFD-120/TLaughren/RKatz/PDavid

DOC: NDA20974.01

43 page(s)

DRAFT

LABELING

REVIEW AND EVALUATION OF CLINICAL DATA

IND/NDA: N20974
SPONSOR: Lilly
DRUG: Fluoxetine HCl (Prozac)
DRUG CATEGORY: Selective serotonin reuptake inhibitor
MATERIAL SUBMITTED: Application to market tablet formulation
CORRESPONDENCE DATE: 3/19/98
DATE RECEIVED: 3/20/98

This NDA submission is for the approval of 10 mg and 20 mg tablets of Prozac. The NDA submission includes draft labeling, CMC information, and report of a bioequivalence study. The draft labeling includes changes to the Description and How Supplied sections, but does not involve any changes under Dosage and Administration.

The bioequivalence study (protocol HCIS) compared oral bioavailability of the 10 mg and 20 mg tablet formulations to marketed 10 mg and 20 mg capsules. A total of 48 subjects were enrolled, with 45 subjects completing. The study design was a cross over study in which subjects received single oral doses of 20 mg on two occasions, as either tablet or capsule formulation; one group received a single 20 mg tablet or capsule and the other group received two 10 mg tablets or capsules. Pharmacokinetic parameters meet requirements for bioequivalence, according to the sponsor. In terms of safety findings, one subject withdrew from the trial due to tachycardia; however, this was in between doses and was many days after the first dose of fluoxetine. In addition, one subject was lost to follow up and one subject moved away before completing the study. The sponsor reported no consistent abnormality was found on clinical laboratories, electrocardiograms, or vital signs. These data were not analyzed by the sponsor beyond inspection for abnormal values.

Conclusions and recommendations: From a clinical standpoint, this NDA may be approved.

/S/

— 10/15/98

Andrew Mosholder, M.D.
Medical Officer, HFD-120

10-15-98

NDA 20-974
Div file
HFD-120 Laughren/David/Mosholder

There are no clinical
issues for this
application.

/S/