CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number : 020051/ S008

Trade Name : GLYNASE PRESTABS

Generic Name: Micronized Glyburide 1.5mg, 3mg and 6mg Tablets

Sponsor : Pharmacia and Upjohn Company

Approval Date: January 10, 1997

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APPLICATION 020051/ S003

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Application Number 020051/ S008

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-051/S-008

JAN 10 1997

Pharmacia & Upjohn Company
Attention: Ms. Janice A. Enzinger
Senior Regulatory Manager
7000 Portage Road
Kalamazoo, MI 49001

Dear Ms. Enzinger:

Please refer to your supplemental new drug application dated October 2, 1996, received October 3, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Glynase PresTab™ (micronized glyburide) 1.5 mg, 3 mg, and 6 mg tablets.

The supplemental application provides for the following changes to the package insert:

1. A paragraph describing the results of a steady-state study in diabetic patients comparing once daily versus twice daily dosing of the same total dose of Glynase PresTabs is added to the "Pharmacokinetics" subsection of the CLINICAL PHARMACOLOGY section;

2. The term "children" is replaced by "pediatric patients" in both the "Pediatric Use" subsectino of the PRECAUTIONS section and in the "Special Populations" subsection of the DOSAGE AND ADMINISTRATION section;

3. The temperature range in the storage section of the HOW SUPPLIED section was changed to reflect the USP standard;

4. The company name was changed from "The Upjohn Company" to "Pharmacia and Upjohn Company."

We have completed the review of this supplemental application, including the submitted draft labeling, 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 draft labeling in the submission dated October 2, 1996. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the draft labeling submitted on October 2, 1996.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or

similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved supplemental NDA 20-051/S-008. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

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 Michael F. Johnston, R.Ph., Consumer Safety Officer, at (301) 443-3510.

Sincerely yours,

1-10-97

Solomon Sobel, M.D.
Director
Division of Metabolic and Endocrine Drug Products (HFD-510)
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 020051/ S008

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEWS

Clinical Pharmacology and Biopharmaceutics Review

NDA:	20-051
Micronized Glyburide 6, 3, and 1.5 mg tablets (Glynase PresTab ®)	DEC 20 1996
Submission Date:	10/2/96
Sponsor:	Pharmacia & Upjohn
Type of Submission:	Labeling Supplement
Reviewer:	Michael J. Fossler, Pharm. D., Ph. D.

Submission

The submission dated 10/2/96 is for micronized glyburide tablets manufactured by Pharmacia and Upjohn. On 9/16/96, the Agency requested that the firm update the **Pharmacokinetics** portion of their labeling to incorporate the results of Study M/5215/0006, *Effect of Dosing Regimen on the Pharmacokinetics and Pharmacodynamics of GLYNASE PresTab Tablets 3 mg in Non-Insulin Dependent Diabetics*. This study, submitted to IND and reviewed by Dr. Albert Chen (see the biopharm review dated 4/26/94) demonstrated that in NIDDM patients given 6 mg GLYNASE either as a single dose or as 3 mg BID, there was no difference in average serum gyburide concentrations over 24 hours, nor was there any difference in 24 hr. plasma glucose levels. There were some small differences in serum insulin response between the two regimens, but they were not clinically significant, since these differences did not affect glucose control.

In addition to the above change, the firm proposes the following additional changes:

- Replacement of the word "children" with "pediatric patients" under the Precautions and Dosage and Administration sections.
- Modification of the storage statement in the How Supplied section for consistency with the current U.S.P. statement for controlled room temperature.
- Change in the firm's name from "Upjohn" to "Pharmacia & Upjohn".

The proposed labeling is attached.

Recommendation

The Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation (HFD-870) has reviewed the submission dated 10/2/96 thoroughly. Based on that review, OCPB recommends acceptance of the addition to the **Pharmacokinetics** section of the labeling for Glynase as proposed by the firm. The modification of the storage statement should be reviewed by the chemist. The other minor changes should be reviewed by appropriate persons within HFD-510.

12/20/96

Michael J. Fossler, Pharm. D., Ph. D.

Division of Pharmaceutical Evaluation II
Office of Clinical Pharmacology and Biopharmaceutics

FT initialed by Hae-Young Ahn, Ph. D., Team Leader 12/20/96

CC: NDA 20-051 (orig., 1 copy), HFD-510(Johnston, Fleming), HFD-850(Lesko), HFD-870(M. Chen, Fossler, Ahn, Drug File, Chron. File, Reviewer File), HFD-340 (Vish)
9/19/96

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 020051/ S008

CORRESPONDENCE

NDA SUPPL FOR SLP

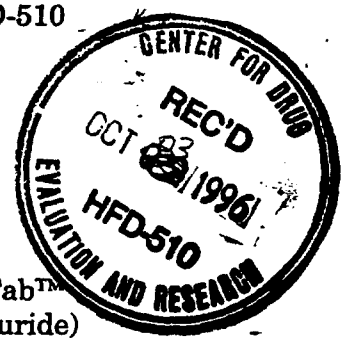
ORIGINAL
NDA SUPPLEMENT

Pharmacia & Upjohn

Office of:
Janice A. Enzinger
Senior Regulatory Manager
US Regulatory Affairs
Telephone No. (616) 833-5633
Facsimile No. (616) 833-8237

October 2, 1996

Division of Metabolism & Endocrine Drug Products, HFD-510
Center for Drug Evaluation and Research
Document Control Room
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857



Re: NDA 20-051
GLYNASE® PresTab™
(reformulated glyburide)

LABELING SUPPLEMENT

Dear Dr. Sobel:

We are supplementing our NDA for GLYNASE® PresTab™ Tablets (NDA #20-051) to propose revisions in the package insert.

A completed User Fee Cover Sheet is provided to this submission. Section 5 of that form indicates that this application does not contain clinical data. It is our understanding that the information provided in the enclosed study report does not meet the user fee definition of clinical data.

Attachment 1 is a mock-up of the proposed insert, which consists of the current approved insert with the requested changes identified in the margins.

As requested in your letter of September 16, 1996, we propose to supplement the Pharmacokinetics section of this insert with information derived from IND Study M/5215/0006. This addition is displayed in column 2 of the attached mock-up.

The study report from that clinical trial (TR 7215-92-044: Effect of Dosing Regimen on the Pharmacokinetics and Pharmacodynamics of GLYNASE® PresTab™ Tablets 3 mg in Non-Insulin Dependent Diabetics [M/5215/0006]) was submitted to IND as Amendment #044 on February 8, 1993. For your convenience, we are including an additional copy of the body of the report (text, tables, figures, and a list of appendices) as Attachment 2 to this submission. Appendices to the study report are available in the original submission to the IND.

We have taken this opportunity to make some additional minor changes in the package insert for GLYNASE® PresTab™ Tablets. As indicated in the attached mock-up, these include the following:

- Replacement of the word "children" with "pediatric patients" in the Pediatric Use portion of the Precautions section (mock-up, column 5) and the Specific Patient Populations portion of the Dosage and Administration section (mock-up, column 8) for consistency with current FDA terminology.

- Modification of the storage statement in the How Supplied section (mock-up, column 8) for consistency with the current USP statement for controlled room temperature.

- Change in the company name from "The Upjohn Company" to "Pharmacia & Upjohn Company" (mock-up, column 8).

Following your approval, the text relating to the pharmacokinetic study will be incorporated into the insert that is current at that time.

Please contact Jan Enzinger at (616) 833-5633 if you have any questions about this labeling supplement. Please send all correspondence to mailstop 0636-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Jan Enzinger

Janice A. Enzinger
Senior Regulatory Manager
US Regulatory Affairs

JAE:jss:10296

REVIEWS COMPLETED
AP
CSO ACTION:
☒ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE