DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-210

JUL 29 1993

Janssen Research Foundation
Attention: Ms. Ruth Wasserman
1125 Trenton-Harbourton Road, P.O. Box 200
Titusville, NJ 08560-0200

Dear Ms. Wasserman:

Please refer to your August 29, 1991 new drug application submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Propulsid (cisapride) Tablets, 10 and 20 mg.

We also acknowledge receipt of your amendments dated April 27 and 30, May 21, June 18, July 1,12 and 14, 1993.

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 enclosed revised draft labeling. Accordingly, the application, with these labeling revisions, is approved, effective as of the date of this letter.

These revisions are terms of the NDA approval. Marketing the product before making the revisions in the product's labeling may render the product misbranded and an unapproved new drug.

Please submit twelve copies of the FPL as soon as available. Seven of the copies should be individually mounted on heavy-weight paper or similar material. The submission should be designated for administrative purposes as "FPL for Approved NDA 20-210." Approval of the submission by FDA is not required before the labeling may be used.

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:

Kati Johnson
Consumer Safety Officer
(301) 443-0487

Sincerely yours,

Robert Temple

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

Enclosure

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APR - 9 1993

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Attention: Ms. Ruth Wasserman
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

Dear Ms. Wasserman:

Please refer to your August 29, 1991 new drug application submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Propulsid (cisapride) Tablets.

We also acknowledge receipt of your amendments dated November 27, December 4, 9, 17, 31, 1991, March 27, September 18, October 19, December 21, 1992, January 28 and February 1, 1993.

We have completed the review of this application as submitted with draft labeling. Before the application may be approved, however, it will be necessary for you to:

1. Submit a satisfactory response to our letter dated February 19, 1993 requesting additional chemistry information.

2. Submit an adequate Environmental Assessment.

3. Commit to assist the FDA in validating the regulatory methods.

4. Submit final printed labeling for the drug. The labeling should be identical in content to the enclosed draft. 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 submit twelve copies of the printed labels and other labeling, seven of which are individually mounted on heavy weight paper or similar material.

We remind you of your commitment to conduct the following post approval studies:

1. Repeat Study 1203 (A Randomized Double-Blind Placebo Controlled MultiCenter Dose Response Trial of Cisapride in the Treatment of Symptoms of Gastroesophageal Reflux Disease) using patient evaluation of nocturnal heartburn as the primary endpoint.

2. A repeat of the autoradiographic Hela cell genotoxicity test.

3. Pharmacologic and toxicologic evaluation of metabolite D.

4. Evaluation of the intersubject and intrasubject pharmacokinetic variability and pharmacokinetic evaluation of metabolite D.

5. A controlled clinical study of granisetron 10 mcg/kg versus 40 mcg/kg in non-cisplatin highly emetogenic chemotherapy regimens.

6. Controlled Holter monitored studies of granisetron versus ondansetron.

In addition, we would appreciate your submitting copies of the introductory promotional material that you propose to use for this product. Please submit one copy to the Division of Gastrointestinal and Coagulation Drug Products and two copies, along with a copy of the package insert, directly to:

Division of Drug Advertising and Labeling, HFD-240
Room 17B-17
5600 Fishers Lane
Rockville, Maryland 20857

Please submit all proposed materials in draft or mock-up form, not final print. Also, please do not use form FD-2253 for this submission; this form is for routine use, not proposed materials.

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 314.110. In the absence of such action FDA may take action to withdraw the application.

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

Should you have any questions, please contact:

Kati Johnson
Consumer Safety Officer
Telephone: (301) 443-0487

Sincerely yours,

12/9/93

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

9/13/93

Enclosure: Draft Labeling

cc:
Original NDA
HFD-180
HFD-181/CSO
HFD-240 (with draft labeling)
HFD-80/DDIR (with draft labeling)
HFD-638/ (with draft labeling)
HFD-100/Dr. Temple
DISTRICT OFFICE
R/D init:
kj/September 8, 1993
kj/September 8, 1993/c:\wp51\cso\n\20239309.0kj

9/13/93

9/8/93

APPROVABLE