CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: 020623

Trade Name: ANZEMET TABLETS

Generic Name: DOLASETRON MESYLATE

Sponsor: HOESCHT MARION ROUSSEL, INC.

Approval Date: 09/11/97

INDICATION(s): FOR THE PREVENTION OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING, AND PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING..

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APPLICATION: 020623

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EA/FONSI	X			
Pharmacology Review(s)	X			
Statistical Review(s)	X			
Microbiology Review(s)				
Clinical Pharmacology Biopharmaceutics Review(s)	X			
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Administrative Document(s)	X			
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CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: 020623

APPROVAL LETTER

NDA 20-623

Hoechst Marion Roussel, Inc.
Attention: Louise Shibley
Marion Park Drive, P.O. Box 9707
Kansas City, MO 64134-0707

Dear Ms. Shibley:

Please refer to your new drug application dated September 28, 1995, received September 29, 1995, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Anzemet (dolasetron mesylate) Tablets.

We acknowledge receipt of your submissions dated March 13, 14, and 28, April 7 and 24, May 12 and 27, June 6 and 9, July 8 and 29, and August 13, 1997. The User Fee goal date for this application is September 30, 1997.

This new drug application provides for 50 and 100 mg tablets indicated for the prevention of chemotherapy-induced nausea and vomiting, and prevention of postoperative nausea and vomiting.

We have completed the review of this 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 enclosed marked-up draft labeling. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed marked-up draft labeling. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

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 NDA 20-623. 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.

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. Should an IND not be required to meet your Phase 4 commitments, please submit protocol, data, and final reports to this NDA as correspondences. In addition, we request under 21 CFR 314.81(b)(2)(vii) that you include in your annual report to this application, a status summary of each commitment. 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."

In addition, please submit three copies of the introductory promotional material 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 Gastrointestinal and Coagulation Drug Products and two copies of both the promotional material and the package insert directly to:

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

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.

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, Supervisory Consumer Safety Officer, at (301) 443-0487.

Sincerely yours,

APPEARS THIS WAY
ON ORIGINAL

/S/ 9/11/97

Paula Botstein, M.D.
Acting Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE

APPEARS THIS WAY
ON ORIGINAL

cc:
Original NDA 20-623 /S/ 9/5/97
HFD-180/Div. files
HFD-180/CSO/K.Johnson
HFD-180/MAdams 9/5/97
HFD-180/EDuffy /S/ 9/5/97
HFD-180/JChoudary
HFD-002/ORM (with labeling) /S/ 9/5/97
HFD-103/Office Director
HFD-101/L.Carter
HFD-820/ONDC Division Director
DISTRICT OFFICE
HF-2/Medwatch (with labeling)
HFD-92/DDM-DIAB (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-735/DPE (with labeling) - for all NDAs and supplements for adverse reaction changes.
HFI-20/Press Office (with labeling)

Drafted by: kj/September 5, 1997/c:\wpfiles\cso\n\20623709.0kj

APPROVAL (AP) [with Phase 4 Commitments]

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.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020623

APPROVABLE LETTER

NDA 20-623

MAR 5 1997

Hoechst Marion Roussel, Inc.
Attention: Louise Shibley
Marion Park Drive, P.O. Box 9707
Kansas City, MO 63134-0707

Dear Ms. Shibley:

Please refer to your new drug application dated September 28, 1995, received September 29, 1995, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Anzemet (dolasetron mesylate) Tablets.

We acknowledge receipt of your submissions dated December 14, 1995 January 16 and 29, February 9 and 15, March 1, April 2, May 21, June 3, August 14, September 12 and 25, and October 11, 1996. The original User Fee goal date for this application was September 29, 1996. Your submission of September 12, 1996 extended the User Fee goal date to December 29, 1996.

We have completed the review of this application as submitted with draft labeling, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit an adequate response to our letter dated December 24, 1996, requesting additional chemistry information. For your convenience, the requests are reiterated below:

DRUG SUBSTANCE

1. Regarding the proposed method of manufacture:

   (a) Revise the description to indicate a specific value or an acceptable range (or limit) of values for the conditions, and amounts, or explain why any of these values are not necessary.

   (b) The synthesis description is inadequate:

      (i) Identify the materials from the

      Describe the procedure, and provide the tests, methods and specifications for the of the

      (ii) Where materials are the specify the amounts of which may be used.

(c) Describe th for each process in the various

(d) For describe the for the

(e) For the range for in the

2. Revise the proposed for reference standard to include testing for Assay.

3. Regarding the proposed

(a) Revise the product release specifications to include the statement that lots which are found to contain an with respect to the will be and the compound investigated.

(b) To assist us in understanding the methods, either revise to indicate the laboratory when they were validated, or specify the for the method and provide method validation data supporting the proposed

(c) Identify the lot numbers and describe the of each of the materials the reference standards used in

DRUG PRODUCT

1. Specify where drug product stability testing will be performed.

2. Regarding the proposed tablet manufacturing and packaging procedures:

(a) Describe the when is found to be outside the acceptable range for lots of

(b) Describe the in the when is found to be present.

(c) Revise the to include
Describe the test, the method and the sampling procedure.

3. Regarding the proposed product release sampling procedure:

(a) The indicate the
collection and of
printed tablets for unspecified testing. Specify the tests to be performed on each of these samples.

(b) Provide a drawing of the used to collect

4. Regarding the proposed product blister packaging components:

(a) Specify whether the to be used for marketing is
printed or unprinted. If the specify the printing and
submit the proposed text.

(b) Describe the acceptance specifications for the
materials. This should include at least an identity test.

(c) The indicates that

may be used as appropriate. Provide a detailed description of the protocol for qualifying the use of an alternate packaging materials and alternate packaging components.

(d) Either withdraw the following proposed packaging components listed below or provide adequate stability and component qualification data to support their approval:

(i)

(ii) material.

(iii) material

5. Regarding your proposed packaging configurations:

   (a) State whether was used in the tested in the primary drug product stability studies. In your packaging configuration description and specifications, please ensure that market packaging configuration(s) correspond to the configuration(s) used in the primary stability studies.

   (b) Either revise the application to delete the proposed use of the for which no stability data has been submitted or provide a protocol for submitting stability and with these

6. Regarding the submitted data:

   (a) Identify the used in the studies. For approval you must provide data showing that each combination meets the

   (b) Identify the blister material used in the studies. For approval you must provide the results from testing which demonstrated that each of the combinations meets the container.

7. Regarding the proposed stability protocol information:

   (a) Revise the stability protocol for commercial batches (volume 1.4/page 127) as follows:

      (i) Specify the the

      (ii) Delete the proposal for after the first three commercial batches. There is insufficient data in the application to support the proposed

   (b) Revise the statement in volume 1.4/page 123 regarding the extension of expiry period, to specify the number of batches of each tablet strength and each package configuration which will be used to support this extension.

In addition, it will be necessary for you to submit final printed labeling (FPL) identical in content to the enclosed marked-up draft labeling. 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, revision of the labeling may be required.

In addition, please submit three copies of the introductory promotional material 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 this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications,
HFD-40
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 314.110. 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.

If you have any questions, please contact Kati Johnson, Consumer Safety Officer, at (301) 443-0487.

Sincerely yours,

APPEARS THIS WAY
ON ORIGINAL

/S/

Paula Botstein, M.D.
Acting Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure: Draft Labeling

APPEARS THIS WAY
ON ORIGINAL

cc:

Original NDA 20-623
HFD-180/Div. Files
HFD-002/ORM
HFD-92/DDM-DIAB
HFD-180/K.Johnson
HFD-180/EDuffy
HFD-180/JChoudary
HFD-103/Office Director
HFD-101/L.Carter
DISTRICT OFFICE
HFD-40/DDMAC (with draft labeling)

/S/ 2/12/97

Drafted by: kj/February 12, 1997/c:\wpfiles\cso\n\20623702/0kj
Initialed by:
Final:

APPROVABLE (AE)