205555/53/54

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-555/S-003/S-004

Trade Name: Axid AR

Generic Name: nizatidine

Sponsor: Whitehall-Robins Healthcare

Approval Date: April 1, 1998

Indications: Treatment of episodic heartburn, acid indigestion and sour stomach.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
20-555/S-003/S-004

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tentative Approval Letter				
Approvable Letter	X			
Final Printed Labeling	X			
Medical Review(s)	X			
Chemistry Review(s)	X			
EA/FONSI				
Pharmacology Review(s)	[redacted]			
Statistical Review(s)	X			
Microbiology Review(s)				
Clinical Pharmacology Biopharmaceutics Review(s)	X			
Bioequivalence Review(s)				
Administrative Document(s)	X			
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-555/S-003/S-004

APPROVAL LETTER

HFD-92
Imaging

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-555/S-003

Whitehall-Robins Healthcare
Attention: Eleanor F. Barbo
Senior Director, Regulatory Affairs
5 Giralda Farms
Madison, NJ 07940-0871

APR - 1 1998

Dear Ms. Barbo:

Please refer to your supplemental new drug application dated December 16, 1996, received December 17, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for nonprescription Axid® AR (nizatidine) Tablets, 75 mg.

We acknowledge receipt of your submissions dated March 19, 25, and 31, 1998. Your submission of March 19, 1998 constituted a complete response to our December 17, 1997 action letter. The User Fee goal date for this application is September 20, 1998.

The supplemental application provides for an additional indication for the drug product: treatment of episodic heartburn, acid indigestion and sour stomach.

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 March 31, 1998. 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 March 31, 1998.

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 20-555/S-003. 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.

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 Over-the-Counter Drug Products (HFD-560) 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

Should a letter communicating important information about this drug product (i.e., a "Dear Doctor" letter) be issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20852-9787

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 Albert Rothschild at (301) 827-2222.

Sincerely,

/S/ 3/31/98

Debra Bowen, M.D.
Director
Division of Over-The-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

/S/ 4-1-98

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

HFD-92
Imaging

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-555/S-004

Whitehall-Robins Healthcare
Attention: Eleanor F. Barbo
Senior Director, Regulatory Affairs
5 Giralda Farms
Madison, NJ 07940-0871

APR - 1 1998

Dear Ms. Barbo:

Please refer to your supplemental new drug application dated March 31, 1997, received April 1, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for nonprescription Axid® AR (nizatidine) Tablets, 75 mg.

We acknowledge receipt of your submissions dated March 31, April 16, December 30, 1997, and March 25 and 31, 1998. The User Fee goal date for this application is April 1, 1998.

The supplemental application provides for a revision to the DIRECTIONS section of the labeling and labels to change the time to take the drug prior to a meal to prevent meal-induced heartburn symptoms from "...one-half hour to one hour before eating ..." to "...right before eating or up to 60 minutes before consuming..." as well as a revision to the graphical representations of the pivotal study results in the package insert concerning the prevention of heartburn symptoms.

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 March 31, 1998. 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 March 31, 1998.

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 20-555/S-004. 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.

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 Over-the-Counter Drug Products (HFD-560) 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

Should a letter communicating important information about this drug product (i.e., a "Dear Doctor" letter) be issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20852-9787

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 Albert Rothschild at (301) 827-2222.

Sincerely,

/S/ 3/31/98

Debra Bowen, M.D.
Director
Division of Over-The-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

/S/ 4-1-98

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-555/S-003/S-004

APPROVABLE LETTER

Attachment 2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-555/S-003

Whitehall-Robins Healthcare
Attention: Eleanor F. Barbo
Director, Regulatory Affairs
5 Giralda Farms
Madison, NJ 07940-0871

DEC 17 1997

Dear Ms. Barbo:

Please refer to your supplemental new drug application dated December 16, 1996, received December 17, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for nonprescription Axid® AR (nizatidine) Tablets.

We acknowledge receipt of your submissions dated February 11 and 25; April 16, and December 12, 1997. The User Fee goal date for this application is December 17, 1997.

The supplemental application provides for an additional indication for the drug product: treatment of episodic heartburn, acid indigestion and sour stomach.

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

1. To conform to 21 CFR 201.61, reverse the order of the drug class name "Acid Reducer" and the established name "Nizatidine Tablets 75 mg" in the statement of identity so that the drug class name follows the established name in all labeling.

2. Because the application does not contain the results of drug-drug interaction studies with multiple drugs, the statement "Axid® AR contains an ingredient, nizatidine, that doctors have prescribed millions of times and has been taken safely with many frequently prescribed medications" is not supported at this time. Either revise this statement, submit data to support this statement, or use the statement in the currently approved labeling.

3. Delete the word "completely" from the text in the third bullet on the back of the package insert.

4. The response rate graph for the relief of heartburn on the back side of the package insert should display only the results from a single study. Because study NZ-95-04 is more convincing than study NZ-95-01, we recommend that the results from study NZ-95-04 be displayed.

5. Delete the "% better" statement from all of the response rate graphs in the package insert.

6. Revise the statement "This pain and discomfort, commonly known as heartburn, can interfere with everyday activities." to "This pain and discomfort is commonly known as heartburn."

Please submit 20 copies of the 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. Additionally, if the February 27, 1997 Federal Register Notice "Over-The-Counter Human Drugs; Proposed Labeling Requirements" [62 FR 9023] becomes final before this application is approved, further revisions of the labeling format may be necessary.

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 supplemental 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.

We remind you that this change may not be implemented until you have been notified in writing that this supplemental application is approved.

If you have any questions, please contact Michael Folkendt, Project Manager, at (301) 443-0487.

Sincerely yours,

/S/

Debra Bowen, M.D.
Director
Division of Over-The-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

/S/ 12-17-97

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research