CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19982_S4

APPROVAL LETTER

14

NDA 19-982/S-004

Wyeth-Ayerst Laboratories
Attention: Karel F. Bernady, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. Bernady:

Please refer to your December 27, 1996 supplemental new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zebeta (bisoprolol fumarate) Tablets, 5 mg and 10 mg.

The supplemental application provides for manufacturing facilities at Rouses Point, NY as an alternate packaging, release testing and stability testing site for Zebeta Tablets.

We have completed the review of this supplemental application and it is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

Sincerely yours,

/S/ 1/14/97

Robert J. Wolters, Ph.D.
Chemistry Team Leader, DNDC I
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA
HFD-110
HFD-110/Project Manager
HFD-92
HFD-232
DISTRICT OFFICE
HFD-810/New Drug Chemistry Division Director
HFD-110/DCunningham/1/10/97;1/14/97
sb/1/14/97;1/14/97
R/D: RWolters

Approval Date: 7/31/92

APPROVAL

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APPLICATION NUMBER:

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CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW	1. ORGANIZATION HFD-110	2. NDA Number 19-982
3. Name and Address of Applicant (City & State) Lederle Laboratories Wyeth-Ayerst Laboratories 170 Radnor-Chester Road St. Davids, PA 19087		4. Supplement(s) Number(s) Date(s) S-004 12/27/96
5. Drug Name ZEBETA	6. Nonproprietary Name Bisoprolol fumarate	8. Amendments & Other (reports, etc) - Dates
7. Supplement Provides For: Manufacturing facilities at Rouses Point, NY as an alternate packaging, release testing and stability testing site for Zebeta tablets.		
9. Pharmacological Category β_1-selective adrenoceptor blocking agent for treatment of hypertension	10. How Dispensed ☒ Rx ☐ OTC	11. Related IND(s)/ NDA(s)/DMF(s) DMF 5387 (Type I)
12. Dosage Form(s) Tablets	13. Potency(ies) 5 mg & 10 mg	
14. Chemical Name and Structure		15. Records/Reports Current ☐ Yes ☐ No Reviewed ☐ Yes ☐ No

16. Comments:

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

The changes will be implemented on 1/27/97.

Zebeta Tablets will continue to be made at their approved manufacturing facility in Gosport, England.

Two other changes - reduced expiration dating for Zebeta Tablets packaged at Rouses Point from 5 years to 3 years. In addition, during the July 19, 1996 telephone conversation Mr. Ressler cited a decrease in the amount of primer coating in the polyvinyl chloride film used in the unit-dose packaging for Zebeta Tablets.

EER requested on 1/3/97. Acceptable - 1/8/97.

17. Conclusions and Recommendations:

AP

18. REVIEWER

Name	Signature	Date Completed
Danute G. Cunningham	/S/	January 10, 1997

Distribution:

☒ Original Jacket ☐ Reviewer ☐ Division File ☐ CSO ☐ District

19982S04.SUP

/S/ 1/13/97

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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CORRESPONDENCE

ORIGINAL

WYETH-AYERST RESEARCH

P.O. BOX 8299, PHILADELPHIA, PA 19101-8299 • (610) 902-3710
FAX: (610)964-5973

Division of American Home Products Corporation

U.S. REGULATORY AFFAIRS

December 27, 1996

NDA No. 19-982
Zebeta®, bisoprolol fumarate, Tablets

Raymond J. Lipicky, M.D., Director
Division of Cardio-Renal Drug Products (HFD-110)
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Attn: Document Control Room 16B-45
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857-1706

NDA NO. 19-982 REF. NO. 2
NDA SUPPL FOR SCM

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

Dear Dr. Lipicky:

Reference is made to Lederle Laboratories New Drug Application No. 19-982 for Zebeta®, bisoprolol fumarate, Tablets. We also reference telephone conversations with Supervisory Chemist, Dr. Robert J. Wolters, by Karel F. Bernady on November 15, 1995 and February 29, 1996, and by Mr. Timothy Ressler on July 19, 1996, concerning adding an alternate site for packaging Zebeta tablets. Finally, we reference our meeting of September 5, 1996 with the Agency's reviewing chemists, wherein we discussed the transfer of manufacturing operations for several Lederle Laboratories products to Rouses Point, New York. A copy of the minutes of this meeting are provided in this submission.

We are filing this supplement to provide for our manufacturing facilities at Rouses Point, New York as an alternate packaging, release testing and stability testing site for Zebeta tablets. A "Special Supplement - Changes Being Effected" is being filed as per agreement with Dr. Wolters. We plan to implement these changes thirty days from the date of this letter.

This supplement provides for the changes listed above. Zebeta tablets will continue to be made at their approved manufacturing facility in Gosport, England. The approved packaging components will be used at the alternate site. Product will be tested and released against the NDA and compendial specifications.

In support of this filing we have included the following: (1) the address and Drug Master File reference for the Rouses Point, New York facility; (2) representative packaging specification tickets for packaging Zebeta tablets; (3) container-closure information for the components used; (4) Certificates of Analyses for the testing of the bulk batches at both the Gosport, England and Rouses Point sites; (5) comparative dissolution profile data on the Zebeta tablets tested at Gosport and at Rouses Point after packaging; (6) marketed product stability protocol; and (7) a commitment to place the first three batches packaged at Rouses Point onto stability testing.

ORIGINAL

We note two other changes. We have reduced the expiration dating for Zebeta tablets packaged at Rouses Point from five years to three years. In addition, during the July 19, 1996 telephone conversation Mr. Ressler cited a decrease in the amount of primer coating in the polyvinyl chloride film used in the unit-dose packaging for Zebeta® tablets. We reiterate our commitment to file one year of room temperature stability data and three months of accelerated data at 40°C/75% RH in the Zebeta Annual Report to support this change.

As per 21 CFR 314.71(b) and per agreement with our Philadelphia District Office, Wyeth-Ayerst hereby certifies that a complete copy of this supplement has been forwarded as a filed copy to the FDA district office at the address below:

Mr. John Podsadowski
Program Coordinator for Field Copy Submission
Buffalo District
U.S. Food and Drug Administration
599 Delaware Avenue
Buffalo, NY 14202

To assist in the Agency's administrative coordination of this supplement we have also provided a copy of the supplement cover letter to the FDA home district office for Wyeth-Ayerst Laboratories located in Philadelphia, PA.

We trust that you will find this supplement satisfactory and that it will be approved at your earliest convenience. If you have any questions, please contact the undersigned at (610) 902-3760 or Ms. Jean Lassen at (610) 902-3762.

Sincerely,

WYETH-AYERST LABORATORIES

Karel F. Bernady, Ph.D.
Director, Marketed Products
U.S. Regulatory Affairs

cc: cover letter w/o attachments
Ms. Debra Pagano
Program Coordinator for Field Copy Submissions
Department of Health and Human Services
Food and Drug Administration
2nd and Chestnut Streets
Philadelphia, PA 19101-2973

KFB/las:zebsupp

WYETH-AYERST RESEARCH

P.O. BOX 8299, PHILADELPHIA, PA 19101-8299 • (610) 902-3710
FAX: (610)964-5973

Division of American Home Products Corporation

U.S. REGULATORY AFFAIRS

December 27, 1996

NDA No. 19-982
Zebeta® , bisoprolol fumarate, Tablets

Mr. John Podsadowski
Program Coordinator for Field Copy Submissions
Buffalo District
U.S. Food and Drug Administration
599 Delaware Avenue
Buffalo, New York 14202

Dear Mr. Podsadowski:

Reference is made to the approved Lederle Laboratories New Drug Application No. 19-982 for Zebeta, bisoprolol fumarate, Tablets.

In conformance with 21 CFR 314.71(b), we hereby are forwarding to you a field copy of our "Special Supplement - Changes Being Effected" of this date to NDA No. 19-982. This supplement provides for our manufacturing facilities at Rouses Point, New York as an alternate packaging, release testing and stability testing site for Zebeta Tablets. Wyeth-Ayerst certifies that this copy is identical in all respects to that provided to the Center in Rockville, MD.

To assist in the Agency's administrative coordination of this supplement we have also provided a copy of the supplement cover letter to Ms. Debra Pagano, Program Coordinator for Field Copy Submissions, at the home district office for Wyeth-Ayerst Laboratories located in Philadelphia, PA.

If there are any questions concerning this "Special Supplement" please contact our representative, Ms. Jean Lassen at (610) 902-3762 or the undersigned at (610) 902-3760.

Sincerely,

WYETH-AYERST LABORATORIES

Karel F. Bernady

Karel F. Bernady, Ph.D.
Director, Marketed Products
U.S. Regulatory Affairs

JL/lm.124b