CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19982_S5

APPROVAL LETTER

NDA 19-982/ S-005

JUN 23 1998

Lederle Laboratories
c/o Wyeth-Ayerst Laboratories
Attention: Diane Mitrione
170 Radnor-Chester Drive
St. Davids, PA 19087

Dear Ms. Mitrione:

Please refer to your supplemental new drug application dated December 22, 1997, received December 24, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zebeta (bisoprolol fumarate) Tablets, 5 mg and 10 mg.

The user fee goal date is June 24, 1998.

The supplemental application provides for:

1. A change in the manufacturing site of Zebeta Tablets, 5 mg and 10 mg, from Gosport, UK to the Ayerst-Wyeth Pharmaceuticals, Inc. (AWPI) facility in Guayama, Puerto Rico.

2. Reduction in batch size for both strengths.

3. Equipment changes to equipment of the same operating principles and design.

4. Operating parameters changes consistent with the equipment and scale changes.

5. Specifications changes for the excipients.

We have completed the review of this supplemental application and it is approved with the understanding that you will continue to monitor degradation products in your on-going stability program and establish specifications if appropriate. These additional specifications should be reported in a Changes Being Effected supplement [21 CFR 314.70 (c) (I)].

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/ 6-23-98

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

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APPLICATION NUMBER:

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CHEMISTRY REVIEW(S)

JUN 23 1998

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-005 12/22/97 (SCM)
5. Drug Name ZEBETA	6. Nonproprietary Name Bisoprolol fumarate	8. Amendments & Other (reports, etc) - Dates
7. Supplement Provides For: 1. Change in manufacturing site of Zebeta Tablets, 5 mg and 10 mg, from Gosport, UK to Ayerst-Wyeth Pharmaceuticals, Inc. (AWPI) facility in Guayama, Puerto, Rico. 2. Reduction in batch size for both strengths. 3. Equipment changes to equipment of the same operating principles and design. 4. Operating parameters changes consistent with the equipment changes and reduction in scale. 5. Specification changes for the excipients.		
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)
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 Cont'd		
17. Conclusions and Recommendations: EER requested on 1/8/98. Acceptable - 6/5/98. In vitro dissolution data provided for these changes have been evaluated by Biopharm reviewer and found to be satisfactory. (See Biopharmaceutics review dated 6/16/98). Issue approval letter with a reminder to the firm of their commitment to monitor degradation products in the on-going stability studies and establish specifications if necessary. Additional specifications should be filed as a CBE supplement.		
18. REVIEWER		
Name Danute G. Cunningham	Signature /S/	Date Completed June 19, 1998
Distribution: ☑ Original Jacket ☐ Reviewer ☐ Division File ☐ CSO		

19982S05.SUP

/S/ 6-19-98

TRANSMITTAL OF ANNUAL REPORTS FOR DRUGS FOR HUMAN USE (21 CFR 314.81)

DATE SUBMITTED: 12-22-97

Form Approved OMB No. 0910-0001
Expiration Date: April 30, 1994
See OMB Statement on Reverse of Part 1

NOTE: This report is required by law *(21 USC 355; 21 CFR 314.81). Failure to report can result in withdrawal of approval of the New Drug Application.*

INSTRUCTIONS

Complete a transmittal form for each application for which an annual report is being submitted. Retain the carbon copy labeled "applicant." Submit the remaining copies of the transmittal form along with two copies of the annual report to FDA.

If any part of the annual report applies to more than one application, list in item 7 all other applications to which such parts apply.

1. NDA OR ANDA NUMBER: N 19982

2. Report No *(FDA Complete)*: Y- 005

APPLICANT NOTE: Reference NDA and Y numbers (entered on Acknowledgement Copy) in any subsequent correspondence regarding report.

4. APPLICANT: Lederle Laboratories, Pearl River, New York 10965

3. CFR SECTION NUMBER *(Antibiotic only)*:

5. DRUG NAME: ZEBETA (bisoprolol fumarate) Tablets, 5mg and 10mg

6 TYPE OF REPORT *(Check one)*: ☐ ANNUAL ☐ OTHER

7. OTHER NDA/ANTIBIOTIC APPLICATION NUMBERS *(List all numbers if any part of report applies to more than one number.)*:

8. PERIOD COVERED BY REPORT

FROM		TO	
YEAR	MONTH	YEAR	MONTH
96	8	97	8

Fold Line

REPORT INFORMATION REQUIRED *(See § 314.81 for description)*

9. *(Enter type of information attached under "Identification." If you have nothing to report, enter None.)*
(INFORMATION IN "9b" and "9c" IS ALWAYS REQUIRED.)

TYPE OF INFORMATION	IDENTIFICATION *(Volume No.(s)/Tab(s)/Page(s) of Report)*
a. SUMMARY OF SIGNIFICANT NEW INFORMATION	"Summary of Significant New Information" tab
b. DISTRIBUTION DATA	"Distribution Data" tab
c. LABELING *(Whether or not previously submitted)*	"Current Package Labeling" tab
d. CHEMISTRY MANUFACTURING AND CONTROLS CHANGES	"Manufacturing and Control Changes" tab
e. NONCLINICAL LABORATORY STUDIES	"Nonclinical Laboratory Studies" tab
f. CLINICAL DATA	"Clinical Data" tab
g. STATUS REPORT POST-MARKETING STUDIES	None
h. STATUS OF OPEN REGULATORY BUSINESS *(Optional)*	None

Fold Line

TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT:
Karel F. Bernady, Ph.D., Director, Marketed Products
U.S. Regulatory Affairs

SIGNATURE: Karel F. Bernady ORIGINAL

APPLICANTS RETURN ADDRESS *(Type within the window envelope tic marks)*:

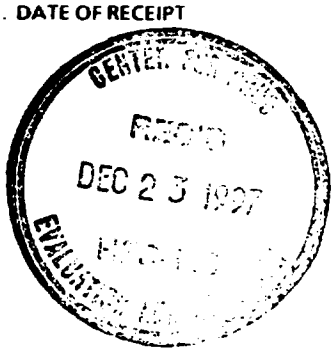
Wyeth-Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-1245

Attn. Karel F. Bernady, Ph.D.

FDA USE ONLY

10. REPORT FILED IN NDA NUMBER: N 19982

11. DATE OF RECEIPT



FORM FDA 2252 (6/93) PREVIOUS EDITION IS OBSOLETE.