# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

*APPLICATION NUMBER:*

**ANDA 62-756 / S-020**

***Name*:** Primaxin® ADD-Vantage® (Imipenem-Cilastatin Sodium for Injection)

***Sponsor*:** Merck Research Laboratories

***Approval Date*:** September 2, 1994

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

# ANDA 62-756 / S-020

## CONTENTS

| Reviews / Information Included in this Review | |
|---|---|
| Approval Letter | X |
| Tentative Approval Letter | |
| Labeling | |
| Labeling Reviews | |
| Medical Review(s) | |
| Chemistry Review | X |
| Bioequivalence Review(s) | |
| Statistical Review(s) | |
| Microbiology Review | |
| Administrative Documents | X |
| Correspondence | X |
| | |

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**ANDA 62-756 / S-020**

# APPROVAL LETTER

AADA 62-756/S-020

Merck Research Laboratories
Attn: Henrietta Ukwu, M.D.
Director, Regulatory Liason
P.O. Box 4, BLA-30A
West Point, PA 19486-004

SEP 2 1994

Dear Madam:

This is in reference to your supplemental antibiotic drug application, dated July 7, 1994, submitted pursuant to Section 314.70 of the Regulations regarding your abbreviated antibiotic application for Primaxin® ADD-Vantage® (Imipenem-Cilastatin Sodium for Injection, MSD)

The supplemental application provides for use of ——— manufactured by ——— at their ——— site as an alternate source in the manufacture of cilastatin sodium.

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 abbreviated antibiotic application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

9/2/94

C. Greg Guyer, Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:
AADA 62-756/S-020
NDA 50-587 @HFD-520
NDA 50-630 @HFD-520
DUP/Division File
HFD-600/RF
HFD-82
FIELD COPY

Endorsements:
HFD-643/EDuffy/ EDuffy 8/30/94
HFD-643/JHarrison/8/29/94 JHarrison 8/30/94
HFD-617/MAnderson/8/29/94 Mark Anderson 8/30/94
X:MSD20S62.756
B:62756S.020
F/T by mw/8/30/94
SUPPLEMENT APPROVAL

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# ANDA 62-756 / S-020

# CHEMISTRY REVIEW

AADA 62-756/S-020

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

NAME AND ADDRESS OF APPLICANT:

Merck Sharp & Dohme Research Laboratories
Attn: Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Liason
Sumneytown Pike
West Point, PA 19486

Contact:
Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Liason
(215) 834-2958
or
Kenneth R. Brown, M.D.
(215) 834-2552

PURPOSE OF AMENDMENT/SUPPLEMENT

The supplemental application provides for use ——————————— manufactured by ——————————— at their ——————— site as an alternate source in the manufacture of cilastatin sodium.

DATE OF SUBMISSION

July 7, 1994

PHARMACOLOGICAL CATEGORY

Antibiotic

TRADE NAME

Primaxin® I.V. ADD-Vantage®

NONPROPRIETARY NAME

Imipenem-Cilastatin Sodium

DOSAGE FORM

Powder for reconstitution

POTENCY

250, 500 mg

RX OR OTC

℞

SAMPLES
N/A

RELATED IND/NDA/DMF
50-587 Primaxin® IV
50-630 Primaxin® IM

STERILIZATION
N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION
N/A

COMPONENTS, COMPOSITION

COMPOSITION

| COMPONENT | 250/250 | 500/500 |
|---|---|---|
| STERILE IMIPENEM MONOHYDRATE | — mg * | —mg ☼ |
| STERILE CILASTATIN SODIUM | — mg * | —mg ☼ |
| STERILE SODIUM BICARBONATE | 10 mg | — mg |
| | — mg | — mg |

* equivalent to 250 mg and — % overage for Imipenem & Cilastatin
☼ equivalent to 500 mg and — % overage for Imipenem & Cilastatin

MANUFACTURING

[redacted]

CONTROLS
N/A

PACKAGING
N/A

STABILITY
N/A

REMARKS AND CONCLUSION

**RECOMMENDATION - APPROVABLE**

| RECALLS | Reviewer | Date Completed |
|---|---|---|
| | Eric P. Duffy | |

The application covered by this review was taken in date order of receipt.

YES _X__ NO ___

cc:
AADA 62-756/S-020
DUP/Division File
HFD-600/RF

Endorsements:
HFD-643/EDuffy/ EDuffy 8/30/94
HFD-643/JHarrison/8/29/94 J Harrison 8/30/94
X:MSD20S62.756
B:62756S.020
F/T by mw/8/30/94

37. **DMF CHECKLIST FOR AADA # 62-756/S-020 REVIEW # 1**

| DMF # | DMF TYPE/SUBJECT/HOLDER | ACTION CODE | RESULT OF REVIEW | DATE REVIEW COMPLETED |
|---|---|---|---|---|
| | I/ | 2 | | |

Comments:

Comments:

Comments:

Comments:

Comments:

Comments:

Comments:

Comments:

APPEARS THIS WAY ON ORIGINAL

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:

(2) Type 1 DMF;
(3) Reviewed previously and no relevant revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under"Comments").

Checklist page 1 of 1

Eric P. Duffy — Reviewer

EDuffy — Signature

8/30/94 — Date

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

## ANDA 62-756 / S-020

# ADMINISTRATIVE DOCUMENTS

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

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DATE: 7/14/94

FROM: Mark Anderson , Consumer Safety Officer

SUBJECT: Special Supplement - Changes Placed into Effect

TO: Document Room

Please make the following entry in the MIS concerning the status of this Special Supplement - Changes Placed into Effect.

| ANDA(s) | SUPPLEMENT(s) | GRANTED | DENIED |
|---|---|---|---|
| 62-756 | S-020 | (GRANTED) | |

This form is to accompany the action package/jacket.

Thank you,

Mark Anderson 7/14/94

Signature of CSO and Date

CC:
ANDA
DIVISION FILE

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

# ANDA 62-756 / S-020

# CORRESPONDENCE

ORIGINAL

These copies are OFFICIAL FDA Copies
not desk copies.

Henrietta N. Ukwu, M.D.
Director
Regulatory Liaison

Merck & Co., Inc.
P.O. Box 4, BLA-30A
West Point PA 19486-0004
Fax 610 397 2962
Tel 610 397 7176
215 652 5000

NDA NO. _____ REF. NO. SC020
NDA SUPPL FOR Facility Rest
SC020 AI

Noted:
TO Mr Harrison
Mark Anderson 7/14/9

MERCK
Research Laboratories

July 7, 1994

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branch
Office of Generic Drugs, (CDER)
FDA Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20857-2773

Dear Mr. Harrison:

**AADA 62-756: PRIMAXIN® I.V. in ADD-Vantage® Vials**
**(Imipenem-Cilastatin Sodium for Injection)**
**Special Supplement - Changes Being Effected**

noted - OK J. Harrison 7/15/94

Pursuant to Section 505(b) of the Food Drug and Cosmetic Act and in accordance with 21 CFR 314.70(c), we submit a supplement to AADA 62-756. As indicated on the attached Form FDA-356h, the supplemental application provides for a change in Item 3 of the approved Abbreviated Antibiotic Application for PRIMAXIN I.V. in ADD-Vantage® Vials.

The supplemental application provides for the inclusion of the ———— ———— facility located at ———— (DMF-——) as the preferred alternative manufacturing site for the ———— in the drug substance cilastatin sodium synthesis.

The manufacturing process of ———— does not differ from that used at the currently approved manufacturing site and the ——facility is equipped with manufacturing process equipment comparable to that used in the ———— ———— manufacturing process at the currently approved manufacturing site. The —— facility received a satisfactory current Good Manufacturing Practices (cGMP) inspection on ————. The inspection covered the general operating procedures utilized at this facility and manufacturing processes similar to that which is used for the manufacture of ————

RECEIVED
JUL 11 1994
GENERIC DRUGS

Received 7-12-94

Attached is Table I which demonstrates that cilastatin sodium, made with production scale ———————————————, conforms to specifications and is comparable to material produced at the currently approved ——— site. Table II provides specifications and test results for ——————————————— ——— manufactured at ———. A revised Section 3a reflects the inclusion of the ——— site in the AADA.

Also attached, are a letter authorizing reference to ——— Drug Master File ——, statements of environmental compliance from ——— management, and the appropriate ——— government official.

Consequently, the ——— facility at ——————— will become an alternate manufacturing site for——————————————— effective immediately.

We consider the filing of this Supplemental New Drug Application to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communication in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

If there are questions or comments concerning this submission, please contact me at (610) 397-7176, or, in my absence, Dr. Kenneth R. Brown at (610) 397-2552.

Sincerely,

Henrietta N. Ukwu, M.D.
Director
Regulatory Liaison

Attachments
Certified No. P 151 656 841

(3) Desk copies w/att.: Ms. Maureen Dillon-Parker, CSO, Div. of Anti-Infective Drug Products, HFD-521, Rm. 12B-05, CDER, FDA, 5600 Fishers Lane, Rockville, MD 20857
Certified No. P 151 656 842
**Please distribute copies to Dr. Roy Suva, and Dr. Rosemary Roberts.**

q/ -- /ukwu/53B