CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 62-756 / S-021

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

***Sponsor*:** Merck Research Laboratories

***Approval Date*:** May 9, 1995

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-021

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-021

APPROVAL LETTER

AADA 62-756/S-021

Merck Sharp & Dohme Research Laboratories
Attn: Henrietta N. Ukwu, M.D.
Director, Regulatory Liaison
Sumneytown Pike
West Point, PA 19486

MAY 9 1995

Dear Sir:

This is in reference to your supplemental antibiotic application, dated August 25, 1994, submitted pursuant to 21 CFR 314.70, regarding your abbreviated antibiotic application for Primaxin® ADD-Vantage® (Imipenem-Cilastatin Sodium for Injection, MSD)

The supplemental application provides for increase in manufacturing

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 drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

5/8/95

Frank O. Holcombe, Jr., Ph.D.
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: 021
AADA 62-756/S-~~010~~
DUP/Division File
HFD-600/RF
HFD-82
FIELD COPY

Endorsements:
HFD-643/EDuffy/5/02/95 EDUFFY 5/4/95
HFD-643/JHarrison/5/02/95 J Harrison 5/8/95
HFD-617/MAnderson/5/03/95 Mark Anderson 5/8/95
X:MSD21S62.756
F/T by kc/5/04/95
SUPPLEMENT APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-021

CHEMISTRY REVIEW

CHEMISTRY REVIEW #1

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

DATE: 5/1/95

FROM: EDuffy/HFD-643

SUBJECT: AADA 62-756/S-021 Merck's Primaxin® ADD-Vantage® (Imipenem-Cilastatin Sodium for Injection, MSD)

TO: AADA 62-756

The firm has submitted supplements to AADA 62-756 and the sister NDAs 50-630/S-012 and 50-587/S-044 for Primaxin® ADD-Vantage® (Imipenem-Cilastatin Sodium for Injection, MSD)

The supplemental application provides for increase in manufacturing

The supplement was approved by HFD-520 3/3/95 (see attached reviews and letters). The same action will be taken by OGD.

cc.
~~AADA 62-756~~ 6/S-021
DUP/Division File
HFD-82
FIELD COPY

Endorsements:
HFD-643/EDuffy/5-1-95 EDuffy 5/4/95
HFD-617/MAnderson/5/03/95
HFD-643/JHarrison/5/02/95
X:\WPFILE\MICHELLE\DUFFY\MSD21S62.756
F/T by kc/5/04/95

NDA SUPPLEMENT REVIEW

CHEMIST'S REVIEW | **1. ORGANIZATION** DAIDP (HFD-520) | **2. NDA NUMBER** 50-630

3. NAME & ADDRESS OF APPLICANT
Merck Sharp & Dohme Research Laboratories
Sumneytown Pike
West Point, PA 19486

4. AF NUMBER

5. SUPPLEMENT(s) NUMBER(s) DATE(s)
SCS-012 10/31/94

6. NAME OF DRUG
Primaxin® I.M.

7. NONPROPRIETARY NAME
Imipenem-Cilastatin Sodium

8. SUPPLEMENT(s) PROVIDES FOR:
SCS-012 Changes in manufacturing [redacted]

9. AMENDMENTS AND OTHER (REPORTS, etc.) DATES
Amendment 4/25/95

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
XXX
Rx OTC

12. RELATED IND/NDA/DMF(s)
NDA 50-587

13. DOSAGE FORM(s)
Recon. powder for I.M.

14. POTENCY(ies)
≈500mg Imipenem/Cilastatin sodium
≈750mg Imipenem/Cilastatin sodium

15. CHEMICAL NAME AND STRUCTURE

Imipenem $C_{12}H_{17}N_3O_4S.H_2O$
(5R,6S)-3-[[2-(formimidoylamino)ethyl]thio]-6-[(R)-1-hydroxyethyl]-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid monohydrate
m.w. 317.36 CAS Registry No. 74431-23-5

Cilastatin Sodium $C_{16}H_{25}N_2NaO_5S$
Sodium (Z)-7-[[(R)-2-amino-2-carboxyethyl]-thil]-2-[(S)-2,2-dimethylcyclopropanecarboxamido]-2-heptenoate
m.w. 380.43 CAS Registry No. 81129-83-1

16. RECORDS AND REPORTS

	Yes	No
CURRENT	XX	
REVIEWED	XX	

17. COMMENTS
The drug is the subject of a monograph, USP 25, page 794.

The changes in [redacted] were implemented in response to a FDA-483 issued after an inspection of Merck's Elkton, VA site between 10/27 - 11/10/93 and an agreement with the Baltimore District.

The proposed increase in manufacturing [redacted] is acceptable from the clinical and safety standpoints (see Supervisory Medical Officer review, of 3/30/95, attached.)

18. CONCLUSIONS AND RECOMMENDATIONS
The supplement is approvable. An approval letter may be issued.

cc: Orig: NDA 50-587
HFD-520 HFD-520/Sheldon HFD-520/Roberts
HFD-520/Buko HFD-520/Dillon-Parker
HFD-520/SBRoy HFD-520/SBRoy:R/D initialed 4/26/95

19. NAME	REVIEWER SIGNATURE	DATE COMPLETED
Suva B. Roy, Ph.D.		4/26/95

DISTRIBUTION ORIGINAL JACKET REVIEWER DIVISION FILE

Redacted 2 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW

NDA 50-630/S-012

Henrietta N. Ukwu, M. D.
Director Regulatory Liaison
Merck Sharp & Dohme Research Laboratories
Sumneytown Pike
West Point, Pennsylvania 19486

Dear Dr. Ukwu:

Reference is made to your supplemental New Drug Application (NDA) dated October 12, 1994, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act for Primaxin® I.M. (Imipenem-Cilastatin Sodium).

We also acknowledge your amendment of April 25, 1995.

The supplemental application provides for changes in the manufacturing [redacted]

We have completed our review and the supplemental application is approved effective as of the date of this letter.

This approval affects only those changes specifically submitted in this supplemental application. Other changes that may have been approved or are pending evaluation are not affected.

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

Sincerely yours,

4/27/95

Suya B. Roy, Ph.D
Acting Supervisory Chemist
Division of Anti-Infective Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-021

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

DATE: 9/9/94

SEP 12 1994

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/021	✓	
62-757	S-010		

This form is to accompany the action package/jacket.

Thank you,

Mark Anderson

Signature of CSO and Date

CC:

ANDA
DIVISION FILE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-021

CORRESPONDENCE

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

These copies are OFFICIAL FDA Copies
not desk copies.

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

August 25, 1994

MERCK
Research Laboratories

Mr. John D. Harrison, Chief
Office of Generic Drugs, CDER, FDA
HFD-635, Room #MPN2
Document Control Room
5600 Fishers Lane
Rockville, Maryland 20857

NDA NO. _____ REF. NO. SC021
NDA SUPPL FOR Manufacturing
SC021AL

Dear Mr. Harrison:

changes were supplemented 8/5/94

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

AADA 62-756: PRIMAXIN I.V.® in ADD-Vantage® Vials
(Imipenem-Cilastatin Sodium for Injection)

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 changes in Item 3 of the approved Abbreviated Antibiotic Drug Application for PRIMAXIN I.V.® in ADD-Vantage® Vials.

In response to FDA-483 observations received during an inspection conducted by FDA from October 27, 1993 to November 10, 1993, at our Elkton, Virginia site, Merck committed to conduct constitution studies in support of the diluents currently approved for the constitution of PRIMAXIN I.V.® in ADD-Vantage® Vials. These studies have recently been completed using a protocol agreed to by the Baltimore District. To assure that PRIMAXIN I.V.® in ADD-Vantage® Vials will:

1) [redacted]

2)

RECEIVED
AUG 2 • 1994
GENERIC DRUGS

ORIGINAL

This supplement provides for a change in the manufacturing ——————— from — to the following :

— (250 mg, ADD-Vantage) and
— (500 mg, ADD-Vantage)

Rationale and justification for these various —— are discussed in Attachment 1.

These changes have been discussed with the Reviewing Chemist, Dr. Suva Roy, in several telephone conversations. In addition, changes to the PRIMAXIN I.V.® in ADD-Vantage® Vials package circular resulting from the constitution studies done in response to the FDA 483 have been submitted August 25, 1994 as a separate labeling supplement.

The manufacturing changes became effective on August 5, 1994 and apply to all packages of PRIMAXIN I.V.® in ADD-Vantage® Vials distributed from the company's manufacturing facilities at West Point.

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

Questions or comments concerning this supplemental application should be directed to Henrietta N. Ukwu, M.D. (610/397-7176) or, in my absence, to Kenneth R. Brown, M.D. (610/397-2552).

Sincerely,

K R Brown for

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

Attachments

Certified No. P 151 563 428