CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 62-756/S-035

Name: Primaxin I.V. in ADD-Vantage Vials
(Imipenem-Cilastatin Sodium for Injection)

Sponsor: Merck & Co., Inc

Approval Date: April 19, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-035

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-035

APPROVAL LETTERS

ANDA 62-756/S-035

Merck & Co. Inc.
Attention: Virginia G. Snyder
P.O. Box 4
Sumneytown Pike, BLA-20
West Point, PA 19486

APR 19 2002

Dear Madam:

This is in reference to your supplemental new drug application, dated December 5, 2001, submitted under section 505 (j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for PRIMAXIN™ I.V. in ADD-Vantage™ Vials, 250 mg and 500 mg.

Reference is also made to your amendment dated ~~March 28~~ April 3 mA, 2002.

This supplemental application, submitted as "Supplement Changes Being Effected in 30 Days", provides for use of the Merck facility in Wilson, North Carolina as an alternate stability testing site for PRIMAXIM™ I.V. in ADD-Vantage™ Vials (Imipenem and Cilistatin), 250 mg and 500 mg.

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

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

H.V. Vandenavan
for Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 62-756/S-035
Division File
Field Copy
HFD-92

Endorsements:

HFD-643/RGanunis/4/1/02 RGanunis 4/15/02

HFD-643/RAdams/4/10/02 R.C. adams 4/15/02

HFD-617/MAnderson/4/12/02 MAnderson 4/16/02

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F/T by dss/4/12/02

APPROVAL

ANDA 62-756/S-035

MAY 13 2002

Merck & Co. Inc.
Attention: Virginia G. Snyder
P.O. Box 4
Sumneytown Pike, BLA-20
West Point, PA 19486

Dear Madam:

This is in reference to your supplemental new drug application, dated December 5, 2001, submitted under section 505 (j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for PRIMAXIN™ I.V. in ADD-Vantage™ Vials, 250 mg and 500 mg.

Reference is also made to your amendment dated March 28, 2002.

This corrects our approval letter of April 19, 2002, in which we erroneously stated that the supplemental application provides for use of the Merck facility in Wilson, North Carolina as an alternate stability testing site for PRIMAXIM™ I.V. in ADD-Vantage™ Vials (Imipenem and Cilistatin), 250 mg and 500 mg. The correct statement is that your Wilson, NC facility will be a test site for cilastatin sodium drug substance used in your PRIMAXIM™ product.

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

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

R. C. Adams for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 62-756/S-035
Division File
Field Copy
~~HFD-92~~

Endorsements:

HFD-643/RAdams/5/13/02 R.C. Adams 5/12/02

HFD-617/MAnderson/5/13/02 M Anderson 5/13/02

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F/T by mda/5/13/02

LETTER OUT - CORRECTION

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-035

CHEMISTRY REVIEW

OFFICE OF GENERIC DRUGS
SUPPLEMENT REVIEW

ANDA 62-756/S-035

NAME AND ADDRESS OF APPLICANT
Merck & Co. Inc.
P.O. Box 4
Sumneytown Pike, BLA-20
West Point, PA 19486

PURPOSE OF SUPPLEMENT
The CBE-30 supplement provides for use of the Merck facility in Wilson, North Carolina as an alternate stability testing site for PRIMAXIM™ I.V. in ADD-Vantage Vials (Imipenem and Cilistatin). The supplement is bundled with NDA 50-587 and NDA 50-630.

DATE OF SUBMISSION
December 5, 2001
~~March 28~~, 2001[2] (amendment)
April 3, 2002 mA
PHARMACOLOGICAL CATEGORY
Antibacterial

TRADE NAME
PRIMAXIN™ I.V. in ADD-Vantage™ Vials

NONPROPRIETARY NAME
Imipenem-Cilastatin for Injection

DOSAGE FORM
Powder

STRENGTHS
250 mg and 500 mg

RX OR OTC
Rx

SAMPLES
N/A

RELATED IND/NDA/DMF
NDA 50-587, Primaxin™ IV for Injection
NDA 50-630, Primaxin™ IM Injectable Suspension

STERILIZATION
N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION - Satisfactory
12/14/01

COMPONENTS/COMPOSITION/MANUFACTURING
N/A

PACKAGING
N/A

CONTROLS/STABILITY - Satisfactory
The firm proposes to use the following alternate stability testing site:

Merck & Co.
4633 Merck Road
Wilson, NC 27893

Telephone Conference: On 3/28/02 the firm was contacted and asked to provide written statement that a PAC-ATLS CBE supplement is appropriate for this supplement. The firm responded that the chemistry section of the supplement, which contained this information, was inadvertently left out of the submission. The chemistry information was submitted on ~~3/28/02~~. 4/3/02 mA

Merck supports their supplement by stating that the following conditions have been met.

- The test methods approved in the application or implemented under 21 CFR 314.70(d) are used.
- All post approval commitments related to the test methods have been fulfilled.
- The new testing facility has the capability to perform the intended testing.
- The new facility has had a satisfactory cGMP inspection within the last 2 years.

REMARKS AND CONCLUSION
Recommended for Approval

RECALLS
N/A

REVIEWER
Ruth Ganunis

DATE COMPLETED
April 1, 2001

cc: ANDA 62-756/S-035
Division File
Field Copy

Endorsements:

HFD-643/RGanunis/4/1/02 RGanunis 4/15/02

HFD-643/RAdams/4/10/02 R.C. Adams 4/15/02

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F/T by dss/4/12/02

APPROVAL

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-035

CORRESPONDENCE

Virginia G. Snyder
Manager
Regulatory Affairs

Merck & Co., Inc.
P.O. Box 4, BLA-20
West Point PA 19486
Tel 484 344 7984
215 652 5000
Fax 484 344 2516

NDA NO. 62-756 REF. NO. SCS-035
NDA SUPP FOR Facility Add. AT

December 5, 2001

MERCK Research Laboratories

EER was requested
(Facility acceptable as a CTL testing site as of 1/2000 per MPQAS
mAnderson

Gary Buehler, Director
Division of Generic Drug Products
Bldg. MPN2, HFD-600, Room 286 (CDER)
Food and Drug Administration
Metro Park North 2
7500 Standish Place
Rockville, MD 20855

OK per 12/7/01

Dear Mr. Buehler:

NDA 50-587: PRIMAXIN™ IV for Injection (Imipenem and Cilastatin)
NDA 50-630: PRIMAXIN™ IM Injectable Suspension (Imipenem and Cilastatin)
AADA 62-756: PRIMAXIN™ IV in ADD-Vantage™ Vials (Imipenem and Cilastatin)

SUPPLEMENT - CHANGES BEING EFFECTED IN 30 DAYS
PAC-ATLS: Post Approval Changes - Analytical Testing Laboratory Sites

Reference is made to the Abbreviated Antibiotic Drug Application for PRIMAXIN™ IV in ADD-Vantage™ Vials cited above and to an October 17, 2001 telephone call between Ms. Susan Lange, OPS (Office of Pharmaceutical Sciences) and Ms. Virginia Snyder (MRL, a Division of Merck & Co., Inc.) in which it was agreed that MRL would bundle the CBE 30s for NDAs 50-587: PRIMAXIN™ IV, NDA 50-630: PRIMAXIN™ IM and AADA 62-756: PRIMAXIN™ IV in ADD-Vantage™ Vials. **As agreed, the supplement will be submitted simultaneously to the Anti-Infective Division for NDAs 50-587 and 50-630 and to this AADA 62-756: PRIMAXIN™ IV in ADD-Vantage™ Vials.**

Pursuant to Section 505(b) of the Food, Drug and Cosmetic Act and in accordance with 506A(d)(3)(B)(i) of the Food and Drug Administration Modernization Act, we submit, for the Agency's review and approval, a supplement to AADA 62-756.

As indicated on the attached Form FDA 356h, this supplemental application provides for changes in the *Chemistry* Section of the approved Abbreviated Antibiotic Drug Application for PRIMAXIN™ IV in ADD-Vantage™ Vials. This supplement provides for use of the Merck facility in Wilson, North Carolina as an alternate stability testing site for cilastatin sodium. The Statement of Organization following this letter describes the sections contained in this application.

In accordance with the Food and Drug Administration Modernization Act of 1997, as indicated in the attached Form 3397, no user fee is required for this supplemental application.

Pursuant to 21 CFR 314.70(a), a complete field copy of this supplement has been submitted to the FDA Philadelphia District Office.

Merck & Co., Inc. is requesting a categorical exclusion for the requirements to prepare an Environmental Assessments under 21 CFR 25.31(a). This supplement meets the requirements of a categorical exclusion under 21 CFR 25.31(a) because it will not increase the use of the active moiety. To the best of the firm's knowledge no extraordinary circumstances exist in regards to this action.

As required by Section 306(k)(1) of the Generic Enforcement Act [21 U.S.C. 335a(k)(1)], we hereby certify that, in connection with this application, Merck & Co., Inc. did not and will not use in any capacity the services of any person debarred under subsections 306(a) or (b) of the Act.

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 communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this supplemental application should be directed to Virginia G. Snyder (484-344-7984) or, in my absence, to Dennis M. Erb, Ph.D. (484-344-7597).

Sincerely,

Virginia G. Snyder
Manager, Regulatory Affairs

Attachments
Federal Express

Desk Copy/att: Mr. Mark D. Anderson, Regulatory Project Manager
HFD-640, Room E251
Federal Express #2

Desk Copies: Ms. Susan Lange, Consumer Safety Officer (cover letter)
HFD-800, Room 13B31
Federal Express #3

Philadelphia District Office, FDA (Item 4 & cover letter)
Federal Express #4

Virginia G. Snyder
Manager
Regulatory Affairs

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OFFICIAL FDA Copies
not desk copies

Merck & Co., Inc.
P.O. Box 4, BLA-20
West Point PA 19486
Tel 484 344 7984
215 652 5000
Fax 484 344 2516

April 3, 2002

Gary Buehler, R.Ph., Director
Division of Generic Drug Products
Bldg. MPN2, HFD-600, Room 286 (CDER)
Food and Drug Administration
Metro Park North 2
7500 Standish Place
Rockville, MD 20855

MERCK
Research Laboratories

SUPPL AMENDMENT
SCB-035
AC

Dear Mr. Buehler:

AADA 62-756: PRIMAXIN™ IV in ADD-Vantage™ Vials (Imipenem and Cilastatin)

General Correspondence

Reference is made to the Abbreviated Antibiotic Drug Application for PRIMAXIN™ IV in ADD-Vantage™ Vials cited above and to a Supplemental Application (CBE-30) submitted on December 5, 2001. Additional reference is made to a March 28, 2002 telephone conversation between Mr. Mark Anderson and Dr. Ruth Ganunis (FDA) and Ms. Virginia Snyder, (MRL, a Division of Merck & Co., Inc.) in which Ms. Snyder was informed that only the administrative section for this supplement had been received and that the *Chemistry* section had been omitted. At Dr. Ganunis' request the *Chemistry* section of the supplement was faxed to her on March 28, 2002. By copy of this letter, we are resubmitting the entire Supplemental Application of December 5, 2001 to insure the completeness of the files.

We apologize for any inconvenience this may have caused.

Questions concerning this submission should be directed to Virginia G. Snyder (484-344-7984) or, in my absence, to Dennis M. Erb, Ph.D. (484-344-7597).

Sincerely,

Virginia G. Snyder
Manager, Regulatory Affairs

Attachments

Federal Express #1

Desk Copies: Mr. Mark D. Anderson, Regulatory Project Manager (cover letter)
HFD-640, Room E251
Federal Express #2

Ms. Debra L. Pagano (Item 4 + cover letter)
Philadelphia District Office
Federal Express #3

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RECEIVED
APR 0 4 2002
OGD / CDER