CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 62-756 / S-030

***Name*:** Primaxin® I.V. in ADD-Vantage® vials
(Imipenem and Cilastatin for Injection)

***Sponsor*:** Merck Research Laboratories

***Approval Date*:** November 29, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-030

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Administrative Documents	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-030

APPROVAL LETTER

ANDA 62-756/S-030

Merck and Co., Inc.
Attention: Charles L. Hyman, M.D.
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

NOV 29 1999

Dear Sir:

This is in reference to your supplemental new drug application, dated March 24, 1999, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for PRIMAXIN® I.V. ADD-Vantage® Vials.

The supplemental application, submitted as a "Prior Approval Supplement" provides for a change in a vendor of a ———— ———— used in the synthesis of active pharmaceutical ingredient imipenem.

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,

11/24/99

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

cc: ANDA 62-756/S-030
Division File
Field Copy

Endorsements:

HFD-643/RGanunis/11/17/99 R. Ganunis 11/22/99
HFD-643/RAdams/11/19/99 R.C. Adams, 11/23/99
HFD-617/MAnderson/11/22/99 M Anderson 11/23/99
V:\ FIRMSAM\MERCK\LTRS&REV\62756s30.AP.DOC
F/T by mda/11/22/99
APPROVAL

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-030

CHEMISTRY REVIEWS

OFFICE OF GENERIC DRUGS
SUPPLEMENT REVIEW

~~ANDA~~ 62-756/S-030

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

PURPOSE OF SUPPLEMENT
Supplement-030 provides for use of [redacted] as a new supplier of [redacted] used in the synthesis of active pharmaceutical ingredient imipenem. This is a bundled supplement.

DATE OF SUBMISSION
Supplement submitted March 24, 1999.

PHARMACOLOGICAL CATEGORY
Antibacterial

TRADE NAME
PRIMAXIN® I.V. ADD-Vantage® Vials

NONPROPRIETARY NAME
Imipenem-Cilastatin Sodium for Injection

DOSAGE FORM
Powder

STRENGTHS
250 mg, 500 mg

RX OR OTC
Rx

SAMPLES
N/A

RELATED IND/NDA/DMF
DMF# [redacted], Type I)
DMF# [redacted], Type II)
NDA 50-587 (PRIMAXIN® I.V., Bundled application)

STERILIZATION
N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION
N/A

COMPONENTS/COMPOSITION/MANUFACTURING/CONTROLS - Satisfactory
The firm proposes to purchase ——————————
from a new vendor, ——————————.
Previously, Merck manufactured the ——————.

In support of this application, the firm provided test data on three batches of ——————— manufactured by ——————— and three batches manufactured by Merck. The firm also provided test results of Imipenem non-sterile, manufactured at lab scale and production scale with ——————— obtained from ——————— and ——————— manufactured by Merck. B.V. Shetty, Ph.D. of the Office of New Drug Chemistry reviewed the submitted information and approved the use of the new ——————— supplier in regard to NDA 50-587 on July 13, 1999. A complete evaluation of the submitted material can be found in that review (copy attached). The supplement has not been reexamined in detail by this reviewer.

Please refer to note in the DMF checklist concerning the status of DMF #———. Since an approval letter has already been sent by the Office of New Drug Chemistry to the firm regarding NDA 50-587/S-051, this supplement will also be recommended for approval.

PACKAGING
N/A

STABILITY
Merck has committed to enter one lot of PRIMAXIN® I.V. in ADD-Vantage® Vials manufactured with ——————— from ——————— into their long term stability program (see attached review).

REMARKS AND CONCLUSION
The supplement is approvable.

RECALLS
N/A

REVIEWER
Ruth Ganunis R. Ganunis

DATE COMPLETED
11/17/99 11/22/99

APPEARS THIS WAY
ON ORIGINAL

DMF CHECKLIST FOR ANDA #62-756 REVIEW #1

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

Comments:

——— II/ ——— 7

Comments: DMF #——— for manufacture of ——— was found inadequate on 8/23/99 by the Office of New Drug Chemistry (B.V. Shetty, review chemist; D. Katague, Team Leader; F.V. LeSane, Project Manager), after approval of NDA 50-587/S-051. The DMF holder responded to the deficiencies on 10/28/99. It appears that the firm has addressed the deficiencies. Since a deficiency letter was sent to the DMF holder, and appropriate protocol requires the same chemist to review the response prior to supplement approval, the DMF was returned to Shetty for review.

Comments:

Comments:

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 revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under "Comments").

Page 1 of 1 . R. Ganunis — Reviewer

l. Ganunis — Signature

11/17/99 11/22/99 — Date

cc: ANDA 62-756/S-030
Division File
Field Copy

Endorsements:

HFD-643/RGanunis/11/17/99 R. Ganunis 11/22/99
HFD-643/Radams/11/19/99 R.C. Adams, 11/23/99
V:\FIRMSAM\MERCK\LTRS&REV\62756s30.AP.DOC
F/T by:mda/11/22/99
APPROVAL

APPEARS THIS WAY
ON ORIGINAL

NDA SUPPLEMENT REVIEW

JUL 7 1999

CHEMIST'S REVIEW

1. **ORGANIZATION**
DAIDP (HFD-520)

2. **NDA NUMBER**
50-587

3. **NAME & ADDRESS OF APPLICANT**
Merck and Co.
Sumneytown Pike
P. O. Box 4, BLA-20
West Point, Pennsylvania 19486

4. **AF NUMBER**

5. **SUPPLEMENT(s)**

NUMBER(s)	DATE(s)
SCM-051	3/24/99

6. **NAME OF DRUG**
PRIMAXIN I.V.

7. **NONPROPRIETARY NAME**
Imipenem-Cilastatin Sodium for Injection

8. **SUPPLEMENT(s) PROVIDES FOR:**
A change in a vendor of _____ used in the synthesis of active pharmaceutical ingredient imipenem.

9. **AMENDMENTS AND OTHER (REPORTS, etc.) DATES**
none

10. **PHARMACOLOGICAL CATEGORY**
Antibiotic

11. **HOW DISPENSED**
XXX
Rx OTC

12. **RELATED IND/NDA/DMF(s)**

13. **DOSAGE FORM(s)**
Powder

14. **POTENCY(ies)**
250 mg, 500 mg

15. **CHEMICAL NAME AND STRUCTURE**

m.w.
CAS Registry No. - -

16. **RECORDS AND REPORTS**

	CURRENT	REVIEWED
XXX Yes		
No		

17. **COMMENTS**
This drug is the subject of a compendial monograph, USP XIII, pg. 793. See items 20-34 for detailed comments.

18. **CONCLUSIONS AND RECOMMENDATIONS**
Recommend approval letter to issue for this supplement.
See attached comments.

cc: Orig: NDA 50-587
HFD-520
HFD-520/Pharm/Ellis
HFD-520/BVShetty
HFD-520/MO/Thompson
HFD-520/CSO/Lesane
HFD-520/DKatague:R/D initialed DBK 7/6/99

19.

NAME	REVIEWER SIGNATURE	DATE COMPLETED
B. V. Shetty	BVShetty 7/6/99	06/07/99

DISTRIBUTION ORIGINAL JACKET REVIEWER DIVISION FILE

20. **Components and Composition** N/A

21. **Facilities and Personnel** N/A

22. **Synthesis** N/A

23. **Raw Material Controls**
    a. New Drug Substance N/A
    b. Other Ingredients N/A

24. **Other Firm(s)** N/A

25. **Manufacturing and Processing** N/A

26. **Container/Closure** N/A

27. **Packaging and Labeling** N/A

28. **Laboratory Controls (In-process and Finished Dosage Form)**

    N/A

29. **Stability** N/A

30. **Control Numbers** N/A

31. **Samples and Results**
    a. Validation N/A
    b. Market Package N/A

32. **Labeling** N/A

NOTE: If labeling is revised, approval letter should be copies to HFD-85, HFD-500, HFD-638 and HFD-735, with a copy of the final or draft label attached.

33. Establishment Inspection

See attached comment #5.

34. Recalls N/A

APPEARS THIS WAY
ON ORIGINAL

Redacted 2 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-030

CORRESPONDENCE

Charles L. Hyman, M.D.
Director
Regulatory Affairs

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Merck & Co., Inc.
P.O. Box 4
West Point PA 19486
Fax 610 397 2516
Tel 610 397 2850
215 652 5000

March 24, 1999

MERCK
Research Laboratories

Mr. Richard C. Adams
Office of Generic Drugs, HFD-643, Room E243
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North 2
7500 Standish Place
Rockville, MD 20855

NDA NO. 62756 REF NO. SC-0:
NDA SUPPL FOR Manufacturer Supp

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

SUPPLEMENTAL NEW DRUG APPLICATION

Dear Mr. Adams:

Pursuant to Section 505(b) of the Food Drug and Cosmetic Act and in accordance with 21 CFR 314.70(b), we submit, for your approval, a supplement to AADA 62-756.

As indicated on the attached Form FDA 356h, this supplemental application provides for changes in Chemistry Section of the approved Abbreviated Antibiotic Drug Application for PRIMAXIN™ I.V. in ADD-Vantage® Vials.

Attached with this letter are all necessary information to support the submission of a supplemental New Drug Application covering the purchase from a vendor of ———— used in the synthesis of active pharmaceutical ingredient imipenem and currently manufactured in-house. The ———— referred to in the approved NDA process and throughout this supplement as ————; will be manufactured by the chosen vendor via the same process in comparable equipment and under approved processing conditions. The chosen vendor, ————, has provided authorization for the FDA to review their DMF on behalf of Merck and Co., Inc.

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.

As required by Section 306(k)(1) of the Generic Drug 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.

RECEIVED
MAR 29
GENERIC DRUGS

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 concerning this supplemental application should be directed to Charles L. Hyman, M.D. (610/397-2850) or, in my absence, to Robert E. Silverman, M.D. (610/397-2944).

Sincerely,

Charles L. Hyman, M.D.
Director
Regulatory Affairs

Attachments

Certified No. P 914 177 626

Desk Copy: Philadelphia District Office, FDA
P 914 177 622

'Letters/AADA 62-756SNDA