CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 62-756/S-003

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

Sponsor: Merck Sharp & Dohme Research Laboratories

Approval Date: March 7, 1991

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APPLICATION NUMBER:

ANDA 62-756/S-003

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APPROVAL LETTER

AADA 62-756/S-003

MAR- 7 1991

Merck Sharp and Dohme Research Laboratories
Attn.: Kenneth R. Brown, Reg. Affairs
West Point, PA 19486

Dear Sir:

Reference is made to your supplemental antibiotic drug application dated June 23, 1989, submitted pursuant to Section 314.70(c), Special Supplement Changes Being Effected, of the Regulations, regarding your abbreviated antibiotic drug application for Primaxin® ADD-Vantage® (Imipenem - Cilastatin Sodium for Injection).

The supplemental application provides for revised "Instructions for Use" copy.

We have completed the review of this supplemental application and it is approved. Our letter of January 8, 1987, detailed the conditions relating to the approval of this abbreviated application.

The material submitted is being retained in our files.

Sincerely yours,

Kyra Johnson for 3-7-91

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:
HFD-638/TPoux
HFD-635
mw/3/6/91/62-756S.003
APPROVAL SUPPLEMENT

3/6/91

CENTER FOR DRUG EVALUATION AND RESEARCH

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LABELING

NDA 62-756

7482202

INSTRUCTIONS FOR USE OF PRIMAXIN®† (Imipenem-Cilastatin Sodium, MSD) IN ADD-Vantage®* VIALS

For IV Use Only.

INSTRUCTIONS FOR USE

To Open Diluent Container.

Peel overwrap from the corner and remove container. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually.

To Assemble Vial and Flexible Diluent Container.
(Use Aseptic Technique)

1. Remove the protective covers from the top of the vial and the vial port on the diluent container as follows:
   a. To remove the breakaway vial cap, swing the pull ring over the top of the vial and pull down far enough to start the opening. (SEE FIGURE 1.) Pull the ring approximately half way around the cap and then pull straight up to remove the cap. (SEE FIGURE 2.) NOTE: DO NOT ACCESS VIAL WITH SYRINGE.

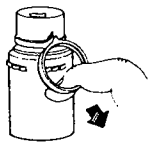

Fig. 1

Fig. 2

   b. To remove the vial port cover, grasp the tab on the pull ring, pull up to break the three tie strings, then pull back to remove the cover. (SEE FIGURE 3.)
2. Screw the vial into the vial port until it will go no further. THE VIAL MUST BE SCREWED IN TIGHTLY TO ASSURE A SEAL. This occurs approximately ½ turn (180°) after the first audible click. (SEE FIGURE 4.) The clicking sound does not assure a seal; the vial must be turned as far as it will go. NOTE: Once vial is seated, do not attempt to remove. (SEE FIGURE 4.)
3. Recheck the vial to assure that it is tight by trying to turn it further in the direction of assembly.
4. Label appropriately.

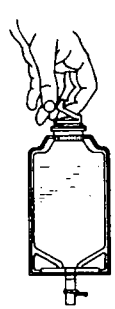

Fig. 3

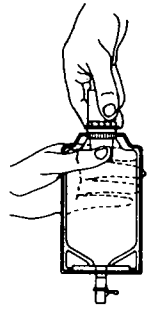

Fig. 4

To Prepare Admixture:

1. Squeeze the bottom of the diluent container gently to inflate the portion of the container surrounding the end of the drug vial.
2. With the other hand, push the drug vial down into the container telescoping the walls of the container. Grasp the inner cap of the vial through the walls of the container. (SEE FIGURE 5.)
3. Pull the inner cap from the drug vial. (SEE FIGURE 6.) Verify that the rubber stopper has been pulled out, allowing the drug and diluent to mix.
4. Mix container contents thoroughly and use within the specified time.

N. B. If the rubber stopper is not removed from the vial and the antibiotic released on the first attempt, the inner cap should be manipulated back into the stopper without removing the drug vial from the diluent container and Step 3 repeated.

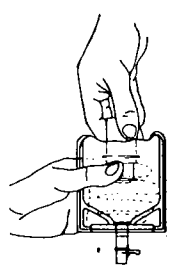

Fig. 5

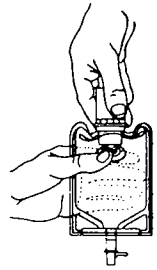

Fig. 6

7482202

Preparation for Administration
(Use Aseptic Technique)

1. Confirm the activation and admixture of vial contents.
2. Check for leaks by squeezing container firmly. If leaks are found, discard unit as sterility may be impaired.
3. Close flow control clamp of administration set.
4. Remove cover from outlet port at bottom of container.
5. Insert piercing pin of administration set into port with a twisting motion until the pin is firmly seated. NOTE: See full directions on administration set carton.
6. Lift the free end of the hanger loop on the bottom of the vial, breaking the two tie strings. Bend the loop outward to lock it in the upright position, then suspend container from hanger.
7. Squeeze and release drip chamber to establish proper fluid level in chamber.
8. Open flow control clamp and clear air from set. Close clamp.
9. Attach set to venipuncture device. If device is not indwelling, prime and make venipuncture.
10. Regulate rate of administration with flow control clamp.

WARNING: Do not use flexible container in series connections.

Stability

PRIMAXIN (Imipenem - Cilastatin Sodium, MSD) 250 or 500 single dose ADD-Vantage® vials should be prepared with ADD-Vantage® diluent containers containing 100 mL of either 0.9 percent Sodium Chloride Injection or 5 percent Dextrose Injection. When prepared with either of these diluents, PRIMAXIN (Imipenem - Cilastatin Sodium, MSD) maintains satisfactory potency for 8 hours at room temperature.

Before administering, see accompanying package circular for PRIMAXIN (Imipenem - Cilastatin Sodium, MSD).

†Registered trademark of MERCK & CO., Inc.
*Registered trademark of ABBOTT LABORATORIES, Inc.

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-003

CORRESPONDENCE

S-003 V
FPL

MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
WEST POINT, PENNSYLVANIA 19486

KENNETH R. BROWN, M.D
GROUP DIRECTOR
REGULATORY AFFAIRS, BIOLOGICS

(215) 834-2552
(215) 661-5000

FPL instructions for the subject 3/6/91 BJ

June 23, 1989

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branch, HFD-235
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Mr. Harrison:

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

ANDA 62-756: Primaxin® ADD-Vantage® (Imipenem-Cilastatin Sodium, MSD)

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 ANDA 62-756.

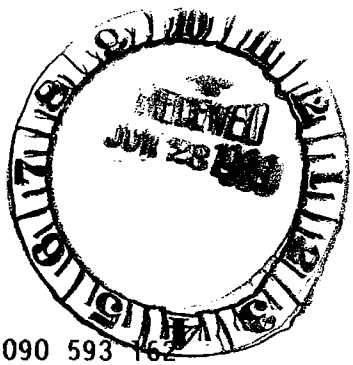
As indicated on the attached Form FDA 356h, the supplemental application provides for changes in Item 4(c) of the approved Abbreviated New Drug Application for Primaxin® ADD-Vantage®.

Attached are copies of the final printed Instructions for Use, a summary of revisions, and an annotated copy of the Instructions for Use. The Instructions for Use have been revised editorially under both Assembly Instructions and Admixture Preparation.

The changes will become effective on or about October 1, 1989 and will apply to all packages of Primaxin® ADD-Vantage® distributed from the company's manufacturing facilities at West Point, Pennsylvania.

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 Kenneth R. Brown, M.D. (215/834-2552) or, in his absence, to David W. Blois, Ph.D. (215/834-2304).



Sincerely yours,

Kenneth R. Brown, M.D.
Group Director
Regulatory Affairs, Biologics

WL/ys/425H
Attachments
Certified No. P 090 593 162

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