CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-517/S-039

APPROVAL LETTER

DF

NDA 50-517/S-039

APR 24 1997

Merck & Co., Inc.
Attention: Henrietta N. Ukwa, M.D.
Director
Regulatory Liaison
P.O. Box 4, BLA-30A
West Point, PA 19486-0004

Dear Dr. Ukwa:

Reference is made to your February 21, 1997 supplemental new drug application submitted under section 507 of the Federal Food, Drug, and Cosmetic Act for Mefoxin® (sterile cefoxitin for injection).

This supplemental application provides an insert for the ADD-Vantage system to be added to the labeling.

We have completed our review of this submission, and find this supplemental application acceptable. Therefore, the application is approved effective as of the date of this letter.

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

Should additional information relating to the safety and effectiveness of this drug product become available, further revision of the labeling may be required.

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

If you have any questions concerning this NDA, please contact Mr. Carmen DeBellas, Project Manager, at 301-827-2125.

Sincerely yours,

/S/ 4.17.97

David W. Feigal, Jr., M.D., M.P.H.
Acting Director
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-517/S-039

APPROVED LABELING

MEFOXIN®
(Sterile Cefoxitin Sodium)

ADMINISTRATION

MEFOXIN may be administered intravenously or intramuscularly after constitution.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Intravenous Administration

The intravenous route is preferable for patients with bacteremia, bacterial septicemia, or other severe or life-threatening infections, or for patients who may be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or impending.

For intermittent intravenous administration, a solution containing 1 gram or 2 grams in 10 mL of Sterile Water for Injection can be injected over a period of three to five minutes. Using an infusion system, it may also be given over a longer period of time through the tubing system by which the patient may be receiving other intravenous solutions. However, during infusion of the solution containing MEFOXIN, it is advisable to temporarily discontinue administration of any other solutions at the same site.

For the administration of higher doses by continuous intravenous infusion, a solution of MEFOXIN may be added to an intravenous bottle containing 5 percent Dextrose Injection, 0.9 percent Sodium Chloride Injection, 5 percent Dextrose and 0.9 percent Sodium Chloride Injection, or 5 percent Dextrose Injection with 0.02 percent sodium bicarbonate solution. BUTTERFLY* or scalp vein-type needles are preferred for this type of infusion.

Solutions of MEFOXIN, like those of most beta-lactam antibiotics, should not be added to aminoglycoside solutions (e.g., gentamicin sulfate, tobramycin sulfate, amikacin sulfate) because of potential interaction. However, MEFOXIN and aminoglycosides may be administered separately to the same patient.

Intramuscular Administration

As with all intramuscular preparations, MEFOXIN should be injected well within the body of a relatively large muscle such as the upper outer quadrant of the buttock (i.e., gluteus maximus); aspiration is necessary to avoid inadvertent injection into a blood vessel.

COMPATIBILITY AND STABILITY

Intravenous

MEFOXIN, as supplied in vials or the bulk package and constituted to 1 gram/10 mL with Sterile Water for Injection, Bacteriostatic Water for Injection, (see PREPARATION OF SOLUTION), 0.9 percent Sodium Chloride Injection, or 5 percent Dextrose Injection, maintains satisfactory potency for 24 hours at room temperature, for one week under refrigeration (below 5°C), and for at least 30 weeks in the frozen state.

These primary solutions may be further diluted in 50 to 1000 mL of the following solutions and maintain potency for 24 hours at room temperature and at least 48 hours under refrigeration:

Sterile Water for Injection‡
0.9 percent Sodium Chloride Injection
5 percent or 10 percent Dextrose Injection‡
5 percent Dextrose and 0.9 percent Sodium Chloride Injection
5 percent Dextrose Injection with 0.02 percent Sodium Bicarbonate solution
5 percent Dextrose Injection with 0.2 percent or 0.45 percent saline solution
Ringer's Injection
Lactated Ringer's Injection‡
5 percent Dextrose in Lactated Ringer's Injection‡
5 percent or 10 percent invert sugar in water
10 percent invert sugar in saline solution
5 percent Sodium Bicarbonate Injection
Neut (sodium bicarbonate)*‡
M/6 sodium lactate solution
NORMOSOL-M in D5-W*‡
IONOSOL B w/Dextrose 5 percent*‡
POLYONIC M 56 in 5 percent Dextrose**
Mannitol 5% and 2.5%
Mannitol 10%‡
ISOLYTE***E
ISOLYTE***E with 5% Dextrose

MEFOXIN, as supplied in infusion bottles and constituted with 50 to 100 mL of 0.9 percent Sodium Chloride Injection, or 5 percent or 10 percent Dextrose Injection, maintains satisfactory potency for 24 hours at room temperature or for 1 week under refrigeration (below 5°C).

MEFOXIN is supplied in single dose ADD-Vantage® vials and should be prepared as directed in the accompanying INSTRUCTIONS FOR USE OF MEFOXIN IN ADD-Vantage® VIALS using ADD-Vantage® diluent containers containing 50 mL or 100 mL of either 0.9 percent Sodium Chloride Injection or 5 percent Dextrose Injection. When prepared with either of these diluents, MEFOXIN maintains satisfactory potency for 24 hours at room temperature.

Limited studies with solutions of MEFOXIN in 0.9 percent Sodium Chloride Injection, Lactated Ringer's Injection, and 5 percent Dextrose Injection in VIAFLEX† intravenous bags show stability for 24 hours at room temperature, 48 hours under refrigeration or 26 weeks in the frozen state and 24 hours at room temperature thereafter. Also, solutions of MEFOXIN in 0.9 percent Sodium Chloride Injection show similar stability in plastic tubing, drip chambers, and volume control devices of common intravenous infusion sets.

After constitution with Sterile Water for Injection and subsequent storage in disposable plastic syringes, MEFOXIN is stable for 24 hours at room temperature and 48 hours under refrigeration.

After the periods mentioned above, any unused solutions or frozen material should be discarded. Do not refreeze.

Intramuscular

MEFOXIN, as constituted with Sterile Water for Injection, Bacteriostatic Water for Injection, or 0.5 percent or 1 percent lidocaine hydrochloride solution (without epinephrine), maintains satisfactory potency for 24 hours at room temperature, for one week under refrigeration (below 5°C), and for at least 30 weeks in the frozen state.

After the periods mentioned above, any unused solutions or frozen material should be discarded. Do not refreeze.

MEFOXIN has also been found compatible when admixed in intravenous infusions with the following:

Heparin 0.1 units/mL at room temperature — 8 hours
Heparin 100 units/mL at room temperature — 24 hours
M.V.I.†† concentrate at room temperature 24 hours; under refrigeration 48 hours
BEROCCA††† C-500 at room temperature 24 hours; under refrigeration 48 hours
Insulin in Normal Saline at room temperature 24 hours; under refrigeration 48 hours
Insulin in 10% invert sugar at room temperature 24 hours; under refrigeration 48 hours

HOW SUPPLIED

Sterile MEFOXIN is a dry white to off-white powder supplied in vials and infusion bottles containing cefoxitin sodium as follows:

No. 3356 — 1 gram cefoxitin equivalent
NDC 0006-3356-45 in trays of 25 vials
(6505-01-119-6005, 1 g 25's).
No. 3368 — 1 gram cefoxitin equivalent
NDC 0006-3368-71 in trays of 10 infusion bottles
(6505-01-195-0649, 1 g infusion bottle 10's).
No. 3357 — 2 gram cefoxitin equivalent
NDC 0006-3357-53 in trays of 25 vials
(6505-01-104-6393, 2 g 25's).
No. 3369 — 2 gram cefoxitin equivalent
NDC 0006-3369-73 in trays of 10 infusion bottles
(6505-01-185-2624, 2 g infusion bottle 10's).
No. 3388 — 10 gram cefoxitin equivalent
NDC 0006-3388-67 in trays of 6 bulk bottles
(6505-01-263-0730, 10 g 6's).
No. 3548 — 1 gram cefoxitin equivalent
NDC 0006-3548-45 in trays of 25 ADD-Vantage® vials
(6505-01-262-9509, 1 g ADD-Vantage® 25's).
No. 3549 — 2 gram cefoxitin equivalent
NDC 0006-3549-53 in trays of 25 ADD-Vantage® vials
(6505-01-263-4531, 2 g ADD-Vantage® 25's).

Special storage instructions

MEFOXIN in the dry state should be stored below 30°C. Avoid exposure to temperatures above 50°C. The dry material as well as solutions tend to darken, depending on storage conditions; product potency, however, is not adversely affected.

*Registered trademark of Abbott Laboratories, Inc.
‡In these solutions, MEFOXIN has been found to be stable for a period of one week under refrigeration.
**Registered trademark of Cutter Laboratories, Inc.
***Registered trademark of American Hospital Supply Corporation.
†Registered trademark of Baxter International, Inc.
††Registered trademark of USV Pharmaceutical Corp.
†††Registered trademark of Roche Laboratories.

MSD MERCK SHARP & DOHME
DIV OF MERCK & CO., INC., WEST POINT, PA 19486, USA

Issued January 1992

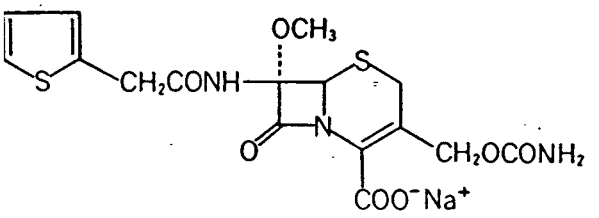
Printed in USA

MSD | MEFOXIN® (STERILE CEFOXITIN SODIUM)

MEFOXIN•
(Sterile Cefoxitin Sodium)

DESCRIPTION

EFOXIN• (Sterile Cefoxitin Sodium) is a semi-synthetic, broad-spec- ı cepha antibiotic sealed under nitrogen for parenteral administration. It is ved from cephamycin C, which is produced by *Streptomyces lactam- ins.* It is the sodium salt of 3-(hydroxymethyl)-7α-methoxy-8-oxo-7-[2-(2- nyl)acetamido]-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylate carba- e (ester). The empirical formula is $C_{16}H_{16}N_3NaO_7S_2$, and the structural ıula is:



:EFOXIN contains approximately 53.8 mg (2.3 milliequivalents) of sodium gram of cefoxitin activity. Solutions of MEFOXIN range from colorless to t amber in color. The pH of freshly constituted solutions usually ranges n 4.2 to 7.0.

CLINICAL PHARMACOLOGY

ical Pharmacology

fter intramuscular administration of a 1 gram dose of MEFOXIN to normal . the mean peak serum concentration was 24 mcg/mL. The peak 20 to 30 minutes. Following an intravenous dose of 1 gram, serum ons were 110 mcg/mL at 5 minutes, declining to less than 1 mcg/mL . The half-life after an intravenous dose is 41 to 59 minutes; after amuscular administration, the half-life is 64.8 minutes. Approximately 85 :ent of cefoxitin is excreted unchanged by the kidneys over a 6-hour period, ılting in high urinary concentrations. Following an intramuscular dose of 1 n, urinary concentrations greater than 3000 mcg/mL were observed. Pro- ecid slows tubular excretion and produces higher serum levels and in- ıses the duration of measurable serum concentrations.

efoxitin passes into pleural and joint fluids and is detectable in antibac- ıl concentrations in bile.

linical experience has demonstrated that MEFOXIN can be administered to ents who are also receiving carbenicillin, kanamycin, gentamicin, ·amycin, or amikacin (see PRECAUTIONS and ADMINISTRATION).

robiology

he bactericidal action of cefoxitin results from inhibition of cell wall syn- ıis. Cefoxitin has *in vitro* activity against a wide range of gram-positive and n-negative organisms. The methoxy group in the 7α position provides FOXIN with a high degree of stability in the presence of beta-lactamases, n penicillinases and cephalosporinases, of gram-negative bacteria. Cefox- is usually active against the following organisms *in vitro* and in clinical ctions:

m-positive
taphylococcus aureus, including penicillinase and non-penicillinase pro- ing strains
taphylococcus epidermidis
eta-hemolytic and other streptococci (most strains of enterococci, e.g., ıptococcus faecalis, are resistant)
treptococcus pneumoniae

m-negative
scherichia coli
lebsiella species (including *K. pneumoniae*)
emophilus influenzae
leisseria gonorrhoeae, including penicillinase and non-penicillinase pro- ing strains
roteus mirabilis
lorganella morganii
roteus vulgaris
rovidencia species, including *Providencia rettgeri*

ierobic organisms
F ·us species
·tococcus species
n species
a. ·es species, including the *B. fragilis* group (includes *B. fragilis, B. asonis, B. ovatus, B. thetaiotaomicron, B. vulgatus*)

IEFOXIN is inactive *in vitro* against most strains of *Pseudomonas* ·a and enterococci and many strains of *Enterobacter cloacae.* in-resistant staphylococci are almost uniformly resistant to

MEFOXIN•
(Sterile Cefoxitin Sodium)

Susceptibility Tests

For fast-growing aerobic organisms, quantitative methods that require measurements of zone diameters give the most precise estimates of antibiotic susceptibility. One such procedure* has been recommended for use with discs to test susceptibility to cefoxitin. Interpretation involves correlation of the diameters obtained in the disc test with minimal inhibitory concentration (MIC) values for cefoxitin.

Reports from the laboratory giving results of the standardized single disc susceptibility test* using a 30 mcg cefoxitin disc should be interpreted according to the following criteria:

Organisms producing zones of 18 mm or greater are considered susceptible, indicating that the tested organism is likely to respond to therapy.

Organisms of intermediate susceptibility produce zones of 15 to 17 mm, indicating that the tested organism would be susceptible if high dosage is used or if the infection is confined to tissues and fluids (e.g., urine) in which high antibiotic levels are attained.

Resistant organisms produce zones of 14 mm or less, indicating that other therapy should be selected.

The cefoxitin disc should be used for testing cefoxitin susceptibility.

Cefoxitin has been shown by *in vitro* tests to have activity against certain strains of *Enterobacteriaceae* found resistant when tested with the cephalosporin class disc. For this reason, the cefoxitin disc should not be used for testing susceptibility to cephalosporins, and cephalosporin discs should not be used for testing susceptibility to cefoxitin.

Dilution methods, preferably the agar plate dilution procedure, are most accurate for susceptibility testing of obligate anaerobes.

A bacterial isolate may be considered susceptible if the MIC value for cefoxitin** is not more than 16 mcg/mL. Organisms are considered resistant if the MIC is greater than 32 mcg/mL.

INDICATIONS AND USAGE

Treatment

MEFOXIN is indicated for the treatment of serious infections caused by susceptible strains of the designated microorganisms in the diseases listed below.

(1) **Lower respiratory tract infections,** including pneumonia and lung abscess, caused by *Streptococcus pneumoniae,* other streptococci (excluding enterococci, e.g., *Streptococcus faecalis*), *Staphylococcus aureus* (penicillinase and non-penicillinase producing), *Escherichia coli, Klebsiella* species, *Hemophilus influenzae,* and *Bacteroides* species.

(2) **Genitourinary infections.** Urinary tract infections caused by *Escherichia coli, Klebsiella* species, *Proteus mirabilis,* indole-positive Proteus (which include the organisms now called *Morganella morganii* and *Proteus vulgaris*), and *Providencia* species (including *Providencia rettgeri*). Uncomplicated gonorrhea due to *Neisseria gonorrhoeae* (penicillinase and non-penicillinase producing).

(3) **Intra-abdominal infections,** including peritonitis and intra-abdominal abscess, caused by *Escherichia coli, Klebsiella* species, *Bacteroides* species including the *Bacteroides fragilis* group***, and *Clostridium* species.

(4) **Gynecological infections,** including endometritis, pelvic cellulitis, and pelvic inflammatory disease caused by *Escherichia coli, Neisseria gonorrhoeae* (penicillinase and non-penicillinase producing), *Bacteroides* species including the *Bacteroides fragilis* group***, *Clostridium* species, *Peptococcus* species, *Peptostreptococcus* species, and Group B streptococci.

(5) **Septicemia** caused by *Streptococcus pneumoniae, Staphylococcus aureus* (penicillinase and non-penicillinase producing), *Escherichia coli, Klebsiella* species, and *Bacteroides* species including the *Bacteroides fragilis* group.***

(6) **Bone and joint infections** caused by *Staphylococcus aureus* (penicillinase and non-penicillinase producing).

(7) **Skin and skin structure infections** caused by *Staphylococcus aureus* (penicillinase and non-penicillinase producing), *Staphylococcus epidermidis,* streptococci (excluding enterococci e.g., *Streptococcus faecalis*), *Escherichia coli, Proteus mirabilis, Klebsiella* species, *Bacteroides* species including the *Bacteroides fragilis* group***, *Clostridium* species, *Peptococcus* species, and *Peptostreptococcus* species.

Appropriate culture and susceptibility studies should be performed to determine the susceptibility of the causative organisms to MEFOXIN. Therapy may be started while awaiting the results of these studies.

In randomized comparative studies, MEFOXIN and cephalothin were comparably safe and effective in the management of infections caused by gram-positive cocci and gram-negative rods susceptible to the cephalosporins. MEFOXIN has a high degree of stability in the presence of bacterial beta-lactamases, both penicillinases and cephalosporinases.

*Bauer, A. W.; Kirby, W. M. M.; Sherris, J. C.; Turck, M.: Antibiotic susceptibility testing by a standardized single disc method, Amer. J. Clin. Path. *45:* 493-496, Apr. 1966. Standardized disc susceptibility test, Federal Register *37:* 20527-20529, 1972. National Committee for Clinical Laboratory Standards: Approved Standard: ASM-2, Performance Standards for Antimicrobial Disc Susceptibility Tests, July 1975.

**Determined by the ICS agar dilution method (Ericsson and Sherris, Acta Path. Microbiol. Scand. [B] Suppl. No. 217, 1971) or any other method that has been shown to give equivalent results.

***B. fragilis, B. distasonis, B. ovatus, B. thetaiotaomicron, B. vulgatus,*

7464705

INSTRUCTIONS FOR USE OF MEFOXIN®* (Cefoxitin for Injection) (Formerly called Sterile Cefoxitin Sodium) 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.

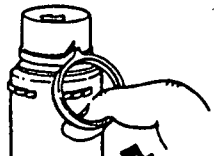


Fig. 1

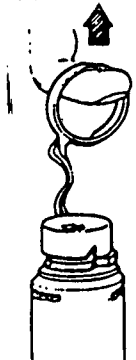


Fig. 2

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

   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

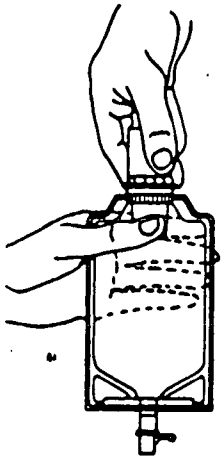


Fig. 4

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.

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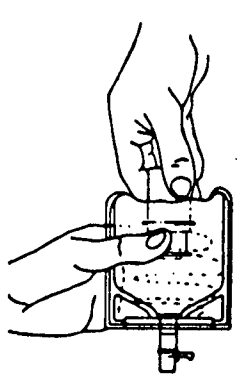

Fig. 5

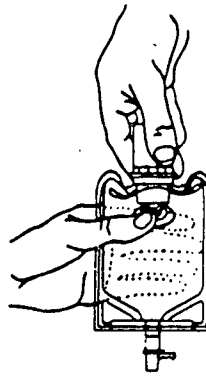

Fig. 6

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, d card 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 twistl motion until the pin is firmly seated. NOTE: See full directions administration set carton.
6. Lift the free end of the hanger loop on the bottom of the vial, brea ing the two tie strings. Bend the loop outward to lock it in the uprig position, then suspend container from hanger.
7. Squeeze and release drip chamber to establish proper fluid level chamber.
8. Open flow control clamp and clear air from set. Close clamp.
9. Attach set to venipuncture device. If device is not indwelling, prim and make venipuncture.
10. Regulate rate of administration with flow control clamp.

WARNING: Do not use flexible container in series connections.

Stability

MEFOXIN (Cefoxitin for Injection) 1 gram or 2 gram single dos ADD-Vantage® vials should be prepared with ADD-Vantage® diluent co tainers containing 50 mL or 100 mL of either 0.9 percent Sodium Chlorid Injection or 5 percent Dextrose Injection. When prepared with either these diluents, MEFOXIN (Cefoxitin for Injection) maintains satisfactor potency for 24 hours at room temperature.

Before administering, see accompanying package circular for MEFOXI (Cefoxitin for Injection).

Issued August 1998

Printed in US

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-517/S-039

ADMINISTRATIVE DOCUMENTS AND CORRESPONDENCE

DIV F

APR - 8 1997

NDA 50-517/S-039

REVIEW OF FINAL PRINTED LABELING (FPL)

APPLICANT: Merck & Co., Inc.
P.O. Box 4, BLA-30A
West Point, PA 19486-0004

DATE OF SUBMISSION: February 21, 1997

DATE OF REVIEW: March 26, 1997

APPEARS THIS WAY ON ORIGINAL

NAMES OF DRUGS:

NDA 50-517 -- Mefoxin (sterile cefoxitin sodium)

GENERIC: See above

SUBMISSION HISTORY:

February 21, 1997: The Applicant submitted supplemental application NDA 50-517/S-039 providing instruction for the use of the ADD-Vantage IV system.

Comments: The labeling submitted in this application was compared to labeling for other ADD Vantage products and was found to be acceptable.

RECOMMENDATIONS: An approval letter should be issued.

/S/

Carmen L. DeBellas, PMS

/S/

Janice Soreth, M.D.

CC:
Orig NDA
50-517
HFD-520
HFD-520/SMO/Sorett
HFD-520/MO/Viraraghavan
HFD-520/CSO/DeBellas
FPL REVIEW

Concurrence:
HFD-520/SCSO/Bona /S/ 1/9/97
HFD-520/DIVDIR/Feigal
/S/ 1/8/97
/S/ 1/8/97

APPEARS THIS WAY
ON ORIGINAL

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Hye-Joo Kim
4/26/01 11:08:23 AM
PHARMACIST

Jerry Phillips
4/27/01 09:30:06 AM
DIRECTOR

Martin Himmel
4/27/01 02:29:09 PM
MEDICAL OFFICER

USER FEE DATA ENTRY/VALIDATION FORM Ver.3 (2/17/94

Div.

NDA # 50577 DOCUMENT ID/LETTER DATE SLR-089 2-21-97

APPLICANT NAME MSD

PRODUCT NAME mefoxin

FORM MUST BE COMPLETED ASAP

1. (YES) User Fee Cover Sheet Validated?

NOTE TO DOCUMENT ROOM:
PLEASE MAKE THE FOLLOWING CHANGES TO THE USER FEE SCREENS:

2. YES (NO) CLINICAL DATA?
(Check YES if contains study reports or literature reports of what are explicitly or implicitly represented by the applicant to be adequate and well-controlled trials. "Clinical data" is not limited data used to modify the labeling to add a precaution that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).)

REF IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION?

3. YES (NO) NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (OTHER THAN SUPPLEMENT)? IF YES, LIST ALL NDA numbers, review divisions & indicate those for which application fees apply.

NDA #	Division		
N_____	_____	FEE	NO FEE
N_____	_____	FEE	NO FEE

4. (YES) NO BIDDING POLICY APPLIED CORRECTLY? NO DATA ENTRY REQUIRED FOR EITHER
(Check YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Check NO if application should be split into more than one application or submitted as an original instead of a supplement. If NO, list resulting NDA numbers, and review divisions.)

NDA #	Division	NDA #	Division
N_____	_____	N_____	_____

5. R (S) PRIORITY OR STANDARD?

/S/ 3/24/97
6. CSO Signature/Date

/S/ 3/27/97
SPSC Concurrence Signature/Date

COPY DISTRIBUTION: ORIGINAL TO RECEIVE AFTER DATA ENTRY, ONE COPY EACH TO DIVISION FILE AND CDR, ASSOCIATE DIRECTOR FOR POLICY ED-5