CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION:NDA 50-632/S-010

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CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 50-632/S-010

Trade Name: AZACTAM

Generic Name:(aztreonam injection)

Sponsor: Bristol-Myers Squibb Company

Approval Date:December 24, 1998

Indication: Provides for the addition of pediatric use statements in the Azactam (aztreonam injection) package insert in which the following sections and subsections are changed:CLINICALPHARMACOLOGY;PRECAUTIONS, Pediatric Use; ADVERSE REACTIONS, Pediatric Adverse Reactions; and DOSAGE AND ADMINISTRATION. In addition, the package insert has been updated in the CLINICAL PHARMACOLOGY, Microbiology subsection and has been revised by editorial changes.

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 50-632/S-010

APPROVAL LETTER

NDA 50-632/S-010

DEC 24 1998

Bristol-Myers Squibb Company
Attention: Joseph A. Linkewich, Pharm.D.
P.O. Box 4000
Princeton, New Jersey 08543-4000

Dear Dr. Linkewich:

Please refer to your supplemental new drug application dated December 19, 1997, received December 29, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Azactam (aztreonam injection).

We acknowledge receipt of your submission dated April 20, 1998.

This supplemental new drug application provides for the addition of pediatric use statements in the Azactam (aztreonam injection) package insert in which the following sections and subsections are changed: CLINICAL PHARMACOLOGY; PRECAUTIONS, Pediatric Use; ADVERSE REACTIONS, Pediatric Adverse Reactions; and DOSAGE AND ADMINISTRATION. In addition, the package insert has been updated in the CLINICAL PHARMACOLOGY, Microbiology subsection and has been revised by editorial changes.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted labeling (package insert submitted April 20, 1998) with the revisions listed below. Accordingly, the supplemental application is approved effective on the date of this letter.

1. Serial commas should be inserted throughout the text.

2. In the DESCRIPTION section:

   In the chemical name, delete the hyphen between "(2S,-3S)."

3. In the CLINICAL PHARMACOLOGY section:

   a. In the first sentence of the first paragraph, insert "aztreonam" between "produced" and "peak."
   b. In the third paragraph, give the full name for "*H.*" i.e., "*Haemophilus*"; add a hyphen between "eight hour"; give the full name for "*Ps.*" i.e., "*Pseudomonas*"; and add a hyphen between "2 g."

c. In the first sentence of the fourth paragraph, "When aztreonam pharmacokinetics were assessed . . . to be comparable (down to 9 months old)." add a hyphen between "9 months."
d. In the sixth paragraph, add a period after "prolonged"; capitalize the "S" in "see"; add a period after "Patients"; and delete the period after the parenthesis. That is, ". . . prolonged. (See DOSAGE AND ADMINISTRATION, Renal Impairment in Adult Patients.) The serum . . . ."
e. In the seventh paragraph, add a hyphen between "1 g" and "2 g" and after "8" and "12."
f. In the eleventh paragraph, change "breast milk" to "human milk."

4. In the WARNINGS section:

In the fifth paragraph, do not capitalize or italicize "*Clostridia*."

5. In the PRECAUTIONS section:

In the Nursing Mothers subsection, change "breast milk" to "human milk."

6. In the ADVERSE REACTIONS section:

Delete all periods placed at the end of the adverse reactions.

These revisions are terms of the approval. Marketing the product before making the revisions, exactly as requested, in the product's final printed labeling (FPL) may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 50-632/S-010." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we

request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, Maryland 20857

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

If you have any questions, contact Mr. Stephen T. Trostle, Regulatory Health Project Manager, at (301) 827-2125.

Sincerely,

Gary Chikami, M.D.
Director
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

cc:
Archival NDA 50-632/SE1-010
HFD-520/Div. files
HFD-520/TL/MO/MAlbuerne MA 12/23/98
HFD-520/TL/Micro/ASheldon AS 12/23/98
HFD-520/Micro/HSilver HS (12/23/98)
HFD-520/TL/Chem/DKatague
HFD-520/Chem/JTimper
HFD-520/TL/Pharm/ROsterberg
HFD-520/Pharm/KSeethaler
HFD-520/LGavrilovich (with labeling) LG 12/22/98
HF-2/MedWatch (with labeling)
HFD-002/ORM (with labeling)
HFD-104/ADRA (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-95/DDMS (with labeling)
HFD-830/DNDC Division Director
DISTRICT OFFICE
HFD-520/STrostle/stt/12/22/98 \n50632ap.010
STT 12/22/98

APPROVAL (AP)

Concurrence only:
HFD-520/C/PMS/JBona for 12/24/98

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 50-632/S-010

APPROVABLE LETTER

SAC
Trostle

NDA 50-580/S-028
NDA 50-632

JUL 18 1997

Bristol-Myers Squibb Company
Attention: Joseph A. Linkewich, Pharm.D.
Director, Marketed Products
U.S. Regulatory Liaison
Worldwide Regulatory Affairs
P.O. Box 4000
Princeton, New Jersey 08543-4000

Dear Dr. Linkewich:

Please refer to your supplemental new drug applications dated June 5, 1996, received June 10, 1996, submitted under section 507 of the Federal Food, Drug, and Cosmetic Act for AZACTAM[R] FOR INJECTION (Aztreonam for Injection, USP), NDA 50-580, and AZACTAM[R] (Aztreonam Injection), NDA 50-632.

These supplemental applications provide for the revision of the package inserts for these products with the requested CLINICAL PHARMACOLOGY changes as a response to our not approvable letter dated May 18, 1995, to NDA 50-632/S-008.

We have completed the review of these supplemental applications as submitted with draft labeling, and they are approvable. Before these applications may be approved, however, it will be necessary for you to submit draft final printed labeling revised as follows:

A. Revise the CLINICAL PHARMACOLOGY- Microbiology and Susceptibility Tests subsection in accordance with the January 26, 1993 letter to all NDA Holders from the Division of Anti-Infective Drug Products, as well as recent discussions within the Division, to read as follows:

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secret and/or

confidential

commercial

information

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

These changes may not be implemented until you have been notified in writing that these supplemental applications are approved.

If you have any questions, please contact Mr. Stephen T. Trostle, Consumer Safety Officer, at (301)-827-2125.

Sincerely yours,

/S/ 07/17/97

Gary K. Chikami, M.D.
Acting Director
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

cc:

Original NDA (50-580/50-632)
HFD-520/Div. Files
HFD-40/DDMAC
HFD-92/DDM-DIAB
HFD-104/TNearing
DISTRICT OFFICE
HFD-520/CSO/STrostle
HFD-520/TL/MO/MAlbuerne
HFD-520/Micro/HSilver
HFD-520/TL/Micro/ASheldon
HFD-520/Pharm/KSeethaler
HFD-520/Chem/JTimper

Concurrence Only:

HFD-520/TL/MO/MAlbuerne MA 7/17/97
HFD-520/TL/Micro/ASheldon AS 7/17/97
HFD-520/Micro/HSilver HVS (7/16/97)
HFD-520/C/PMS/JBona JB 7/14/97

Drafted: 04/25/97/JBona
Revised and final typed: 07/14/97/STrostle \n50580ae.028
ST 07/14/97

APPROVABLE (AE)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 50-632/S-010

MEDICAL REVIEW(S)

AUG 11 1998

Medical Officer's Review of NDA Supplement

NDA 50-632/SEI-010

Applicant: Bristol Myers Squibb Company
P.O. Box 4000
Princeton, NJ

Date of Submission: December 19, 1997
Date Received: December 29, 1997
Date of Amendment: April 20, 1998
Date Review completed: June 22, 1998

Product Identification:
Trade Name: AZACTAM®
Generic Name: Aztreonam injection
Drug Class: Monobactam

Dosage Form: Injection

Route of Administration: Intravenous

How Supplied:
AZACTAM (aztreonam injection) in Galaxy® plastic container (PL2040) is supplied as a frozen, 50mL single-dose intravenous solution as follows:

1-g aztreonam/50 mL container
2-g aztreonam/50 mL container

Purpose of Supplement

The applicant submitted draft Final Printed Labeling (FPL) incorporating all revisions exactly as specified in the Division's letter dated August 20, 1996.

In addition, further changes were effected in the CLINICAL PHARMACOLOGY, PRECAUTIONS (Pediatric Use Subsection), ADVERSE REACTION (Pediatric Adverse Reactions Subsection), and DOSAGE ADMINISTRATION sections of the package insert. These changes have been approved and were implemented in the AZACTAM® (aztreonam for injection) package insert, NDA 50-580, S-008 (submitted May 18, 1987, and approved November 1, 1996; Final Printed Labeling submitted January 27, 1997, and approved June 10, 1997.

Discussion of Labeling

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information

Comment: The revisons are acceptable.

/S/

M.S. Albuerne, M.D.,
Medical Team Leader

cc: Orig NDA
HFD-520
HFD-520/MO
HFD-520/Pharm/
HFD-520/Micro/
HFD-520/Chem/
HFD-520/CSO/
HFD-520/Biopharm

Concurrence:
HFD-520/Div. Dir/Chikami

/S/

5/11/98