CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 50-632/S-010

CHEMISTRY REVIEW(S)

NDA SUPPLEMENT REVIEW

CHEMIST'S REVIEW Review #1

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

2. **NDA NUMBER** 50-632

3. **NAME & ADDRESS OF APPLICANT**
Bristol-Myers Squibb Co.
P.O.Box 4000
Princeton, NJ 08543-4000

4. **AF NUMBER**

5. **SUPPLEMENT(s) NUMBER(s) DATE(s)** SE1-010; 12/29/97

6. **NAME OF DRUG** Aztreonam

7. **NONPROPRIETARY NAME** Azactam

8. **SUPPLEMENT(s) PROVIDES FOR:**
the labeling changes pertaining to clinical pharmacology with editorial changes to chemical nomenclature.

9. **AMENDMENTS AND OTHER (REPORTS, etc.) DATES**

10. **PHARMACOLOGICAL CATEGORY** Antimicrobial

11. **HOW DISPENSED** XXX Rx OTC

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

13. **DOSAGE FORM(s)** for injection

14. **POTENCY(ies)** 500mg/ 1g/ 2g/ vial

15. **CHEMICAL NAME AND STRUCTURE**
$C_{13}H_{17}N_5O_8S_2$; 435.43 CAS-78110-38-0
Aztreonam

16. **RECORDS AND REPORTS**
CURRENT
Yes
REVIEWED
Yes

17. **COMMENTS**
This is a supplement that pertains to the "Clinical Pharmacology" section of the labeling. On review of the sections pertaining to chemistry it is observed a hyphen in the chemical name should not be present.

18. **CONCLUSIONS AND RECOMMENDATIONS**
Recommend approval letter to depend on clinical review by the medical officer. Include the statement, "the chemical name should not have a hyphen before the '...3S...'.

Orig: NDA 50-580
HFD-520/
HFD-520/Alam/Pharm
HFD-520/HSilver/Micro
HFD-520/Katague: initialed DBK 3/11/98
HFD-520/Meyerhoff/MO
HFD-520/Trostle/CSO
HFD-520/JTimper/Chem

19. **REVIEWER**

NAME J. Timper

SIGNATURE /S/ 3/10/98

DATE COMPLETED 3/10/98

DISTRIBUTION ORIGINAL JACKET REVIEWER DIVISION FILE

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NDA SUPPLEMENT REVIEW

CLINICAL MICROBIOLOGIST'S REVIEW #1

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

2. **NDA NUMBER** 50-632

3. **NAME & ADDRESS OF APPLICANT**
Bristol-Myers Squibb Company
P.O. Box 4000
Princeton, New Jersey 08543-4000
Contact Person(s):
Joseph A. Linkewich, Pharm.D.,
Director, Marketed Products,
U.S. Regulatory Liaison, Worldwide Regulatory Affairs,
Tel: (609)--252-5761

4. **AF NUMBER** N/A

5. SUPPLEMENT(s)
NUMBER(s) DATE(s)

6. **NAME OF DRUG**
AZACTAM®

7. **NONPROPRIETARY NAME**
aztreonam injection

8. **SUPPLEMENT(s) PROVIDES FOR:**
Updated draft labeling on the **CLINICAL PHARMACOLOGY -- Microbiology** subsection and the **Susceptibility Tests** subsection, respectively.

9. **AMENDMENTS AND OTHER DATES (REPORTS, etc.)** N/A

10. **PHARMACOLOGICAL CATEGORY**
Antibiotic/Certain Other Antibiotic Drugs

11. **HOW DISPENSED**
Rx

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

a. Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, New Jersey 08543-4000, AZACTAM® (aztreonam for injection, USP), NDA 50-580 (Approved 12/31/86).

b. Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, New Jersey 08543-4000, AZACTAM® (aztreonam injection) in single dose Viaflex® Plus Plastic Container (PL 146®) containing either 1 g or 2 g aztreonam, NDA 50-632 (Approved 5/24/89).

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13. **DOSAGE FORM(s)**
Injection: In a 50 mL single-dose Galaxy® plastic container (PL 2040). The drug product is stored frozen.

14. **POTENCY(ies)**
Each 50 mL single-dose Galaxy® plastic container (PL 2040) contains:

- 1 gram aztreonam per 50 mL GALAXY® plastic container (= 20 mg aztreonam per mL); and

-- 2 grams aztreonam per 50 mL GALAXY® plastic container (= 40 mg aztreonam per mL).

15. **CHEMICAL NAME AND STRUCTURE**

Chemical Name	=	See 1996 USAN, on pp. 71 & 72
Structure	=	See 1996 USAN on page 72
Molecular Formula	=	$C_{13}H_{17}N_5O_8S_2$
Molecule Weight	=	435.44
CAS #	=	*CAS-78110-38-0*

16. **RECORDS AND REPORTS:** CURRENT Yes; REVIEWED Yes

17. **COMMENTS**

This supplement was submitted in response to the Agency's "not approvable" letter, on NDA 50-632/S-008, and dated 5/18/96. The supplement (50-632/S-008) provided for an additional new container, the GALAXY® plastic bag (PL 2040), to package the 1-gram and 2-gram potencies. One request in the "not approvable" was to revise the drug product's labeling on the **CLINICAL PHARMACOLOGY -- Microbiology** and **Susceptibility Tests** subsections, respectively. The labeling was requested to be revised and submitted as a separate supplement according to the Agency's "TO ALL NDA HOLDERS" letter dated 1/26/93 and recent recommendations within the Division.

This drug is the subject of the compendial monographs, 21 CFR §455.4 (aztreonam), 21 CFR §455.204b (aztreonam injection), & 23 USP (Aztreonam) on page 155 & 23 USP (Aztreonam Injection) on pages 155 & 156, respectively.

The original application NDA 50-580, AZACTAM® (aztreonam for injection, USP) was approved on 12/31/86 and is cross-referenced in this supplemental labeling application.

18. **CONCLUSIONS AND RECOMMENDATIONS**

We recommend that an "approvable" letter be issued for this supplement.

19.

REVIEWER NAME	SIGNATURE	DATE COMPLETED
Harold V. Silver	(11/26/96) /S/	11/26/96

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 50-632/S-010

MICROBIOLOGY REVIEW(S)

OCT 27 1998

DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS (HFD-520)
Microbiological Review of Labeling Supplement

NDA#: 50-632 **REVIEW #:** 2 **REVIEW DATE:** 8/31/98

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
NDA 50-632: SE1-010 (N) SLR-009 (BL) & SEI-010 (BL)	12/19/97 4/20/98	12/24/97 4/23/98	8/25/98

NAME & ADDRESS OF APPLICANT:

Bristol-Myers Squibb Company
P.O. Box 4000
Princeton, New Jersey 08543-4000

CONTACT PERSON:

Joseph A. Linkewich, Pharm. D.,
Director, U.S. Regulatory Liaison, Worldwide Regulatory Affairs,
Tel: (609) 252-5761

SUBMISSION REVIEWED:
SUPPLEMENT PROVIDES FOR:

The Supplement, NDA 50-632, It provided updated draft labeling on the **CLINICAL PHARMACOLOGY – Microbiology** and **Susceptibility Tests** subsections and **REFERENCES** section, respectively.

DRUG PRODUCT NAME:

aztreonam:

Proprietary:	AZACTAM®
Non-Proprietary/USAN:	aztreonam injection
Code Name:	SQ 26776
CAS No.:	*CAS-8068-28-8*

ANDA Suitability Petition/DESI/Patent Status: N/A

PHARMACOLOGICAL CATEGORY/INDICATION:

Monobactam Antibiotic Drug

DOSAGE FORM:

Injection: In a 50 mL single-dose Galaxy® plastic container (PL 2040). The antibiotic drug product is stored frozen.

STRENGTH/POTENCY:

Each 50 mL single-dose GALAXY® plastic container (PL 2040) contains:

- 1 gram aztreonam per 50 mL GALAXY® plastic container (= 20 mg aztreonam per mL); and
- 2 grams aztreonam per 50 mL GALAXY® plastic container (= 40 mg aztreonam per mL).

ROUTE OF ADMINISTRATION: Intravenous only

DISPENSED: _x_ Rx ___ OTC

CHEMICAL NAME, STRUCTURAL & MOLECULAR FORMULA, MOL. W.T.:

aztreonam

Chemical Name/Structure	=	See 1998 USAN (Pages 75 & 76)
Molecular Formula	=	$C_{13}H_{17}N_5O_8S_2$
Molecular Weight	=	435.44
CAS #:	=	*CAS-78110-38-0*

AMENDMENT(S):

The Amendment to the Supplement is the Applicant's response to the Agency's "approvable" letter, dated 7/18/97, on requested labeling changes, on NDA 50-632/ and on requested labeling changes, on NDA 50-632/SEI-010, on 8/20/96.

RELATED DOCUMENTS (if applicable):

a. Bristol-Myers Squibb Company, NDA 50-580, AZACTAM® (aztreonam for injection, USP), and "approved" on 12/31/86.

b. Bristol-Myers Squibb Company, NDA 50-632, AZACTAM® (aztreonam injection) in single dose Viaflex® Plus Plastic Container (PL 146®) containing either 1 g or 2 grams of aztreonam, and "approved" on 5/24/89.

c. Bristol-Myers Squibb Company, NDA 50-632, AZACTAM® (aztreonam injection) in single dose AZACTAM® (aztreonam) in Galaxy® Plastic Container (PL 2040) for IV Use, and "approved" on 5/24/89. It contained either 1 g or 2 grams of aztreonam.

CONSULTS: N/A

REMARKS/COMMENTS:

This drug is the subject of the compendial monographs 23 USP (Aztreonam), on page 155, and 23 USP (Aztreonam injection), on page 155, respectively.

CONCLUSIONS:

From the microbiological perspective, an "approval" letter should be issued to Bristol-Myers Squibb Company, after negotiation of the most current revised "draft" labeling on NDA 50-632 SEI-010. This includes all the Agency's labeling recommendations on the **CLINICAL PHARMACOLOGY – Microbiology** and **Susceptibility Tests** subsections, and the **REFERENCES** section, found in this Review on pages 7 to 12, 17 to 21, and 22 to 27, respectively.

CLINICAL MICROBIOLOGICAL REVIEW

TABLE OF CONTENTS

INTRODUCTION

The Amendment to the Supplement is the Applicant's response to the Agency's "approvable" letter, dated 7/18/97, on requested labeling changes, on NDA 50-632 and on requested labeling changes, on NDA 50-632/SEI-010, on 8/20/96.

Notes to Reader:

1. Applicant's revisions:

- Addition/Replacement/Revision = highlighted (e.g. AZACTAM now written as aztreonam).

2. Microbiologist's revisions:

- Deletion = ~~strikeout~~ and highlighted (e.g. ~~AZACTAM~~); and

- Addition/Replacement/Revision = highlighted (e.g. AZACTAM now written as aztreonam).

Redacted 22

pages of trade

secret and/or

confidential

commercial

information

From the microbiological perspective, an "approval" letter should be issued to Bristol-Myers Squibb Company, after negotiation of the most current revised "draft" labeling on NDA 50-632 and SEI-010. This includes all the Agency's labeling recommendations on the **CLINICAL PHARMACOLOGY – Microbiology** and **Susceptibility Tests** subsections, and the **REFERENCES** section, found in this Review on pages 7 to 12, 17 to 21, and 22 to 27, respectively.

/S/

Harold V. Silver
Clinical Microbiology Reviewer
DAIDP/HFD-520

cc: Orig. NDA 50-632
HFD-638
520/Division File
HFD-520/Micro/HVSilver
HFD-520/TLMO/Malbueme
HFD-520/TLPharm/Kseethaler
HFD-520/Chem/JTimper
HFD-520/ProjMgr/STrostle
HFD-520/REV by HVS:10/07;10/27/98
Filename: 50632S9.FIN
APPROVAL

Concurrence Only:
HFD-520/DivDir/GChikami
HFD-520/DepDvDir/LGavrilovich
HFD-520/TLMicro/ATSheldon
R/D init. by ATSheldon:
RD# 1 initialed 9/9/98
Final 10/26/98
10/27/98
10/28/98