



NDA 50-580/S-033  
NDA 50-632/S-011

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

Dear Dr. Linkewich:

Please refer to your supplemental new drug applications dated August 24, 2000, received August 30, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Azactam<sup>®</sup> (aztreonam for injection, USP) (NDA 50-580) and Azactam<sup>®</sup> (aztreonam injection) (NDA 50-632). We note that these applications are subject to the exemption provisions contained in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

We acknowledge receipt of your submissions dated November 21, 2001.

These supplemental new drug applications provide for geriatric use information submitted in compliance with the geriatric use labeling regulations as found in 21 CFR 201.57 (f)(10).

We have completed the review of these supplemental applications, 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 agreed upon labeling text and with the revisions listed below. Accordingly, these supplemental applications are approved effective on the date of this letter.

The revisions are as follows:

### **Geriatric Use**

Clinical studies of AZACTAM did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.<sup>7-10</sup> In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

In elderly patients, the mean serum half-life of aztreonam increased and the renal clearance decreased, consistent with the age-related decrease in creatinine clearance.<sup>1-4</sup> Since aztreonam is known to be substantially excreted by the kidney, the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have

decreased renal function, renal function should be monitored and dosage adjustments made accordingly (see **DOSAGE AND ADMINISTRATION: Renal Impairment in Adult Patients and Dosage in the Elderly**).

AZACTAM contains no sodium.

## REFERENCES

1. Naber KG, Dette GA, Kees F, Knothe H, Grobecker H. Pharmacokinetics, *in vitro* activity, therapeutic efficacy, and clinical safety of aztreonam vs. cefotaxime in the treatment of complicated urinary tract infections. *J Antimicrob Chemother* 1986; 17:517-527.
2. Creasey WA, Platt TB, Frantz M, Sugerman AA. Pharmacokinetics of aztreonam in elderly male volunteers. *Br J Clin Pharmacol* 1985; 19:233-237.
3. Meyers BR, Wilkinson P, Mendelson MH, *et al*. Pharmacokinetics of aztreonam in healthy elderly and young adult volunteers. *J Clin Pharmacol* 1993; 33:470-474.
4. Sattler FR, Schramm M, Swabb EA. Safety of aztreonam and SQ 26,992 in elderly patients with renal insufficiency. *Rev Infect Dis* 1985; 7 (suppl 4):S622-S627.
5. National Committee for Clinical Laboratory Standards. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*—Fifth Edition. Approved Standard NCCLS Document M7-A5, Vol. 20, No. 2, NCCLS, Wayne, PA, January 2000.
6. National Committee for Clinical Laboratory Standards. *Performance Standards for Antimicrobial Disk Susceptibility Tests*—Seventh Edition. Approved Standard NCCLS Document M2-A7, Vol. 20, No 1, NCCLS, Wayne, PA, January 2000.
7. Deger F, Douchamps J, Freschi E, *et al*: Aztreonam in the treatment of serious gram-negative infections in the elderly. *Int J Clin Pharmacol Ther and Toxicol* 1988; 26: 22-26.
8. Knockaert DC, Dejaeger E, Nestor L, *et al*: Aztreonam-flucloxacillin double beta-lactam treatment as empirical therapy of serious infections in very elderly patients. *Age and Aging* 1981; 20:135-139.
9. Roelandts F. Clinical use of aztreonam in a psychogeriatric population. *Acta Clin Belg* 1992; 47:251-255.
10. Andrews R, Fasoli R, Scoggins WG, *et al*. Combined aztreonam and gentamicin therapy for pseudomonal lower respiratory tract infections. *Clin Therap* 1994; 16:236-252.

11. National Committee for Clinical Laboratory Standards. *Performance Standards for Antimicrobial Susceptibility Testing*—Eleventh Informational Supplement, NCCLS Document M100-S11, Vol. 21, No 1, NCCLS, Wayne, PA, January 2001.

The final printed labeling (FPL) must be identical, and include the revisions indicated, to the submitted draft labeling (package insert submitted November 21, 2001). These revisions are terms of the approval of these applications.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no 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 50-580/S-033, 50-632/S-011." 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-42  
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 Professional" 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, MD 20857

Please submit one market package of the drug product when it is available.

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

NDA 50-580/S-033

NDA 50-632/S-011

Page 4

If you have any questions, call Susmita Samanta, M.D., Regulatory Project Manager, at (301) 827-2125.

Sincerely,

*{See appended electronic signature page}*

Janice M. Soreth, M.D.

Director

Division of Anti-Infective Drug Products

Office of Drug Evaluation IV

Center for Drug Evaluation and Research

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

/s/

-----  
Janice Soreth  
3/25/02 03:01:12 PM