CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050823Orig1s000

SUMMARY REVIEW

Deputy Division Director's Action Summary Memorandum

Date	June 13, 2011
From	Katherine Laessig, MD
Subject	Action Summary Memo
NDA/BLA # Supplement#	NDA 50-823
Applicant	B. Braun Medical, Inc.
Date of Submission	August 13, 2010
PDUFA Goal Date	June 13, 2011
Proprietary Name / Established (USAN) names	Ceftazidime for Injection and Dextrose Injection in the Duplex® Container
Dosage forms / Strength	1 g and 2 g
Proposed Indication	1. Lower respiratory tract infections 2. Skin and skin structure infections 3. Bacterial septicemia 4. Bone and joint infections 5. Gynecologic infections 6. Intra-abdominal infections 7. Central nervous system infections (b) (4) [redacted]
Recommended:	Approval for indications 1-7

1.0 Background

Ceftazidime is an injectable, cephalosporin in the β-lactam class of antibacterial agents. Its mechanism of action is bactericidal via inhibition of cell wall synthesis by binding to penicillin-binding proteins found in the bacterial cell wall of both Gram-positive and Gram-negative bacteria. The applicant, B. Braun Medical, Inc., has submitted NDA 50-823 in support of 1 and 2 g Ceftazidime for Injection and Dextrose for Injection in the Duplex Container. The application is submitted under 505(b)(2) of the FD&C Act, contains no new clinical studies, and relies on the Agency's previous finding of safety and effectiveness for the reference listed drug product, ceftazidime for injection (FORTAZ®, manufactured by GlaxoSmithKline, NDA 50-578, approved 7/19/85).

The indications for which the applicant is seeking approval are identical to those approved for FORTAZ and are listed above, with the exception of empiric therapy for sepsis and intraperitoneal dialysis and continuous ambulatory dialysis.

This memo will summarize elements of all relevant reviews by discipline. For more detailed discussions, please refer to the CDTL memo by Dr. Janice Pohlman, the CMC review by Dr. Milton Sloan, the Product Quality Microbiology review by Dr. Steven Fong, the review of the safety update by Dr. Alma Davidson, and consults by DMEPA and DDMAC. Note that there is no new pharmacology/toxicology, clinical pharmacology, clinical microbiology, or other clinical data contained in this application.

2.0 Summary of Chemistry, Manufacturing, and Controls

This application is recommended for approval by the CMC reviewer, Dr. Milton Sloan and by the Product Quality Microbiology reviewer, Dr. Steven Fong. Ceftazidime is the drug substance and has a USP monograph. (b) (4)

Ceftazidime for Injection, USP (sterile bulk), manufactured by (b) (4) is a sterile (b) (4) mixture of ceftazidime pentahydrate, USP and (b) (4) sodium carbonate, USP. Ceftazidime for Injection USP and Dextrose for Injection USP in the Duplex (b) (4) Container is sterile, nonpyrogenic and packaged in a single use, dual chamber container. The finished drug product consists of sterile Ceftazidime for Injection USP in one chamber and 5% Dextrose for Injection USP in the other chamber. The two chambers are separated by a peelable seal which is activated prior to use. The peelable foil is removed to permit the powder to be inspected. To reconstitute the drug with the diluent vehicle, the peelable seal is activated by applying pressure on the diluent chamber, followed by activation of the second seal between the drug chamber and the forward compartment containing the administration port.

Ceftazidime for Injection USP and Dextrose for Injection USP in the Duplex Container is expected to remain stable on storage throughout the proposed shelf life of 9 months at 25°C, for seven days after the removal of the foil strip, for twelve hours after activation/reconstitution at 25°C or 3 days under refrigeration (5°C). Therefore, the Applicant's proposed expiry of nine months under room temperature conditions was found to be acceptable.

All facilities including that of the Applicant, (b) (4), and Irvine, CA have been found to be acceptable by the office of Compliance as noted in the Establishment Evaluation System (EES) reports.

3.0 Summary of Safety Update

The medical reviewer, Dr. Alma Davidson, recommends approval of this application as does the CDTL, Dr. Janice Pohlman. The safety evaluation was based on recent literature relevant to the clinical safety of ceftazidime and dextrose solution as provided by the applicant, and a separate literature search conducted by Dr. Davidson. The Office of Surveillance and Epidemiology-Division of Pharmacovigilance II was consulted for analysis of selected adverse drug reactions associated with ceftazidime in the AERS database. Based on the literature and the results of the AERS database search, language has been added to the postmarketing adverse reactions section of the label as follows: nephropathy which may be severe (e.g. renal failure). Articles related to allergic reactions to dextrose-containing solutions in patients with a history of corn allergy/hypersensitivity support the addition of language to the Warnings and Precautions section of the label, as follows:

"Hypersensitivity reactions, including anaphylaxis, have been reported with administration of dextrose containing products. These reactions have been reported in patients receiving high concentrations of dextrose (i.e. 50% dextrose). The reactions have also been reported when corn-derived dextrose solutions were administered to patients with or without a history of hypersensitivity to corn products."

4.0 Summary of Other Regulatory Issues

DMEPA has provided recommended revisions for the container and container labeling, as well as for the carton labeling that have been accepted by the Applicant. DDMAC has provided edits to the package insert.

This application did not require a pediatric assessment under PREA since the drug product does not contain or involve a new 1) active ingredient(s); 2) indication(s); 3) dosage form; 4) dosage regimen; or 5) route of administration.

5.0 Regulatory Action

I concur with the findings and recommendations of the review team that this application contains sufficient information to support approval of Ceftazidime for Injection and Dextrose for Injection 1 and 2 g.

Katherine A. Laessig, M.D.

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/s/

KATHERINE A LAESSIG
06/13/2011