CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-821

SUMMARY REVIEW

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 05-04-10

FROM: Katherine A. Laessig, M.D.
Deputy Director
Division of Anti-infective and Ophthalmology Products

TO: Division File

SUBJECT: Deputy Division Director's Decisional Memo for NDA 50-821 cefepime for injection USP and dextrose for injection USP in the Duplex® III Container, 1 g in 50 mL and 2 g in 50 mL

1.0 Background

This is the 2nd cycle for this 505(b)(2) application for cefepime injection in Duplex container. The applicant submitted information to address the deficiencies in the complete response action letter of July 21, 2009, on November 6, 2009. Please refer to my decisional memo of July 21, 2009, for further details regarding the first review cycle. In brief, the application received a complete response because the Office of Compliance had issued a withhold status because the manufacturing sites were not in compliance with Good Manufacturing Practices. There was the potential for pending action against the contracted drug substance manufacturing facility, (b) (4) The site had been issued a 483 after inspection listed multiple violations. In addition, the supporting DMF (b) (4) had a deficient status.

This memo will summarize elements of reviews that were necessary to evaluate the resubmission, specifically chemistry, manufacturing, and controls, and clinical.

2.0 Summary of Chemistry, Manufacturing, and Controls

This application is recommended for approval by the CMC reviewer, Milton Sloan, PhD, because the Office of Compliance has issued a final overall site recommendation of acceptable. The applicant has submitted an updated DMF that has been found to be adequate. The applicant has agreed to the proposed

labeling revisions and there are no outstanding inspection issues or labeling comments.

3.0 Summary of Safety

The applicant submitted a safety update as required, which consisted of a review of publications covering the 120 day period from February 10, 2009, to October 22, 2009. Their search yielded 86 new publications, the majority of which dealt predominantly with in vitro issues, efficacy, and PK/PD. Eight related to the safety of cefepime and have been reviewed by Dr. Alma Davidson. One of the articles discusses an association between cefepime use and non-convulsive status epilepticus, which will be added to the package insert. There were no other new safety signals identified, and Dr. Davidson recommends approval of this application. The medical officer team leader, Dr. Janice Pohlman, concurs with this recommendation.

4.0 Other Regulatory Issues

The application does not have a requirement to conduct pediatric studies because it is not for new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. It should also be noted that the RLD contains pediatric use information for all ages except neonates < 2 months.

The Division of Medication Error Prevention and Analysis conducted a review of the carton and container labels, and have provided the following recommendations:

A. Cefepime/Dextrose Duplex Carton (all strengths)

1. Present the strength “Equivalent to 1 g Cefepime (5% w/v Dextrose)” and “Equivalent to 2 g Cefepime (5% w/v Dextrose)” in the same font size as or greater than the company logo “B|BRAUN”

B. Cefepime/Dextrose Duplex Container Label (all strengths)

1. Delete the statement “U.S. Patent Nos. D388.168… and 6,996.951” and include this information in the insert labeling.
2. Delete the statement “Duplex® Drug Delivery System” and “Duplex is a registered trademark of B. Braun Medical Inc.” and include this information in the insert labeling.
3. Delete B. Braun Medical Inc.’s address as this information is included in the insert labeling.

C. Cefepime/Dextrose Duplex Container Label - Drug Chamber Label (all strengths)

1. Revise the statement (b) (4) with “Peel foil strip only when ready for use to visually inspect drug prior to reconstitution”
2. Delete the statement ‘(b) (4) as this information is included in the Container Label.

These comments have been conveyed to the applicant. They have the potential to make the presentation clearer, but do not necessarily represent a safety concern and will likely be implemented post-approval.

5.0 Recommendation

I agree with the recommendation of the review team that since the CMC deficiencies have been satisfactorily resolved, and as the applicant and the Division have agreed upon the package insert, this application will be approved.

Katherine A. Laessig, M.D.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50821	ORIG-1	B BRAUN MEDICAL INC	CEFEPIME

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/s/

KATHERINE A LAESSIG
05/06/2010