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RESEARCH**

*APPLICATION NUMBER:*

**50-817**

**CLINICAL PHARMACOLOGY AND  
BIOPHARMACEUTICS REVIEW(S)**

NDA#	50-817
PRODUCT	Cefepime Hydrochloride
FORMULATION	Cefepime Injection in GALAXY Containers, 1g/50ml and 2g/100ml
SUBMISSION DATE	February 28, 2007
SUBMISSION TYPE	Original 505(b)(2) NDA
SPONSOR	Baxter Healthcare Corporation, 1620 Waukegan Road, McGaw Park, IL 60085
REVIEWER	Jeffrey J. Tworzyanski, Pharm.D.
ACTING TEAM LEADER	Charles R. Bonapace, Pharm.D.

## CLINICAL PHARMACOLOGY REVIEW

### BACKGROUND:

Baxter Healthcare Corporation submitted a New Drug Application (NDA) to obtain approval to market cefepime injection in GALAXY containers 1g/50 ml and 2g/100 ml. In a teleconference between the Agency and the sponsor on April 24, 2006, the Agency agreed that no bioequivalence or bioavailability studies would be needed to support this application. Based on 21 CFR 320.22(b), the in vivo bioavailability or bioequivalence of the drug product may be self-evident if 1) it is a parenteral solution intended solely for administration by injection, and 2) contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application. Baxter's proposed premixed Cefepime Injection products are designed to be "ready to use" versions of cefepime hydrochloride (Maxipime) that require no reconstitution prior to use. The indications, route of administration, and dosing regimen (frequency and duration) for Baxter's IV products will be identical to Maxipime when reconstituted for IV administration.

A comparison of the formulations of Maxipime in Abbott's ADD-VANTAGE system and Baxter's proposed premixed Cefepime Injection products is shown in the table below.

	MAXIPIME for Injection (ADD-VANTAGE Vial)	Reconstituted MAXIPIME (ADD-VANTAGE)	Baxter Premixed Cefepime Injection
Doses of Cefepime (as Cefepime Hydrochloride)	1g  2g	1g/50ml 1g/100ml 2g/50ml 2g/100ml	1g/50ml   2g/100ml
L-Arginine	Approximately 725 mg/g cefepime	Approximately 725 mg/g cefepime	Approximately 725 mg/g cefepime
Diluent	None	5% Dextrose or 0.9% Sodium Chloride	<del>5% Dextrose or 0.9% Sodium Chloride</del>
Hydrochloric Acid	None <sup>2</sup>	None <sup>2</sup>	Used for pH adjustment
pH	N/A	4.0-6.0	4.0-6.0
Osmolality	N/A	Approximately 469 mOsmol/kg (measured by Baxter)	Iso-osmotic (Approximately 300 mOsmol/kg)

N/A: Not Applicable

<sup>2</sup>

b(4)

b(4)

Baxter Healthcare Corporation requested a waiver of the requirements for evidence of *in vivo* bioavailability data. The sponsor states that "the proposed product is a ready to use version of MAXIPIME, the reference listed drug (NDA 50-679, held by Bristol-Myers Squibb, approved on 1/18/96). The safety and effectiveness of the proposed drug product is based on the Agency's previous determination of the safety and effectiveness of MAXIPIME." The product's self-evident *in vivo* bioavailability is based on the fact that Cefepime Injection in GALAXY containers is intended solely for administration by injection, having the same active and inactive ingredients, in the same concentration to the reconstituted drug product that is the subject of an approved full new drug application. Based on 21 CFR 320.22(b), the sponsor meets the requirements for granting a waiver of evidence of *in vivo* bioavailability for parenteral products intended solely for administration by injection. No further studies are necessary to support the *in vivo* bioavailability of Cefepime injection in GALAXY containers.

**LABELING RECOMMENDATIONS:**

The reviewer has no labeling comments.

**RECOMMENDATIONS:**

This application was reviewed by the Office of Clinical Pharmacology, Division of Clinical Pharmacology 4, and found to be acceptable from a clinical pharmacology point of view.

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Jeffrey J. Tworzyanski, Pharm.D.  
Office of Clinical Pharmacology  
Division of Clinical Pharmacology 4

RD/FT Initialed by Charles R. Bonapace, Pharm.D., \_\_\_\_\_  
Acting Team Leader

cc:

Division File: NDA 50-817

HFD-520 (CSO/Hyon)

HFD-520 (MO/Davidson, Nambiar)

HFD-880 (Division File, Lazor, Reynolds, Bonapace, Tworzyanski)

CDR (Clin. Pharm.)

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/s/

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Jeffrey Tworzyanski  
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