CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-796

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

Clinical Pharmacology and Biopharmaceutics Review
Division of Pharmaceutical Evaluation III

NDA:	50-796
Drug:	Ceftriaxone Sodium/Dextran Injection in Duplex Container
Sponsor:	B Braun Medical Inc.
Date of Submission:	6/18/04
Type of Submission:	Original NDA (505(b)(2) application)
Reviewer:	Venkateswar R. Jarugula, Ph.D.

1. EXECUTIVE SUMMARY

B. Braun Medical Inc. has submitted this 505(b)(2) NDA for ceftriaxone for Injection and Dextrose for Injection in the DUPLEX container based on the reference listed drug, ROCEPHIN®. The NDA 50-585 for ROCEPHIN was approved on December 21, 1984. Ceftriaxone for Injection and Dextrose for Injection in the DUPELX container is intended for intravenous use only. It is indicated for the identical intravenous clinical indications as the reference listed drug, ROCEPHIN. Previously B. Bruan has secured approval of two antibiotics with Duplex container: Cefazolin for Injection USP and Dextrose Injection USP in the DUPLEX container (NDA 50-779, approved on 7/27/00) and Cefuroxime for Injection USP and Dextrose Injection USP in the DUPLEX Container (NDA 50-780, approved on 02/21/01).

The DUPLEX container is a patented drug delivery system consisting of a dual chamber, PVC free, DEHP-free and latex-free [redacted] container. The diluent chamber contains 50 ml of sterile dextrose diluent and the drug chamber contains either 1 g or 2 g ceftriaxone powder. Ceftriaxone for Injection and Dextrose Injection in the DUPLEX container contains the same active ingredient in the identical amounts as the reference listed drug, ROCEPHIN. Hence, in accordance with 21 CFR320.22(b)(1), the sponsor's request for a waiver for submission of evidence demonstrating the in vivo bioavailability data can be granted.

In the current submission, the sponsor provided an updated label with respect to drug interactions. The purpose of this review is to evaluate the drug interactions update in the label.

The following labeling language should be included in the Drug Interaction section of the label:

[redacted]

2. RECOMMENDATION

NDA 50-796 has been reviewed by the Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation III and it is acceptable from Clinical Pharmacology and Biopharmaceutics perspective. Please convey the Labeling comments to the sponsor as appropriate.

Venkateswar R. Jarugula, Ph.D.

RD initialed by Arzu Selen, Ph.D., Deputy Director, HFD-880 _____

FT signed by Arzu Selen, Ph.D., Deputy Director, HFD-880_____

cc: NDA50-796, HFD-520 (Nambiar, Davidson), HFD-880 (Lazor, Selen, Jarugula), CDR (B.Murphy for Drug).

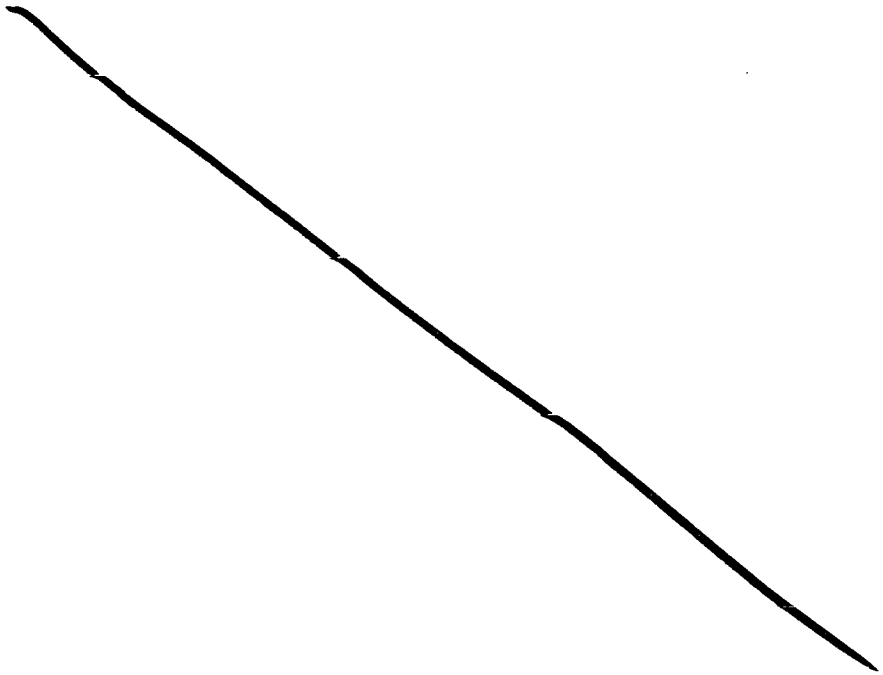
3 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Clin Pharm/Bio- 1



3.2 Biopharmaceutics

3.2.1 How does the formulation of the proposed product compare with the reference listed drug product, ROCEPHIN?

The composition of the proposed product and the RLD, ROCEPHIN are summarized in the table below:

Table 2. Formulation comparison between ROCEPHIN and B.Braun's Ceftriaxone

Component	ROCEPHIN (RLD)	B.Braun Ceftriaxone
Ceftriaxone Free Acid	1g	1g
Dextrose Injection (reconstitution diluent)		
Ceftriaxone Free Acid		
Dextrose Injection (reconstitution diluent)		

1 After reconstitution

As noted above the B.Braun's Ceftraixone in Duplex container contains identical amount of active ingredient, ceftriaxone, as that of ROCEPHIN, the RLD. To make the reconstituted product in the DUPLEX container iso-osmotic, the Dextrose concentration was adjusted.

3.2.2 What is the relative bioavailability of the proposed drug product compared to the approved product (reference listed drug)?

The sponsor of the current application did not conduct any bioavailability studies or clinical studies. The NDA is a 505(b)(2) application based ROCEPHIN for injection, the reference listed product (RLD). Ceftriaxone for Injection and Dextrose Injection in the DUPLEX container contains the same active ingredient in the identical amounts as the reference listed drug, ROCEPHIN. The changes in Dextrose concentration in DUPLEX container should not have any impact on the bioavailability of ceftriaxone as the proposed product is intended for intravenous administration. Therefore, in accordance with 21 CFR320.22(b)(1), the sponsor request for a waiver for submission of evidence demonstrating the in vivo bioavailability data can be granted.

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/s/

Venkateswar Jarugula
4/18/05 09:47:20 AM
BIOPHARMACEUTICS

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4/18/05 10:07:52 AM
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