CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-796

CHEMISTRY REVIEW(S)

NDA 50-796

Ceftriaxone/Dextrose injection in Duplex container®

B Braun Inc.

Andrew Yu
DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS, HFD-520

Table of Contents

Chemistry Review Data Sheet

1. NDA 50-796

2. REVIEW #:1

3. REVIEW DATE: 1/20/05

4. REVIEWER: Andrew Yu

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
IND 67794	3/3/04
Pre-IND (NDA) 67794 meeting minute	5/13/04
NDA checklist review	8/4/04

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
NDA 50-796 (Original Submission)	6/21/04
NDA 50-796 BC (Deletion of comparability protocol)	1/27/05
NDA 50-796 BC (Update of stability data)	2/ 11/05
NDA 50-796 BC (Add [redacted])	2/15/05 (Faxed in on 2/14/05) Microbiology information
NDA 50-796 BC (Response to deficiency)	3/14/05
NDA 50-796 BC (Container & container label)	3/23/05

7. NAME & ADDRESS OF APPLICANT:

Executive Summary Section

Name:	B Braun Inc
Address:	B. Braun Medical Inc. 2525 McGaw Avenue, P.O. Box 19791, Irvine, CA 92623-9791
Representative:	Richard Bourne, VP, Regulatory Affairs
Telephone:	(610) 596-2517

8. DRUG PRODUCT NAME/CODE/TYPE: Injection

a) Proprietary Name: Ceftriaxone/Dextrose injection in Duplex container®
b) Non-Proprietary Name (USAN): Ceftriaxone sodium
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):
- Chem. Type: 5
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(2)

10. PHARMACOL. CATEGORY: Anti-infective

11. DOSAGE FORM: Injection

12. STRENGTH/POTENCY: 1 and 2 g

13. ROUTE OF ADMINISTRATION: IV

14. Rx/OTC DISPENSED: __x_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

Executive Summary Section

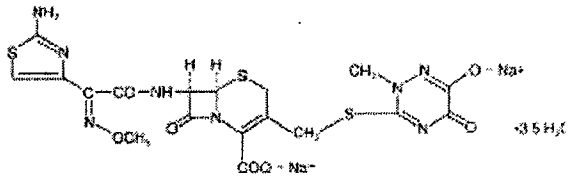
_____SPOTS product – Form Completed

___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Ceftriaxone sodium $C_{18}H_{16}N_8Na_2O_7S_3\ 3.5H_2O$
(6R,7R)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-8-oxo-3-[[(1,2,5,6-tetrahydro-2-methyl-5,6-dioxo-as-triazin-3-yl)thio]-methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7^2-(Z)-(O-methyloxime), disodium salt, sesquaterhydrate CAS: 104376-79-6

M.W. 661.60



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
[redacted]	II	[redacted]	[redacted]	1	Inadequate. Adequate	1/23/05 3/30/05	Reviewed by OGD., S. Zuk Reviewed by A. Yu
	II			1	Inadequate Adequate	1/21/05 3/30/05	Reviewed by OGD., S. Zuk Reviewed by A. Yu

Executive Summary Section

III		1	Adequate	1/13/97	Fina copolymer was reviewed by RO. Riggleman and reviewed 6/1/04 by A. Yu
III		1	Adequate	6/1/04	Deficiency letter issued in 6/2/94 by R. M. Patel and responded by DMF holder. Reviewed by A. Yu for [redacted]
III		4	Adequate		Not in contact with drug diluent. See review for 50-780 on 10/25/00 by S. Pagay on the same duplex container
III		4	Adequate		Not in contact with drug diluent. Reviewed for 50-780 on 10/25/00 by S. Pagay on the same duplex container
III		4	Adequate	6/25/02	Not in contact with drug diluent. See review for 50-780 on 10/25/00 by S. Pagay on the same duplex container
III		3	Adequate	3/10/03	E. Chikhale

					HFD-510. Fasson adhesive is adequate.
	III		4	Adequate	Not in contact with drug diluent
	III		3	Adequate	2/05/01	Adequate by Gantam Basak, NAM.

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION STATUS	DATE	REVIEWER
EES	Acceptable	11/1/04	Janine D Ambrogio
Pharm/Tox	Pending	3/30/05	Terry Peters
Biopharm	None		V. Jarugula
LNC	None (not new drug)		
Methods Validation		1/12/05	Method validated by FDA lab not recommended, reviewed by A. Yu
EA	Categoric exclusion waiver found acceptable	6/12/05	Andrew Yu
Microbiology	Acceptable	3/30/05	John Metcaffe

The Chemistry Review for NDA 50-796

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Recommend approval from CMC view point. The label is pending final revision; all other CMC deficiencies are resolved, and all facility inspections are acceptable.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

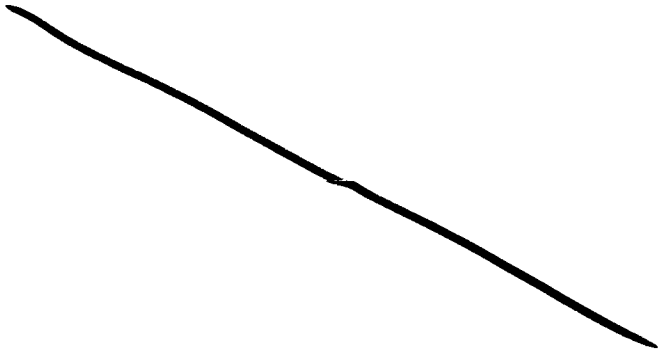
A. Description of the Drug Product(s) and Drug Substance(s)
Ceftriaxone sodium is a semi-synthetic broad spectrum cephalosporin antibiotic for parenteral administration. Its molecular formula is $C_{18}H_{16}N_8Na_2O_7S_3\,3.5H_2O$. Ceftriaxone sodium drug substance is available as the sodium salt, and is a white crystalline powder with a molecular weight of 661.60. Ceftriaxone sodium contains approximately 83 mg (3.6 mEq) of sodium per gram of Ceftriaxone activity. Ceftriaxone for Injection USP and Dextrose Injection is a sterile, nonpyrogenic, single use, packaged combination of Ceftriaxone Sodium and Dextrose Injection (diluent) in the DUPLEX sterile container. The DUPLEX Container is a flexible dual chamber container.

Excessive moisture and heat can cause decomposition of Ceftriaxone sodium. Under the dry storage conditions employed in manufacturing, Ceftriaxone sodium is stable and several known and unknown impurities are adequately controlled with specifications in the DMF. B Braun used the USP and a developed and validated analytical methods for Ceftriaxone, related impurities, and stability study. Ceftriaxone/Dextrose injection in Duplex™ are injections each containing 1 and 2 g Ceftriaxone activity after reconstitution. Dextrose hydrous USP has been added to the diluent to adjust the product to be iso-osmotic (approximately 1.87 g and 1.11 g to 1 g and 2 g dosages, respectively). Hydrous Dextrose content are [redacted] in the 1 g and 2 g doses, respectively. The product is packaged in Duplex container containing 50 mL of final solution after reconstitution.

Executive Summary Section

B. Description of How the Drug Product is Intended to be Used
Ceftriaxone for Injection USP and Dextrose Injection is indicated for the treatment of several types of infections when caused by susceptible organisms including lower respiratory tract infections, skin and skin structure infections, urinary tract infections and other indicated infections described in the package insert. Ceftriaxone for Injection USP and Dextrose Injection is a sterile, injection for single use. The 1 and 2 g injections are available in 50 mL injection in Duplex and provides an approximately iso-osmotic solution after reconstitution. The proposed storage condition is: Store the unactivated unit at 20-25°C (68-77°F). Excursions permitted to 15-30°C (59-86°F). Following reconstitution (activation), the product must be used within 24 hours if stored at room temperature or within 7 days if stored under refrigeration.

C. Basis for Approvability or Not-Approval Recommendation



III. Administrative

A. Reviewer's Signature

B. Endorsement Block

ChemistName/Date: Same date as draft review
ChemistryTeamLeaderName/Date
ProjectManagerName/Date

C. CC Block

58 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

*Withheld Track Number: Chemistry-*1

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

/s/

Andy Yu
4/18/05 04:23:05 PM
CHEMIST

Jim Vidra
4/18/05 04:27:52 PM
CHEMIST