CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-780

CHEMISTRY REVIEW(S)

AUG 7 200

REVIEW FOR HFD-520

OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805
Microbiologist's Review #1 of NDA 50-~~779~~ 780

August 2, 2000

A. 1. APPLICATION NUMBER: 50-780

APPLICANT: B. Braun Medical, Inc.
2525 McGaw Avenue
P.O. Box 19791
Irvine, CA 92623-9791
(tel) 949-660-2401

2. **PRODUCT NAME:** Cefuroxime for Injection USP and Dextrose Injection USP in the DUPLEX™ Container

3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:** Dual chamber plastic container. The diluent chamber contains 50 mL of sterile iso-osmotic dextrose solution, and the drug chamber contains either 750 mg or 1.5 gram of the sterile API. For intravenous administration.

4. **METHODS OF STERILIZATION:** [redacted]

5. **PHARMALOGICAL CATAGORY and/or PRINCIPLE INDICATION:** Cephalosporin class antibiotic indicated for treatment of serious infections due to susceptible organisms.

6. **DRUG PRIORITY CLASSIFICATION:** S

B. 1. DATE OF INITIAL SUBMISSION: April 17, 2000

2. **DATE OF CONSULT:** May 18, 2000

3. **ASSIGNED FOR REVIEW:** June 12, 2000

4. **RELATED DOCUMENTS:** NDA 50-779

C. REMARKS: The bulk sterile active pharmaceutical ingredient is the subject of the approved [redacted] The sterilization process validation information of NDA 50-780 is identical to that submitted under 50-779 (approved 7/27/00).

D. CONCLUSIONS:

The submission is recommended for approval for microbiology issues concerning sterility assurance. Specific comments are provided in section "E. REVIEW NOTES".

/S/ 8/2/00
Neal Sweeney, Ph.D.

/S/ 8/7/00

cc: NDA 50-780
HFD-520/Division File
HFD-520/B. Duvall-Miller (P.M.)
HFD-520/ S. Pagay (Chem.)
HFD-805/Consult File/N. Sweeney

Drafted by: N. Sweeney, August 2, 2000
R/D initialed by P. Cooney, August 2, 2000

13 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 50-780 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 25-Oct-00

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	17-Apr-00	24-Apr-00	27-Apr-00

NAME & ADDRESS OF APPLICANT: B. Braun Medical Inc.
2525 McGaw Avenue
P.O.Box 19791
Irvine, CA 92623-9791

DRUG PRODUCT NAME
Proprietary: Cefuroxime for Injection USP and Dextrose Injection USP in the Duplex Container
Nonproprietary/USAN: NA
Code Names/#'s: NA
Chemical Type/
Therapeutic Class: 5S

ANDA Suitability Petition/DESI/Patent Status:
N/A [if applicable]

PHARMACOLOGICAL CATEGORY/INDICATION:
Antiinfective

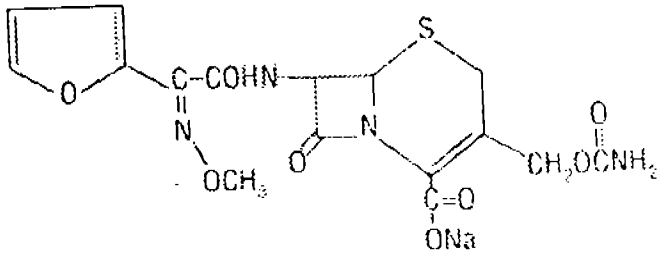
DOSAGE FORM: Powder for reconstitution
STRENGTHS: 0.75 g and 1.5 g

ROUTE OF ADMINISTRATION: Injectable
DISPENSED: X Rx _____ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT: $C_{16}H_{15}N_4NaO_8S$, 446.37

Sodium (6R,7R)-7-[2-(2-furyl)glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate,7^2-(Z)-(O-methyloxime), carbamate (ester)

CAS # 56238-63-2



SUPPORTING DOCUMENTS:

RELATED DOCUMENTS (if applicable):

NDA 50-779 - Cefazolin for Injection and Dextrose for Injection in the Duplex Container. The novel package concept is identical to this NDA.

CONSULTS:

ONDC microbiology for Sterilization validation: The review is completed, and recommended for approval (August 7, 2000). The reviewer indicated that the bulk sterile drug substance is the subject of approved The sterilization process validation information is identical to that submitted under NDA 50-779 which has been approved.

Labeling and Nomenclature committee: Pending

Facilities inspection for Drug substance and Drug product has been completed and the facilities are acceptable (drug substance 5/22/2000 and drug product 7/7/2000)

REMARKS/COMMENTS:

The basis of review for the manufacturing section, packaging components, packaging controls, facilities for the drug product manufacturing, sterilization validation is similar for this application and for the approved NDA 50-779. If

appropriate, reference will be made to CMC reviews for NDA 50-779.

CONCLUSIONS & RECOMMENDATIONS:

The application is not approvable. Please see the attached attached CMC draft of comments and recommendations.

/S/ 10/25/00
Shrikant N. Pagay, Ph.D., Review Chemist

cc: Orig. NDA 50-780
HFD-520/Division File
HFD-520/Pagay/
HFD-520/~~JAlexander~~ J Pahlman
HFD-520/~~Osterberg~~ K. Seethala
HFD-520/Altie
HFD-520/Duvall-Miller
HFD-520/DRoss
R/D Init by: Team Leader/Chem: DKatague /S/ 10/26/00

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DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 50-780 **CHEM.REVIEW #:** 2 **REVIEW DATE:** 1-Feb-01

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	17-Apr-00	24-Apr-00	27-Apr-00
Amendment	21-Dec-00	22-Dec-00	01-Jan-01

NAME & ADDRESS OF APPLICANT: B. Braun Medical Inc.
2525 McGaw Avenue
P.O.Box 19791
Irvine, CA 92623-9791
Contact: John D'Angelo, (949)660-2401

DRUG PRODUCT NAME

Proprietary:	Cefuroxime for Injection USP and Dextrose Injection USP in the Duplex Container
Nonproprietary/USAN:	NA
Code Names/#'s:	NA
Chemical Type/ Therapeutic Class:	**5S**

ANDA Suitability Petition/DESI/Patent Status:
N/A [if applicable]

PHARMACOLOGICAL CATEGORY/INDICATION:
Antiinfective

DOSAGE FORM: Powder for reconstitution
STRENGTHS: 0.75 g and 1.5 g

ROUTE OF ADMINISTRATION: Injectable
DISPENSED: __X__ **Rx** _____ **OTC**

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT: $C_{16}H_{15}N_4NaO_8S$, 446.37

Sodium (6R,7R)-7-[2-(2-furyl)glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate,7^2-(Z)-(O-methyloxime), carbamate (ester)

CAS # 56238-63-2

SUPPORTING DOCUMENTS:

RELATED DOCUMENTS (if applicable):

NDA 50-779 - Cefazolin for Injection and Dextrose for Injection in the Duplex Container. The novel package concept is identical to this NDA.

CONSULTS:

ONDC microbiology for Sterilization validation: The review is completed, and recommended for approval (August 7, 2000). The reviewer indicated that the bulk sterile drug substance is the subject of approved [redacted] The sterilization process validation information is identical to that submitted under NDA 50-779 which has been approved.

Labeling and Nomenclature committee: ??????

Facilities inspection for Drug substance and Drug product has been completed and the facilities are acceptable (drug substance 5/22/2000 and drug product 7/7/2000)

Method validation: Satisfactory based on review. The method verification is in progress by FDA lab but will not hold NDA approval for this item.

REMARKS/COMMENTS:

The basis of review for the manufacturing section, packaging components, packaging controls, facilities for the drug product manufacturing, sterilization validation is similar to the approved NDA 50-779 since both applications are for the Duplex® container. If appropriate, reference will be made to CMC reviews for NDA 50-779.

CONCLUSIONS & RECOMMENDATIONS:

The application is not approvable. Please see the attached CMC draft of comments and recommendations.

Shrikant N. Pagay, Ph.D.,
Review Chemist

cc: Orig. NDA 50-780
HFD-520/Division File
HFD-520/Pagay/
HFD-520/JAlexander
HFD-520/Osterberg
HFD-520/Altie
HFD-520/Duvall-Miller
HFD-520/DRoss
R/D Init by: Team Leader/Chem: DKatague _____

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DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 50-780 **CHEM.REVIEW #:** 3 **REVIEW DATE:** 8-Feb-01

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	17-Apr-00	24-Apr-00	27-Apr-00
Amendment	21-Dec-00	22-Dec-00	01-Jan-01
Response to Review 1 comments			
Telecon - 8-Feb-01 discussion of review 2 comments with the applicant			
Amendment	12-Feb-01	12-Feb-01	12-Feb-01
Response to review 2 comments			
General correspondance for concurrence on Regulatory specifications	16-Feb-01	16-Feb-01	16-Feb-01

NAME & ADDRESS OF APPLICANT: B. Braun Medical Inc.
2525 McGaw Avenue
P.O.Box 19791
Irvine, CA 92623-9791
Contact: John D'Angelo, (949)660-2401

DRUG PRODUCT NAME

Proprietary:	Cefuroxime for Injection USP and Dextrose Injection USP in the Duplex Container
Nonproprietary/USAN:	NA
Code Names/#'s:	NA
Chemical Type/ Therapeutic Class:	5S

ANDA Suitability Petition/DESI/Patent Status:
N/A [if applicable]

PHARMACOLOGICAL CATEGORY/INDICATION:
Antiinfective

DOSAGE FORM: Powder for reconstitution
STRENGTHS: 0.75 g and 1.5 g

ROUTE OF ADMINISTRATION: Injectable
DISPENSED: __X__ **Rx** _____ **OTC**

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT: $C_{16}H_{15}N_4NaO_8S$, 446.37

Sodium (6R,7R)-7-[2-(2-furyl)glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate,7^2-(Z)-(O-methyloxime), carbamate (ester)

CAS # 56238-63-2

SUPPORTING DOCUMENTS:

RELATED DOCUMENTS (if applicable):

NDA 50-779 - Cefazolin for Injection and Dextrose for Injection in the Duplex Container. The novel package concept is identical to this NDA.

CONSULTS:

ONDC microbiology for Sterilization validation: The review is completed, and recommended for approval (August 7, 2000). The reviewer indicated that the bulk sterile drug substance is the subject of approved [redacted] The sterilization process validation information is identical to that submitted under NDA 50-779 which has been approved.

Labeling and Nomenclature committee: No consultation was required since the drug product name is a USP Monograph Title.

Facilities inspection for Drug substance and Drug product has been completed and the facilities are acceptable (drug substance 5/22/2000 and drug product 7/7/2000)

Methods validation: Satisfactory based on review. The method verification is in progress by FDA lab but will not hold NDA approval for this item.

REMARKS/COMMENTS:

This review covers the following items in that order:
Review of 2/12/01 Amendment
Manufacturing facilities
Status of Establishment inspections
Regulatory specifications
Post approval commitments

CONCLUSIONS & RECOMMENDATIONS:

Recommend approval for the chemistry, manufacturing and controls for this application. The CMC information that should be communicated to the applicant is provided as Attachment 1. The regulatory specifications concurred by the applicant (2/16/01 correspondence sent via fax) are provided in Attachment 2.

Shrikant N. Pagay, Ph.D.,
Review Chemist

cc: Orig. NDA 50-780
HFD-520/Division File
HFD-520/Pagay/
HFD-520/JAlexander
HFD-520/Osterberg
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