

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*

**50-739**

**50-749**

**CHEMISTRY REVIEW(S)**

**DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS**  
Review of Chemistry, Manufacturing, and Controls  
**NDA #: 50-749 CHEM.REVIEW #: 1 REVIEW DATE: 5-June-97**

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	30-Dec-96	31-Dec-96	1-Jan-97
AMENDMENT/AC	10-Jan-97	13-Jan-97	15-Jan-97
AMENDMENT/AC	24-Jan-97	27-Jan-97	28-Jan-97

NAME & ADDRESS OF APPLICANT: Parke-Davis Pharmaceutical  
Research  
Division of Warner-Lambert Co.  
2800 Plymouth Road,  
P.O.Box 1047  
Ann Arbor, MI 48106-1047

Contact: Dr. Paul Chen  
Phone: (313) 996-2623

DRUG PRODUCT NAME  
Proprietary: Omnicef® Oral Suspension  
Nonproprietary/USAN: Cefdinir  
Code Names/#'s:  
Chemical Type/  
Therapeutic Class: 38

ANDA Suitability Petition/DESI/Patent Status:  
N/A

PHARMACOLOGICAL CATEGORY/INDICATION: Anti-infective/ For  
treatment of mild to moderate infections.

DOSAGE FORM: Oral Suspension  
STRENGTHS: 125 mg/5 mL  
ROUTE OF ADMINISTRATION: Oral  
DISPENSED:  Rx  OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,  
MOL. WT:

C<sub>14</sub>H<sub>13</sub>N<sub>5</sub>O<sub>5</sub>S<sub>2</sub> M.W. 395.42

[6R-[6α,7B(Z)]]-7-[[ (2-amino-4-thiazolyl) (hydroxyamino) acetyl] amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2ene-2-carboxylic acid

Figure 1: Cefdinir Structural Formula



**SUPPORTING DOCUMENTS:**

IND /  
DMF

DMF

Packaging Components:  
DMF /

**RELATED DOCUMENTS (if applicable):** None

**CONSULTS:**

EA review completed; Fonsi Issued 6/9/97

Nomenclature Committee for trade name Omnicef - Not acceptable to the committee (similar name - Omnipen is a marketed product). Clinical and Project management plans to overrule the recommendation.

Establishment Inspection - Submitted Date 1/27/97. Three drug substance facilities are acceptable (2/5/97). The drug product is pending.

Methods validation - Submitted Date 2/12/97

**REMARKS/COMMENTS:**

The structure relates to cefixime, the acetate group at the ( / is replaced by / )

50 and 100 mg cefdinir capsules were approved in Japan in 1991.

The drug substance is also known as FK482.

NDA 50-749  
Parke-Davis/Warner-Lambert  
Omnicef for Oral Suspension 125 mg/5 mL

page 3

All deficiencies for each Section (example: item 1, 2 etc.) of the Drug Substance and the Drug product are listed at the end of respective sections and compiled

**CONCLUSIONS & RECOMMENDATIONS:**

The application is not approvable for manufacturing and controls under section 507 of the Act. Specific items which are not approvable are identified under the following headings: Drug Substance [Specifications and Analytical methods]; Drug Product [Manufacturer, Specifications and Methods for Drug Product, Container/Closure System, Stability]; Investigational Formulations and Labeling.

Please note that the drug substance related issues based on DMF/ /and related DMF's/ ((intermediates) were addressed to the DMF holder.

The establishment inspection, methods validation and approval of the brand name are pending.

IS/ <sup>D</sup>  
\_\_\_\_\_  
Shrikant N. Pagay, Ph.D. 7/17/97  
Review Chemist

cc: Orig. NDA 50-749 (other NDA's may be included if appropriate)

HFD-520/Division File Filename:N50-749

HFD-520/S.Pagay

HFD-520/Soreth/Viraghavan/Hamilton

HFD-520/Osterberg

HFD-520/Altaie

HFD-520/DuVall-Miller

HFD-520/Katague R/D Init by: Katague

B/K 7/21/97

**DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS**

Review of Chemistry, Manufacturing, and Controls

**NDA #:** 50-749 **CHEM.REVIEW #:** 2 **REVIEW DATE:** 1-Dec-97

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	30-Dec-96	31-Dec-96	1-Jan-97
AMENDMENT/AC -Street address for	10-Jan-97	13-Jan-97	15-Jan-97
		Plants	
AMENDMENT/AC -Summary of MV package (item 4 of NDA)	24-Jan-97	27-Jan-97	28-Jan-97
AMENDMENT/BC -Response to DRAFT deficiency letter (Review 1)	13-Aug-97	14-Aug-97	14-Aug-97
AMENDMENT/BZ -Update of stability data	27-Aug-97	28-Aug-97	28-Aug-97
AMENDMENT -MV dissolution method	29-Sep-97 (desk copy)		30-Sep-97
AMENDMENT/ -Final draft container label	16/Oct-97	17-Oct-97	17-Oct-97
AMENDMENT/BB Response to Biopharm recommendations for the dissolution method and specifications.	20-Oct-97	21-Oct-97	21-Oct-97
AMENDMENT/ -18 month stability data + Container label revision for storage of reconstituted suspension	07-Nov-97 (desk copy)		08-Nov-97
AMENDMENT -Amendment to Post approval stability protocol	18-Nov-97 (desk copy)		19-Nov-97
AMENDMENT -Response to draft Post-Approval Commitments.	25-Nov-97 (desk copy)		26-Nov-97

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Contact: Dr. Paul Chen  
Phone: (313) 996-2623

**DRUG PRODUCT NAME**

**Proprietary:**

**Nonproprietary/USAN:**

**Code Names/#'s:**

**Chemical Type/**

**Therapeutic Class:**

Omnicef® Oral Suspension  
Cefdinir

38

NDA 50-749  
Parke-Davis/Warner-Lambert  
Omnicef for Oral Suspension 125 mg/5 mL

page 2

ANDA Suitability Petition/DESI/Patent Status:

N/A

PHARMACOLOGICAL CATEGORY/INDICATION: Anti-infective/ For treatment of mild to moderate infections.

DOSAGE FORM:

Oral Suspension

STRENGTHS:

125 mg/5 mL

ROUTE OF ADMINISTRATION:

Oral

DISPENSED:

X  Rx   OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,  
MOL.WT:

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SUPPORTING DOCUMENTS:

IND   
DMF

DMF

NDA 50-749 Chemistry review 1.

Packaging Components:

DMF

NDA 50-749  
Parke-Davis/Warner-Lambert  
Omnicef for Oral Suspension 125 mg/5 mL

page 4

**CONCLUSIONS & RECOMMENDATIONS:**

The application is not approvable for manufacturing and controls under section 505(b) of the Act.

The establishment inspection is pending.

The firm was requested in a meeting on November 21, 1997 to consider the recommendation listed under list of Chemistry Deficiencies and Comments

TSI  
Shrikant N. Pagay, Ph.D.  
Review Chemist  
12/1/97

cc: Orig. NDA 50-749 (other NDA's may be included if appropriate)  
HFD-520/Division File  
HFD-520/S.Pagay/date  
HFD-520/Soreth/Viraghavan/Hamilton  
HFD-520/Osterberg  
HFD-520/Sheldon  
HFD-520/Debellas  
HFD-520/Katague R/D Init by: Katague DB/K 12/1/97  
Filename:N50-749

**DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS**  
**Review of Chemistry, Manufacturing, and Controls**  
**NDA #:** 50-749 **CHEM.REVIEW #:** 3 **REVIEW DATE:** 2-Dec-97

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	30-Dec-96	31-Dec-96	1-Jan-97
AMENDMENT/AC	10-Jan-97	13-Jan-97	15-Jan-97
-Street address for Plants			
AMENDMENT/AC	24-Jan-97	27-Jan-97	28-Jan-97
-Summary of MV package (item 4 of NDA)			
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-Response to draft Post-Approval Commitments.			
AMENDMENT	26-Nov-97 (desk copy)		28-Nov-97
-Response to draft Post-Approval Commitments.			

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**Therapeutic Class:** 38

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**STRENGTHS:**

125 mg/5 mL

**ROUTE OF ADMINISTRATION:**

Oral

**DISPENSED:**

     X      Rx      OTC

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:**

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**SUPPORTING DOCUMENTS:**

IND /  
DMF

DMF

NDA 50-749 Chemistry review 1.

Packaging Components:

DMF /

**RELATED DOCUMENTS (if applicable):** None

**CONSULTS:**

EA review completed; Fonsi Issued 6/9/97 - attached to CMC Review 2.

Nomenclature Committee for trade name Omnicef - Not.

acceptable to the committee (similar name - Omnipen is a marketed product). As a post-approval commitment, the firm will monitor prescription errors resulting from similarity of different brand names starting with OMNI.

Establishment Inspection - Submitted Date 1/27/97

Methods validation - Completed-November 12, 1997

**REMARKS/COMMENTS:**

The structure relates to cefixime, the acetate group at the  
/ is replaced by /

The drug substance is also known as FK482.

**CONCLUSIONS & RECOMMENDATIONS:**

Recommend approval of this application for manufacturing and controls under section 505(b) of the Act.

The drug substance is recommended for approval under NDA 50-739.

IS/ P  
\_\_\_\_\_  
Shrikant N. Pagay, Ph.D. 12/2/97  
Review Chemist

cc: Orig. NDA 50-749 (other NDA's may be included if appropriate)

HFD-520/Division File

HFD-520/S.Pagay/date

HFD-520/Soreth/Viraghavan/Hamilton

HFD-520/Osterberg

HFD-520/Sheldon

HFD-520/Debellas

HFD-520/Katague R/D Init by: Katague

Eilename:N50-749 DBK 12/2/97