Malandrucco

JUL - 1 1999

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
REVIEW OF CHEMISTRY, MANUFACTURING, AND CONTROLS

NDA 21-035	**CHEM. REVIEW # 1**	**REVIEW DATE** 21-MAY-99	
SUBMISSION TYPE	**DOCUMENT DATE**	**CDER DATE**	**ASSIGNED DATE**
ORIGINAL	01-FEB-99	03-FEB-99	18-FEB-99

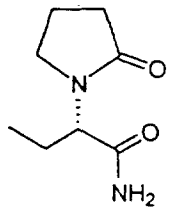
NAME AND ADDRESS OF APPLICANT ucb Pharma, Inc.
1950 Lake Park Drive
Smyrna, GA 30080

DRUG PRODUCT NAME

Proprietary:	Kepra
Nonproprietary/USAN:	Levetiracetam (filed for USAN name 18-MAY-99)
Code Name/Number:	ucb L059, ucb 22059
Chem. Type/Ther. Class:	1S

PHARMACOLOGICAL CATEGORY/INDICATION	Anticonvulsants	
DOSAGE FORM	Tablets	
STRENGTHS	250 mg, 500 mg, and 750 mg	
ROUTE OF ADMINISTRATION	Oral	
DISPENSED	XXX RX	___OTC
SPECIAL PRODUCTS	___ Yes	XXX NO

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA
(S)-(-)-α-ethyl-2-oxo-1-pyrrolidine acetamide
(oxo-2-pyrrolidinyl-1) 2 butyramide-(S)
(S)-(-)-α-ethyl-pyrrolidone acetamide



$C_8H_{14}N_2O_2$
Mol. Wt. 170.21
CAS Registry #: 102767-28-2

SUPPORTING DOCUMENTS: IND [redacted] DMF [redacted]
RELATED DOCUMENTS: None

CONSULTS: The proposed trademark "Kepra" was found acceptable by the CDER Labeling and Nomenclature Committee. The EER was requested on 01-APR-99 [redacted] The [redacted] is being prepared.

REMARKS/COMMENTS: The sponsor applied for an USAN name (levetiracetam) on May 18, 1999. The sponsor has requested a 24-month expiration date. A list of questions and comments, which were communicated to the sponsor, are found at the end of this review. No statistical analysis was provided to support the stability data. Very little stability data (3 months) was provided for the proposed commercial packaging.

CONCLUSIONS & RECOMMENDATIONS: The CMC information is not approvable at this time because stability data for the drug product is incomplete. The sponsor has agreed to update the stability data for the drug product and submit a statistical analysis. In addition, the sponsor has agreed to provide additional information to show comparability between the original drug product packaging and the proposed commercial packaging (as discussed in the pre-NDA meeting).

/S/
Thomas F. Oliver, Ph.D., Chemist

cc: Orig. NDA 21-035
HFD-120
HFD-120/TOliver
HFD-120/PM/MMalandrucco
HFD-120/MGuzewska
R/D Init by: MEG /S/ 7.1.99

Filename: n21035

Malandrucco

SEP 29 1999

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
REVIEW OF CHEMISTRY, MANUFACTURING, AND CONTROLS

NDA 21-035 **CHEM. REVIEW # 2** **REVIEW DATE** 28-SEP-99

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AMENDMENT .N(BC)	15-JUN-99	16-JUN-99	17-JUN-99
AMENDMENT .N(BC)	06-JUL-99	07-JUL-99	07-JUL-99
AMENDMENT .N(BC)	30-AUG-99	31-AUG-99	01-SEP-99
AMENDMENT .N(BC)	24-SEP-99	27-SEP-99	28-SEP-99

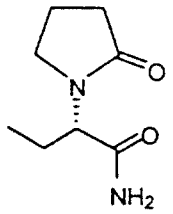
NAME AND ADDRESS OF APPLICANT ucb Pharma, Inc.
1950 Lake Park Drive
Smyrna, GA 30080

DRUG PRODUCT NAME

Proprietary:	Kepra
Nonproprietary/USAN[1999]:	Levetiracetam (name adopted by USAN on July 28, 1999)
Code Name/Number:	ucb L059, ucb 22059
Chem. Type/Ther. Class:	1S

PHARMACOLOGICAL CATEGORY/INDICATION	Anticonvulsants
DOSAGE FORM	Tablets
STRENGTHS	250 mg, 500 mg, and 750 mg
ROUTE OF ADMINISTRATION	Oral
DISPENSED	XXX RX ___OTC
SPECIAL PRODUCTS	___ Yes XXX NO

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA
-)-(S)-α-ethyl-2-oxo-1-pyrrolidineacetamide, and
1-pyrrolidineacetamide, α-ethyl-2-oxo-, (αS)-o



$C_8H_{14}N_2O_2$
Mol. Wt. 170.21
CAS Registry #: 102767-28-2

SUPPORTING DOCUMENTS: IND [redacted] DMF [redacted]
RELATED DOCUMENTS: None
CONSULTS: The proposed trademark "Kepra" was found acceptable by the CDER Labeling and Nomenclature Committee. However, the sponsor has changed the trademark to "Keppra" due to problems in Europe. The CDER Labeling and Nomenclature Committee is reviewing the new name. An inspection is scheduled for September 27-October 1, 1999 [redacted] The [redacted] is being prepared.

REMARKS/COMMENTS: The stability data supports a tentative 24-month expiration date for the bottles and a tentative 12 month expiration date for the blisters. The sponsor has addressed the questions we submitted in a letter date [18-JUN-99]. The final drug substance and drug product specification [redacted]

CONCLUSIONS & RECOMMENDATIONS: The CMC information is approvable pending a satisfactory EER report. The three remaining issues: 1) acceptable EER report, 2) acceptable finding by the CDER Labeling and Nomenclature Committee for "Keppra", and 3) commitment to a 3 month bulk stability expiration with stability testing [redacted]

/S/
Thomas F. Oliver, Ph.D., Chemist

cc: Orig. NDA 21-035
HFD-120
HFD-120/TOliver
HFD-120/PM/MMalandrucco
HFD-120/MGuzewska
R/D init by: MES /S/ 9.29.99

Filename: n21035

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
REVIEW OF CHEMISTRY, MANUFACTURING, AND CONTROLS NOV 17 1999

NDA 21-035 **CHEM. REVIEW # 3** **REVIEW DATE** 17-NOV-99

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AMENDMENT .N(BC)	05-OCT-99	06-OCT-99	06-OCT-99

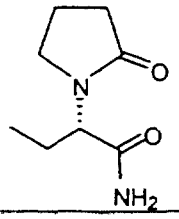
NAME AND ADDRESS OF APPLICANT ucb Pharma, Inc.
1950 Lake Park Drive
Smyrna, GA 30080

DRUG PRODUCT NAME

Proprietary:	**Keppra**
Nonproprietary/USAN[1999]:	Levetiracetam (name adopted by USAN on July 28, 1999)
Code Name/Number:	ucb L059, ucb 22059
Chem. Type/Ther. Class:	1S

PHARMACOLOGICAL CATEGORY/INDICATION	Anticonvulsants	
DOSAGE FORM	Tablets	
STRENGTHS	250 mg, 500 mg, and 750 mg	
ROUTE OF ADMINISTRATION	Oral	
DISPENSED	XXX RX	___OTC
SPECIAL PRODUCTS	___ Yes	XXX NO

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA
(-)-(S)-α-ethyl-2-oxo-1-pyrrolidineacetamide, and
1-pyrrolidineacetamide, α-ethyl-2-oxo-, (αS)-



$C_8H_{14}N_2O_2$
Mol. Wt. 170.21
CAS Registry #: 102767-28-2

SUPPORTING DOCUMENTS: IND [redacted] DMF [redacted]
RELATED DOCUMENTS: None
CONSULTS: The new proposed trademark **"Keppra"** was found **acceptable by OPDRA** (recommendation is attached at the end of review) [Note: The original proposed name "Kepra" was approved by the CDER's Labeling and Nomenclature Committee on 09-APR-99; sponsor switched to Keppra due to problems in Europe]. The EER was found acceptable [redacted] The [redacted] is being prepared.

REMARKS/COMMENTS: The stability data supports a tentative 24-month expiration date for the bottles and a tentative 12 month expiration date for the blisters. The sponsor has committed to the 3-month bulk stability (fax 15-NOV-99) expiration with stability testing on the first commercial batch of bulk drug product (each strength).

[redacted]

CONCLUSIONS & RECOMMENDATIONS: Recommend **APPROVAL**. The ***HOW SUPPLIED*** section should be revised to read: **250 mg tablets are blue** and the **500 mg tablets are yellow**.

/S/
Thomas F. Oliver, Ph.D., Chemist

cc: Orig. NDA 21-035
HFD-120
HFD-120/TOliver
HFD-120/PM/MMalandrucco
FD-120/MGuzewska
.VD Init by: MEG 11.17.99

/S/

Filename: n21035.03