CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-014

CHEMISTRY REVIEW(S)

Malandrucco

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

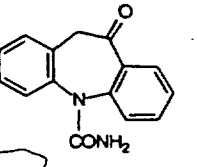
DEC 14 1999

NDA#: 21-014 **CHEMISTRY REVIEW: # 3** **DATE REVIEWED:** 13-DEC-99

Submission Type		Document Date	CDER Date	Assigned Date
ORIGINAL		25-SEP-98	28-SEP-98	
AMENDMENTS	(BF)	24-AUG-99	25-AUG-99	27-AUG-99
	(BC)	2-SEP-99	8-SEP-99	8-SEP-99
	(BC)	20-SEP-99	21-SEP-99	21-SEP-99
	(AZ)	15-NOV-99	16-NOV-99	16-NOV-99

NAME AND ADDRESS OF APPLICANT: Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover,
NJ 07936-1080

DRUG PRODUCT NAME:
Proprietary: Trileptal™
Nonproprietary/Established/USAN: oxcarbazepine [USAN applied 12-JUL-99]
Code Name/#: GP 47680
Chem. Type/Therapeutic Class: 1 S
DESI/PATENT STATUS: No patent application relating to the product as of filing date.
PHARMACOLOGICAL CATEGORY / INDICATION: Anticonvulsant
DOSAGE FORM: Tablets
STRENGTH(S): 150, 300, 600 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: XX Rx ___ OTC
SPECIAL PRODUCTS: No
CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA: 10, 11-Dihydro-10-oxo-5H-dibenz[b,f]azepine-5-carboxamide
$C_{15}H_{12}N_2O_2$ **Mol. Weight:** 252.27 **CAS:** 28721-07-5



SUPPORTING DOCUMENTS: DMF
RELATED DOCUMENTS: IND
CONSULTS: The proposed trademark "Trileptal" is accepted by the CDER Labeling and Nomenclature Committee. Site inspections completed (OC recommendation acceptable, June 7, 1999). Methods Validation to be submitted.

REMARKS / COMMENTS: This review consists of two parts: Part I: Review and evaluation of the responses provided by Novartis to the AE letter of 24-SEP-99, and Part II: Review of other amendments. Novartis' responses to both CMC comments are adequate. The proposed 24-month expiration date is supported by the stability data of Trileptal Tablets.

CONCLUSIONS AND RECOMMENDATIONS: Recommend Approval.

cc: Orig. NDA 21-014
HFD-120/Division File
HFD-120/DChristodoulou
HFD-120/MMalandrucco
HFD-120/MGuzewska/R/D Init by: MG
HFD-810/JSimmons

/S/ 12.14.99

/S/
Danae D. Christodoulou, Ph.D., Review Chemist

Filename: N21014n4.doc

Malandrucco

AUG 5 1999

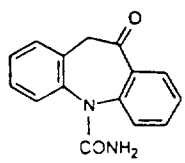
DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA#: 21-014 **CHEMISTRY REVIEW: # 2** **DATE REVIEWED:** 30-JUL-99

Submission Type	Document Date	CDER Date	Assigned Date
ORIGINAL	25-SEPT-98	28-SEPT-98	
AMENDMENTS	14-JUN-99	15-JUN-99	18-JUN-99
	16-JUN-99	17-JUN-99	18-JUN-99
	24-JUN-99	25-JUN-99	28-JUN-99
	16-JUL-99	19-JUL-99	22-JUL-99

NAME AND ADDRESS OF APPLICANT: Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover,
NJ 07936-1080

DRUG PRODUCT NAME:
Proprietary: **Trileptal™**
Nonproprietary/Established/USAN: oxcarbazepine [USAN applied 12-JUL-99]
Code Name/#: GP 47680
Chem. Type/Therapeutic Class: **1 S**
DESI/PATENT STATUS: No patent application relating to the product as of filing date.
PHARMACOLOGICAL CATEGORY / INDICATION: Anticonvulsant
DOSAGE FORM: Tablets
STRENGTH(S): 150, 300, 600 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: XX Rx ___ OTC
SPECIAL PRODUCTS: No
CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA: 10, 11-Dihydro-10-oxo-5H-dibenz[b,f]azepine-5-carboxamide
$C_{15}N_2O_2$ **Mol. Weight**: 252.27 **CAS**: 28721-07-5



SUPPORTING DOCUMENTS: DMF
RELATED DOCUMENTS: IND
CONSULTS: The proposed trademark "Trileptal" is accepted by the CDER Labeling and Nomenclature Committee. Site inspections completed (OC recommendation acceptable, June 7, 1999). Methods Validation to be submitted.

REMARKS / COMMENTS: Novartis provided responses to the CMC deficiencies. A 36-month retest date for the drug substance is supported by real time stability data from . Revised specifications and post-approval stability commitments for the drug product have been provided (Am. July 16, 1999). The 24-month expiration date is supported by real time stability data.

CONCLUSIONS AND RECOMMENDATIONS: Recommend NDA 21-014 is Approvable.
The following recommendations should be communicated to the sponsor:
1. Rounding the purity factor (reference standard) to the first decimal (rounding to 100% not acceptable).
2. Including one batch (300 mg strength) tablets packaged in blisters in the post-approval stability commitment to cover all prevalent marketed packaging configurations.

cc: Orig. NDA 21-014
HFD-120/Division File
HFD-120/DChristodoulou
HFD-120/MMalandrucco
HFD-120/MGuzewska/R/D Init by: MG
HFD-810/CHoiberg

/S/

Danae D. Christodoulou, Ph.D., Review Chemist

Filename: N21014n2.doc

/S/ 8.5.99

Malandrucco

JUL 19 1999

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA#: 21-014 **CHEMISTRY REVIEW: # 1** **DATE REVIEWED:** 16-Jul-99

Submission Type	Document Date	CDER Date	Assigned Date
ORIGINAL	25-SEPT-98	28-SEPT-98	7-OCT-98
AMENDMENTS	04-APR-99	06-APR-99	
	23-APR-99	26-APR-99	

NAME AND ADDRESS OF APPLICANT: Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover,
NJ 07936-1080

DRUG PRODUCT NAME:
Proprietary: **Trileptal™**
Nonproprietary/Established/USAN: oxcarbazepine [USAN accepted 1999]
Code Name/#: GP 47680
Chem. Type/Therapeutic Class: **1 S**
DESI/PATENT STATUS: No patent application relating to the product as of filing date.
PHARMACOLOGICAL CATEGORY / INDICATION: Anticonvulsant
DOSAGE FORM: Tablets
STRENGTH(S): 150, 300, 600 mg
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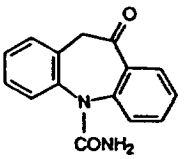

SUPPORTING DOCUMENTS: OMF
RELATED DOCUMENTS: IND
CONSULTS: The proposed trademark "Trileptal" is accepted by the CDER Labeling and Nomenclature Committee. The EER report is attached all facilities comply. MV to be submitted after methods deficiencies have been addressed.

REMARKS / COMMENTS: The deficiencies were communicated.

Updated 18-month stability data for the drug substance, and 24-month data for the drug product have been provided in the April 5, 1999 amendment. The 24-month expiration date is supported by real time stability data.

CONCLUSIONS AND RECOMMENDATIONS: Recommend NDA 21-014 Not Approvable.

/S/

Danae D. Christodoulou, Ph.D., Review Chemist

cc: Orig. NDA 21-014
HFD-120/Division File
HFD-120/DChristodoulou
HFD-120/MMalandrucco
HFD-120/MGuzewska/R/D Init.by: MG
HFD-810/CHoiberg

/S/ 7.19.99

Filename: N21014n.doc