CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-285

CHEMISTRY REVIEW(S)

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

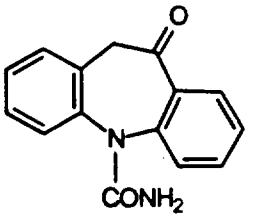
NDA#: 21-285 **CHEMISTRY REVIEW: # 1** **DATE REVIEWED: 02-May-01**

Submission Type	Document Date	CDER Date	Assigned Date
ORIGINAL	28-JUL-00	31-JUL-00	8-AUG-00
AMEND. N-BC	22-SEP-00	26-SEP-00	27-SEP-00
AMEND. N-BC	04-OCT-00	05-OCT-00	06-OCT-00
AMEND. N-BC	06-FEB-01	07-FEB-01	07-FEB-01
AMEND. N-BC	27-FEB-01	28-FEB-01	28-FEB-01
AMEND. N-BB	16-MAR-01	21-MAR-01	21-MAR-01

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 29-SEP-99; not in USP 2000 dictionary]
Code Name/#: GP 47680
Chem. Type/Therapeutic Class: **3 S**

DESI/PATENT STATUS: No patent application relating to the product as of filing date
PHARMACOLOGICAL CATEGORY / INDICATION: Anticonvulsant
DOSAGE FORM: Oral suspension
STRENGTH(S): 6% (60 mg/ml)
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: 252.28
CAS: 28721-07-5

SUPPORTING DOCUMENTS: DMF
NDA 21-014 Trileptal (oxcarbazepine) Tablets; IND
RELATED DOCUMENT: IND
CONSULTS: EA (Acceptable); Microbiology (Pending); Statistical analysis of stability data (See Review Notes, p. 28); MV (To be submitted).

REMARKS / COMMENTS: The deficiencies have been communicated to the sponsor in the IR letter of 9-APR-01. The packaging DMF provides supplementary information to support the Additional information about the has been requested [on 22-MAR-01 from the DMF US Representative]. The 36 month expiration date requested by the sponsor is not supported by stability data (maximum 12-month data for one batch and supportive data). The Dissolution method and specification is Q= after 30 min, USP apparatus 2, paddle at 75rpm, 37°C, 900 ml 1% aqueous dodecyl sulfate.

CONCLUSIONS AND RECOMMENDATIONS: Recommend NDA 21-285 is Approvable at this time.
(See deficiencies-IR Letter attached).

cc: Orig. NDA 21-285
HFD-120/Division File
HFD-120/DChristodoulou
HFD-120/MFanari
HFD-120/MGuzewska/R/D Init.by: MG
HFD-810/JSimmons

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

Filename: n21285.doc

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

48 pages

ATTACHMENT 1

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21285/000
Priority: S
Org Code: 120
Stamp: 31-JUL-2000 Regulatory Due: 31-MAY-2001
Action Goal:
District Goal: 01-APR-2001
Applicant: NOVARTIS PHARMS
59 RT 10
EAST HANOVER, NJ 079361080
Brand Name: TRILEPTAL(OXCARBAZEPINE) 60MG/ML ORAL
Established Name:
Generic Name: OXCARBAZEPINE
Dosage Form: SUS (SUSPENSION)
Strength: 6%

FDA Contacts: M. FANARI (HFD-120) 301-594-5526 , Project Manager
D. CHRISTODOULOU (HFD-810) 301-594-5554 , Review Chemist
M. GUZEWSKA (HFD-120) 301-594-5571 , Team Leader

Overall Recommendation:

ACCEPTABLE on 18-APR-2001 by M. GARCIA (HFD-322) 301-594-0095

Establishment: 9617227
NOVARTIS PHARMA INC
SITE INDUSTRIEL DE HUNINGUE
HUNINGUE, , FR
DMF No:
AADA No:

Profile: LIQ
OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 10-JAN-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION
Responsibilities: FINISHED DOSAGE LABELER
FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER

Establishment: 2416082
NOVARTIS PHARMA INC (CIBA)
OLD MILL RD
SUFFERN, NY 10901
DMF No:
AADA No:

Profile: LIQ
OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 02-OCT-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION
Responsibilities: FINISHED DOSAGE LABELER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER

Establishment: 9611204
NOVARTIS PHARMA INC (SANDOZ)
LICHSTRASSE 35
KLYBECK, BASEL, SZ 4002
DMF No:
AADA No:

Profile: CTL
OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 12-JAN-2001
Responsibilities: FINISHED DOSAGE RELEASE TESTER

ATTACHMENT 1 (contd.)

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: **9614433**
NOVARTIS PHARMANALYTICA SA

LOCARNO, , SZ

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **03-OCT-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE STABILITY TESTER**

Establishment: [redacted]

DMF No:
AADA No:

Profile: **LIQ** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **16-OCT-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities [redacted]

Establishment: [redacted]

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **18-APR-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: [redacted]

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/s/

Danae Christodoulou
5/23/01 11:06:37 AM
CHEMIST

Maryla Guzewska
5/23/01 11:23:21 AM
CHEMIST

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

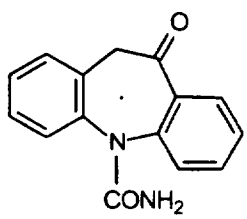
NDA#: 21-285 **CHEMISTRY REVIEW: # 2** **DATE REVIEWED:** 23-May-01

Submission Type	Document Date	CDER Date	Assigned Date
ORIGINAL	28-JUL-00	31-JUL-00	8-AUG-00
AMEND. N-BC	19-APR-01	23-APR-01	23-APR-01
AMEND. N-BC	30-APR-01	01-MAY-01	01-MAY-01
AMEND. N-BC	04-MAY-01	07-MAY-01	16-MAY-01
AMEND. N-BL	20-APR-01	23-APR-01	24-APR-01
AMEND. N-BL	07-MAY-01	08-MAY-01	16-MAY-01
AMEND. N-BL	11-MAY-01	14-MAY-01	16-MAY-01
AMEND. N-BC	22-MAY-01		Reviewed from facsimile

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 29-SEP-99; not in USP 2000 dictionary]
Code Name/#: GP 47680
Chem. Type/Therapeutic Class: **3 S**

DESI/PATENT STATUS: No patent application relating to the product as of filing date
PHARMACOLOGICAL CATEGORY / INDICATION: Anticonvulsant
DOSAGE FORM: Oral suspension
STRENGTH(S): 6% (60 mg/ml)
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: 252.28
CAS: 28721-07-5

SUPPORTING DOCUMENTS: DMF [redacted] s)
NDA 21-014 Trileptal (oxcarbazepine) Tablets; IND [redacted]
RELATED DOCUMENT: IND [redacted]
CONSULTS: EA (Acceptable); Microbiology (Acceptable for lot-by-lot testing); Statistical analysis of stability data (Acceptable for 24 months expiry); MV (To be submitted), OPDRA, DDMAC.

REMARKS / COMMENTS: Review #2 addresses responses to deficiencies (Amendments of 19-APR-01, 30-APR-01 and 4-MAY-01), microbiology review, revised stability commitment for microbiological testing and labeling. Additional information on the packaging DMF [redacted] We recommend 24-month expiration dating based on real time stability data on the suspension formulation for the US market. The final Dissolution method and specification accepted by the Biopharm Division is: Q= [redacted] after 30 min, USP apparatus 2, paddle at 75 rpm, 37°C, 900 ml 1% aqueous dodecyl sulfate. The microbiological testing will be performed on a lot-by-lot basis. The proposal for skip-lot testing may be submitted post-approval. Overall OC recommendation is "Acceptable" (EER, Attach. 1).

CONCLUSIONS AND RECOMMENDATIONS: Recommend NDA 21-285 is Approved with 24-month expiration dating.

cc: Orig. NDA 21-285
HFD-120/Division File
HFD-120/DChristodoulou
HFD-120/MFanari
HFD-120/MGuzewska/R/D Init.by: MG
HFD-810/JSimmons

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

Filename: n21285.2a.doc

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

18 pages

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/s/

Danae Christodoulou
5/23/01 11:24:38 AM
CHEMIST

Maryla Guzewska
5/23/01 01:08:51 PM
CHEMIST

APPEARS THIS WAY
ON ORIGINAL

ATTACHMENT 1

27-APR-2001

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21285/000
Stamp: 31-JUL-2000 Regulatory Due: 31-MAY-2001
Applicant: NOVARTIS PHARMS
59 RT 10
EAST HANOVER, NJ 079361080

Priority: S Org Code: 120
Action Goal: District Goal: 01-APR-2001
Brand Name: TRILEPTAL(OXCARBAZEPINE) 60MG/ML ORAL
Established Name:
Generic Name: OXCARBAZEPINE
Dosage Form: SUS (SUSPENSION)
Strength: 6%

FDA Contacts: M. FANARI (HFD-120) 301-594-5526 , Project Manager
D. CHRISTODOULOU (HFD-810) 301-594-5554 , Review Chemist
M. GUZEWSKA (HFD-120) 301-594-5571 , Team Leader

Overall Recommendation:

ACCEPTABLE on 18-APR-2001 by M. GARCIA (HFD-322) 301-594-0095

Establishment: 9617227
NOVARTIS PHARMA INC
SITE INDUSTRIEL DE HUNINGUE
HUNINGUE, , FR

DMF No:
AADA No:

Profile: LIQ OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 10-JAN-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: FINISHED DOSAGE LABELER
FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER

Establishment: 2416082
NOVARTIS PHARMA INC (CIBA)
OLD MILL RD
SUFFERN, NY 10901

DMF No:
AADA No:

Profile: LIQ OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 02-OCT-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: FINISHED DOSAGE LABELER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER

Establishment: 9611204
NOVARTIS PHARMA INC (SANDOZ)
LICHSTRASSE 35
KLYBECK, BASEL, SZ 4002

DMF No:
AADA No:

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 12-JAN-2001

Responsibilities: FINISHED DOSAGE RELEASE TESTER

ATTACHMENT 1 (contd.)

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: **9614433**
NOVARTIS PHARMANALYTICA SA

LOCARNO, , SZ

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **03-OCT-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE STABILITY TESTER**

Establishment: [redacted]

DMF No:
AADA No:

Profile: **LIQ** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **16-OCT-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: [redacted]

Establishment: [redacted]

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **18-APR-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: [redacted]

APPEARS THIS WAY ON ORIGINAL