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

DESIGN/PATENT STATUS:
No patent application relating to the product as of filing date

PHARMACOLOGICAL CATEGORY / INDICATION:
Anticonvulsant

DOSE 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_{19}H_{20}N_{2}O_{2}
Mol. Weight: 252.28
CAS: 28721-07-5

SUPPORTING DOCUMENTS:
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 add. 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=____ iter 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).

c: Orig. NDA 21-285
HFD-120/Division File
HFD-120/Christodoulou
HFD-120/Manari
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
FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NOVARTIS PHARMS
59 RT 10
EAST HANOVER, NJ 079361000

Priority: $ Org Code: L20
Stamp: 31-JUL-2000 Regulatory Due: 31-MAY-2001
Action Goal: District Goal: 01-APR-2001
Brand Name: TRILEPTAL (OXCARBAZEPIONE)
Established Name: OXCARBAZEPIONE
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. GUZIEWSKA (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

Profile: LIQ OAI Status: NONE
Responsibilities: FINISHED DOSAGE LABELER
Last Milestone: OC RECOMMENDATION FINISHED DOSAGE MANUFACTURER
Milestone Date: 18-JAN-2001 FINISHED DOSAGE PACKAGER
Decision: ACCEPTABLE FINISHED DOSAGE RELEASE TESTER
Reason: DISTRICT RECOMMENDATION

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

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

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

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

(Continued on next page)
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Establishment: 9614833
NOVARTIS PHARMANALYTICA SA
LOCARNO, SZ

Profile: CTL
Last Milestone: OC RECOMMENDATION
Milestone Date: 03-OCT-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Profile: LIQ
Last Milestone: OC RECOMMENDATION
Milestone Date: 16-OCT-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Profile: CTL
Last Milestone: OC RECOMMENDATION
Milestone Date: 16-APR-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: FINISHED DOSAGE STABILITY TESTER
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

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

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

APPEARS THIS WAY
ON ORIGINAL
DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDAS: 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

DES/PATENT STATUS: No patent application relating to the product as of filing date
PHARMACOLOGICAL CATEGORY / INDICATION: Anticonvulsant
DOSEAGE 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-dibenzo[b,f]azepine-5-carboxamide
C_{18}N_{2}O_{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 (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 s)

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: Qr 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/MPGuzezska/R/D Init.by: MG
HFD-810/SSimmons

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

Filename: n21285.2a.doc
THIS SECTION WAS DETERMINED NOT TO BE RELEASABLE

18 pager
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/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
### 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:** OXCARBAZEPINE  
**Generic Name:** SUS (SUSPENSION)  
**Dosage Form:** 6%  
**Strength:**  

**FDA Contacts:**  
M. FANARI (HFD-120)  
D. CHRISTODOULOU (HFD-810)  
M. GUZIEWSKA (HFD-120)  
301-594-5526, Project Manager  
301-594-5554, Review Chemist  
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  
**Responsibilities:** FINISHED DOSAGE LABELER  
FINISHED DOSAGE MANUFACTURER  
FINISHED DOSAGE PACKAGER  
FINISHED DOSAGE RELEASE TESTER

**Profile:** LIQ  
**Last Milestone:** OC RECOMMENDATION  
**Milestone Date:** 10-JAN-2001  
**Decision:** ACCEPTABLE  
**Reason:** DISTRICT RECOMMENDATION

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

**Profile:** LIQ  
**Last Milestone:** OC RECOMMENDATION  
**Milestone Date:** 02-OCT-2000  
**Decision:** ACCEPTABLE  
**Reason:** DISTRICT RECOMMENDATION

**Establishment:** 9611204  
NOVARTIS PHARMA INC (SANDOZ)  
LICHTSTRASSE 35  
KLYBECK, BASEL, SZ 4002  
**DMF No:**  
**AAD No:**

**Profile:** CTL  
**Last Milestone:** OC RECOMMENDATION  
**Milestone Date:** 12-JAN-2001  
**Responsibilities:** FINISHED DOSAGE RELEASE TESTER
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Establishment: 9614433
NOVARTIS PHARMANALYTICA SA
LOCARNO, SZ

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

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

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

APPEARS THIS WAY ON ORIGINAL