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

NDAs: 20-796

CHEMISTRY REVIEW: # 1

DATE REVIEWED: 13-Jul-98

Submission Type Letter Date CDER Stamp Date Assigned Date
ORIGINAL 24-OCT-97 24-OCT-97 [Assigned Date]
RESUBMISSION 23-DEC-97 24-DEC-97
N(BC) - EA/ categorical exclusion 24-APR-98 27-APR-98
N(BC) - packaging site 01-MAY-98 04-MAY-98
AMENDMENT 08-MAY-98 11-MAY-98

NAME AND ADDRESS OF APPLICANT:
Orion Corporation
P.O. Box 65
Fin-02101
Espoo, Finland

DRUG PRODUCT NAME:
Proprietary: Comtan®
Nonproprietary/Established/USAN: entacapone [INN, USAN name is pending]
Code Name/#: OR-611
Chem. Type/Therapeutic Class: 1 S


PHARMACOLOGICAL CATEGORY / INDICATION: Parkinson's disease, adjunct to levodopa/dopa therapy

DOSE FORM:

STRENGTH(S):

ROUTE OF ADMINISTRATION:

DISPENSED: XX Rx OTC

SPECIAL PRODUCTS:

CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:
(E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethyl-2-propenamide (CAS)
(E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethylylacrylamide (IUPAC)
CAS No. 1309929-57-6

Mol. Formula: C₁₈H₁₇N₃O₅ Mol. Weight: 305.29

SUPPORTING DOCUMENTS: DMF

RELATED DOCUMENTS: IND

CONSULTS: Tradename consulted to nomenclature committee on 30-OCT-97, no recommendation available.

REMARKS / COMMENTS:

Conclusions and Recommendations:
Recommend Information Request letter to sponsor.

cc: Orig. NDA [NDA number] 20796
HFD-120/Division File
HFD-120/MHeimann
HFD-120/TWheelous
HFD-120/AGuzewska/R/D Init by: Mr.-98
HFD-810/Choiberg

Martha R. Heimann, Ph.D., Review Chemist
Filename: 7/16/98
DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA#: 20-796

CHEMISTRY REVIEW: # 2

DATE REVIEWED: 11-Dec-98

Submission Type
N(BC)
N(BC)
N(BL)
N(BC) - Method validation package

Letter Date     CDER Stamp Date     Assigned Date
30-SEP-98       01-OCT-98           01-OCT-98
11-NOV-98       13-NOV-98           13-NOV-98
24-NOV-98       25-NOV-98           25-NOV-98
02-DEC-98       03-DEC-98           03-NOV-98

NAME AND ADDRESS OF APPLICANT:
Orion Corporation
P.O. Box 65, Fin-02101
Espoo, Finland

DRUG PRODUCT NAME:
Proprietary:
Nonproprietary/Established/USAN: entacapone [USAN letter dated 27-AUG-97]
Code Name/#:
Chem. Type/Therapeutic Class: 1S


PHARMACOLOGICAL CATEGORY / INDICATION:
Parkinson's disease, adjunct to levodopa/dopa therapy

DOSSAGE FORM:
Tablets

STRENGTH(S):
200 mg

ROUTE OF ADMINISTRATION:
Oral

DISPENSED:

SPECIAL PRODUCTS:
No

SUPPORTING DOCUMENTS:

CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:
(E)-2-Cyano-3-(3,4-dihtydryoxy-5-nitrophenyl)-N,N-dietyl-2-propenamide (CAS)
(E)-2-Cyano-3-(3,4-dihtydryoxy-5-nitrophenyl)-N,N-dietylacrylamide (IUPAC)

CAS No. 130929-57-6
Mol. Formula: C_{14}H_{12}N_{3}O_{5}   Mol. Weight: 305.29

RELATED DOCUMENTS: IND

CONSULTS: Tradename consult was returned by Nomenclature committee on 23-FEB-98 - Acceptable

REMARKS / COMMENTS: Deficiencies identified in NDA Review #1 and DMP

Establishment evaluations are complete, with acceptable overall compliance recommendation dated 04-AUG-1998. Revised Methods Validation is adequate and methods validation is being initiated.

CONCLUSIONS AND RECOMMENDATIONS:
Recommend approval. Action letter needs standard method validation statement and final container labeling should be reviewed when submitted.

cc: Orig. NDA 20-768
HFD-120/Division File
HFD-120/Heimann
HFD-120/TVheelius
HFD-120/MSzewska/R/D Init. by: MG
HFD-810/Choiberg

Martha R. Heimann, Ph.D., Review Chemist
File date: D:WORDWP#NDAIN20-796N20-795.002.DOC

12/11/98

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

NDA#: 20-796
Submission Type: N(BC)
NAME AND ADDRESS OF APPLICANT: Orion Corporation
P.O. Box 65, Fin-02101 Espoo, Finland

DRUG PRODUCT NAME:
Proprietary: CONTAN®
Nonproprietary/Established/USAN: entacapone [USAN letter dated 27-AUG-97]
Code Name#: OR-611
Chem. Type/Therapeutic Class: '1 S

DATE REVIEWED: 21-SEP-99
Letter Date 25-MAY-99
CDER Stamp Date 26-MAY-99
Assign Date 27-MAY-99


PHARMACOLOGICAL CATEGORY / INDICATION: Parkinson's disease, adjunct to levodona/dopa therapy

DOSSAGE FORM:
Tablets

STRENGTH(S):
200 mg

ROUTE OF ADMINISTRATION:
Oral

DISPENSED: XX Rx ___ OTC

SPECIAL PRODUCTS:
No

CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:
(E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethyl-2-propenamide (CAS)
(E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethylacrylamide (IUPAC)
CAS No. 130929-57-6
Mol. Formula: C_{14}H_{15}N_{3}O_{5} Mol. Weight: 305.29

CONSULTS: Tradename consult was returned by Nomenclature committee on 23-FEB-98 - Acceptable

REMARKS / COMMENTS:

CONCLUSIONS AND RECOMMENDATIONS:
CMC information is adequate to support approval of the proposed commercial formulation. Action letter needs standard method validation statement and final container labeling should be reviewed when submitted.

cc: Orig. NDA 20-768
HFD-120/Division File
HFD-120/MHeimann
HFD-120/TWhealous
HFD-120/MGuzewska/R&D Init. by: MG
HFD-810/JSSimmons

Marta R. Heimann, Ph.D., Review Chemist
Filename: D:\WORD#WP\NDAW20-796IN20-796.003.DOC