

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

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JUL 15 1998

NDA#: 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	
RESUBMISSION	23-DEC-97	24-DEC-97	[Assigned Date]
N(BC) - EA/categorical exclusion	24-APR-98	27-APR-98	27-APR-98
N(BC) - packaging site	01-MAY-98	04-MAY-98	05-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

DESI/PATENT STATUS: US Patent Nos. 5,446,194 (expiry 8/29/2012), 5,135,950 (expiry 10/31/2010), 4,963,590 (expiry 11/27/2007) and 5,112,861 (expiry 5/12/2009)

PHARMACOLOGICAL CATEGORY / INDICATION: Parkinson's disease, adjunct to levodopa/dopa therapy  
DOSAGE FORM: Tablets  
STRENGTH(S): 200 mg  
ROUTE OF ADMINISTRATION: Oral  
DISPENSED:  Rx  OTC  
SPECIAL PRODUCTS: No

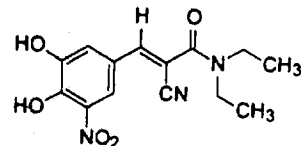
CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:

(E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethyl-2-propenamamide (CAS)

(E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethylacrylamide (IUPAC)

CAS No. 130929-57-6

Mol. Formula: C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>O<sub>5</sub> 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:

Most are relatively minor and could be resolved quickly. Establishment evaluations requested on 03-MAR-98. Initial site inspections are complete, with field/compliance recommendations still pending. Methods Validation will not be initiated until all deficiencies in analytical method and validation have been addressed by the sponsor.

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/MGuzewska/R/D Init. by: MF  
HFD-810/CHOiberg

Martha R. Heimann, Ph.D., Review Chemist  
Filename:

15-98  
ISI

ISI  
7/13/98

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

NDA#: 20-796

CHEMISTRY REVIEW: # 2

DATE REVIEWED: 11-Dec-98

Submission Type

	Letter Date	CDER Stamp Date	Assigned Date
N(BC)	30-SEP-98	01-OCT-98	01-OCT-98
N(BC)	11-NOV-98	13-NOV-98	13-NOV-98
N(BL)	24-NOV-98	25-NOV-98	25-NOV-98
N(BC) - Method validation package	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: COMTAN®  
Nonproprietary/Established/USAN: entacapone [USAN letter dated 27-AUG-97]  
Code Name/#: OR-611  
Chem. Type/Therapeutic Class: 1 S

DESI/PATENT STATUS: US Patent Nos. 5,446,194 (expiry 8/29/2012), 5,135,950 (expiry 10/31/2010), 4,963,590 (expiry 11/27/2007) and 5,112,861 (expiry 5/12/2009)

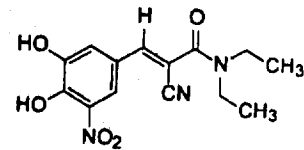
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STRENGTH(S): 200 mg  
ROUTE OF ADMINISTRATION: Oral  
DISPENSED:  Rx  OTC  
SPECIAL PRODUCTS: No

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CAS No. 130929-57-6

Mol. Formula: C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>O<sub>5</sub> Mol. Weight: 305.29



SUPPORTING DOCUMENTS:

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 DMF

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/MHeimann  
HFD-120/TWheeler  
HFD-120/MGuzewska/R/D Init. by: MG  
HFD-810/CHOiberg

12/11/98  
Martha R. Heimann, Ph.D., Review Chemist

Filename: D:\WORD\WP\NDA\N20-796\N20-796.002.DOC

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DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS SEP 21 1999  
Review of Chemistry, Manufacturing, and Controls

NDA#: 20-796

CHEMISTRY REVIEW: # 3

DATE REVIEWED: 21-SEP-99

Submission Type

Letter Date

CDER Stamp Date

Assigned Date

N(BC)

25-MAY-99

26-MAY-99

27-MAY-99

NAME AND ADDRESS OF APPLICANT:

Orion Corporation  
P.O. Box 65, Fin-02101  
Espoo, Finland

DRUG PRODUCT NAME:

Proprietary:

COMTAN®

Nonproprietary/Established/USAN: entacapone [USAN letter dated 27-AUG-97]

Code Name#: OR-611

Chem. Type/Therapeutic Class: 1 S

DESI/PATENT STATUS: US Patent Nos. 5,446,194 (expiry 8/29/2012), 5,135,950 (expiry 10/31/2010), 4,963,590 (expiry 11/27/2007) and 5,112,861 (expiry 5/12/2009)

PHARMACOLOGICAL CATEGORY / INDICATION:

Parkinson's disease, adjunct to levodopa/dopa therapy

DOSAGE FORM:

Tablets

STRENGTH(S):

200 mg

ROUTE OF ADMINISTRATION:

Oral

DISPENSED:

XX Rx

    OTC

SPECIAL PRODUCTS:

No

CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:

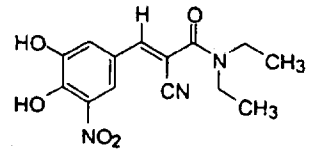
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(E)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethylacrylamide (IUPAC)

CAS No. 130929-57-6

Mol. Formula: C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>O<sub>5</sub>

Mol. Weight: 305.29



SUPPORTING DOCUMENTS:

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/TWheelous  
HFD-120/MGuzewska/R/D Init. by: MG  
HFD-810/JSimmons

15/ 9/21/99  
Martha R. Heimann, Ph.D., Review Chemist

Filename: D:\WORD\WP\#NDA\N20-796\N20-796.003.DOC

15/ 9/21/99