CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-224

Chemistry Review(s)

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

NDA #: 21-224 **CHEM.REVIEW #** 3 **REVIEW DATE: 08-JUN-01**

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment	26-APR-01	27-APR-01	30-APR-01

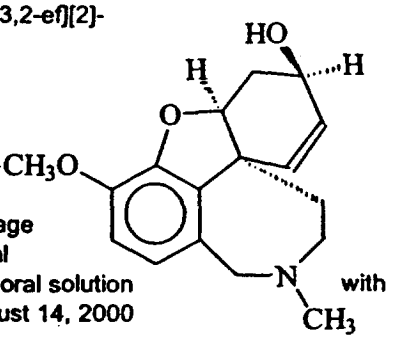
NAME & ADDRESS OF APPLICANT: Janssen Pharmaceutica
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

DRUG PRODUCT NAME
Proprietary: REMINYL (galantamine Hydrobromide) Oral Solution
Nonproprietary/USAN: Galantamine Hydrobromide
Code Name/#:
Chem.Type/Ther.Class: Acetylcholine Esterase Inhibitor

PHARMACOL.CATEGORY/INDICATION: AD

DOSAGE FORM: Oral Solution
STRENGTHS: 4 mg/ mL
ROUTE OF ADMINISTRATION: Oral
DISPENSED: XXXX Rx_____OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
(4aS,6R,8aS)-4a,5,9,10,11,12-hexahydro-3-methoxy-11-methyl-6*H*-benzofuro[3a,3,2-ef][2]-benzodiazepin-6-ol hydrobromide
$C_{17}H_{22}BrNO_3$; Molecular Weight: 368.27;
CAS #: 1953-04-0 (hydrobromide); 357-70-0 (base)



SUPPORTING DOCUMENTS: DMF[ ](galantamine HBr); NDA 21-169 (REMINYL Tablets)
RELATED DOCUMENTS:
REMARKS/COMMENTS: Response to AE letter including: 1) Combination Package Insert reflecting both the tablet and oral solution formulations with the relevant oral solution language highlighted (Attachment 1), and 2) Instructions for Use for the oral solution illustrations modified in response to comments received from the Division on August 14, 2000 (Attachment 2).

CONCLUSIONS & RECOMMENDATIONS : The detailed illustrated instruction leaflet fulfills the CMC request and completes CMC review. Recommend approval of NDA 21-224.

/S/ 6/8/01

W. Janusz Rzeszotarski, Ph.D., Chemist

cc:
Orig. NDA 21-224
HFD-120
HFD-120/WJRzeszotarski
HFD-120/MFanari
HFD-120/MEGuzewska
R/D Init by:MEG

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FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21224/000**
Stamp: **03-FEB-2000** Regulatory Due: **27-JUN-2001**
Applicant: **JANSSEN RES FDN**

Priority: **3S** Org Code: **120**
Action Goal: District Goal: **04-OCT-2000**
Brand Name: **REMINYL (GALANTAMINE) 4MG/ML ORAL SOLUTI**
Established Name:
Generic Name: **GALANTAMINE**
Dosage Form: **LIQ (LIQUID)**
Strength: **4 MG/ML**

FDA Contacts:
M. FANARI (HFD-120) 301-594-5526 , Project Manager
W. RZESZOTARSKI (HFD-120) 301-594-2850 , Review Chemist
M. GUZEWSKA (HFD-120) 301-594-5571 , Team Leader

Overall Recommendation:

ACCEPTABLE on 16-OCT-2000 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: **9610028**
JANSSEN PHARMACEUTICA NV
30, B-2340
BEERSE, , BE

DMF No:
AADA No:

Profile: **LIQ** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **11-AUG-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

Establishment:

DMF No:
AADA No:

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

Responsibilities:

Fanari

OCT 30 2000

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

NDA #: 21-224 **CHEM.REVIEW # 2** **REVIEW DATE: 25-OCT-00**

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AMENDMENT	04-AUG-00	06-AUG-00	06-AUG-00
AMENDMENT	16-OCT-00	18-OCT-00	18-OCT-00

NAME & ADDRESS OF APPLICANT: Janssen Pharmaceutica
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

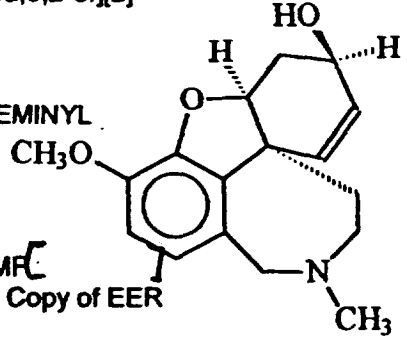
DRUG PRODUCT NAME

Proprietary: REMINYL (galantamine Hydrobromide) Oral Solution
Nonproprietary/USAN: Galantamine Hydrobromide
Code Name/#:
Chem.Type/Ther.Class: Acetylcholine Esterase Inhibitor

PHARMACOL.CATEGORY/INDICATION: AD

DOSAGE FORM: Oral Solution
STRENGTHS: 4 mg/ mL
ROUTE OF ADMINISTRATION: Oral
DISPENSED: XXXXX Rx_____OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
4aS,6R,8aS)-4a,5,9,10,11,12-hexahydro-3-methoxy-11-methyl-6*H*-benzofuro[3a,3,2-ef][2]-
benzodiazepin-6-ol hydrobromide
$C_{17}H_{22}BrNO_3$; Molecular Weight: 368.27;
CAS #: 1953-04-0 (hydrobromide); 357-70-0 (base)



SUPPORTING DOCUMENTS: DMF [ ] galantamine HBr); NDA 21-169 (REMINYL Tablets)
RELATED DOCUMENTS:
REMARKS/COMMENTS: Response to IR letters of August 4 & 14, 2000.

CONCLUSIONS & RECOMMENDATIONS: The deficiencies observed in the DMF [ ] and in this NDA have been resolved. Recommend the approval of NDA 21-224. Copy of EER included..

c:
Orig. NDA 21-224
HFD-120
HFD-120/WJRzeszotarski
HFD-120/MFanari
HFD-120/MEGuzewska
HFD Init by:MEG

[S]
W. Janusz Rzeszotarski, Ph.D., Chemist

S 10/30/00

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AUG 14 2000

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

NDA#: 21-224 **CHEM.REVIEW #** 1 **REVIEW DATE:** 10-AUG-00

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	02-FEB-00	04-FEB-00	11-FEB-00

NAME & ADDRESS OF APPLICANT: Janssen Pharmaceutica
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

DRUG PRODUCT NAME
Proprietary: REMINYL (galantamine Hydrobromide) Oral Solution
Nonproprietary/USAN: Galantamine Hydrobromide
Code Name/#:
Chem.Type/Ther.Class: Acetylcholine Esterase Inhibitor

PHARMACOL.CATEGORY/INDICATION: AD

DOSAGE FORM: Oral Solution
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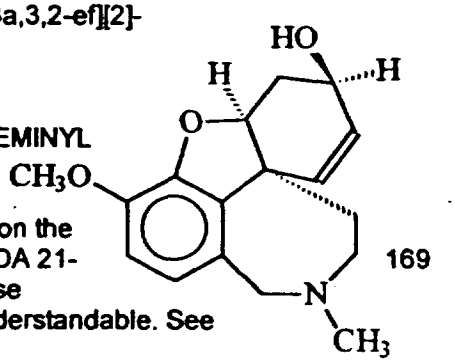

169

SUPPORTING DOCUMENTS: DMF[ ](galantamine HBr); NDA 21-169 (REMINYL Tablets)
RELATED DOCUMENTS:
REMARKS/COMMENTS: A second NDA for galantamine hydrobromide based on the DMF supported API. The same reservations that have to be answered for the NDA 21- apply here. A complicated, difficult to use container/closure system requires close examination and the package insert needs reediting to make the instructions understandable. See the two consecutive IR letters. EER submitted.

CONCLUSIONS & RECOMMENDATIONS: Recommend NDA 21-224 approvable subject to resolution of deficiencies in the DMF and in the NDA. Draft Letter enclosed.

cc:
Orig. NDA 21-224
HFD-120
HFD-120/WJRzeszotarski
HFD-120/MFanari
HFD-120/MEGuzewski
R/D Init by:MEG 8/15/2000

W. Janusz Rzeszotarski, Ph.D., Chemist

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