CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-414

CHEMISTRY REVIEW(S)

CHEMISTRY

NDA 20-414
Pyridostigmine Bromide
Tablets, 30 mg.

Classification: 3P

Date	Document	Tab
	Labeling & Nomenclature Review: NO TRADE NAME PROPOSED	
3-24-94	Supervisory Memorandum RE: RTF; Stan Blum, Ph.D.	A
4-25-94	EA: Memorandum to File: Comments for RTF ltr	B
	Review # 1 (DRAFT)	C
5-3-94	EA Review # 1: Glen Jon Smith	D
5/5/94	REFUSE TO FILE action letter date	
9-22-94	Agency Letter to DMF Holder	E
9-3-96	Memoranda (3) regarding status of foreign inspections	F
9-25-96	DMF # —— Review # 1, Janusz Rzeszotarski, Ph.D.	G
9-25-96	DMF # —— Review # 1, Janusz Rzeszotarski, Ph.D.	H
9-30-96	Chemistry Rev. # 1: Janusz Rzeszotarski, Ph.D.	I
3-11-97	EMail regarding status of foreign inspections	J
3-19-97	Agency Letter to DMF # —— holder	K
3-19-97	Agency Letter to DMF # —— holder	L
3-19-97	Supervisory Memorandum, Stan Blum, Ph.D.	M
3-21-97	EA Memorandum "comments on draft review", Nancy Sager, PhD	Mc
4-11-97	EER: for NDS & NDP	N
1/3/2003	Re-Submission under SubPart I "Animal Rule"	
9-29-1999	NDA 9-829 S-014: Chemistry Review, Janusz Rzeszotarski, Ph.D. "This is a review of the ICN 60 mg immediate release tablet" - includes 9/30/1999 "N9-829/S-014" Approval letter	O
1-22-2003	Chemistry Rev. # 1, Janusz Rzeszotarski, Ph.D.	P
2-5-2003	Chemistry Rev. # 2, Janusz Rzeszotarski, Ph.D.	Q

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

NDA #: 20-414 **CHEM.REVIEW #** 2 **REVIEW DATE: 04-FEB-03**

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment	30-JAN-03	30-JAN-03	30-JAN-03
Amendment	04-FEB-03	04-FEB-03	04-FEB-03

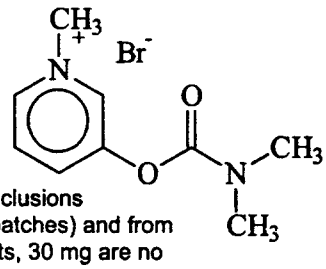
NAME & ADDRESS OF APPLICANT: Office of the Surgeon General
Department of the Army
Fort Detrick, MD 21702-5012

DRUG PRODUCT NAME
Proprietary: Pyridostigmine Bromide USP 30 mg Tablets
Nonproprietary/USAN: Pyridostigmine Bromide
Code Name/#: none
Chem.Type/Ther.Class: Acetylcholine Esterase Inhibitor

PHARMACOL.CATEGORY/INDICATION: Nerve Gas Antidote

DOSAGE FORM: Tablets
STRENGTHS: 30 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: XXXXX Rx_____OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Pyridinium, 3-[[(dimethylamino)carbonyl]oxy]-1-methyl-, bromide
CAS NUMBER: 101-26-8; (Br^-); 155-97-5 (pyridostigmine)
MOLECULAR WEIGHT: 261.12; CHEMICAL FORMULA: $C_9H_{13}BrN_2O_2$



SUPPORTING DOCUMENTS: IND —— NDA 09-829 (ICN); DMF ——
DMF —— DMF ——
RELATED DOCUMENTS: none
REMARKS/COMMENTS: The sponsor has requested that Hoffman-La Roche (H-LR) facility in Welwyn, UK be added as an alternate manufacturer of the specific batches (see Conclusions below) of the drug product. That facility manufactured the drug product from 1/91 to 12/91 (8 batches) and from 10/95 to 3/98 (21 batches), and was in GMP compliance in 1996. Since Pyridostigmine Tablets, 30 mg are no longer manufactured at the Welwyn, UK facility, no additional evaluations of this site are requested at this time. The attached spreadsheets lists the batches manufactured by H-LR within the last twelve (12) years and for which some of the SLEP testing results are provided. Also attached are the results of five (5) years stability testing by H-LR of five (5) of the more recent (1995-98) batches and the certificates of their release analysis. The H-LR drug product is of different formulation and was manufactured under the DMF —— The ICN drug product is manufactured under the DFM —— provided in support of the January 3, 2003 submission. The SLEP program does not include testing for degradants, which were monitored during the five years of HL-R stability studies. That deficiency severely impacts the value of SLEP data, and therefore, our recommendation to grant the ten years expiration date for the ICN manufactured drug product is contingent upon the sponsor's commitment to place all the batches on stability and to monitor the degradants. Using the available extrapolation techniques one can only assume that the H-LR batches kept under constant refrigeration for a period of up to ten (10) years are expected to be within the degradant specifications. The H-LR batches older than ten (10) years do not have the release CoAs and an attempt to obtain them failed. The policy of HL-R, as stated, was to destroy any records older than ten years (see the attached E-mail).
CONCLUSIONS & RECOMMENDATIONS: It is recommended to approve Hoffmann-La Roche as an alternative manufacturer of pyridostigmine bromide USP, 30 mg tablets. The following twenty (20) lots of the drug product: PYA563, PYA564, PYA 565, PYA567, PYA568, PYA569, PYA570, PYA571, PYA572, PYA573, PYA553, PYA554, PYA555, PYA556, PYA557, PYA 559, PYA560, PYA561, PYA562, and PYA566 appear to be within specifications and appropriate for dispensing. It is recommended that the older (manufactured in 1991) H-LR batches 101514, 104522, 105528, 105529, 105531, 105533, 105534, and 112538 kept by the sponsor be dispensed only after being analyzed for the assay, degradants and dissolution.
cc: Orig. NDA 20-414
HFD-120
HFD-120/WJRzeszotarski
HFD-120/RNighswander
HFD-120/MEGuzewska
Init by:MEG
Init by J.E. Simmons

W. Janusz Rzeszotarski, Ph.D., Chemist

filename: E:\msword\N20-414R.002.doc

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/s/

Janusz Rzeszotarski
2/5/03 10:32:31 AM
CHEMIST

Maryla Guzewska
2/5/03 11:43:53 AM
CHEMIST

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

NDA #: 20-414 **CHEM.REVIEW # 1** **REVIEW DATE: 10-JAN-03**

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment	07-JAN-03	07-JAN-03	07-JAN-03

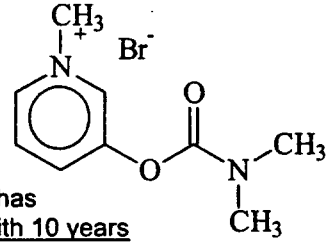
NAME & ADDRESS OF APPLICANT: Office of the Surgeon General
Department of the Army
Fort Detrick, MD 21702-5012

DRUG PRODUCT NAME
Proprietary: Pyridostigmine Bromide USP 30 mg Tablets
Nonproprietary/USAN: Pyridostigmine Bromide
Code Name/#: none
Chem.Type/Ther.Class: Acetylcholine Esterase Inhibitor

PHARMACOL.CATEGORY/INDICATION: Nerve Gas Antidote

DOSAGE FORM: Tablets
STRENGTHS: 30 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: XXXXX Rx_____OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Pyridinium, 3-[[(dimethylamino)carbonyl]oxy]-1-methyl-, bromide
CAS NUMBER: 101-26-8; (Br^-); 155-97-5 (pyridostigmine)
MOLECULAR WEIGHT: 261.12
CHEMICAL FORMULA: $C_9H_{13}BrN_2O_2$



SUPPORTING DOCUMENTS: IND ——— NDA 09-829 (ICN); DMF —— (ICN), DMF ———
RELATED DOCUMENTS: none
REMARKS/COMMENTS: Drug product initially manufactured by Hoffmann-La Roche under DMF ——— ICN purchased DMF —— (also property of HL-R) and moved manufacturing to Montreal, Quebec, Canada. The 60 mg tablet (Mestinon) has exactly the same formulation as 30 mg tablet. The recommendation for approval with 10 years expiration date is based on the combined review of the DMFs —— (ICN) and ——— (Hoffmann-La Roche) and the NDA 20-414 (above), and the approved NDAs 09-829, 09-830 and 11-665 (all ICN). The DMF —— covers manufacturing by ICN of 30 mg tablet, which is directly proportional to the approved Mestinon (pyridostigmine bromide) Tablet, 60 mg (NDA 09-829). Although the previously manufactured by Hoffmann-La Roche and ——— 30 mg tablets had different formulation their bioequivalency with the ICN tablet has been proven and their stability under refrigeration for periods exceeding 10 year proven under the SLEP (Shelf-Life Extension Program). Given the scarcity of accelerated stability data, and the extraordinary handling procedures under the battlefield conditions - the following warning should be posted: a) on the unit package and shipping container: "The contents not to be used if the package is removed from refrigeration for more than a total of six months", and b) on the immediate container (blister); "Discard after three months of issue".
CONCLUSIONS & RECOMMENDATIONS: recommend the approval of NDA 20-414 with ten (10) years expiration date.
cc: Orig. NDA 20-414
HFD-120
HFD-120/WJRzeszotarski
HFD-120/RNighswander
HFD-120/MEGuzewska
R/D Init by:MEG

W. Janusz Rzeszotarski, Ph.D., Chemist

filename: E:\msword\N20-414R.001.doc

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/s/

Janusz Rzeszotarski
1/22/03 10:40:03 AM
CHEMIST

Maryla Guzewska
1/22/03 10:49:41 AM
CHEMIST

NDA 20-414

Pyridostigmine Bromide Tablet, USP, 30 mg

U. S. Army

W. Janusz Rzeszotarski, Ph.D.

Division of Neuropharmacological Drug Product

HFD-120

Table of Contents

CHEMISTRY NDA REVIEW DATA SHEET

1. **NDA 20-414** (Pyridostigmine Bromide Tablet, USP, 30 mg)
2. **CHEMISTRY REVIEW # 1**
3. **REVIEW DATE:** 09-JAN-2003
4. **REVIEWER:** W. Janusz Rzeszotarski, Ph.D.

5. **PREVIOUS DOCUMENTS**

Previous Documents	Document Date
Original	07-MAR-94
Resubmission	24-MAY-96
Major Amendment	20-JUN-96
Major Amendment	03-JAN-03
Minor Amendment	07-JAN-03

6. **SUBMISSION BEING REVIEWED**

Major Amendment	03-JAN-03
Minor Amendment	07-JAN-03

7. **NAME AND ADDRESS OF APPLICANT**

Office of the Surgeon General
Department of the Army
Fort Detrick, MD 21702-5012

8. **DRUG PRODUCT NAME**

Proprietary:	Pyridostigmine Bromide Tablet, USP, 30 mg
Nonproprietary/USAN [1966]	Pyridostigmine Bromide
Code Name/Number:	None
Chem.Type/Ther. Class:	3P

9. **LEGAL BASIS FOR SUBMISSION** N/A

10. **PHARMACOLOGICAL CATEGORY/INDICATION**

Pyridostigmine bromide is intended to produce acetylcholinesterase inhibition in humans as part of a medical program to provide protection against soman nerve agent poisoning effects.

11. **DOSAGE FORM:** Tablet

12. **STRENGTHS** 30 mg

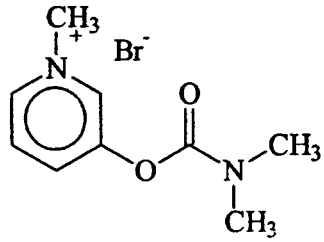
13. **ROUTE OF ADMINISTRATION** Oral

14. **DISPENSED** XXX RX

15. **SPOTS** XXX NO

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA

3-hydroxy-1-methylpyridinium bromide dimethylcarbamate



CAS NUMBER: 101-26-8; (Br^-); 155-97-5 (pyridostigmine)

MOLECULAR WEIGHT: 261.12

CHEMICAL FORMULA: $C_9H_{13}BrN_2O_2$

17. RELATED SUPPORTING DOCUMENTS

A. DMFs

DMF#	Type	Holder	Item Referenced	Code	Status	Date Review	Comments
[redacted]	II	ICN	Drug Product	1	Adequate	09-JAN-03	Manufacture
	II	Hoffmann-La Roche	Drug Product	1	Adequate	25-SEP-96	Manufacture
	II	[redacted]	Drug Substance	1	Adequate	24-JUN-96	Synthesis

B. Other Documents

Document	Application #	Description
IND	[redacted]	
NDA	09-829	ICN Mestinon (Pyridostigmine Bromide) Tablets
NDA	09-830	ICN Mestinon (Pyridostigmine Bromide) Injectable
NDA	11-665	ICN Mestinon (Pyridostigmine Bromide) Syrup

16. STATUS

Consults/CMC Related Matters	Recommendation	Date	Reviewer
Bioequivalence	Acceptable	07-AUG-96	Mahmood
EES	Acceptable (on profile)	07-JAN-03	Ferguson
Methods Validation	Pending		
EA Categorical Exclusion	Requested and granted	09-Jan-03	Rzeszotarski

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SEP 29 1999

CHEMISTS REVIEW

1. ORGANIZATION: HFD-120

2. NDA NUMBER: **09-829**

4. SUPPLEMENT NUMBERS/DATES: **S-014**
LETTERDATE: 11-MAR-99
STAMPDATE: 16-MAR-99

5. AMENDMENTS/REPORTS/DATES:
LETTERDATE: 31-MAR-99; 26-APR-99; 30-JUN-99; 09-JUL-99; 23-JUL-99;05-AUG-99
STAMPDATE: 26-APR-99; 29-APR-99; 30-JUN-99; 12-JUL-99; 26-JUL-99; 09-AUG-99

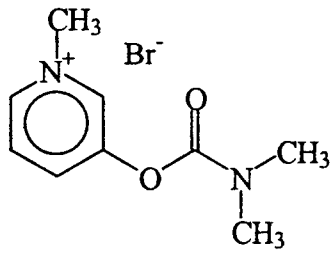
6. REC'D BY CHEMIST: 23-MAR-99, 05-APR-99; 29-APR-99;30-JUN-99; 12-JUL-99; 26-JUL-99; 09-AUG-99

7. APPLICANT NAME AND ADDRESS: ICN Pharmaceuticals, Inc.
3300 Hyland Avenue
Costa Mesa, CA 92628

8. NAME OF DRUG: Mestinon (pyridostigmine bromide) Tablets

9. NONPROPRIETARY NAME: Pyridostigmine bromide

10. CHEMICAL NAME/STRUCTURE: 3-hydroxy-1-methylpyridinium bromide dimethylcarbamate



11. DOSAGE FORM(S): Tablets

12. POTENCY(IES): 60 mg

13. PHARM. CATEGORY: Myasthenia gravis

14. HOW DISPENSED: XXX (Rx) (OTC)

15. RECORDS AND REPORTSCURRENT: XXX (YES) (NO)

16. RELATED IND/NDA/DMF(S): IND [redacted]; NDAs 11-665, 15,193.

17. SUPPLEMENT PROVIDES FOR: change to a new manufacturing, packaging and quality control site at ICN Canada Ltd., 1956, rue Bourdon, Montreal, Quebec, Canada H4M 1V1.

18. COMMENTS: The finished product is currently manufactured by Hoffmann-La Roche (Roche), 340 Kingsland Street, Nutley, New Jersey, 07110-1199 (Roche), and is owned by ICN Pharmaceuticals Inc. (ICN), 3300 Hyland Avenue, Costa Mesa, California 92626. In October 1988, ICN purchased the product from Roche, but Roche has continued to manufacture, pack and perform quality control testing for ICN. Ownership of this NDA was transferred to ICN effective August 7, 1997. ICN now intends to manufacture, pack, and perform quality control testing for this product. Except as mentioned in this supplement, all other conditions in the application remain the same. Specially: the manufacturing process, testing and controls for the active new drug substance remain unchanged. On March, 25th, 1999 I have requested from Mr Anil Hiteshi of ICN to provide the Agency with a resubmitted supplement where the pages are numbered. On 13-APR-99 I requested from Mr Hiteshi explanation why the methods and MV for [redacted] included in the application. On 14-APR-99 in view of scarcity of real-time data I discussed with Mr Hiteshi the expiry date. RFI letter was sent to ICN on 30-JUN-99 and a satisfactory answer was received on 26-JUL-99. See Review Notes. EER acceptable as of 16-JUL-99 (see attached).

19. CONCLUSIONS/RECOMMENDATIONS: Recommend NDA 09-829/S-014, as amended, approved with 18 months expiration date. Draft Letter enclosed.

20. REVIEWER NAME	SIGNATURE	DATE COMPLETED
W. Janusz Rzeszotarski, Ph.D.	/S/	28-SEP-99

cc:
ORIG: NDA 09-829
HFD-120
HFD-120/TWheelous
HFD-120/WJRzeszotarski
INIT: MEG /S/ 29.99

filename: e:\msword\n09829s.014

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ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: NDA 9829/014
Stamp: 16-MAR-1999
Regulatory Due: 16-JUL-1999
Applicant: ICN PHARMS
3300 HYLAND AVE
COSTA MESA, CA 92626
Priority: 1S
Org Code: 120

Action Goal:
District Goal: 11-JUN-1999
Brand Name: MESTINON TABLETS
Estab. Name:
Generic Name: PYRIDOSTIGMINE BROMIDE

Dosage Form: (TABLET)
Strength: 60 MG

Application Comment:
FDA Contacts: T. WHEELOUS (HFD-120) 301-594-5504 , 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-JUL-1999 by M. EGAS (HFD-322) 301-594-0095

Establishment: 9690016
ICN CANADA LTD
1956 BOURDON ST
MONTREAL, , CA

DMF No:
AADA:
Responsibilities: FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER
Profile: TCM
OAI Status: NONE
Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	24-MAR-1999				RZESZOTARS
SUBMITTED TO DO	25-MAR-1999	GMP			EGASM
ASSIGNED INSPECTION	25-MAR-1999	GMP			EGASM
INSPECTION SCHEDULED	09-JUL-1999		16-JUL-1999		IRIVERA
INSPECTION PERFORMED	16-JUL-1999		16-JUL-1999		EGASM
DO RECOMMENDATION	16-JUL-1999			ACCEPTABLE INSPECTION	EGASM
BASED ON INVESTIGATOR'S COMMENTS ONLY					
OC RECOMMENDATION	16-JUL-1999			ACCEPTABLE DISTRICT RECOMMENDATION	EGASM

DMF: [redacted] **DMF Type:** II

Title: Pyridostigmine Bromide Tablets USP 30 mg

1. CHEM REVIEW # 1 **2. REVIEW DATE:** 25-SEP-96

3. DMF INFORMATION REVIEWED:

Type of Submission	Date of Submission	Location of Information
Original	10-MAY-96	

4. PREVIOUS DOCUMENTS

Type of Document	Date of Document	Comment
None		

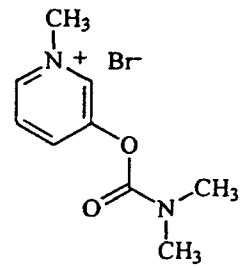
5. NAME & ADDRESS OF DMF HOLDER AND REPRESENTATIVE(S):

NAME: Roche Products Limited
ADDRESS: 40 Broadwater Road, Welwyn Garden City, Hertfordshire, England
REPRESENTATIVE: Mr Jeremy Brace, Department of Regulatory Affairs
TELEPHONE: +44 1707 365612 FAX: +44 1707 377838

U.S. AGENT (if necessary): None
NAME: N/A
ADDRESS: N/A
REPRESENTATIVE: N/A
TELEPHONE: N/A

6. ITEM REVIEWED:

NAME: Pyridostigmine Bromide
CHEMICAL NAME: Pyridinium, 3[[(dimethylamino)carbonyl]oxy]-1-methyl, bromide
CAS NUMBER: 101-26-8
MOLECULAR WEIGHT: 261.12
CHEMICAL FORMULA: $C_9H_{13}BrN_2O_2$
STRUCTURAL FORMULA:



7. DMF REFERENCED FOR:

NDA\ANDA\AADA\IND: 20-414
APPLICANT NAME: The Office of the Surgeon General, United States Army
LOA DATE: 10-MAY-1996
DRUG PRODUCT NAME: Pyridostigmine Bromide Tablets USP 30 mg
DOSAGE FORM: Tablet CODE: 500
STRENGTH: 30 mg
ROUTE OF ADMINISTRATION: Oral CODE: 001

8. SUPPORTING DOCUMENTS: None

9. CURRENT STATUS OF DMF:

DATE OF LAST UPDATE OF DMF: Original
DATE OF MOST RECENT LIST OF COMPANIES FOR WHICH LOA's HAVE BEEN PROVIDED:
The Office of the Surgeon General, United States Army

10. CONSULTS: None

11. REMARKS:

12. CONCLUSIONS: INADEQUATE

13. COMMENTS: Numerous deficiencies, see the DRAFT LETTER.

/S/
W. Janusz Rzeszotarski, Ph.D.
Chemist, HFD-810

/S/
Stanley W. Blum, Ph.D.
Team Leader, HFD-810

cc:
DMF (2 copies)
HFD-120/Division File NDA 20-414
HFD-120/CSO/RNighswander
HFD-810/SChemist/SWBlum
R/D Init by: /S/ - 3/19/97

F/T DMF

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

NDA #: 20-414 **CHEM.REVIEW #** 1 **REVIEW DATE: 30-SEP-96**

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	24-MAY-96	28-MAY-96	28-MAY-96

NAME & ADDRESS OF APPLICANT: Department of the Army
Office of the Surgeon General
Falls Church, VA 22041-3258

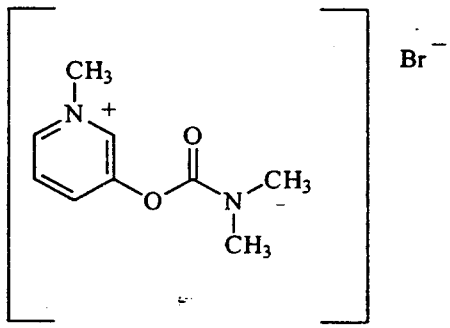
DRUG PRODUCT NAME
Proprietary: None
Nonproprietary/USAN: Pyridostigmine Bromide Tablets
Code Name/#:
Chem.Type/Ther.Class: Acetylcholinesterase inhibitor

PHARMACOL.CATEGORY/INDICATION: NAPS

DOSAGE FORM: Tablets
STRENGTHS: 30 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: XXXXX Rx_____OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

3-{[(dimethylamino)carbonyl]oxy}-1-methylpyridinium bromide



$C_9H_{13}BrN_2O_2$; Molecular Weight: 261.12;
CAS #: 101-26-8

SUPPORTING DOCUMENTS: INDs ——— (Dept of the Army); NDAs 9-829; 9-830; 11-665; 15-193 (Mestinon, Hoffmann-La Roche; NDA 17-398 (Regnol, Organon).
RELATED DOCUMENTS:
REMARKS/COMMENTS: A drug product derived directly from Mestinon (pyridostigmine bromide tablets) 60 mg for myasthenia gravis and Mestion 30 mg for military use in the United Kingdom, Canada, Switzerland and Denmark. Drug substance is to be manufactured in ——— although the participation of the former is in doubt (see N020414.M01 and the attachements). Therefore only the reviews of DMFs ——— and ———(Hoffmann-La Roche) have been completed. The drug product is manufactured under contract by Hoffmann-La Roche UK (DMF ———). The DMFs ——— are inadequate due to numerous deficiencies and do not support the NDA. Both manufacturing facilities have to be inspected before the application can be approved.

CONCLUSIONS & RECOMMENDATIONS: Recommend NDA 20-414 **NOT APPROVED** until the completion of establishment inspections and successful updating of DMFs ———

cc:Orig. NDA 20-414
HFD-120
HFD-120/WJRzeszotarski
HFD-120/RNighswander
HFD-120/SWBlum
R/D Init by:SWE /S/ 3/19/97

/S/
W. Janusz Rzeszotarski, Ph.D., Chemist

filename: N020414.000

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DMF. **DMF Type:** II

Title: Pyridostigmine Bromide

1. CHEM REVIEW # 1 **2. REVIEW DATE:** 25-SEP-96

3. DMF INFORMATION REVIEWED:

Type of Submission	Date of Submission	Location of Information
Original	28-MAR-96	

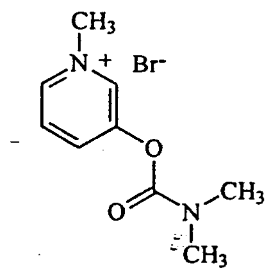
4. PREVIOUS DOCUMENTS

Type of Document	Date of Document	Comment
Original	11-APR-94	

5. NAME & ADDRESS OF DMF HOLDER AND REPRESENTATIVE(S):

U.S. AGENT (if necessary): None
NAME: N/A
ADDRESS: N/A
REPRESENTATIVE: N/A
TELEPHONE: N/A

6. ITEM REVIEWED:
NAME: Pyridostigmine Bromide
CHEMICAL NAME: Pyridinium, 3[[(dimethylamino)carbonyl]oxy]-1-methyl, bromide
CAS NUMBER: 101-26-8
MOLECULAR WEIGHT: 261.12
CHEMICAL FORMULA: $C_9H_{13}BrN_2O_2$
STRUCTURAL FORMULA:



7. DMF REFERENCED FOR:
NDA\ANDA\AADA\IND: 20-414
APPLICANT NAME: The Office of the Surgeon General, United States Army
LOA DATE: 10-MAY-1996
DRUG PRODUCT NAME: Pyridostigmine Bromide Tablets USP 30 mg
DOSAGE FORM: Tablet CODE: 500
STRENGTH: 30 mg
ROUTE OF ADMINISTRATION: Oral CODE: 001

8. SUPPORTING DOCUMENTS: None

9. CURRENT STATUS OF DMF:

DATE OF LAST UPDATE OF DMF: Previous Original filed on 11-APR-94
DATE OF MOST RECENT LIST OF COMPANIES FOR WHICH LOA's HAVE BEEN PROVIDED:
The Office of the Surgeon General, United States Army
Roche Products Limited, England

10. CONSULTS: None

11. REMARKS:

12. CONCLUSIONS: INADEQUATE

13. COMMENTS: Numerous deficiencies, see the DRAFT LETTER.

/S/

W. Janusz Rzeszotarski, Ph.D.
Chemist, HFD-810

/S/

Stanley W. Blum, Ph.D.
Team Leader, HFD-810

cc:
DMF (2 copies)
HFD-120/Division File NDA 20-414
HFD-120/CSO/RNighswander
HFD-810/SChemist/SWBlum
R/D Init by: 3/19/97

F/T DMF

11 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.