

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-175**

**CHEMISTRY REVIEW(S)**



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

Nighswander  
JUN 29 2000

NDA #: 21-175

CHEM.REVIEW # 2

REVIEW DATE: 29-JUN-00

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Response to IR Letter	01-JUN-00	02-JUN-00	02-JUN-00

NAME & ADDRESS OF APPLICANT:

Department of the Army  
504 Scott Street  
Fort Detrick, MD 21702-5012

DRUG PRODUCT NAME

Proprietary:

None

Nonproprietary/USAN:

Atropine/Pralidoxime Multi-chamber Injector

Code Name/#:

NAADS, or MA, or ?

Chem.Type/Ther.Class:

2012002

PHARMACOL.CATEGORY/INDICATION:

Antidote for nerve gas

DOSAGE FORM:

Injection (multi-chamber auto-injector)

STRENGTHS:

2.1 mg/0.7 mL atropine + 600 mg/2.0 mL

pralidoxime

ROUTE OF ADMINISTRATION:

IM

DISPENSED:

XXXXX Rx \_\_\_\_\_ OTC

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

Atropine: benzeneacetic acid,  $\alpha$ -(hydroxymethyl)-8-methyl-8-azabicyclo[3.2.1] oct-3-yl ester, endo -(±)-

C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub>; Molecular Weight: 289.38;

CAS #: 51-55-8

Pralidoxime chloride: pyridinium, 2-

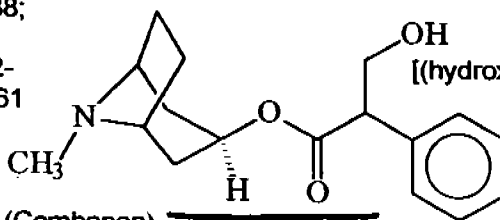
C<sub>7</sub>H<sub>9</sub>ClN<sub>2</sub>O; Molecular Weight: 172.61

CAS # 51-15-0

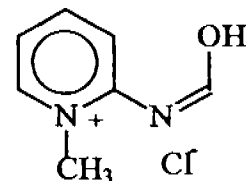
SUPPORTING DOCUMENTS:

NDAs: 14-134 (Protopam

Chloride); 17-106 (Atropen); 18-986 (Combopen);



[(hydroxyimino)methyl]-1-methyl-, chloride



RELATED DOCUMENTS:

REMARKS/COMMENTS: A response to IR Letter of April 11, 2000. The application was determined not approvable due to unjustified, excessive levels of degradants and impurities proposed. The response addressed the issue and the corrected specifications are now fully acceptable. The system is to replace the now available kit known as MK I NAAK which contains the current nerve agent antidotes: AtroPen and ComboPen. The NAADS will deliver atropine (2.1 mg in 0.7 ml) and pralidoxime chloride (600 mg in 2 ml) from one (two-chamber) auto-injector, through a single needle for self-aid and buddy-aid of service members who have been exposed to organophosphorous nerve agents.

CONCLUSIONS & RECOMMENDATIONS: Recommend the approval of NDA 21-175. Copy of acceptable EER enclosed.

cc:

Orig. NDA 21-175

HFD-120

HFD-120/WJRzeszotarski

HFD-120/RNighswander

HFD-120/MEGuzewska

R/D Init by:MEG

*IS/* 29/00

*IS/*  
W. Janusz Rzeszotarski, Ph.D., Chemist

FDA CDER EES  
ESTABLISHMENT EVALUATION REQUEST  
SUMMARY REPORT

Application: NDA 21175/000  
Stamp: 06-DEC-1999 Regulatory Due: 06-JUN-2000  
Applicant: US ARMY  
504 SCOTT ST  
FORT DETRICK, MD 217025012

Priority: 3P  
Action Goal:  
Brand Name: ATROPINE/PRALIDOXIME  
CHLORIDE 2.1MG OF  
Established Name:  
Generic Name: ATROPINE/PRALIDOXIME  
CHLORIDE 2.1MG OF  
Dosage Form: INJ (INJECTION)  
Strength: 2.1MG/0.7ML//600MG/2ML

Org Code: 120

District Goal: 07-APR-2000

FDA Contacts: R. NIGSWANDER (HFD-120)  
W. RZESZOTARSKI (HFD-120)  
M. GUZEWSKA (HFD-120)

301-594-2850 , Project Manager  
301-594-2850 , Review Chemist  
301-594-5571 , Team Leader

Overall Recommendation:

**ACCEPTABLE on 06-JUN-2000 by M. EGAS (HFD-322) 301-594-0095**

Establishment: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

DMF No: \_\_\_\_\_  
AADA No: \_\_\_\_\_

Profile: CSN OAI Status: NONE  
Last Milestone: OC RECOMMENDATION  
Milestone Date: 06-JUN-2000  
Decision: ACCEPTABLE  
Reason: DISTRICT RECOMMENDATION

Responsibilities: \_\_\_\_\_  
\_\_\_\_\_

Establishment: 1950222  
MERIDIAN MEDICAL TECHNOLOGI  
2555 HERMELIN DR  
SAINT LOUIS, MO 63144

DMF No:  
AADA No:

Profile: SVS OAI Status: NONE  
Last Milestone: OC RECOMMENDATION  
Milestone Date: 08-MAY-2000  
Decision: ACCEPTABLE  
Reason: DISTRICT RECOMMENDATION

Responsibilities: \_\_\_\_\_  
\_\_\_\_\_

Establishment: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

DMF No: \_\_\_\_\_  
AADA No: \_\_\_\_\_

Profile: CSN OAI Status: NONE  
Last Milestone: OC RECOMMENDATION

Responsibilities: \_\_\_\_\_  
\_\_\_\_\_

FDA CDER EES  
ESTABLISHMENT EVALUATION REQUEST  
SUMMARY REPORT

Milestone Date: **14-FEB-2000**  
Decision: **ACCEPTABLE**  
Reason: **BASED ON PROFILE**

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Establishment: \_\_\_\_\_  
DMF No: \_\_\_\_\_  
AADA No: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

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Profile: **CSN**                      OAI Status: **NONE**                      Responsibilities: \_\_\_\_\_  
Last Milestone: **OC RECOMMENDATION**  
Milestone Date: **26-APR-2000**  
Decision: **ACCEPTABLE**  
Reason: **DISTRICT RECOMMENDATION**

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APPEARS THIS WAY  
ON ORIGINAL

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ON ORIGINAL

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

NDA #: 21-175

CHEM.REVIEW # 3

REVIEW DATE: 26-SEP-01

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AZ	15-AUG-01	15-AUG-01	16-AUG-01

NAME & ADDRESS OF APPLICANT:

Department of the Army  
504 Scott Street  
Fort Detrick, MD 21702-5012

DRUG PRODUCT NAME

Proprietary:

Nonproprietary/USAN:

Code Name/#:

Chem.Type/Ther.Class:

PHARMACOL.CATEGORY/INDICATION:

DOSAGE FORM:

STRENGTHS:

ROUTE OF ADMINISTRATION:

DISPENSED:

None

Atropine/Pralidoxime Multi-chamber Injector

NAADS, or MA, or ?

2012002

Antidote for nerve gas

Injection (multi-chamber auto-injector)

2.1 mg/0.7 mL atropine + 600 mg/2.0 mL

pralidoxime

IM

XXXXX Rx \_\_\_\_\_ OTC

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

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Pralidoxime chloride: pyridinium, 2-

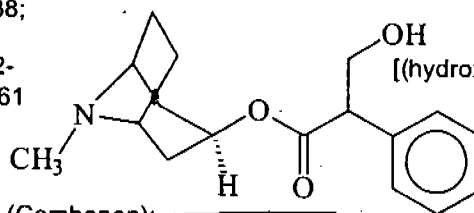
C<sub>7</sub>H<sub>9</sub>ClN<sub>2</sub>O; Molecular Weight: 172.61

CAS # 51-15-0

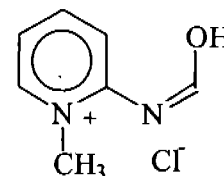
SUPPORTING DOCUMENTS:

NDA: 14-134 (Protopam

Chloride); 17-106 (Atropen); 18-986 (Combopen);



[(hydroxyimino)methyl]-1-methyl-, chloride



RELATED DOCUMENTS:

REMARKS/COMMENTS: A response to AE Letter of June 6, 2001. Part 1 of CMC report was reviewed in review #2 as response to IR letter and recommended AP. This review addresses only the part # 2 of CMC response to AE Letter requesting the \_\_\_\_\_ The data requested has been included in the report RP-346 attached with the response. In accordance to ICE recommended guidelines, the following \_\_\_\_\_ cycles were to be performed. From batch 9MI082 100 units were subjected to a \_\_\_\_\_ study cycling between \_\_\_\_\_ Units from this batch held at 25°C served as controls. At the conclusion of the study the units were submitted to Analytical Services for appearance, Atropine and Pralidoxime assays, \_\_\_\_\_ Units were also submitted to

Quality Control for functionality testing.

CONCLUSIONS & RECOMMENDATIONS: The information provided indicates that there is no difference in the analytical results between the \_\_\_\_\_ and control samples. No CMC concerns to provided draft labeling and package labels. Recommend the approval of NDA 21-175. Copy of acceptable EER attached.

cc:

Orig. NDA 21-175

HFD-120

HFD-120/WJRzeszotarski

HFD-120/RNighswander

HFD-120/MEGuzewska

R/D Init by:MEG

W. Janusz Rzeszotarski, Ph.D., Chemist

28-SEP-2001

Page 1 of 2

FDA CDER EES  
ESTABLISHMENT EVALUATION REQUEST  
SUMMARY REPORT

Application: NDA 21175/000 Priority: 3P Org Code: 120  
 Stamp: 06-DEC-1999 Regulatory Due: 15-FEB-2002 Action Goal: District Goal: 07-APR-2000  
 Applicant: US ARMY Brand Name: ATROPINE/PRALIDOXIME  
 C/O OFFICE OF SURGEON GENERAL CHLORIDE 2.1MG OF  
 504 SCOTT ST ATTN MCMR-RCQ-R Established Name:  
 FORT DETRICK, MD 217025012 Generic Name: ATROPINE/PRALIDOXIME  
 CHLORIDE 2.1MG OF  
 Dosage Form: INJ (INJECTION)  
 Strength: 2.1MG/0.7ML//600MG/2ML

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

Overall Recommendation:  
**ACCEPTABLE on 06-JUN-2000 by EGASM**

Establishment: \_\_\_\_\_ DMF No: \_\_\_\_\_  
 \_\_\_\_\_ AADA No: \_\_\_\_\_  
 \_\_\_\_\_

Profile: CSN OAI Status: NONE Responsibilities: \_\_\_\_\_  
 Last Milestone: OC RECOMMENDATION  
 Milestone Date 06-JUN-2000  
 Decision: ACCEPTABLE  
 Reason: DISTRICT RECOMMENDATION

Establishment: 1950222 DMF No: \_\_\_\_\_  
 MERIDIAN MEDICAL TECHNOLOGI AADA No: \_\_\_\_\_  
 2555 HERMELIN DR  
 ST LOUIS, MO 63144

Profile: SVS OAI Status: NONE Responsibilities: FINISHED DOSAGE  
 Last Milestone: OC RECOMMENDATION MANUFACTURER  
 Milestone Date 08-MAY-2000  
 Decision: ACCEPTABLE  
 Reason: DISTRICT RECOMMENDATION

Establishment: \_\_\_\_\_ DMF No: \_\_\_\_\_  
 \_\_\_\_\_ AADA No: \_\_\_\_\_  
 \_\_\_\_\_

Profile: CSN OAI Status: NONE Responsibilities: \_\_\_\_\_  
 Last Milestone: OC RECOMMENDATION

Milestone Date **14-FEB-2000**  
Decision: **ACCEPTABLE**  
Reason: **BASED ON PROFILE**

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Establishment: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

DMF No: \_\_\_\_\_  
AADA No: \_\_\_\_\_

Profile: CSN                      OAI Status: NONE  
Last Milestone: **OC RECOMMENDATION**  
Milestone Date **26-APR-2000**  
Decision: **ACCEPTABLE**  
Reason: **DISTRICT RECOMMENDATION**

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Responsibilities: \_\_\_\_\_  
\_\_\_\_\_

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL