UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND
READINESS

MEMORANDUM FOR SECRETARY OF THE ARMY
SECRETARY OF THE NAVY
SECRETARY OF THE AIR FORCE
CHAIRMAN, JOINT CHIEFS OF STAFF
DIRECTOR, DEFENSE LOGISTICS AGENCY

SUBJECT: Requirements Associated with the Food and Drug Administration Approval of Pyridostigmine Bromide Tablets as a Nerve Agent Pretreatment

On February 5, 2003, the Food and Drug Administration (FDA) approved the use of pyridostigmine bromide (PB) tablets for nerve agent pretreatment against Soman. The approval provides the Department of Defense (DoD) with a product that will enhance force health protection against chemical threats. However, as part of the approval process, certain logistical and medical record keeping requirements were identified. This memorandum addresses clinical requirements applicable to use of PB. Nothing in this memorandum affects conditions of employment of civilian employees.

First, use of PB must be recorded in servicemembers' personal medical records and the automated information data system (e.g., MEDPROS, SAMS, AFCITA, CHCS, PDTS, if archived). I recommend recording individual issue of PB tablets in a manner that will facilitate these record-keeping requirements.

Second, due to the product's temperature-stability profile, PB tablets must be issued to personnel within 3 months if removed from refrigeration and stored at controlled room temperature (59 - 86 degrees F, or 15 - 30 degrees C). PB tablets must be discarded/destroyed 90 days after they are issued to individuals, whether they were previously stored in a refrigerator or at controlled room temperature. Services must establish plans to issue replacement stocks of PB tablets to servicemembers every 90 days, if there is a continuing threat of exposure to Soman. Because of the need to dispose of PB tablets issued to personnel after 90 days, Services should consider the availability of replacement stocks when establishing a basis of initial issue (i.e. some units may want to issue only one packet/sleeve of PB instead of two to each servicemember to reduce potential wastage).

Third, an interim patient package insert must be provided with each packet of PB tablets. Services will comply with the instructions at attachment 1 with regard to the distribution and dispensing of the interim patient package insert. This plan also calls for the replacement of all retained pre-approval stocks of PB tablets within five years.

Fourth, the approval of the product resulted in the creation of approved labeling by the Food and Drug Administration (package insert for health care providers). The requirements for

distribution of this approved labeling to physicians, physician assistants, pharmacists, nurses, and medics are provided at attachment 2.

Fifth, the approval of PB was accompanied by the need to ensure all servicemembers and other affected personnel are properly trained in the history, use, drug action and side effects associated with this product. Long term, this training should be incorporated into each Service's training activities. More urgent, however, is the requirement to provide adequate training and information to deployed servicemembers. A new revised interim patient package insert is being quickly fielded and distributed with PB, providing new information (attached). In addition, a briefing package is available (attached).

Sixth, Services will maintain electronic/hard copy medical records of personnel to whom PB is distributed or offered. These records may be required for surveys or studies to determine safety and medical benefit of PB. Services will make available to representatives of the US Army Medical Research and Materiel Command, or their contractors when requested, non-classified electronic rosters of such personnel — and hard copy/electronic medical records generated as part of the military operation — for FDA-required post-marketing studies to determine safety and medical benefit of PB. Additionally, incorporation of data obtained on PB use should be made part of ongoing longitudinal health studies (e.g., Millennium Cohort Study).

Finally, post-deployment questionnaires should include a new line documenting whether the individual did or did not take these medical countermeasures during the deployment and whether they perceived that they experienced any adverse reactions from the medication.

David S. C. Chu

Attachments:
As stated

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

MAR 2 5 2003

ACTION MEMO

FOR: UNDER SECRETARY OF DEFENSE (PERSONNEL AND READINESS)

FROM: William Winkenwerder, Jr., MD, Assistant Secretary of Defense (Health Affairs)

SUBJECT: Policy for Requirements Associated with the Food and Drug Administration Approval of Pyridostigmine Bromide Tablets as a Nerve Agent Pretreatment

- On February 5, 2003, the Food and Drug Administration (FDA) approved the use of pyridostigmine bromide (PB) tablets for nerve agent pretreatment. The approval provides the Department of Defense (DoD) with a product that will enhance force health protection against chemical threats. However, as part of the approval process, certain logistical and medical record keeping requirements were identified.

- First, use of PB must be recorded in individual's, servicemember's, and other military operations personnel's medical records.

- Second, due to the product's temperature stability profile to degrade when stored outside refrigeration, any PB issued to servicemembers must be discarded/destroyed after 90 days.

- Third, an interim patient package insert must be provided with each packet of PB tablets at time of dispensing. Services will comply with the instructions at Enclosure 1 with regard to the distribution and dispensing of the interim patient package insert. This plan also calls for the replacement of all retained pre-approval stocks of PB tablets within five years.

- Fourth, the approval of the product resulted in the creation of approved labeling by the FDA (package insert for health care providers). The requirements for distribution of this approved labeling to physicians, physician assistants, pharmacists, nurses, and medics is provided at Enclosure 2.

- Fifth, the approval of PB was accompanied by the need to ensure all servicemembers and other personnel taking part in all military operations are properly trained in the history, use, drug action and side effects associated with this product. Long term, this training should be incorporated into each

Service's training activities. More urgent, however, is the requirement to provide adequate training and information to deployed servicemembers. A new revised interim patient package insert is being quickly fielded and distributed with PB, providing new information (attached). In addition, a briefing package is available (attached).

- Sixth, Services will make available to representatives of the US Army Medical Research and Materiel Command, or their contractors, as requested non-classified electronic rosters of personnel taking part in the military operation and hard copy/electronic medical records generated as part of the military operation for FDA required post-marketing studies to determine safety and medical benefit of pyridostigmine bromide. Additionally, incorporation of data-obtained on pyridostigmine bromide use should be made part of ongoing longitudinal studies (e.g., Millennium Cohort Study).

- This action establishes new policy.

RECOMMENDATION: USD (P&R) approve and sign the memo at TAB A

COORDINATION: TAB B

Prepared by: Salvatore M. Cirone, FHP/R, 703-575-2679, PCDOCS#

Tab

B

Department of Defense
Pyridostigmine Bromide Tablets, 30 mg
Licensure Transition Logistics Plan

1. **Issue**. The licensure/New Drug Application (NDA) approval for Pyridostigmine Bromide (PB) tablets under the "Animal Rule" by the Food and Drug Administration (FDA) created a unique opportunity for the Department of Defense (DoD). Normally, products labeled as Investigational New Drugs (INDs) must be withdrawn from the field once NDA approval is achieved. Unlike most investigational products, PB tablets are distributed to worldwide locations for contingency use rather than for "research" purposes. For this reason, removal of IND-labeled material from the field immediately after NDA approval would be detrimental to force health protection and national defense. In order to meet requirements for ready access to PB tablets, a Transition Logistics Plan was developed to cover the interim between current status with pre-approval PB in the field and conversion to new product manufactured post FDA approval. DoD must now execute that plan. Key aspects of this plan are described below.

2. **Background.** DoD, through the Services, must communicate and issue the new, approved, detailed labeling for PB tablets (hereafter called the package insert) to all health care providers. DoD must provide all personnel receiving PB tablets with new patient information. The FDA is permitting the DoD to use an interim product information sheet (hereafter referred to as the patient package insert) to replace the current patient package insert enclosed in the IND-labeled PB inventory. The Services must ensure personnel receive these new patient package inserts. DoD must replace all retained IND-labeled PB inventory with newly licensed product over a maximum period of five years from the NDA approval date (5 February 2008).

3. **DoD Transition Logistics Plan.** There are three key aspects of the Transition Logistics Plan.

a. The Services must distribute the approved package insert to all physicians and health care providers, down to the medic-level. The approved package insert provides detailed clinical information needed for the safe, appropriate prescribing of PB tablets and monitoring of personnel for safety and effectiveness. Due to the short time frame between approval of the NDA and potential use of PB tablets, a multi-pronged approach, employing numerous methods such as e-mail, official DoD messages, website pages, and hardcopy will be performed by the Services. More information about the provision of the approved package insert can be found in the Annex titled "Distribution Plan for Approved Labeling of Pyridostigmine Bromide (Package Insert for Health Care Providers)".

b. The Services must execute a comprehensive plan to ensure all Service members receiving the current IND-labeled PB tablets also receive an interim patient package insert regarding the approval of this drug by the FDA under the Animal Rule. To fulfill that requirement the Services will remove the old patient package insert from sleeves of IND-labeled PB tablets and issue replacement interim patient package inserts at the time these tablets are dispensed (the interim plan).

c. The Services will execute the phased replacement of IND-labeled product with appropriately labeled, licensed PB tablets over a maximum of 5 years from NDA approval (the

replacement plan). More specific details of both the interim plan and the replacement plan are provided below.

d. Interim Plan – Provision of interim patient package insert. The Services will ensure Service members receive the appropriate interim patient package insert. These inserts replace the current patient package inserts enclosed with the IND-labeled inventory. The following language will be added to the interim patient package inserts:

Please remove and discard previous information provided in the PB packet and replace it with this information sheet.

This Information Sheet also updates the information on the cardboard sleeve and foil pack containing your PB.

* **The US Food and Drug Administration (FDA) has approved 30 mg PB tablets as a pretreatment against a Soman nerve gas attack. Therefore, PB is no longer considered investigational when used as a nerve agent pretreatment against Soman.**

* **Discard your PB tablets 3 months after issue.**

You must read the following information about PB to find out more about its risks and benefits and how to use it.

The Services will instruct personnel to remove the old, IND patient package inserts from sleeves of IND-labeled PB tablets at time of dispensing and replace those with new, interim patient package inserts. These new patient package inserts must be issued with the IND product after licensure, because removal of the current IND-labeled inventory from the field, and replenishment of this materiel with licensed product would be detrimental to military readiness and potential contingency operations.

These interim patient package inserts will be distributed by the Services' Medical Logistics Agencies and the Defense Logistics Agency. Ten sheets will be distributed with each pouch containing ten sleeves of PB tablets. These required interim patient package inserts will be attached or banded to each Mylar pouch/bag containing ten sleeves of PB tablets while in storage and distribution, and must accompany the materiel throughout the supply chain to point of dispensing.

DoD will issue a Medical Materiel Quality Control Message through medical logistics channels directing the Services to distribute the interim patient package inserts to all sites possessing PB tablets. Additionally, the message will direct sites to dispense/issue these interim patient package inserts, one insert with each sleeve of PB tablets.

Services will confirm receipt of the interim patient package inserts at each receiving location and will provide detailed directions for issue/dispensing of these with each sleeve of PB tablets throughout the chain of custody and issue.

e. Replacement Plan. DoD must replace current IND-labeled product with licensed product within a reasonable period. DoD proposed a phased approach for the replacement of IND-labeled product over a maximum of five years from the NDA approval date. The Services will continue to use retained IND-labeled PB inventory, dispensed with the interim patient package insert during this transition period. All retained IND-labeled stocks of PB tablets will be replaced with newly manufactured material over a maximum of 5 years (approximately 20% of stocks each year). All IND-labeled stocks of PB tablets will be replaced with newly produced PB tablets not later than 5 February 2008.

4. **Conclusion.** Careful execution of the DoD PB Transition Logistics Plan supports DoD's needs for force health protection and a reasonable transition to replace IND-labeled product with licensed PB tablets.

Distribution Plan for Approved Labeling of Pyridostigmine Bromide

(Package Insert for Health Care Providers)

Background. The Department of Defense (DoD) has pre-positioned large amounts of pyridostigmine bromide (PB) tablets labeled as investigational drugs for force health protection purposes. The recent Food and Drug Administration approval of the New Drug Application (NDA) now requires communication of the approved labeling to health care providers. This paper describes the DoD plan to provide health care providers the approved labeling of pyridostigmine bromide.

Plan. Due to the short time frames between the approval of the NDA and a potential need for use of the product, a multi-pronged approach is proposed.

a. Services to utilize e-mail notifications (attachment of the .pdf version of the approved package insert) through major subordinate commands to all physicians and other health care providers (down to medic level). U.S. Army to include notification to those health care personnel assigned outside of the U.S. Army Medical Command (e.g., Forces Command, 8th Army, U.S.Army Reserve Command). For those organizations with an e-mail system that has return receipt, utilize the return receipt option to document receipt of the message by the health care providers. Notification of services to include National Guard/Reserve units in addition to active duty forces. Electronic mail routes to also include health care information system (composite health care system mail messaging).

b. Joint Staff to notify combatant commanders and command surgeons of the approved labeling and the requirement to distribute the labeling to health care providers of their respective component services. Emphasis to be placed on distribution of information to deployed and deploying medical personnel, particularly Reserves, who are deployed and may not be able to access their normal e-mail.

c. Services to provide information to health care providers in hard copy at mobilization stations for reserve and active forces.

d. DoD and Services will prominently post a message to web sites used by health care providers in the course of their routine business. Include link with pdf down-load and html viewed versions of approved label. Potential sites may include (not exhaustive list):

Department of Defense:

Assistant Secretary of Defense for Health Affairs
Deployment Link (Deployment Health Support)
Deployment Health Clinical Center

TRICARE
The Military Vaccines Web Site
Anthrax Vaccine Program
Pharmacoeconomic Center
Uniformed Services University of Health Sciences
Armed Forces Epidemiological Board
DoD GulfLINK

U.S. Air Force:

Surgeon General of the Air Force
Air Force Medical Treatment Facilities
Air Force Link
Air National Guard
Air Force Wing Commands
Air Force Institute for Environment, Safety and Occupational Health Risk Analysis

U.S. Army:

Surgeon General of the Army (Army Medicine)
Army Medical Department Center and School
Army Regional Medical Commands and Medical Treatment Facilities
Army Link
Army Reserve On-line (U.S. Army Reserve Command)
The Army National Guard (National Guard Bureau)
U.S. Army Medical Research and Materiel Command
U.S. Army Medical Materiel Development Activity
U.S. Army Medical Materiel Activity
U.S. Army Medical Research Institute of Chemical Defense
U.S. Army Center for Health Promotion and Preventive Medicine
U.S. Army Pharmacy
U.S. Army Soldier and Biological Chemical Command
U.S. Army Knowledge On-line
U.S. Army PERSCOM

U.S. Navy:

Surgeon General of the Navy
Bureau of Medicine and Surgery
Navy Medical Treatment Facilities
Navy On-line Link
Naval Reserve Force
Naval Medical Information Management Center
Navy Pharmacy
Naval Health Research Center
Navy Environmental Health Center

Virtual Naval Hospital
U.S. Marines
Marines Life Line
Marine Corps Manpower and Reserve Affairs
Marine Corps Anthrax Vaccine Program

e. DoD to inform other Federal departments that may have direct or indirect roles in support of DoD, e.g., Department of Transportation (U.S. Coast Guard), Central Intelligence Agency, Homeland Defense, Department of Justice, Department of State, Department of Veterans Affairs, Department of Health and Human Services, Department of Energy.

f. Defense Logistics Agency to include approved package insert with any newly procured PB.

g. DoD to coordinate with publisher of Military Medicine to include story of PB approval and package insert in next possible edition. Services to coordinate with Public Affairs Officers to use other forums to make announcement (e.g., Army's MEDCOM Mercury).

Department of Defense

Pyridostigmine Bromide Tablets, 30 mg

Licensure Transition Logistics Plan

Issue The licensure/New Drug Application (NDA) approval for Pyridostigmine Bromide (PB) tablets under the "Animal Rule" by the Food and Drug Administration (FDA) created a unique opportunity for the Department of Defense (DoD). Normally, products labeled as Investigational New Drugs (INDs) must be withdrawn from the field once NDA approval is achieved. Unlike most investigational products, PB tablets are distributed to worldwide locations for contingency use rather than for "research" purposes. For this reason, removal of IND-labeled material from the field immediately after NDA approval would be detrimental to force health protection and national defense. In order to meet requirements for ready access to PB tablets, a Transition Logistics Plan was developed to cover the interim between current status with pre-approval PB in the field and conversion to new product manufactured post FDA approval. The DoD must now execute that plan. Key aspects of this plan are described below.

Background The DoD, through the Services, must communicate and issue the new, approved, detailed labeling for PB tablets (the package insert) to all health care providers. The DoD must provide all personnel receiving PB tablets with new patient information. The FDA is permitting the DoD to use an interim product information sheet (the patient package insert) to replace the current patient package insert enclosed in the IND-labeled PB inventory. The Services must ensure personnel receive these new patient package inserts. The DoD must replace all retained IND-labeled PB inventory with newly licensed product over a maximum period of five years from the NDA approval date (February 5, 2008).

DoD Transition Logistics Plan There are three key aspects of the Transition Logistics Plan.

1. The Services must distribute the approved package insert to all physicians and health care providers, down to the medic-level. The approved package insert provides detailed clinical information needed for the safe, appropriate prescribing of PB tablets and monitoring of personnel for safety and effectiveness. Due to the short time frame between approval of the NDA and potential use of PB tablets, a multi-pronged approach, employing numerous methods such as e-mail, official DoD messages, website pages, and hardcopy will be performed by the Services. More information about the provision of the approved package insert can be found in the Annex titled "Distribution Plan for Approved Labeling of Pyridostigmine Bromide (Package Insert for Health Care Providers)."

2. The Services must execute a comprehensive plan to ensure all servicemembers receiving the current IND-labeled PB tablets also receive an interim patient package insert regarding the approval of this drug by the FDA under the Animal Rule. To fulfill that requirement, the Services will remove the old patient package insert from sleeves of IND-labeled PB tablets

and issue replacement interim patient package inserts at the time these tablets are dispensed (the interim plan).

3. The Services will execute the phased replacement of IND-labeled product with appropriately labeled, licensed PB tablets over a maximum of 5 years from NDA approval (the replacement plan). More specific details of both the interim plan and the replacement plan are provided below.

Interim Plan - Provision of interim patient package insert The Services will ensure servicemembers and other personnel receive the appropriate interim patient package insert. These inserts replace the current patient package inserts enclosed with the IND-labeled inventory. The following language will be added to the interim patient package inserts:

- **Please remove and discard previous information provided in the PB packet and replace it with this information sheet.**
- **This Information Sheet also updates the information on the cardboard sleeve and foil pack containing your PB.**
- **The US Food and Drug Administration (FDA) has approved 30 mg PB tablets as a pretreatment against a Soman nerve gas attack. Therefore, PB is no longer considered investigational when used as a nerve agent pretreatment against Soman.**
- **Discard your PB tablets 3 months after issue.**
- **You must read the following information about PB to find out more about its risks and benefits and how to use it.**

The Services will instruct personnel to remove the old, IND patient package inserts from sleeves of IND-labeled PB tablets at time of dispensing and replace those with new, interim patient package inserts. These new patient package inserts must be issued with the IND product after licensure, because removal of the current IND-labeled inventory from the field and replenishment of this materiel with licensed product would be detrimental to military readiness and potential contingency operations.

The Services' Medical Logistics Agencies and the Defense Logistics Agency will distribute these interim patient package inserts. Ten sheets will be distributed with each pouch containing ten sleeves of PB tablets. These required interim patient package inserts will be attached or banded to each Mylar pouch/bag containing ten sleeves of PB tablets while in storage and distribution, and must accompany the materiel throughout the supply chain to point of dispensing.

DoD will issue a Medical Materiel Quality Control Message through medical logistics channels directing the Services to distribute the interim patient package inserts to all sites possessing PB tablets. Additionally, the message will direct sites to dispense/issue these interim patient package inserts, one insert with each sleeve of PB tablets.

Services will confirm receipt of the interim patient package inserts at each receiving location and will provide detailed directions for issue/dispensing of these with each sleeve of PB tablets throughout the chain of custody and issue.

Replacement Plan The DoD must replace current IND-labeled product with licensed product within a reasonable period. DoD proposed a phased approach for the replacement of IND-labeled product over a maximum of five years from the NDA approval date. The Services will continue to use retained IND-labeled PB inventory, dispensed with the interim patient package insert during this transition period. All retained IND-labeled stocks of PB tablets will be replaced with newly manufactured material over a maximum of five years (approximately 20% of stocks each year). All IND-labeled stocks of PB tablets will be replaced with newly produced PB tablets not later than February 5, 2008.

Conclusion Careful execution of the DoD PB Transition Logistics Plan supports DoD's needs for force health protection and a reasonable transition to replace IND-labeled product with licensed PB tablets.

Important Information
Rx Only
February, 2003

Pyridostigmine Bromide (PB) 30 mg

- Please remove and discard previous information provided in the PB packet and replace it with this information sheet.
- This information sheet also updates the information on the cardboard sleeve and foil pack containing your PB.
- The US Food and Drug Administration (FDA) has approved 30 mg PB tablets as a pretreatment against a Soman nerve gas attack.
- Therefore, PB is no longer considered investigational when used as a nerve agent pretreatment against Soman.
- Discard your PB tablets 3 months after issue.
- You must read the following information about PB to find out more about its risks and benefits and how to use it.

Protection against Chemical Warfare Agents

Pyridostigmine bromide is approved for protection against the chemical nerve agent Soman (GD). Other chemical nerve agents include Sarin (GB), Tabun (GA) and VX. Nerve agents work by making your muscles weak. They can make you lose control of your muscles. You can die if your breathing muscles are paralyzed.

Your main protection against chemical weapons is your chemical protective mask and battle dress overgarment. You also have other items to help you if you are exposed to chemical warfare agents. These items are:

Two antidotes (atropine and 2-PAM) —that are part of the MARK I Nerve Agent Antidote Kit or ATNAA (Antidote Treatment - Nerve Agent Autoinjector).

Pyridostigmine Bromide (PB) — PB is approved as a pretreatment against a Soman nerve agent attack. The approval is based on safety studies in humans and effectiveness (how well it works) studies conducted in animals. The FDA has approved PB based only on animal studies of effectiveness because it is not ethical to do these studies in humans. Human studies would require exposing people to the deadly effects of nerve agents, risking poisoning them or even killing them. Studies in monkeys and guinea pigs show

that pretreatment with PB makes the antidotes (atropine and 2-PAM) work better against Soman (GD). PB pretreatment in animals has not been shown to make the antidotes work better against other nerve agents. Based on the animal studies of whether PB works against Soman, it is thought that any potential benefits from use of PB occur only if:

(1) PB is taken within 8 hours before, but not right before, exposure to the nerve agent Soman. (If PB is taken right before (when the nerve gas attack alarm is given) or during nerve agent exposure, it may not work and may make the effects of Soman worse).

(2) Atropine and 2-PAM are used when symptoms of nerve agent poisoning occur.

How To Take Your PB

(1) Your chain of command will tell you when it is time to take PB. This decision will be based on the threat of exposure to Soman nerve agents.
(2) You must take 1 tablet of PB every 8 hours until your chain of command tells you to stop taking PB.
(3) Do not take PB more often than you are told. **Do not double up on your dose if you miss taking it.**
(4) There is no known advantage to taking extra PB right before Soman exposure.
(5) No further PB should be taken after nerve agent exposure has occurred.
(6) Instead of taking more PB after nerve agent exposure has occurred, if you experience most of the **MILD** symptoms of nerve agent poisoning, you should **IMMEDIATELY** hold your breath **(DO NOT INHALE)** AND PUT ON YOUR PROTECTIVE MASK. Then administer atropine and 2-PAM (*one* MARK I kit or *one* ATNAA).
(7) Contact your unit medical officer if side effects from PB continue and limit duty performance.

Who should not take PB

Do not take PB if you:

- Have a history of bowel or bladder blockage (obstruction);
- Are overly sensitive to anticholinesterase medicines (certain drugs used during surgery like physostigmine, edrophonium, neostigmine, and ambenonium);

Tell your doctor or medic before taking PB if you:

- Are pregnant;
- Have asthma;
- Are allergic to bromide;
- Take blood pressure medicine;
- Have high eye pressure (glaucoma).

Also, tell your doctor about all your other medical conditions you may have including heart problems, or reflux esophagitis (GERD).

Side Effects

Side effects include stomach cramps, watery eyes, gas, blurred vision, diarrhea, runny nose, nausea, difficulty or tightness in breathing, frequent urination, acid stomach (including heartburn or reflux), increased salivation, tingling of fingers, toes, arms, and legs, sweating, muscle twitching or weakness, headaches, muscle cramps, and dizziness. Most side effects are mild and will go away without treatment. If your side effects do not go away, see your unit doctor or medic. This is not a complete list of symptoms that may occur. See your unit doctor right away if your side effects are very bad or for any symptoms that concern you.

PB has been safely used and has been FDA approved for over 40 years in the U.S. to treat a disease called myasthenia gravis (MG). Human studies of PB at doses intended for military use have found PB to be generally safe.

About your rights and welfare:

DOD may collect information on the use of PB to help decide how best to protect deployed forces in the future. Information that identifies you will remain private (confidential). However, the FDA may review any data collected by DoD for the purpose of evaluating PB. Direct questions about your rights and welfare to your unit medical officer, or e-mail questions to hsrrb@det.amedd.army.mil.

For more information about PB:

Talk to your unit medical officer or medic. You can also e-mail questions about PB directly to the U.S. Army Medical Research and Materiel Command at address hsrrb@det.amedd.army.mil.

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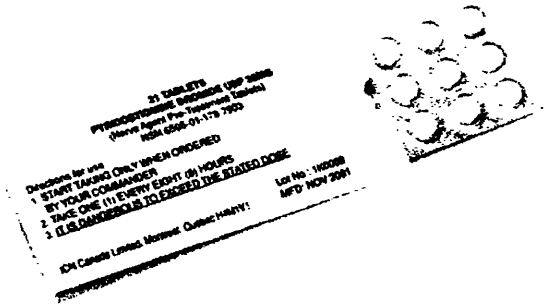
Fort Detrick, MD 21702-5012

USAMMDA 30206450

Pyridostigmine Bromide Service Member's Briefing

What you need to know



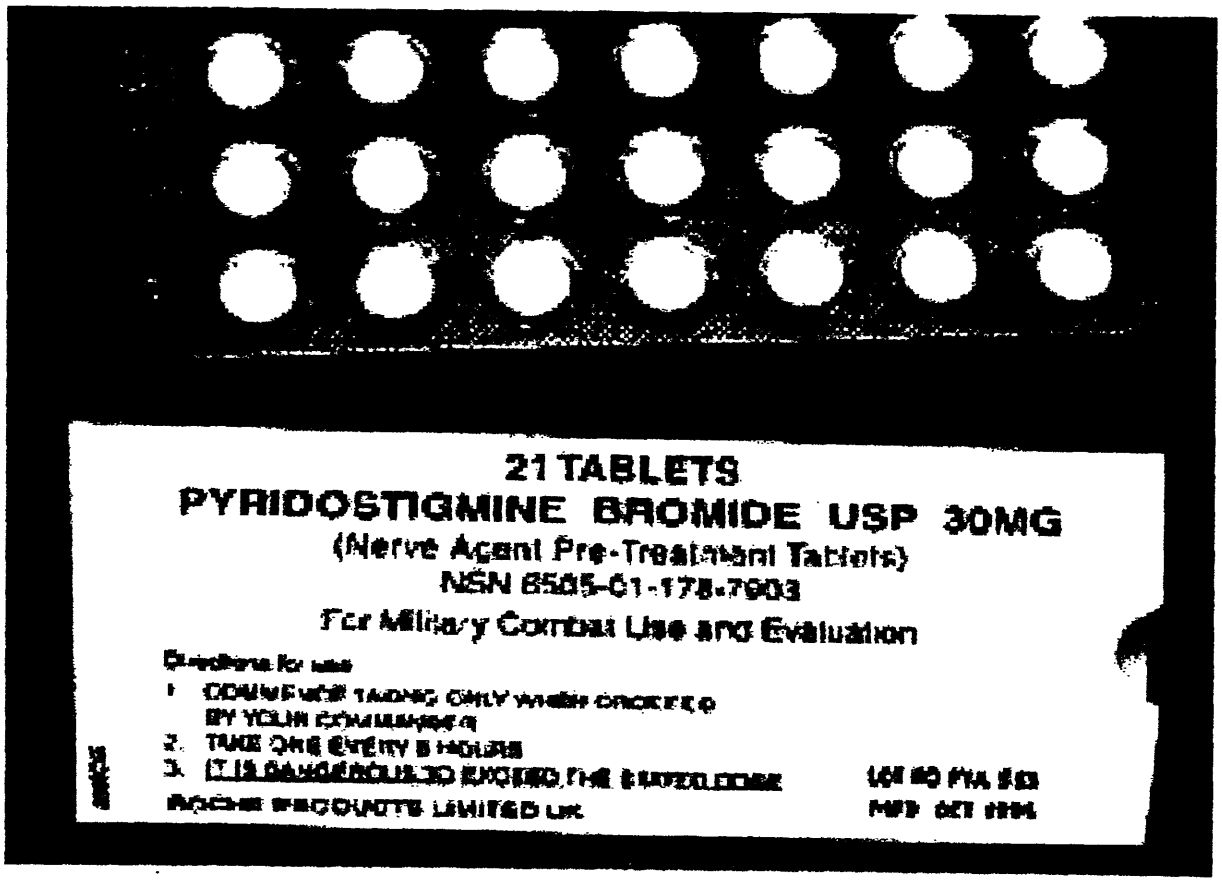
Speaker's Name/Title

Organization

Pyridostigmine Bromide (PB): What, Why and How

- This information brief will describe the use of **PB** in military operations as a protection against the nerve agent **Soman**.
- It is important for you to understand why we need PB, how it works, and how to use it.
- PB is an oral medication that comes as small tablets. It must be taken **BEFORE** a Soman nerve agent attack. **AFTER** an attack, the nerve agent antidotes that are in your MARK I kit must still be used to treat the effects of the nerve agent.
- Your **PRIMARY PROTECTION** against chemical weapons is your protective mask and battle dress overgarment (MOPP gear).

Pyridostigmine Bromide Tablets (PB Tabs)

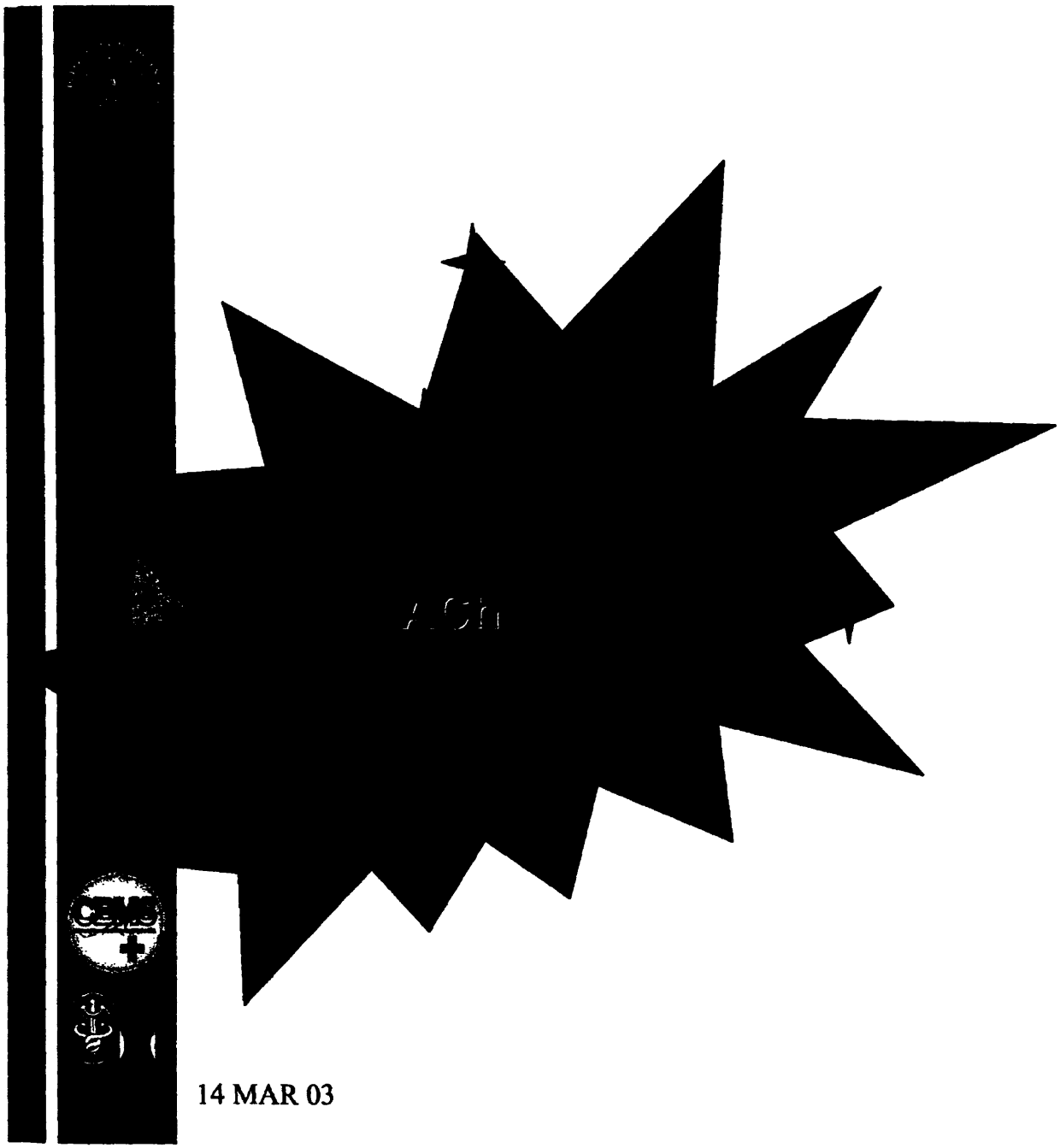


Nerve Agents: Symptoms

- Remember the signs and symptoms of nerve agents. See STP 21-1-SMCT: Soldier's Manual of Common Tasks.
- Some of these symptoms may be absent:
  - unexplained runny nose
  - muscle twitching
  - unexplained sudden headache
  - stomach cramps
  - excessive drooling
  - nausea
  - tightness of chest
  - difficulty seeing

Nerve Agents

- Nerves work by sending out a chemical (acetylcholine - **ACh**) which causes a muscle to contract or twitch. Another chemical (acetylcholinesterase - **AChE**) stops the ACh from working, which allows the muscle to relax. These chemicals occur naturally in your body.
- Nerve Agents attack the body's nervous system by preventing AChE from breaking down ACh. Too much ACh causes a constant state of muscle contraction. If not treated by antidotes, this overworking of the muscles eventually results in muscle failure, collapse, and death.
- Nerve agents work within a few seconds and some even work after treatment with the MARK I kit & CANA.



14 MAR 03


AChE
Nerve
Agent
ACh
ACh
ACh

Pretreatment with PB Tabs

- Pretreatment with PB tabs has been shown to increase the effectiveness of the MARK I antidote kit against nerve agent **Soman** in animal studies.
- PB must be used **PRE-EXPOSURE ONLY**. It does not eliminate the requirement to use the MARK I kit after exposure to treat symptoms of nerve agent poisoning.
- If you have been exposed or exhibit symptoms to nerve agents, **STOP** taking your PB tabs and use the atropine and 2-PAM chloride autoinjectors in your MARK I kit.

PB Tabs: FDA Approval

- PB tabs FDA-approved for over 40 years to treat Myasthenia Gravis - a chronic disease of the muscles
  - higher doses
  - longer period of time.
- FDA-approved as pretreatment for exposure to the nerve agent **Soman** in February 2003
  - Approval based on results from studies in animals as human trials would require exposing people to the deadly effects of nerve agents – which would not be ethical.
  - Use with MOPP gear and all other NBC countermeasures

Reasons you should <u>not</u> take PB

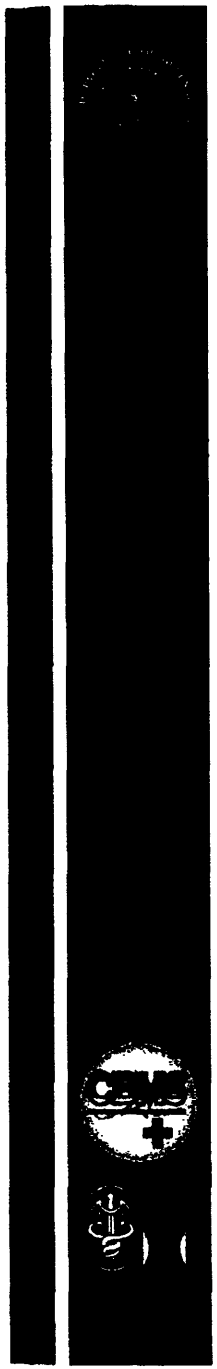
- Mechanical intestinal or urinary obstruction
- Hypersensitivity to anticholinesterase agents

Medical Conditions in which PB should be used with caution:

- Asthma
- Stomach ulcers or reflux esophagitis
- High blood pressure (b-blocker medication) or other heart problems
- Glaucoma
- Allergy to bromide
- Pregnancy

How to Take PB (1 of 2)

- Your commander will instruct you to begin taking PB tablets.
- Take one (1) PB tablet every eight (8) hours for a total of three (3) tablets in a day - for a period not to exceed 14 days.
- To be effective, PB must be taken within the previous 8 hours before an attack
- Continue to take PB tabs until either:
  - **Your Commander tells you to stop**
  - **Your Medical Officer tells you to stop**
  - **You finish two blister packs (42 tabs)**
  - **You have been exposed to nerve agent**



How to Take PB Tabs (2 of 2)

- Remember, PB tabs are for pretreatment only! If there is a Soman nerve agent attack and/or you develop symptoms of nerve agent poisoning (such as drooling, twitching, excessive sweating) use your atropine and 2-PAM chloride autoinjectors. **DO NOT** continue to take PB.
- If you miss a dose of PB, **DO NOT** double up at the next dose – take only one tablet for the next dose.

Temporary Side Effects That May Occur

- **Most Common**: gas, diarrhea, stomach cramps, frequent urination
- **Less Common**: headaches, dizziness, stomach cramps, nasal drip, urinary retention, nausea, dehydration
- **Short Term Side Effects that are similar to Nerve Agent Poisoning: (you will know you are experiencing PB side effects as they appear within 30-60 minutes of taking PB)**

  tightness in chest, tingling of extremities, muscle twitching, frequent urination, muscle weakness, increased drooling, muscle cramps, watery eyes/blurred vision. **You should seek medical attention if these or other symptoms persist or worsen.**
- **Long Term Side Effects**: no long term side effects have been found

PB Tabs: Key Points

- **FOLLOW ALL INSTRUCTIONS**
- Report serious side effects of PB to your Medical personnel
- Keep all of your PB tabs for turn-in upon redeployement
- **Feel free to ask questions – your complete understanding is important**