SKIN EXPOSURE REDUCTION PASTE AGAINST CHEMICAL WARFARE AGENTS (SERPACWA)

DESCRIPTION

SKIN EXPOSURE REDUCTION PASTE AGAINST CHEMICAL WARFARE AGENTS (SERPACWA) is a viscous white paste containing a 50:50 mixture of a perfluoroalkylpolyether (PFPE) and a polytetrafluoroethylene (PTFE).

PFPE has the empirical formula C_xF_{2x+1}-[O-CF(CF_3)-CF_2]$_n$-(O-CF_2)$_m$-O-C_yF_{2y+1} where x, y=1, 2 or 3 and n/m > 40. PTFE has the empirical formula $(CF_2CF_2)_n$.

The PFPE CAS number is: 69991-67-9.
The PTFE CAS number is: 9002-84-0.

CLINICAL PHARMACOLOGY

SERPACWA is not absorbed through intact human skin in detectable amounts. The systemic absorption of SERPACWA was evaluated under simulated usage conditions. Subjects were exposed to SERPACWA for four hours daily for two consecutive days according to package directions. For one hour each day the subjects experienced a period of light exercise under Mission Oriented Protective Posture 2 (MOPP 2) conditions (Battle Dress Uniform overgarment and overboots worn). At the end of each 4 hour period the subjects were allowed to remove residual SERPACWA via showering. NMR analysis of urine samples for both organic (limit of detection 0.3ppm) and inorganic fluorine (limit of detection 2ppm) revealed no detectable levels of fluorine from either component of SERPACWA.

Pharmacology

Mechanism of Action:

SERPACWA serves as a physical barrier that may reduce or delay exposure of skin to chemical warfare agents (CWA). SERPACWA has no other known action.

Nonclinical and Clinical Studies:

Nonclinical Studies:

In controlled laboratory studies on animals, SERPACWA has been shown to reduce or delay skin exposure to a variety of CWA including: sulfur mustard (HD), a blistering agent; the nerve agents soman (GD), thickened soman (TGD), and VX; T-2 mycotoxin, a skin necrosis agent; and CS, a lacrimating riot control gas.

In vitro, concentrated liquid sulfur mustard (HD) and thickened soman (TGD) did not penetrate a thin (0.15 mm) layer of SERPACWA covering M8 Chemical Agent Detector Paper after continuous exposure for more than six hours.

In vivo studies designed to assess penetration of CWA applied directly to the skin of anesthetized rabbits with and without SERPACWA pretreatment demonstrated limited, but significant, protection by SERPACWA against 4-hour challenges with sulfur mustard (HD), T-2 Toxin, soman (GD) and VX.

SERPACWA applied prior to a 4-hour challenge with 1 µl liquid sulfur mustard (HD) substantially reduced the size of the lesions. Those lesions present at the SERPACWA-treated sites were less severe. Application of SERPACWA was also shown to block all macroscopic signs of dermal irritation 24 to 48 hours following a 6-hour challenge with T-2 toxin and signs of erythema following a 15 minute exposure to 1.0% CS.

Under controlled laboratory conditions the majority of anesthetized rabbits pretreated with SERPACWA survived a 4 hour challenge with lethal concentrations of soman (GD) or VX. In comparison, almost all animals died within 4 hours of soman (GD) or VX exposure in the absence of SERPACWA. Blood acetylcholinesterase (AChE) activity associated with exposure to soman (GD), thickened soman (TGD) or VX was significantly higher in most animals pretreated with SERPACWA compared to unprotected animals. However, almost all of the animals exposed to soman (GD), and approximately two-thirds of the animals exposed to VX experienced some loss of blood AChE activity, indicative of CWA penetration of the SERPACWA barrier.

The relevance of these studies in anesthetized animals under controlled conditions of SERPACWA application and exposure to CWA to actual field use conditions is not quantifiable. The limited, but significant, protection that was provided in animals was critically dependent on complete coverage of exposure sites. The barrier properties and safety of SERPACWA under conditions of wear time greater than 4 hours were not assessed.

The use of insect repellents containing DEET, some camouflage paints (loam and sand), and possibly permethrin, reduced but did not completely eliminate the protective effects of SERPACWA. Further testing showed that wiping off DEET with a dry towel prior to application of SERPACWA partially restored protection afforded by SERPACWA.

Clinical Studies:

SERPACWA has been shown to reduce or delay exposure of skin to chemicals used as surrogates for chemical warfare agents in human trials. However, SERPACWA did not provide complete protection in every tested subject. These surrogates include methyl nicotinate, a skin irritant and vasodilator, and urushiol, a resin contained in plants like poison ivy.

A clinical study was performed to evaluate SERPACWA's ability to reduce the severity of dermatitis resulting from four hours of continuous contact with urushiol (poison ivy resin) in acetone solution in 50 healthy human volunteers with a history of sensitivity to urushiol. Subjects with a history of allergic reactions to glycols, cosmetics, or skin care products were excluded from this study. Sites on the ventral forearms of subjects were wiped with 70% isopropyl alcohol and allowed to air dry. Sites were pretreated with SERPACWA. One hour later, each subject had a matched pair of SERPACWA-pretreated and untreated sites exposed to equal volumes of a urushiol solution. To test SERPACWA at a range of urushiol doses, equal volumes of a more concentrated urushiol solution were applied to a different matched pair of SERPACWA-pretreated and untreated sites on each subject. The sites were left undisturbed for 4 hours, then washed off with a soapless cleanser and water. Based on photographs taken 4 days after urushiol challenge, two blinded physician observers independently scored the contact dermatitis severity, with a score of 0.0 corresponding to no reaction, and a score of 4.0 corresponding to a bullous, ulcerative reaction.

The following table shows the contact dermatitis scores recorded for the test sites.

	Number of Test Sites By Score			
	SERPACWA-treated Sites		SERPACWA-untreated Sites	
Scores After High Dose Challenge	Scorer #1	Scorer #2	Scorer #1	Scorer #2
0	60	58	5	4
0.5	20	19	31	22
1.0	14	15	36	
1.5	1	2	12	22
2.0	1	1	9	14
2.5			3	4
3.0		1		3
3.5				4
4.0				
	SERPACWA-treated Sites		SERPACWA-untreated Sites	
Scores After Low Dose Challenge	Scorer #1	Scorer #2	Scorer #1	Scorer #2
0	64	59	6	7
0.5	21	27	39	27
1.0	9	5	27	26
1.5	2	3	13	19
2.0			10	7
2.5		2	1	4
3.0				5
3.5				1

The contact dermatitis scores at each matched pair of SERPACWA-treated and SERPACWA-untreated sites were compared. The mean differences in the contact dermatitis scores were 0.7 to 1.0 point lower for sites pretreated with SERPACWA compared to matched sites not treated with SERPACWA. The degree to which SERPACWA reduced the development of dermatitis was varied among individuals, between the different observers, and between different urushiol dosages. Not all SERPACWA-treated subjects were completely protected from a urushiol reaction, but SDERPACWA-treated sites exhibited dermatitis scores lower than the SERPACWA-untreated matched sites. The observed reduction in contact dermatitis scores may not predict the degree of protection SERPACWA would provide to humans from exposure to CWA.

A clinical study was performed to determine whether perspiration, induced during the time interval between SERPACWA application and exposure of subjects to a cutaneous irritant, disrupted barrier properties of the product. Subjects with a history of allergic reactions to glycols, cosmetics, or skin care products were excluded from this study. SERPACWA was applied to selected sites on the ventral forearm skin of 37 healthy normal subjects, who were then exposed to conditions that induce active perspiration. Following this exposure, sites pretreated with SERPACWA and sites not treated with SERPACWA were challenged with the dermal irritant/vasodilator methyl nicotinate for 2 minutes. Intraindividual comparisons of laser Doppler velocimetry (LDV) measured at methyl nicotinate-challenged sites showed substantially less cutaneous vasodilation from methyl nicotinate exposure in SERPACWA**B**treated sites compared to SERPACWA-untreated sites. Not all SERPACWA-treated sites were completely protected from methyl nicotinate-induced vasodilation. The degree to which SERPACWA reduced methyl nicotinate-induced vasodilation was variable among individuals. The LDV analysis was corroborated using a Draize visual scoring method. The observed reduction in LDV scores may not predict the degree of protection SERPACWA would provide to humans from exposure to CWA.

INDICATIONS AND USAGE

SERPACWA is indicated only in conjunction with MOPP gear to reduce or delay the absorption of chemical warfare agents through the skin when SERPACWA is applied prior to exposure. SERPACWA was not tested for protection against chemical warfare agents in humans. SERPACWA was not tested in conjunction with MOPP gear in the presence of a CWA surrogate (see NONCLINICAL and CLINICAL STUDIES Sections). SERPACWA is not intended to be a replacement for or to be used without any portion of the MOPP gear. The ability of SERPACWA to reduce exposure to CWA or CWA surrogates has not been studied beyond 5 hours after application.

SERPACWA should only be used under threat of imminent CWA attack. SERPACWA should not be used in training exercises, due to the potential risk of polymer fume fever (See PRECAUTIONS Section).

WARNINGS

SERPACWA is intended for cutaneous use only. Do not apply to the eyes or to mucous membranes. The safety of SERPACWA and its barrier properties when applied to abraded skin or skin with wounds has not been investigated.

PRECAUTIONS

General:

The handling of smoking products, such as cigarettes, by personnel who have even small amounts of SERPACWA on their hands may result in contamination of these products with SERPACWA. Smoking of products contaminated with the PTFE component of SERPACWA generates harmful fumes. A flu-like syndrome called polymer fume fever has been reported in individuals who have been exposed to fumes generated by the burning of PTFE, such as fumes generated by the smoking of cigarettes contaminated with PTFE powder. The severity of this syndrome depends upon the amount of exposure and the number of exposures. Polymer fume fever should not be regarded as a transitory or benign condition. The long-term health significance of smoking products contaminated with PTFE has not been characterized. While patients with mild manifestations of this syndrome appear to have self-limited symptoms without lasting effects, a patient with a more severe manifestation of this syndrome developed interstitial pulmonary fibrosis. The risk associated with smoking products contaminated with SERPACWA has not been characterized. Because the paste-like consistency of SERPACWA could possibly enable it to adhere more efficiently to smoking products than does PTFE powder, the risk of polymer fume fever, and its degree of severity, may be higher following SERPACWA exposure to smoking products than the historical risk associated with handling of cigarettes by personnel exposed to PTFE powder exposure.

Personnel should not touch smoking products after they have applied SERPACWA to their skin surface. Personnel are advised to wash their hands thoroughly to remove all visible traces of SERPACWA prior to handling smoking products. Smoking products may become contaminated even if there are no visible traces of SERPACWA on the hands. Some, but not all individuals with polymer fume fever reported that the tobacco smoke had an unusual or unpleasant taste.

If the smoke has an unusual taste, this may be indicative of product contamination. Under these circumstances, personnel should cease smoking and discard the potentially-contaminated products. Even in the absence of an unusual or unpleasant taste, the smoking product may still be contaminated, so smoking should be avoided after use of SERPACWA. Clothing or other materials exposed to SERPACWA, including SERPACWA packaging, should not be destroyed by burning, because of the release of toxic fumes.

In animal studies, the presence of insect repellent containing DEET (N,N-diethyl-m-toluamide) has been demonstrated to significantly reduce the barrier effects of SERPACWA. The use of water to remove products containing DEET reduces the barrier effect of SERPACWA, while removal of insect repellent with dry gauze partially restores a barrier effect for SERPACWA. Though the relevance of the results of these animal studies to humans is unknown, it is recommended that products containing DEET be removed with a dry towel or cloth before SERPACWA is applied.

EFFECT OF DEET PRODUCT AND PRODUCT REMOVAL METHODS ON SERPACWA EFFICACY WHEN CHALLENGED WITH HD

Pretreatment Agents	N	Test Conditions	Product Removal Method	Lesion Area Ratio (%)	
				Arithmetic Mean (95% C.I.)	Geometric Mean (95% C.I.)
None	8	-		100	
SERPACWA	32	-		27 (11, 43)	26 (15, 46)
DEET PRODUCT + SERPACWA	32	A	None	91 (16, 166)	82 (41, 166)
DEET PRODUCT + SERPACWA	8	B	None	92 (70, 114)	77 (59, 102)
DEET PRODUCT + SERPACWA	8	C	moist towelette	122 (85, 158)	97 (72, 132)
DEET PRODUCT + SERPACWA	8	C	dry gauze	48 (32, 64)	39 (29, 52)

a) DEET product was applied 3 hours prior to SERPACWA applications.
b) DEET product was applied approximately 12 minutes prior to SERPACWA applications.
c) DEET product was applied for 3 hours then removed just prior to SERPACWA applications by either a moist towelette (alcohol-free, dilute soap solution) or a dry gauze pad.

Some camouflage paints (loam and sand) and possibly permethrin also reduced the protective effects of SERPACWA.

Studies in humans were not conducted with CW or surrogate agents using SERPACWA in the presence of insect repellents containing DEET, or loam and sand camouflage paints, or permethrin. It is not known whether DEET affects the barrier properties of SERPACWA or whether it is the other ingredients in this product.

Information for Personnel:

Personnel using SERPACWA should receive the following information and instructions:

1. SERPACWA is to be applied to skin in conjunction with and prior to the wearing of MOPP gear. In the event of CWA attack, SERPACWA may be unable to reduce or delay the absorption of CWA through the skin unless used in conjunction with MOPP gear.

2. The duration of SERPACWA's ability beyond 5 hours to reduce or delay the absorption through the skin of chemical warfare agents is not known. SERPACWA's ability to reduce or delay the absorption through the skin of chemical warfare agent surrogates has been demonstrated in humans.

3. The handling of smoking products such as cigarettes by personnel who have even small amounts of SERPACWA on their hands may result in contamination of these products with SERPACWA. Smoking products contaminated with SERPACWA generates harmful fumes. A flu-like syndrome called polymer fume fever has been reported in individuals who have been exposed to smoke contaminated with a component of SERPACWA. The severity of this syndrome depends upon the amount of exposure and the number of exposures. Polymer fume fever should not be regarded as a transitory or benign condition. The long-term risk associated with smoking products contaminated with SERPACWA has not been characterized.

   Personnel should not touch smoking products after they have applied SERPACWA to their skin surface. Personnel are advised to wash their hands thoroughly to remove all visible traces of SERPACWA prior to handling smoking products. Smoking products may become contaminated even if there are no visible traces of SERPACWA on the hands. Some, but not all, individuals with polymer fume fever reported that the tobacco smoke had an unusual or unpleasant taste.

If the smoke has an unusual taste this may be indicative of product contamination. Under these circumstances, personnel should cease smoking and discard the potentially-contaminated products. Even in the absence of an unusual or unpleasant taste, the smoking product may still be contaminated, so smoking should be avoided. Clothing or other materials, exposed to SERPACWA, including SERPACWA packaging, should not be destroyed by burning, because of the release of toxic fumes.

4. DEET products should be removed with a dry towel or cloth before SERPACWA is applied. Do not use water or a moist towelette.

5. Some camouflage paints (loam and sand) may reduce the protective effects of SERPACWA.

6. The potential for interaction between SERPACWA and a skin decontaminating kit has not been characterized. However, in animals, the protection provided by a SERPACWA-like product and the M291 Skin Decontaminating Kit was superior to the protection provided by the M291 Skin Decontaminating Kit alone.

Drug Interactions:

There have been no studies of the interaction of SERPACWA with any other drugs, and no drug-specific interactions were noted during any clinical trials. DEET products have been demonstrated to reduce the effect of SERPACWA. SERPACWA has been shown to have no effect on the M40 Chemical Protective Mask seal, but the compatibility between MOPP gear materials or battle dress uniform and SERPACWA has not been characterized.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

The genotoxicity and carcinogenicity potential of SERPACWA was not evaluated. However, PFPE was negative in the standard Ames Assay at concentrations up to 5000 µg/plate. Nonclinical information was not submitted to assess the potential effect of SERPACWA on fertility.

Pregnancy Category:

Pregnancy Category C: Animal developmental toxicology studies have not been conducted with SERPACWA.

It is also not known whether SERPACWA can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. SERPACWA should be given to a pregnant woman only if clearly needed.

Nursing Mothers:

Because the effects of SERPACWA ingestion have not been studied in humans, caution should be exercised when SERPACWA is applied by a nursing woman.

Pediatric Use:

The safety and effectiveness of this product have not been established in pediatric patients.

Geriatric Use:

The safety and effectiveness of this product have not been established in patients 65 years and older.

ADVERSE REACTIONS

Tests conducted in humans demonstrated that topical application of SERPACWA is not associated with acute skin irritation or with allergic sensitization. Exposure of SERPACWA-treated skin to ultraviolet light was not associated with skin irritation or allergic sensitization. SERPACWA application to 20% of body surface area did not impair normal heat exchange for personnel who were exposed to an environment that simulated the effects of wearing MOPP 4 gear. In the clinical trials in which a single dose of SERPACWA was applied to humans and left in place for a five hour period, no adverse events were found to be associated with SERPACWA use.

OVERDOSAGE

There is no human experience with ingestion of SERPACWA. Tests conducted in rats demonstrated no acute ill effects associated with ingestion of up to 3240 mg/kg. The human equivalent dose is approximately 32 grams for a 60 kg adult. The consequences of exceeding the recommended topical dosage are unknown.

DOSAGE AND ADMINISTRATION

Apply the SERPACWA by hand onto the skin until there is a barely noticeable white film layer. Apply the entire contents of the 84-gram package of SERPACWA evenly to the areas of the skin (as outlined in Instructions for Use for Military Personnel below) prior to donning MOPP gear.

Instructions for Use for Military Personnel:

This product is intended for use prior to exposure to CWA and only in conjunction with MOPP gear.

The barrier properties of SERPACWA may be reduced if any insect repellents and/or camouflage paints remain on the skin surfaces to which SERPACWA is applied.

Before you put on the chemical protective overgarment, use a dry towel to wipe off the sweat, insect repellent, camouflage paint, sand or dirt from your skin at the areas shown in the picture below and on the label.

Tear open the packet and squeeze about one third of the pouch into the palm of your hand and rub it evenly around the wrists (site 1), neck (site 2), and boot tops of lower legs (site 3) until it forms a white film which is barely noticeable. Remove the remaining two thirds of the SERPACWA from the pouch and rub it evenly onto your armpits (site 4), groin area (site 5), and waistline (site 6).

After the product is applied, if exposure to CWA is either confirmed or suspected, follow the appropriate protocol for decontamination.

For removal of SERPACWA in the absence of exposure to CWA, scrub the sites with a dry towel, or if possible, with a cloth using both soap and water. For personnel who smoke, hands should have no visible traces of SERPACWA prior to handling of smoking products. If smoking products have an unusual or unpleasant taste during smoking, this may indicate that the products have been contaminated with SERPACWA. Personnel are advised to cease smoking and discard such potentially-contaminated products. Even in the absence of an unusual or unpleasant taste, the smoking product may still be contaminated, so smoking should be avoided.

Clothing or other materials exposed to SERPACWA, including SERPACWA packaging, should not be destroyed by burning, because of the release of toxic fumes.

HOW SUPPLIED

SERPACWA is supplied as an olive drab (green) pouch which contains 84 grams of SERPACWA (sufficient for one application per individual). Store between 20° and 30° C.

Dispensing information as of February 17, 2000.

Package Revised [Month/Year] ***(Front side of pack)*****:**

SKIN EXPOSURE REDUCTION PASTE AGAINST CHEMICAL WARFARE AGENTS (SERPACWA)

Ingredients: Polytetrafluoroethylene and perfluoroalkylpolyether
Manufacturing Date: Lot No.
Net: 84 g

CAUTION: For military use only. For external use only. This product, product packaging, and clothing or other materials exposed to SERPACWA should not be destroyed by burning due to the release of toxic fumes. Avoid getting SERPACWA on smoking products. Clean hands thoroughly before handling smoking products. Smoking should be avoided during and after applying SERPACWA.

Store between 20° and 30° C.

Manufactured for U.S. Army by:

McKesson BioServices
14665 Rothgeb Drive
Rockville, MD 20850

Package Revised [Month/Year] ***(Back side of pack)*****:**

INSTRUCTIONS FOR USE FOR MILITARY PERSONNEL:

This product is intended for use prior to exposure to CWA and only in conjunction with MOPP gear.

Before you put on the chemical protective overgarment, use a dry towel to wipe off the sweat, insect repellent, camouflage paint, sand or dirt from your skin at the areas shown in the picture below and on the label. The barrier properties of SERPACWA may be reduced if any insect repellents and/or camouflage paints remain on the skin surfaces to which SERPACWA is applied.

Tear open the packet and squeeze about one third of the pouch into the palm of your hand and rub it evenly around the wrists (site 1), neck (site 2), and boot tops of lower legs (site 3) until it forms a white film which is barely noticeable. Remove the remaining two thirds of the SERPACWA from the pouch and rub it evenly onto your armpits (site 4), groin area (site 5), and waistline (site 6).

After the product is applied, if exposure to CWA is either confirmed or suspected, follow the appropriate protocol for decontamination.

For removal of SERPACWA in the absence of exposure to CWA, scrub the sites with a dry towel, or if possible, with a cloth using both soap and water. For personnel who smoke, hands should have no visible traces of SERPACWA prior to handling of smoking products. If smoking products have an unusual or unpleasant taste during smoking, this may indicate that the products have been contaminated with SERPACWA. If this occurs, personnel are advised to cease smoking and discard the potentially–contaminated products. Even in the absence of an unusual or unpleasant taste, the smoking product may still be contaminated, so smoking should be avoided. Clothing or other materials exposed to SERPACWA and SERPACWA packaging should not be destroyed by burning, because of the release of toxic fumes.