Uniform Formulary Beneficiary Advisory Panel

Meeting Summary
June 27, 2005
Washington, D.C.

Panel Members Present:

- John Class
- Deborah Fryar
- Marshall Hanson
- Sydney Hickey
- Rance Hutchings
- Lisa LeGette
- Jeffrey Lenow
- Robert Washington

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. Major (MAJ) Travis Watson, the Designated Federal Officer (DFO), called the proceedings to order at 8:00 A.M.

Opening Comments

After reviewing the layout of the facility for those present, MAJ Watson reviewed the rules under which the Panel will operate: (1) only the Panel will participate in the meeting; (2) only the Panel may address questions to the briefers; (3) audience comments and interaction must be confined to the time allotted on the agenda (0830-0930) and then only to individuals designated and approved to address the Panel as private citizens; and (4) private citizen comments may be submitted in writing.

MAJ Watson next introduced two new Panel members: Mr. John Class (replacing Dr. Schwartz) and Mr. Marshall Hanson.

MAJ Watson announced that the first order of business would be for the Panel to select a chairperson, who must come from the Panel and cannot be a military person. MAJ Watson asked the Panel to vote for a chair using ballots provided and to vote for only one person. Election will be by simple majority. Only the name of the Chairperson will be announced. In the event of a tie, the process will be repeated. The person elected will serve as Chair for one year and no individual can serve for two consecutive terms. Duties of the Chair will include leading the Panel through the agenda; leading the Panel in discussions of DoD Pharmacy and Therapeutics Committee (P&T Committee) recommendations; and coordinating necessary meeting preparations with the Designated Federal Officer and the Senior Consultant, Mr. Martel.

A Panel member asked what the voting procedure would be for a second ballot in the event a simple majority is not obtained on the first ballot. MAJ Watson said if that happens, the re-vote will be between the top two vote getters from the first ballot.

After the first ballot, a second vote was required between Mr. John Class and Ms. Sydney Hickey. On the second ballot, Ms. Hickey was elected to Chair the Panel.

Meeting Objectives

MAJ Watson reviewed the objectives of today's meeting:

- To discuss the recommendations of the DoD P&T Committee resulting from the meeting on 17-19 May 2005 in San Antonio, Texas.
- To discuss drugs in the PDE-5 inhibitor drug class, the topical antifungal drug class and the Multiple Sclerosis Disease Modifying Drug (MS-DMD) class.
- Review the P&T Committee's recommendations, make comments and forward to the Director, TRICARE Management Activity (TMA) for final decision to approve, disapprove or modify the recommendations.
- Entertain private citizen comments from 8:30 until 9:30.

MAJ Watson announced that the summary of the meeting are being recorded. All comments made at today's meeting are for the record and will be published.

Public Comments

MAJ Watson opened the public comment session by reviewing the rules:

- Up to twelve people who may have signed up to address the Panel will be given a maximum of five minutes each using the microphone. The time limit will be strictly enforced.
- The time is set aside for public comment only. Product endorsements, presentations of marketing strategies or comments from industry are not appropriate.
- Comments or questions from the public at other times will not be acknowledged.

One individual signed up to offer a public comment and was heard at this time.

Comments by Lori Brantley

Ms. Brantley introduced herself as a retired Lieutenant Colonel from the United States Air Force, married twenty-two years with an eleven year old daughter. She had twenty-one years of active service, fourteen of those with Multiple Sclerosis (MS). Her symptoms began after completing her Master's Degree in 1988; unfortunately, no treatments were available.

The first medication available to treat MS was Betaseron, which she started using in February, 1995. When Avonex became available in 1996, her doctor suggested she consider switching medications because Avonex seemed to meet her needs better as an active duty person. Last September, she started using Avonex. She had very few side effects and the once a week injection was more convenient for the traveling she required.

The FDA approved another medication for treating relapsing-remitting MS: Rebif. Being a former intelligence officer with an investigative mind, she thought she would try it. Her doctor reluctantly gave her his blessing. When she experienced some rather severe side effects she quickly returned to Avonex.

Ms. Brantley said she has always been an active person. She played varsity basketball and ran outdoor track and cross country at Virginia Tech and competed in marathons. She even played basketball for Peterson Air Force Base's women's basketball team. That was following her first MS exacerbation. She said she doesn't think she would have been able to be this active for this long if it weren't for Avonex.

MS is a chronic, progressive disease. It attacks the central nervous system: the core of our bodies and the core of our beings. Everyone is vulnerable. Yes, being told you have MS can send you into a tailspin, but in the same breath, the doctor can tell you about a variety of medications that you have at no cost or very little cost.

Ms. Brantley said she believes these medications are essential to maintaining a quality force. Without them, the money that the American people invested in her would have been lost. Her career would have ended abruptly. She said she thinks its important for us to give our military members the same opportunity she had to take these treatments. We owe it to the American people to seek every opportunity to capitalize on their investment. It's a win-win situation. Military members must know their country is behind them 100 percent. And that 100 percent includes the medications to treat relapsing-remitting MS. Avonex must be part of the survival kit.

Written Comments Submitted for the Record

MAJ Watson next read additional written comments that have been submitted for the Panel's consideration.

The documents are summarized below, appended in full to this report as Appendix 2 and posted on the Panel's website at http//tricare.osd.mil/pharmacy/bap.

Letter No. 1

Submitted jointly by two corporate officials of Pfizer Global Pharmaceuticals, the maker of Viagra. The letter states that the possibility that Viagra (sildenafil citrate) will no longer be covered by the Department of Defense will: challenge the purposes of the Uniform Formulary; have a significant impact on DoD beneficiaries currently being treated for erectile dysfunction, over 90 percent of whom receive Viagra; and will likely cause an administrative burden and could introduce unforeseen costs.

The writers state that there are "important differences in the depth and breadth of clinical data favoring Viagra® as a preferred agent" and summarize the results of clinical trials. They indicate it is difficult to draw conclusions about the relative efficacy of PDE-5 agents based on randomized placebo controlled trials. They state that studies conducted to date have failed to demonstrate that Cialis® and Levitra® were "not inferior to Viagra®."

The writers also state that the cardiovascular safety profile of Viagra® is well established, that the drug has shown significant benefit in treating pulmonary arterial hypertension (PAH) patients and has been approved by the FDA as Revatio® for treatment of PAH.

Additional costs to the DoD system might result from patients either continuing to use Viagra® or switching back after trying a competitor.

The writers disagree with the P&T Committee's conclusions that the three PDE-5 agents are comparable and ask that the BAP members and Dr. Winkenwerder disagree with them also.

Letter No. 2

The second letter received contained the comments that were offered orally by Ms. Brantley during the "Public Comment" session and included in the record above.

Letter No. 3

Submitted by a 64-year-old retired Viet Nam-era naval veteran and father of an active duty navy pilot. The letter states that both men are erectile dysfunction (ED) patients who have benefited from Viagra. The writer requests that Viagra continue to remain available. The letter states that the efficacy and safety of Viagra have been extensively researched through clinical trials over the past ten years. It has been tested in patients with cardiovascular disease and spinal cord injury, those taking antidepressant and hypertensive medications and following treatment for prostate cancer. The writer's son, a survivor of testicular cancer, also uses Viagra successfully. Discontinuing the availability could have a negative impact on sexual relations and morale for such patients.

Letter No. 4

Submitted by a retired Marine suffering from prostate cancer due to agent orange. The letter asks that DoD keep Viagra in the inventory of medicines for both active and retired military. The letter states that the individual has tried other products and trusts only Viagra. Many others in his prostate cancer support group have similar feelings about Viagra.

Ms. Hickey noted that the statement in the first paragraph of letter number one, stating "Viagra would no longer be covered by the Department of Defense," is not true. The agent would be moved to the third tier for payment, but would continue to be covered by the Department of Defense. She asked that the situation be clarified for the record. MAJ Watson confirmed that Ms. Hickey's understanding is correct.

Other Administrative Matters

MAJ Watson asked if the Panel had other administrative matters to be addressed. Ms. Hickey said several corrections are needed to the minutes of the last meeting and asked about establishing a process for making corrections. It was suggested and decided that the Panel be given an opportunity to review the summary before it is posted. MAJ Watson noted there are time constraints -- both the Panel summary and the P&T Committee minutes must be included in the package that goes to Dr. Winkenwerder. Ms. Hickey acknowledged the need for a fast turnaround time on the review and said it would be acceptable to send the summary out to the Panel with a date by which replies must be received so the recommendations can be forwarded. Her concern is that an incorrect summary not be posted on the website.

Ms. Hickey also asked that, in the future, presentation slides such as those posted on the Beneficiary Advisory Panel (BAP) website be sent directly to the Panel members, preferably before they are made public.

Overview of the Review Process

Commander (CDR) Denise Graham opened the briefing on behalf of the DoD Pharmacoeconomic Center (PEC), outlining the broad types of analysis that are conducted by the Center on drug class agents for the DoD Uniform Formulary. She introduced the other individuals who would be briefing the Panel today: Captain (CAPT) Don Nichols, a P&T Committee Physician Consultant and family practice specialty leader, and Major Wade Tiller, an Air Force pharmacist and cost analysis specialist. She said their purpose is to present an overview of the analysis presented to the P&T Committee.

CDR Graham said the Code of Federal Regulations establishes procedures for including pharmaceutical agents in the Uniform Formulary based on clinical effectiveness and relative cost effectiveness. The presentation to the Panel will not provide the same in-depth analysis given to the P&T Committee. Instead, the Panel will receive a summary of what was provided to the P&T Committee. This includes:

1. A brief overview of the relative clinical effectiveness analysis considered by the P&T Committee.
2. A general overview of the relative cost-effectiveness analysis. The overview will be general because PEC staff are unable to disclose the actual costs used in the cost model. The overview will include the factors used to evaluate the cost of the agents in relation to their safety, effectiveness and clinical outcomes.
3. The DoD P&T Committee's Uniform Formulary recommendations, based on their collective professional judgment, after reviewing both the clinical and relative cost effectiveness of the three drug classes: Phosphodiesterase-5 (PDE-5) inhibitors, topical antifungal agents and the Multiple Sclerosis Disease Modifying Drugs (MS-DMD).
4. The P&T Committee's transition recommendations as to the effective date of change for agents being switched from formulary to non-formulary.

Based on the Code of Federal Regulations, any such changes may not be longer than 180 days from the final decision.

CDR Graham advised the Panel that CAPT Don Nichols will present the briefing on PDE-5 inhibitors, Maj. Tiller will present the briefing on topical antifungals and she will present the briefing on MS-DMD.

PDE-5 Inhibitor Drug Class Review

CAPT Nichols began the briefing by indicating that the P&T Committee's clinical review considered the relative safety, tolerability and efficacy of drugs in the PDE-5 class. Three PDE-5 drugs are marketed in the U.S.:

- Sildenafil (brand name Viagra),
- Vardenafil (brand name Levitra), and
- Tadalafil (brand name Cialis).

PDE-5 agents are considered the gold standard for treating erectile dysfunction.

In the 12-month period ending January 31, 2005, 142,333 patients were prescribed PDE-5 inhibitors. The class is ranked 46th in Military Health System (MHS) drug class expenditures. Since January, new prescriptions at all three points of service have included, 9 million in Military Treatment Facilities (MTFs), 11.7 million in the retail network and 4 million in the mail order program. Based on the number of tablets dispensed, Sildenafil was the most-used drug, followed by Tadalafil and Vardenafil.

Relative Clinical Effectiveness

In evaluating the relative clinical effectiveness of PDE-5 agents, the P&T Committee examined the following key questions: (1) Are the available PDE-5 inhibitors relatively similar in efficacy, safety, tolerability and other factors? (2) Is it clinically acceptable to designate one or more PDE-5 drugs as "non formulary" on the Uniform Formulary?

Data sources used for clinical evaluation include randomized clinical trials, published articles, information from the FDA website and information provided by additional manufacturers' tests. All PDE-5 inhibitors have FDA-approved indications for the treatment of erectile dysfunction. There are no head-to-head trials comparing the efficacy of the three PDE-5 inhibitors. The available placebo-controlled trials and meta-analyses were reviewed. Although all PDE-5s were found to be clinically effective when compared to placebo, variability in study design, demographics and outcome measures precluded the ability to designate one PDE-5 as clinically superior. A difference in duration of action exists among these agents. The duration of action of sildenafil and vardenafil is approximately four hours; tadalafil has a half-life of 17.5 hours. There is no evidence to suggest clinical superiority based on differences in the duration of action.

Non-FDA approved uses for sildenafil (Viagra) include the treatment of primary pulmonary hypertension and radical prostatectomy. Since the meeting, sildenafil has been approved for the treatment of primary arterial hypertension.

The P&T Committee concluded that all PDE-5 inhibitors have similar relative clinical effectiveness for treating erectile dysfunction.

Regarding safety and tolerability, the P&T Committee found that the PDE-5s were not significantly different with respect to major contraindications, drug interactions and adverse drug reactions. Co-administration with nitrates is contraindicated. Interactions with alpha blockers indicate starting at the lowest recommended PDE-5 dosage. Vardenafil has demonstrated a slight increase in QT intervals; patients with class 1-A or class III antiarrythmics should avoid taking vardenafil. The most common side effect associated with PDE-5s is headaches. Sildenafil is associated with more visual side effects where tadalafil is associated with back pain.

The P&T Committee concluded that all three PDE-5s have similar safety and tolerability profiles.

The P&T Committee's overall conclusion regarding the clinical effectiveness of PDE-5 inhibitors was that, for purposes of the DoD Uniform Formulary clinical review, none of the PDE-5 inhibitors have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness or clinical outcome over the other PDE-5 inhibitors.

Relative Cost Effectiveness

CAPT Nichols next discussed the P&T Committee's consideration of the relative cost effectiveness of the three PDE-5 agents. The P&T Committee evaluated the costs of the agents in relation to the safety, effectiveness and clinical outcomes of the other agents in the class. The information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 C.F.R. 199.21(e)(2). Several analyses were used to determine the relative cost effectiveness of agents within the PDE-5 inhibitor therapeutic class. A pharmacoeconomic analysis using cost minimization techniques was conducted based on the clinical review's conclusion that the efficacy, safety, and tolerability between all agents were roughly equivalent. A series of cost-effectiveness analyses were then conducted to confirm the results of the cost-minimization analysis (CMA). Cost-effectiveness analyses were also used to evaluate differences in the duration of action between the agents.

Results of the cost-minimization and cost-effectiveness analyses showed vardenafil (Levitra) to be the most cost-effective PDE-5 inhibitor across all points of service (MTF, retail and mail order), followed by sildenafil (Viagra) and tadalifil (Cialis). This was true even when taking into consideration differences in the duration of action between the agents.

The results of the above analyses were then incorporated into a budget impact analysis (BIA), which accounted for other factors and costs associated with a potential decision regarding formulary status of PDE-5 inhibitors within the Uniform

Formulary. These factors included: market share migration, cost reduction associated with non-formulary cost shares, medical necessity processing fees, and switch costs. The results of the budget impact analysis further confirmed the results of the cost-minimization analysis and cost-effectiveness analysis.

The P&T Committee concluded that sildenafil and tadalafil were not cost-effective relative to vardenafil. Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of PDE-5 inhibitors and other relevant factors, the P&T Committee recommended that the status of sildenafil and tadalafil be changed from "formulary" to "non-formulary" on the Uniform Formulary and that vardenafil maintain "formulary" status at the formulary cost share.

Committee Action: The P&T Committee voted to recommend non-formulary status on the Uniform Formulary for sildenafil and tadalafil, with vardenafil maintaining formulary status on the Uniform Formulary at the formulary cost share.

Implementation Plan

Because a substantial number of patients is currently receiving either sildenafil or tadalafil from one of the three MHS pharmacy points of service (128,007 patients – 90 percent of all patients receiving PDE-5 inhibitors) the P&T Committee proposed a 90-day transition period for implementation of the decision to change sildenafil and tadalafil to non-formulary drugs. Patients wishing to fill prescriptions for sildenafil or tadalifil at retail network pharmacies or the TMOP would then have to pay the non-formulary cost share, unless medical necessity for these agents is established by the beneficiary and their provider.

MTFs will not be allowed to have sildenafil or tadalafil on their local formularies. MTFs will be able to fill non-formulary requests for these agents only if both of the following conditions are met: (1) the prescription must be written by a MTF provider, and (2) the beneficiary and their provider must establish medical necessity for these agents. MTFs may (but are not required to) fill a prescription for sildenafil or tadalafil written by a non-MTF provider to whom the patient was referred, as long as medical necessity has been established.

Committee Action. The P&T Committee recommended an effective date no later than the first Wednesday following a 90-day implementation period. The implementation period will begin immediately following the approval by the Director, TMA.

Beneficiary Advisory Panel Questions and Comments

Dr. Lenow asked whether it would be safe to say that the approach to reviewing these drugs was evidence-based, since the Cochrane collaboration was referenced. CAPT Nichols answered in the affirmative. Dr. Lenow also asked if the PEC used expert reviews beyond meta analyses or as a partial reviewer for a Cochrane search? He noted that Cochrane doesn't answer all questions and asked whether PEC used expert panels or outside authorities on the subject. The answer again was "yes." Dr. Lenow asked whether that occurred in this case. CAPT Nichols said that it did. Dr. Lenow

asked about the review process used at PEC and how many people participate in it. He said he was especially interested in how the process works when there are differences of opinion. How does PEC break ties? How does it reach consensus? CAPT Nichols said the initial work on all projects is conducted by a physician and a pharmacist. CDR Graham added that once the basic review work has been completed, the rest of the staff provide comments. Dr. Lenow asked if the PEC had the capacity, or the budget, to send its opinions out for a second opinion - to an outside reviewer with no axe to grind, for example. CDR Graham said that the PEC staff look at other public opinions, look at outside articles and consult with the Veterans Affairs people about the views of their providers to make sure that the findings aren't too far afield. But the time pressures and the role of the P&T Committee in the process don't always allow a broader look. Dr. Lenow said he didn't mean to second-guess the work, but this is a new process and, with this topic in particular, he thinks it might be important to take into account the collateral impact of the decision. He said the letters received indicate that there might be a time when the PEC would want an independent analysis or a "tie breaker" vote. He said sometimes issues go beyond evidence-based rationale. In those cases, for the future, PEC might want to have outside help available.

Mr. Hanson, referring back to the comments received, noted that the Panel is dealing with some drugs that will benefit retirees that have been directly affected by military operations – exposure to agent orange, for example, which has been found to increase the risk of prostate cancer.

Sildenafil has strengths of 25, 50 and 100 milligrams while the other two have smaller sizes. Mr. Hanson asked if this means that sildenafil is a stronger pill - because the sizes are bigger - or is it a different mixture of fillers to where a 20 milligram pill of vardenafil is as strong as a 100 milligram pill of sildenafil. The answer provided was that comparisons between agents can't be made based on the size of the tablets. Mr. Hanson also noted that the patent expiration date for vardenafil is August 2008 and asked if this is an indication that there might be a generic version of any of these drugs by then. CDR Graham said that is a possibility. Nobody really knows what will happen then, but August 2008 is the earliest there might be a generic version.

Mr. Class asked what the PEC studies showed about how many beneficiaries might shift from using Viagra to using Cialis? Moving the drug to the third tier will cause a shift somewhere. Maj Tiller said the shift would be away from both Viagra and Cialis to using Levitra. He said PEC runs a number of models using various assumptions. In this case, the baseline assumption is that DoD will be able to shift 80 percent of the market share from non-formulary to formulary. That is a significant figure. Studies have shown that shifts do occur when the P&T Committee makes such a decision. The 80 percent assumption was also subjected to a series of sensitivity analyses - from 0 percent to 99 percent - in order to test the confidence of the basic assumption compared to other scenarios. For this particular class, the budget impact analysis looked at every possible combination of the three agents as "formulary" versus "non formulary." The "break even" point was 25 percent - a shift to 25 percent of market share for vardenafil was needed to support the option. Mr. Class asked about the figures cited in the letter from Pfizer that there was only a six

percent shift away from Viagra among patients and that 22-27 percent of those later switched back. If that situation occurs here, the beneficiaries are going to go to retail and DoD won't realize the benefits. CDR Graham said beneficiaries will still be able to get Viagra and Cialis from retail and mail order points of service, but not at the lower cost unless they can meet the "medical necessity" criteria.

Mr. Washington asked when the other two PDE-5 inhibitors - Cialis and Levitra - were approved. The answer is that Cialis was approved in August 2003 and Levitra in November 2003. Mr. Washington noted that Viagra was the first to be introduced to the formulary, so the majority of people are taking it. He asked if any tests had been done to determine how effective one might be compared to the others and if the beneficiaries were ever told or surveyed to determine the possible effects of a switch to non-formulary. CDR Graham said rigorous tests were conducted, but not head-to-head. She said consulting beneficiaries probably wouldn't provide the answers to Mr. Washington's questions because most patients wouldn't have tried either of the other two agents – especially if one was working for them – so they wouldn't know whether one was more effective than another. She also said that if the formulary drug didn't work for an individual, that person would be able to use the medical necessity criteria to get one of the other agents.

Ms. Hickey asked whether the same would be true of DoD providers. Since only 10 percent of the population was using the drug now being recommended for formulary, wouldn't providers also have limited professional experience with that drug? CAPT Nichols agreed that would be correct. She asked whether the analysis had taken into consideration the length of time Viagra had been on the market compared to the other two drugs in this class. CAPT Nichols answered in the affirmative.

Ms. Hickey asked if the economic analysis used the proposed new federal rule under which there would be federal pricing at the retail pharmacy or the current rule. The answer provided was that the analysis used the current rule. Maj Tiller said that for the economic analysis, the baseline was set at current market prices. Full cost avoidance was determined by looking at the current prices and the new prices and determining the market share shift. Federal Ceiling Prices were not looked at for any of these particular agents.

Ms. Hickey asked if the economic analysis considered that the pricing would move a significant number to the mail order point of service where the co-payment is much less – even less than beneficiaries are now paying retail. Maj Tiller replied that another assumption used in the model is that when market share is migrated from one product to another product, the patient also migrates within that point of service. In other words, a patient on sildenafil in the mail order program will be assumed to migrate to Levitra within that point of service. The same is true for the MTF and the retail. Ms. Hickey reiterated her understanding that the analysis did not consider that people using the retail pharmacy in this class would migrate to the mail order pharmacy where the cost would be less. CDR Graham said there is a quantity limit restriction on any prescription filled in this class. In response to a question about what that limit is, the answer was 6 tablets every 30 days. Ms. Hickey said it would have been helpful to include information in the briefing to the effect that these drugs do require prior authorization and there is a quantity limit. But she still believes

people will migrate to the mail order pharmacy because it's going to be less expensive than what they are currently paying in the retail pharmacy. In that case, the cost analysis, which assumes patients will stay in the same venue, might not be quite as accurate as it is assumed to be.

Mr. Hanson said that the early introduction of Viagra compared to the other two drugs created certain patterns of use, as evidenced by the commercials for Levitra and Cialis where these drugs are trying to obtain part of the market segment. The briefers have already said that at least a 15-17 percent shift in the formulary would be needed to be successful. He asked whether the issue of "formulary" versus "non-formulary" distribution would be revisited if the hoped-for shift does not occur and people decide to stay with the product they are currently using. The answer provided was that all decisions are subject to review, but PEC has no plans now to review this class again. CDR Graham said the PEC actively monitors every formulary decision made for results, but there are no plans for a routine "second look" here because of the number of other drug classes out there that have yet to be reviewed.

Mr. Class asked how much of a difference the medical necessity criteria would make in where patients get their prescription filled. CDR Graham replied that, of the three points of service, MTFs have the greatest number of users for sildenafil. MTFs have budgetary pressures and one of the things that will help create the market shift is that there may be a drop in the price. Also, MTF providers will have to meet the medical necessity criteria burden for their patients. Her view is that for these reasons the MTF providers are the most likely to respond to the change. The mail order and retail points of service are not DoD's own providers so they won't be as directly affected.

Mr. Class asked whether the assumption is that most of the 58,000 MTF patients now using the three drugs will shift to Levitra. CDR Graham replied that after the change, Levitra will be the only PDE-5 inhibitor available from the MTF formulary without a "medical necessity" exception.

Mr. Class noted that at the last meeting, the P&T Committee had recommended moving just one of seven available agents in a particular class to the "non formulary" category. This time, however, more than 90 percent of the patients will be affected by the change since the agent being maintained on the formulary has the lowest percentage of use. His understanding was that the Department wasn't going to be real aggressive with this process. Now over 100,000 folks will have to go for a "medical necessity," which is a tremendous hassle factor. He thought we weren't going to do that and asked for an explanation. Maj Tiller replied that fewer patients would be affected by this decision than were affected by the angiotensin receptor blockers (ARB) decision made last time.

Ms. Fryar said she is concerned about the 90-day implementation period, which doesn't seem like nearly enough time for a phase-in. She believes that a minimum period of 120 days would be more effective.

Ms. Hickey agreed with Ms. Fryar. One reason is that the Department really doesn't know how effective the limited publicity has been in notifying people about the Nexium transition and won't know until the middle of July. A 120-day

implementation period would at least give the Department a chance to look at a more effective notification process. She also recognized that the majority of people affected by this decision get their medication at the MTF and will be much easier to notify.

Ms. Hickey also asked whether it would have made a difference to the PEC or the P&T Committee if they had known at the time of their decision that the FDA has approved Viagra for the treatment of PAH? CAPT Nichols said it wouldn't have made a difference because the population to be treated is so small.

Ms. Hickey asked whether patients using the drugs in this class will need new pre-authorizations, either for patients moving to Levitra or those already on Levitra? The answer given by CDR Graham and the staff was that patients with a pre-authorization who are moving to the formulary drug do not need a new pre-authorization. Also, because of an administrative change, pre-authorizations no longer expire (they used to last only for one year).

Ms. Hickey said a reading of the literature suggests that these drugs are effective only if there is a psychological component through sexual stimulation; without it the medicine won't work. She asked, "If somebody believes strongly in Viagra, is that going to inhibit their ability to use Levitra? Or was that even looked at?" CAPT Nichols answered that Ms.Hickey's understanding is correct and the analysis didn't specifically consider it. CDR Graham added that the psychological component is the reason why pre-authorization is required for this class of drugs; without it there would be no covered benefit under the program.

Mr. Washington, noted that a "medical necessity" determination will be necessary for patients to obtain Viagra. He asked what would happen if the providers, who control the prescriptions, write large numbers of "medical necessity" prescriptions for Viagra and the expected market share change doesn't happen. CAPT Nichols answered that the three drugs are very similar in outcome, so the scenario is not likely to occur. CDR Graham added that the Viagra numbers are high because it was available first. But MTF providers are most likely to prescribe the agent that's most readily available on the shelf. The providers will be given information and literature to show that all PDE-5 inhibitors are capable. Given the availability and the price along with this, she believes the providers will be encouraged to try the formulary agent. If therapeutic failures occur, the providers will have the opportunity to go back.

Mr. Hutchings said, in regard to safety, his organization is finding that most patients are using 100 milligram doses. He asked about the maximum dose for elderly patients. The answer provided was that it would be a clinical preference, probably 50 milligrams unless that dose didn't work.

Mr. Hutchings also asked about the interaction between nitrate and Viagra. His organization found that there is a one percent to two percent incidence of patients taking both. CAPT Nichols said that would also be a decision made between the patient and the practitioner. CDR Graham said that for prescriptions filled at MTFs, a safety warning would come up when the prescription is filled and the provider would be able to override it or change the prescription.

Mr. Hutchings asked why this would even be a factor. He is looking at this drug class as a lifestyle issue for most patients. Other than quality of life, he sees no health factor involved with this class. CDR Graham said that TRICARE has decided to cover these medications, which is the standard they use. TMA has determined to make effective coverage benefits for those patients have an organic component. Her organization doesn't make coverage decisions; it makes quality decisions based on what the plan covers. Their concern is to have the most cost-effective agents available on the Uniform Formulary.

Mr. Hanson agreed that it's important to do it this way. Military members are exposed to risks – such as Agent Orange. We don't know the reactions to some of the "clinical cocktails" used in Desert Storm and even today. We are placing people in situations where they could be exposed to something that can make them impotent. In such cases, being in the military is depriving the individuals of quality of life. Most Desert Storm veterans would agree that treatment for this is a medical necessity. Mr. Hanson noted that the majority of Viet Nam era veterans have retired and are in the PRIME program or entering into the TRICARE for Life program. He is concerned that if they are currently taking Viagra, they will have to go back and re-enter the system to continue to get it. Most retirees like or prefer to go to an MTF to get a prescription filled. He asked what an individual who is now in the network but not being treated by an MTF would have to go through to re-establish medical necessity.

Discussion indicated that the individual would only have to re-establish medical necessity if he is using an MTF. Individuals referred out to a network provider by an MTF may have to re-establish necessity, depending on what the MTF decides. But the beneficiary has two other points of service he can go to – the mail order pharmacy or the retail pharmacy – although the cost would be higher ($22 cost share).

Dr. Lenow said he is very sensitive to the need for cost containment. He realizes TMA is neither empowered to define benefits nor negotiate tougher lines with the pharmaceutical companies. His concern is for the patient who will be really upset that he can no longer continue taking a medication that has been working. Dr. Lenow said he can make an argument - in the case of ARBs, for example - that another medication will treat the problem just fine. However, with people's emotions involved he needs to know and be comfortable with the reasoning that went into the decision – the mechanics of the process. He asked about the nitty-gritty review work that went into the decision before the summary review. He said right now he is more or less taking the PEC's word for the competency of the evidence-based review. He is comfortable doing that because he's comfortable with the process and the laboratory people he's met. But he would like to know whether the Panel members are entitled to ask for examples of the review process that occurred, or to see some of the opinions rendered by outside consultants. He would like to make his own evidence-based review in the event he is confronted with what the panel did so he can comfortably say: "That was a sound decision."

CDR Graham said she understands Dr. Lenow's concerns. She said it is important, too, to have confidence in the P&T Committee members. The Surgeon General has

picked the members to be representative of the services and the disciplines, and they were responsible for selecting the studies. In this class, there were no head-to-head studies of all three agents. The next step is to evaluate studies comparing agents to each other. If those don't exist or aren't sufficient, the Committee uses placebo studies.

Dr. Lenow replied that he understands what the situation was. But, if possible, he would like to get his hands on the actual opinions of the reviewers before making a decision. He asked whether such information would be available to BAP members or not.

CDR Graham asked whether he was looking for the full set of slides used for the P&T Committee. Dr. Lenow said he wanted to "see the homework." The crux of the issue is to be able to see how people approach the decision. He thinks it would be worthwhile for the BAP at a future date to review the whole process once to "see how the sausage is made."

Mr. Burleson of the Office of General Counsel said that he would like to take the question under advisement and get back to the Panel. He noted that the P&T Committee role is larger than just what the BAP gets to look at. It is important not to violate those roles.

Mr. Hutchings commented that he has been on the P&T Committee, and he knows that their processes are good and would be comfortable with almost anything that came from them.

Mr. Hutchings also asked about the current authorizations for the organics, which were covered in March. His impression is that these covered 97 percent or more. His question is whether the whole prior authorization process is capturing the people we want to capture. In reply, CDR Graham read from a report of changes in the use of PDE-5 inhibitors. Over the ten months prior to March 2005, approximately 94 percent of all beneficiaries requesting PDE-5s received approval. She also summarized the three most common reasons for refusal. She cited several steps used to assess the impact of prior authorization criteria. She said the bottom line is if the prior authorizations don't meet the criteria, then the prescriptions won't go ahead through the process.

Ms. Hickey asked whether the PDE rejections were all due to the lack of a prior authorization or whether some of the rejections were because there were drug interactions. The answer was that all were due to the lack of prior authorizations. The process takes place at the patient-provider level. If there are interactions to be considered, the prescriptions come back at the pharmacy as "requires prior authorization."

Mr. Hutchings asked how far back the pharmacies check for drug interaction. He said a lot of people hold nitrates for several months before using them, for example. The answer provided was that as long as the drug is still active, the system triggers a response. Mr. Hutchings said his concern is there might be an interaction with a drug that was prescribed months ago that the system might miss because of its age at the

time a viagra prescription was filled. CDR Graham offered to provide additional information on this question.

Mr. Class asked how much money this decision would save DoD assuming the market shift works out as envisioned. Maj Tiller said the analysis looked at three different time horizons. All the costs associated with the market share shift, new prescriptions, telephone consultations, medical necessity determinations and the change in co-pay are incorporated into the first year. In the first year, there would be a little over $4 million in savings from the decision. In the second year, a lot of the one-time costs will have occurred, so the cost avoidance will be $5 million. The total savings over three years will be over $13 million.

In response to a follow up question, Maj Tiller said the cost avoidance figure is based on "current market share" and "current price." Cost avoidance is the change resulting from the recommendation.

Ms. Hickey said one of the things it might be interesting to look at, not at the next meeting but at the one after that, would be information on the market share of Nexium and related drugs. The purpose would be to look at whether the organization is getting what it expected to get, or close to it. She said it would be important for the Panel to see that the whole process is actually doing something. CDR Graham agreed, saying that PEC should get that kind of information to the Panel.

Mr. Class noted that without head-to-head studies or other studies comparing all three agents to show that they are different, the conclusion was reached that they must be the same. He asked how, lacking such studies, that conclusion could be reached. CAPT Nichols and CDR Graham answered that it is rare to have head-to-head studies of all the agents in a class. However, the studies used were controlled and rigorous. They do tell whether each individual agent is efficacious in treating what it is supposed to treat. Additionally, the studies show how effective the agent is compared against a placebo. These studies are very good and indicate how the drug will perform in a controlled situation. Right now there are no studies with similar outcome measures for this class that can be pulled together using a meta-analysis. The process involves applying the best clinical judgment to the information that is available. When additional research becomes available, PEC looks at it.

Mr. Class asked whether more time might not suggest that one or the other of these agents in this class is more effective. CDR Graham replied that her organization is confident they know the efficacy from the placebo tests. Mr. Class expressed concern about whether those tests really give a good picture, considering the population class we are dealing with. CDR Graham offered to provide additional information to the Panel on how the studies are conducted. Mr. Class said the problem is not with the process; it's with the information available on which to decide whether or not to question a recommendation.

Ms. Hickey said the public letters had raised questions in the minds of the Panel. Additional information, such as that available to the P&T Committee - might give the members more comfort in dealing with such issues. CDR Graham and CAPT Nichols

discussed the differences in the placebo studies referred to in one of the letters, which were the cause of the questions.

Before opening the issue to further comment and a vote among Panel members, Ms. Hickey asked the DFO to clarify whether or not she would vote, as Chairperson. She said Colonel Young had said he would not vote unless there was a tie, and asked if the same rule would apply to her. The DFO replied that the Chairperson could decide, in the event of a tie, what the recommendation would be, but that the Chairperson should vote.

Ms. Hickey opened for discussion the question of whether the Panel agrees with the P&T Committee recommendation to move Levitra to formulary status and Viagra and Cialis to non-formulary status.

A question was asked about the possibility of recommending a longer period of time for the implementation. Ms. Hickey noted that implementation recommendations are voted upon separately. In answer to a follow-up question about whether that vote would be a straight "yes or no" vote, Ms. Hickey said the Panel would vote on whether to concur or not concur with the P&T Committee's recommendation.

Another member asked whether the Panel would vote on all three conclusions (relative clinical effectiveness, relative cost effectiveness and implementation period). Ms. Hickey replied that the Panel would be voting on the P&T Committee's recommendations, not necessarily on what they found.

BAP Vote on the Recommendations

On the question of moving Levitra to formulary status and Viagra and Cialis to non-formulary status, the Panel vote was a four-four tie.

The P&T Committee recommended a 90-day transition period for implementation of the decision to change sildenafil and tadalafil to non-formulary drugs on the Uniform Formulary. Chairperson Hickey noted that there have been comments from Panel members suggesting that the time should be extended to at least 120 days.

The vote on the recommended 90-day transition period was: 0 concurring, 8 non-concurring.

Ms. Hickey asked for a Panel vote on a 120-day transition period. Seven members voted to concur with a 120-day period; 1 member voted to not concur.

Dr. Lenow clarified his non-concurrence with the 120-day option by saying he favored the full 180-day period allowed by law.

Additional Panel Comments on the Vote

After a break, Ms. Hickey summarized the actions of the BAP before asking individual members to comment. Regarding the tie vote on the formulary status issue, Ms. Hickey said she believes some Panel members felt they didn't see enough

evidence that the particular medicine selected for formulary status might be more or less efficacious than the others. The large number of people affected – over 90 percent of the beneficiaries are on medications other than that recommended for formulary status - might not be best from a psychological point of view.

Dr. Lenow qualified his comments. He said he voted to concur, although his comments might have suggested otherwise, because he thought the review was "right on." He believes there should be second opinions from time to time as a quality matter and thinks the recommendations should be sent out for review to ensure their quality. His own experience with the drug class does not suggest there are differences among the agents significant enough to challenge the recommendations. He recognizes it is an emotional issue, but thinks with a decent explanation and good counseling most patients will be reasonable enough to try alternatives since they will still have options. He said there is never perfect evidence; it is always necessary to use best evidence. People have to understand that. However, he said he would still like to have access to additional information if that wouldn't compromise the process and that it would make him feel better about his decision.

He also questioned the statement that this decision would affect a smaller number of people than the decision made at the first meeting. The ARBs decision would only affect a small number. The Nexium example is better because that affected a lot of people. He asked to have that matter clarified.

Ms. Hickey said that one reason she had heard for the concurrence was that it was the "lesser of all evils."

Mr. Hutchings said he voted to concur because, overall, it was the correct recommendation. He found no reason not to concur. He also agreed that more information would have been helpful.

Ms. Hickey asked that the comments for the record also include the fact that some Panel members have asked to see some of the information provided to the P&T Committee that went into their decision. The letter from the drug company had raised the issue of knowing whether the tests used were valid or not valid.

Regarding the implementation decision, Dr. Lenow said he felt that, because of the sensitivity of the recommended action, a little more time in the planning might be prudent. He affirmed his preference for 180 days.

Ms. Hickey noted that other comments on the preference for 120 days instead of 90 result from not knowing how effective the Department will be in implementing the recommendations from the last meeting. That won't be known until July 17. The additional 30 days would provide time to deal with any significant problems that come along.

Topical Antifungal Drug Class Review

Maj Wade Tiller of the DoD Pharmacoeconomic Center presented the briefing to the Panel on dermatological topical antifungals.

Relative Clinical Effectiveness

Maj Tiller said the evaluation of the relative clinical effectiveness took into consideration the relative safety, tolerability and effectiveness of drugs in this class. The dermatological topical antifungal class includes topical products used to treat fungal infection. The class specifically excludes: vaginal products (such as Miconazole vaginal cream), oral doses used to treat onychomycosis (such as Lamisil tablets), preparations applied on nail beds (such as Ciclopirox or Nail Laquer), products used in combination with corticoid steroids, and products only available over the counter (OTC) and not in prescription strength (such as Tinactin). The dermatological topical antifungal class includes:

The following in the "azole" class:

- Clotimazole (Lotrimin)
- Econozole (Spectazole)
- Ketoconazole (Nizoral)
- Miconazole (Monistat Derm)
- Oxiconazole (Oxistat)
- Sertaconazole (Ertaczo)
- Sulfaconazole (Exelderm).

The following in the "allylamine" class:

- Butenafine (Mentax)
- Naftifine (Naftin)

Additionally, the following were included:

- Ciclopirox cream, a substituted pyridone
- Nystatin (Mycostatin), a polyene.

The topical formulation of terbinafine (Lamisil) was specifically excluded from the class, as it is now solely available in a non-prescription product.

On average, 51,000 prescriptions per month are filled in this drug class. The top three are: (1) clotrimazole (15,000 prescriptions per month); (2) econazole (12,000 prescriptions per month); and Nystatin (8,000 prescriptions per month). Ciclopirox is number four at 4,000 prescriptions a month. The five most common conditions for which topical antifungals are used are:

- Tinea pedis (athletes foot)
- Tinea cruris (jock itch)

- Tinea corporis (ringworm)
- Tinea versacolor (blotchy skin)
- Cutaneous candidiasis (heat rash)

Clotrimazole, econazole, ketoconazole, miconazole and ciclopirox are approved for all five indications. Oxiconazole, sertaconazole and butenafine are approved for the first four indications, but not for cutaneous candidiasis. Naftifine is approved for the first three indications, but not for candidiasis or tinea versacolor. Sertaconazole is only approved for tinea pedis and nystatin is only approved for candidiasis.

Based on the relative clinical effectiveness, the P&T Committee concluded that the Uniform Formulary should include at least one agent from the azole sub-class, one agent from the allylamine sub-class, ciclopirox and nystatin.

Within each sub-class, there is no evidence to support the superiority of one agent over another in terms of efficacy, safety, tolerability or outcome. The topical antifungals do differ in terms of structure, mechanism of action, cost, current utilization patterns, available dosage formulations and duration of therapy.

The DoD P&T Committee reached its conclusions after answering the following key questions based of relative clinical effectiveness of use: (1) Are there differences in the relative clinical effectiveness of the topical antifungals? (2) Are there differences in the safety and tolerability profiles of the topical antifungals? (3) What are the clinical coverage requirements for topical antifungals? (e.g. do we really need at least one agent from the azole sub-class, one agent from the allylamine sub-class, ciclopirox and nystatin on the Uniform Formulary?)

The data sources considered in evaluating topical antifungals included information from randomized clinical trials, which were used to produce the DoD topical antifungal review class. Additional published clinical trials were found using MEDLINE search, major medical journals and manufacturers press releases. Manufacturers were invited to present new data and the FDA website was monitored. Provider opinion was solicited to determine clinical coverage requirements.

Regarding differences in the relative clinical effectiveness of topical antifungals (key question No. 1), Maj Tiller said the relative effectiveness was reviewed for tinea pedis, tinea cruris, tinea corporis, cutaneous candidiasis and tinea versacolor.

- For tinea pedis, the review found that allylamines were slightly more efficacious than the azoles, but that result depended on which published articles were used in the evaluation. Overall, the cure rates were similar. There was no difference when individual azoles were compared to each other or when individual allylamines were compared to each other. The efficacy of ciclopirox was similar to the azoles. Nystatin is not effective for tinea pedis. Overall, there is no evidence to support that one individual agent is superior to another for treating tinea pedis.
- For tinea cruris, tinea corporis and tinea versicolor, there were no systematic reviews and no head to head trials of individual treatment agents. There is no

evidence to support that one individual agent is superior to another for treating tinea cruris, tinea corporis or tinea versicolor.

- For cutaneous candidiasis, there are no systematic reviews. One head to head trial comparing nystatin with clotrimazole showed similar efficacy. The conclusion reached was that there is no evidence to support that any one topical antifungal agent is superior to another for treating cutaneous candidiasis.

Regarding differences in the safety and tolerability of topical antifungals (key question No. 2), the topical antifungals are recognized as safe therapeutic agents. Several of the products (clotrimazole, miconazole, butenafine) are available without prescription in the same concentration and dosage form as the prescription product. Hypersensitivity is the only contraindication listed in the package inserts of the topical antifungals. Adverse reactions reported most commonly with the topical antifungals include itching, burning and erythema, which are also the most common symptoms of the conditions these agents are used to treat. Package inserts list adverse reactions in the range of one to three percent. The P&T Committee concluded topical antifungal agents have similar safety and tolerability profiles.

The clinical coverage requirements for topical antifungals (key question No. 3) showed, based on opinions solicited from DoD providers, that clinicians requested both an azole and an allylamine on the Uniform Formulary due to the differences in the mechanism of action and the duration of therapy. Patients who do not respond to a drug in one class can be treated with a drug in the other class. Nystatin was also recognized as required for the treatment of cutaneous candiasis. The P&T Committee recommended that the Uniform Formulary should include at least one agent from the azole sub-class, one agent from the allylamine sub-class and nystatin. The P&T Committee also agreed that it would be efficacious to include agents that have different mechanisms of action, a wide number of approved FDA indications and those that are approved for use in younger populations.

Based on the relative clinical effectiveness analysis, the P&T Committee concluded that the Uniform Formulary should include at least one agent from the azole and substituted pyridone sub-class, one agent from the allylamine sub-class and nystatin. For each sub-class, there was no evidence of the superiority of one agent over another in terms of safety, efficacy or tolerability. The P&T Committee also concluded that topical antifungals do differ in terms of structure, mechanism of action, cost, current utilization patterns, available dosage formulations and duration of therapy.

Relative Cost Effectiveness

In comparing the relative cost effectiveness, the P&T Committee evaluated the cost in relation to safety, effectiveness and clinical outcomes of each agent against other agents in the class. Information considered by the P&T Committee included, but was not limited to, sources of information listed in the Code of Federal Regulations. To determine the relative cost effectiveness of agents in the antifungal therapeutic class, two separate economic analyses were performed: a cost-minimization analysis and a budget impact analysis. From the preceding relative clinical effectiveness evaluation, the P&T Committee formed two primary conclusions: (1) the Uniform Formulary

should include at least one agent from the azole and substituted pyridone sub-class, one agent from the allylamine sub-class and nystatin; and (2) within each sub-class there is no evidence to support the superiority of one agent over another in terms of safety, effectiveness or clinical outcomes.

Given the conclusions, two different cost-minimization analyses were conducted for each sub-class using different measures of cost: the weighted average cost per gram, and the weighted average annual cost of treatment per unique user. In general, the results of the CMAs revealed that:

- Miconazole was the most cost-effective agent in the azole and substituted pyridone sub-class;
- Naftifine and butenafine were similar in relative cost effectiveness in the allylamine sub-class; and
- Nystatin was the most cost-effective agent relative to all topical antifungals.

More specifically, within the allylamine sub-class, naftifine was more cost-effective relative to butenafine at the MTF and TMOP points of service, whereas butenafine was more cost-effective relative to naftifine at the retail point of service. Examination of the cost continuum further suggested that a cluster of agents (nystatin, miconazole, clotrimazole and ketoconazole) were more cost-effective relative to the other agents within the therapeutic class (i.e., butenafine, ciclopirox, econazole, naftifine, oxiconazole, sertaconazole and sulconazole).

The results of the cost-minimization analyses were subsequently incorporated into a budget impact analysis. A BIA accounts for other factors and costs associated with a potential decision to recommend that the status of one or more topical antifungals be changed from "formulary" to "non formulary" status. These other factors and costs include market share migration, cost reduction associated with non-formulary cost shares, and medical necessity processing fees. The goal of the budget impact analysis was to identify a group of antifungal agents to be included on the Uniform Formulary which best met the majority of the clinical needs of the DoD population at the lowest cost to the MHS, given the P&T Committee's decision to include on the Uniform Formulary at least one agent from the azole and substituted pyridone sub-class, one agent from the allylamine sub-class and nystatin. The BIA results revealed that a group of topical antifungals that included nystatin, miconazole, clotrimazole, ketoconazole, butenafine and naftifine best achieved this goal when compared to other combination groups of antifungals. Thus this group was determined to be more cost-effective relative to other combination groups.

The P&T Committee concluded that econazole, sulconazole, ciclopirox, oxiconazole and sertaconazole were not cost-effective relative to the other topical antifungals.

Based on its collective professional judgment, the P&T Committee voted to recommend formulary status for 6 topical antifungal agents: nystatin, miconazole, clotrimazole, ketoconazole, butenafine and naftifine. The P&T Committee recommended non-formulary status under the Uniform Formulary for five topical antifungals: econazole, sulconazole, ciclopirox, oxiconazole and sertaconazole.

Implementation Plan

Because topical antifungals are used for acute rather than chronic infections and patients are unlikely to require a change in existing therapy, the P&T Committee voted to recommend a 30-day transition period for implementing the decision to change econazole, sulconazole, ciclopirox, oxiconazole and sertaconazole to non-formulary drugs under the Uniform Formulary.

The number of patients who received these drugs at all MHS points of service from February 1, 2004, to January 31, 2005, was 49,742 patients, representing less than 13 percent of all patients who were prescribed topical antifungals. MTFs are not allowed to have non-formulary pharmaceuticals on their local formulary. MTFs can fill requests for non-formulary agents only if both of the following conditions are met: (1) the prescription must be written by an MTF provider; and (2) the beneficiary and his or her provider have established medical necessity for the agents. MTFs may, but are not required to, fill a non-formulary prescription written by a non-MTF provider to whom the patient was referred as long as medical necessity has been established.

The P&T Committee voted to recommend an effective date of 30 days from the final decision date (the date that the P&T Committee minutes are signed by the Director, TMA, approving the Committee's recommendation).

Beneficiary Advisory Panel Questions and Comments

The Chairperson, Ms. Hickey, opened the floor to questions from the Beneficiary Advisory Panel.

In answer to a question from Mr. Hutchings about whether the cost analysis was done using the prices of generic agents, Maj Tiller said ciclopirox cream is available in generic form, whereas other formulations are not. For that agent, the cost included the generic price for the cream. They were bundled together. Econazole is also available generically now and the generic price was used for that agent. Maj Tiller also said that the prices for generics relative to the other products are high.

In answer to a follow-up question about the possibility of a price drop over time, Maj Tiller said that ketoconozole has been available generically for a long time, and there was a considerable difference between nystatin and ketoconazole. He said there is no guarantee that the generic form of ciclopirox will even come close to ketoconazole. There is a clear separation. And, based on the analysis of relative clinical effectiveness, ciclopirox wouldn't add anything for treating the DoD population to the other agents that are included in the Uniform Formulary.

Ms. LeGette asked how this would work from the perspective of the patient who is using a generic that has now become a non-formulary agent? What is the process at the retail pharmacy if the drug goes to third tier? The answer, provided by staff, was that the drug would be available, but at a $22 co-pay because it is non-formulary.

Mr. Class asked if it wouldn't be confusing for beneficiaries to have generic drugs moved to the third tier. The policy has been that if there is a generic available, the beneficiary should use it.

Mr. Hanson asked the same question in relation to econazole, for which there is now a generic. He asked what's going to be offered as a generic and what will go to non-formulary status. CDR Graham said the whole drug itself, whether it's econazole or the generic version, goes to non-formulary. She noted that not all generics are cost-effective. In general, the generic cost is less than the branded cost, but that doesn't hold true for all generics.

Mr. Burleson read a new regulation requiring generic substitution: "In cases in which there is clinical justification for a brand-name drug in lieu of a generic equivalent, the generic substitution policy is waived. When a blanket purchase agreement, incentive price agreement, government contract or other circumstances result in a branded pharmaceutical agent being the most cost-effective agent for purchase by the Government, the P&T Committee may also designate the drug to be cost-shared at the generic rate."

Mr. Class said he doesn't think generics are necessarily the best answer, but it's what the system has pushed everyone to. This represents another new wrinkle: just because it's generic doesn't mean you'll be able to get it.

Ms. Hickey asked whether it is conceivable that somebody at a $22 co-pay for 30 days would be paying more than the drug costs. The answer given was that it isn't.

Mr. Hutchings said his concern is that generic prices will fluctuate when they come on the market and then, a year from now, will have low costs. He said he's looking for assurances that the prices will continue to be monitored on the generics. CDR Graham said this is another situation, like PDE-5 inhibitors, where ongoing monitoring will be conducted once the Uniform Formulary recommendations are accepted. This is the first time a generic has been recommended to go into the "non-formulary" category. It will be up to PEC to watch and take action when the price finally drops.

Mr. Hanson asked whether any topical antifungals will be available in the generic category. The answer given was "yes" - with the exception of two brand products, all of the recommendations have generic equivalents. Mr. Hanson asked if there is anything in tier 1. The answer was nystatin, clotrimazole and miconazole would be available in tier 1 at the generic co-pay share.

Ms. Hickey observed that one of the things looked at was medications used for the pediatric population and asked which drugs those are. The answer was nystatin is commonly prescribed for the pediatric population and clotrimazole may be prescribed for ages two and up. Ms. Hickey asked about drugs for pediatric use in the third sub-class (allylamines). The answer provided was that the safety and efficacy of the allylamine sub-class has not been established for populations under the age of twelve. Ms. Hickey said a comment to that effect included in the read-ahead material would have been helpful.

Ms. Hickey also asked that future presentations use the common terms for diseases as well as the latin terms.

Mr. Hutchings observed that it might be more effective to have Lamisil available with a co-pay. CDR Graham said it doesn't fall in the category of a "covered benefit."

BAP Vote

Chairperson Hickey called for a vote on the P&T Committee recommendation that the status of econazole, sulconazole, ciclopirox, oxiconazole and sertaconazole be changed from "formulary" to "non formulary," with butenafine, clotrimazole, ketoconazole, miconazole, naftifine and nystatin maintaining "formulary" status. The vote was 8-0 with all Panel Members concurring with the recommendation.

The Chair next called for a vote on the implementation plan. The P&T Committee proposed a 30-day transition period for implementation of the decision to change econazole, sulconazole, ciclopirox, oxiconazole and sertaconazole from "formulary" to "non formulary" drugs on the Uniform Formulary. Three Panel members voted to concur. Four Members cast non-concur votes. One member abstained.

Additional Comments on Vote

The Chair asked for comments from those who voted to not concur. Mr. Hutchings said the change will take more time than the 30-day window allows. He said he would recommend 90 days to avoid any undue hardship.

Mr. Class said he had a problem with the logistics and that 90 days seems like a more reasonable period.

Ms. Fryar noted that the 30 days shouldn't be a problem for the MTFs.

The Chair asked for a vote on a 90-day transition period from among the members who non-concurred with the 30 days period. All four members concurred with a 90-day period. Mr. Hanson said he was abstaining because he lacked expertise.

The rationale for the 90 day recommendation to TMA, provided by the Chair, was that the Panel is new to the process. The first time for implementing anything will happen July 17. She would like to see how the notification process works before moving to a 30-day implementation period.

Dr. Lenow said that for agents like this it shouldn't matter much. He doesn't see this as a consumer issue.

Mr. Class added a comment to the effect that there needs to be an educational process by TMA to explain the generic policy and why people will have to pay $22 for drugs they are now paying $3 for.

Ms. Hickey agreed, noting that the beneficiary population has gotten used to the phrase "generic substitution."

Mr. Hanson also said it would be helpful if future presentations could include a chart that groups drugs into "Tier One," "Tier Two" and "Non Formulary."

After the lunch break, Chairperson Hickey continued the discussion, indicating that there may be a systemic problem in implementing the non-formulary recommendations for antifungals. She asked Lisa LeGette to describe the problem.

Ms. LeGette said the problem arises with communications. Since there will be generics on the non-formulary tier, they will have to be processed as a $22 co-pay. Currently on the Express Scripts commercial side, all generics are covered at the lowest co-pay. In the TRICARE Retail Pharmacy program, brand prescriptions that have generic versions available are actually rejected. In the case of a drug like Loprox (ciclopirox), the brand name would be rejected. The potential here is that the branded product would be rejected, even though we have been communicating to beneficiaries that all non-formulary products will still be covered but merely at the $22 co-pay. She said the need is to think through the communications and tailor them when things like this come up.

Mr. Class noted that the Panel might want to suggest that the communication needs be taken into account before making a final decision.

Ms. Hickey said she would like the Panel to reaffirm its decision regarding the formulary/non-formulary recommendations, but that the Department should be aware of the possibility of a systemic problem and it does not want a beneficiary to be rejected from having the drug at all. Dr. Winkenwerder and the TMA staff should look carefully at the implementation of the recommendation and what might happen in the retail pharmacy program to prevent any total rejections from occurring.

The Panel agreed with the recommendations as noted earlier, but stressed the need to be clear in the communications regarding implementation to avoid potential complications.

Multiple Sclerosis Disease Modifying Drugs Class Review

CDR Graham presented the findings and recommendations of the P&T Committee on the drug class: Multiple Sclerosis Disease Modifying Drugs.

Relative Clinical Effectiveness

CDR Graham said the evaluation of the relative clinical effectiveness of the four Multiple Sclerosis Disease Modifying Drugs (MS-DMDs) took into account information regarding their safety, effectiveness and clinical outcomes. Currently there are four drugs that have been approved for the treatment of relapsing-remitting multiple sclerosis, all of which are biologics:

1. intramuscular interferon (IFN) beta 1-a (brand name Avonex)
2. subcutaneous IFN beta 1-a (brand name Rebif)
3. subcutaneous IFN beta 1-b (brand name Betaseron), and
4. A subcutaneous polypeptide mixture, glatiramer acetate (brand name Copaxone)

The MS-DMD class has been available for twelve years and is currently ranked 33rd in Military Health System expenditures. In the 2004 fiscal year, 36, 296 MS-DMD prescriptions were dispensed at a total expenditure of $41.5 million at all three points of service. The MS population in DoD is small – approximately 6,500 beneficiaries out of 9 million.

All four MS-DMDs are indicated by FDA for the treatment of patients with relapsing forms of MS to decrease the frequency of clinical exacerbations. Avonex and Rebif also have the additional indication of delaying the accumulation of physical disability. Based on the relative clinical effectiveness reviews, the P&T Committee concluded that all four MS-DMDs have similar clinical effectiveness. Their conclusion was reached after answering the following questions: (1) are there differences in the efficacy of disease modifying drugs for MS? and (2) are there differences in the safety and tolerability profiles of MS-DMDs?

In answering these questions, the P&T Committee evaluated information from randomized clinical trials, additional clinical trials found in a MEDLINE search, major medical journals and manufacturer press sheets. Professional society proceedings (such as the American Academy of Neurology) were also reviewed to find additional published clinical trials. Manufacturers were invited to present new data and the FDA website was monitored.

CDR Graham said, regarding efficacy, that the clinical trials in this class were difficult to review, detailing several of the inherent problems with the test methods, measures and scores. All the interferons and glatiramer are indicated for the treatment of patients with relapsing forms of MS to decrease the frequency of clinical exacerbations. Avonex and Rebif also claim to delay the accumulation of physical disability. A Cochrane Systematic Review of all the available trials through 200 found only a modest reduction in exacerbations and disability following treatment of the relapsing-remitting MS with interferons. Another Cochrane Systematic Review of trials available through 2003 concluded that glatiramer had a modest reduction in exacerbations but no beneficial effect on disease progression. A decrease in exacerbations does not necessarily correlate to the progression of disease.

There is no compelling evidence to support the superiority of one agent over another. All beta interferons and glatiramer have a modest protective effect on disease exacerbations. Interferon beta 1-a agents (Rebif and Avonex) have shown to have a modest protective effect on disease disability and therefore may have a marginal benefit over glatiramer.

The conclusion was that there is no evidence that any one MS-DMD is more efficacious than the others.

Regarding safety and tolerability, the P&T Committee agreed there is no evidence that any one MS-DMD is preferable to the others. These medications are generally well tolerated and adverse events are dose related. The most common side effects were local injection site reactions for the subcutaneous drugs and flu-like symptoms for the intramuscular drugs. Additionally, a self-limiting allergic reaction (shortness of breath, palpitations and anxiety) may be seen with glatiramer. All the MS-DMDs have similar safety and tolerability profiles with only rare incidences of true serious side effects. CDR Graham detailed some of these rare incidents.

All the interferons are pregnancy category C and glatiramer is pregnancy category B. Drug interaction studies have not been performed with the interferons or glatiramer. The drugs have been prescribed together with cortocoid steroids, antidepressants and oral contraceptives without adverse effects.

The P&T Committee's conclusion regarding the overall clinical effectiveness of drugs in this class was that there is no conclusive evidence to support any of the MS-DMDs having a significant, clinically meaningful therapeutic advantage over the others in terms of safety, effectiveness or clinical outcomes.

Relative Cost Effectiveness

In considering the relative cost effectiveness of pharmaceutical agents in this class the P&T Committee evaluated the costs of the agents in relation to the safety, effectiveness and clinical outcomes of the other agents in the class. Information considered by the P&T Committee included, but was not limited to, sources of information listed in the Code of Federal Regulations.

Cost minimization techniques determined that the overall weighted average cost per day of therapy for the MS-DMDs was lowest for Avonex, followed by glatiramer and Betaseron. Rebif was determined have the highest average cost per day of treatment.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, other relevant factors (i.e. the relative uniqueness of each agent and the low expectation that patient behavior would be affected by formulary status), the P&T Committee recommended that all MS-DMDs maintain UF status with the formulary cost share.

P&T Committee Recommendation

The Uniform Formulary recommendation, taking into consideration the conclusions noted above, was that all MS-DMDs should maintain their "formulary" status with the formulary cost share.

Implementation Plan

Since no changes were recommended, an implementation plan was not required.

Beneficiary Advisory Panel Questions and Comments

Ms. Hickey asked whether, even though there is no implementation plan, the recommendation would show as being effective on the system if included in the formulary. CDR Graham said it would.

A question was asked about the cost of the drugs to the MHS. CDR Graham confirmed that the cost was $41.5 million in fiscal year 2004.

Beneficiary Advisory Panel Vote

The Panel unanimously voted (8-0) to concur with the recommendations of the P&T Committee that all of the agents in the MS-DMD drug class should maintain their status as "formulary" drugs in the DoD Uniform Formulary.

No vote was needed on implementation.

Panel Comments on the Process

MAJ Watson asked the Panel members if they had comments regarding the process used for today's meeting. He said he already had noted that the Panel would like to have 2-3 days to review the summary before it is forwarded to Dr. Winkenwerder and would like to have copies of the presentation materials before they are posted to the website. MAJ Watson said the date for submitting the summary of this meeting to Dr. Winkenwerder had already been set, but the staff would try to get the summary to the Panel in time to allow a review. In the future, the additional time will be built into the planning.

Chairperson Hickey said it is necessary to decide who will answer some of the questions that the Panel raises. As an example, she noted the question arising at the previous meeting about staggered implementation time periods for patients already on a drug as opposed to new prescriptions. Her understanding is that this approach may not be feasible, but an answer should be provided to the Panel. There was also a question about whether the Panel could have knowledge of what the recommendations to the P&T Committee are. Her question is: "What is the process for answering the Panel regarding these questions?" It needs to be clarified.

Ms. Hickey expressed her appreciation to the members of the public who provided comments, to the presenters, to MAJ Watson and the staff and to those who attended the meeting.

Mr. Hutchings suggested that the agendas for future meetings should include, after the questions, time for a discussion among the Panel members of the recommendations. Mr. Burleson said the Panel members could talk among themselves and decide what process they want to use for coming to a decision. Mr. Martel said his understanding, though, is that the Panel cannot conduct deliberations as a group unless it is public. All discussions and conclusions must be published.

The Panel also discussed the need or desirability of having the Panel meeting focus on new information instead of just repeating the information that is already posted on the website. Ms. Hickey asked whether there is a requirement that the formal information from the P&T Committee must be presented to the Panel.

Mr. Class said he is unsure of the value of just reading through information that was already provided to the Panel in the read ahead. CDR Graham said what the PEC presenters try to do is provide the Panel with just the key information from very extensive P&T Committee deliberations. Mr. Hanson said a combination of read-ahead material and presentations gives him a better understanding. He wouldn't want to make the presentations too brief and have to rely on the materials sent out ahead of time.

It was agreed that DoD should get back to the Panel about how much and what information provided to the P&T Committee can be shared with the Panel.

Mr. Hutchings acknowledged that the Panel isn't allowed to know specific price information, but said he would find it helpful to have more information about costs as used in the cost effectiveness analysis - perhaps a range of costs or indexed cost information comparing the relative costs of the drugs. Several other Panel members agreed that it would be useful to have something more. CDR Graham said her organization will look into the possibilities and get back to the Panel. She agreed it would be good for the Panel to know the potential impact in terms of cost savings. Perhaps a continuum showing where the various agents fall along it could be developed.

Mr. Hanson also asked that the write-up include information about some of the key assumptions used, such as expectations regarding market share shift.

MAJ Watson announced that the next meeting of the Beneficiary Advisory Panel would be held on September 28, 2005, at the Naval Heritage Center in Washington, D.C. The official announcement will be published in the *Federal Register*. The summary of this meeting should be posted on the website around the second or third week in July.

MAJ Watson closed the meeting at 1:10 P.M.

Brief Listing of Acronyms Used in This Summary

Abbreviated terms are spelled out in full in this summary; when they are first used, the acronym is listed in parentheses immediately following the term. All of the terms used as acronyms are listed below for easy reference. The term "Panel" in this summary refers to the "Uniform Formulary Beneficiary Advisory Panel," the group whose meeting is the subject of this report.

- ARB - angiotensin receptor blockers (a drug class)
- BAP - Uniform Formulary Beneficiary Advisory Panel (the "Panel" referred to above)
- BIA - Budget Impact Analysis
- CAPT - Captain (U.S. Navy)
- CDR - Commander (U.S. Navy)
- CFR - Code of Federal Regulations
- CMA - Cost-Minimization Analysis
- DFO - Designated Federal Officer
- DoD - Department of Defense
- ED - erectile dysfunction
- IFN - interferon
- Maj - Major (U.S. Air Force)
- MAJ - Major (U.S. Army)
- MHS - Military Health System
- MS - multiple sclerosis
- MS-DMD - Multiple Sclerosis Disease Modifying Drugs (a drug class)
- MTF - Military Treatment Facility
- OTC - Over the counter
- PA - Prior Authorization
- PAH - Pulmonary arterial hypertension
- P&T - Committee - DoD Pharmacy and Therapeutics Committee
- PDE-5 - Phosphodiesterase Type 5 Inhibitors (a drug class)
- PEC - DoD Pharmacoeconomic Center
- TMA - TRICARE Management Activity
- TMOP - Tricare Mail Order Pharmacy
- UF - DoD Uniform Formulary

Letters Submitted for Panel Consideration

Letter No. 1

June 16, 2005

Tricare Management Activity
Beneficiary Advisory Panel
c/o Mr. Richard Martel
5111 Leesburg Pike, Suite 810
Falls Church, VA 22041

Messrs. Chairman and Members of the Panel:

We are submitting this statement as an interested party with a unique composite of perspectives on the issue of Uniform Formulary (UF) determinations for the Phosphodiesterase 5 (PDE5) Inhibitor class. It is recognized that the stated purpose of the UF was to create a "uniform, consistent and equitable pharmacy benefit" that will provide adequate access to beneficiaries across the entire Military Health System. This objective is being challenged by the possibility that Viagra® (sildenafil citrate) will no longer be covered by the Department of Defense. This decision will have a significant impact on DoD beneficiaries currently treated for erectile dysfunction (ED) since the majority of these patients '(>90%) receive Viagra<8>. In addition, this will likely result in significant administrative burden and potentially introduce unforeseeable costs to the entire TriCare Network.

There are important differences in the depth and breadth of clinical data favoring Viagra@ as a preferred agent.[1] Over the past 10 years, the clinical efficacy and safety of Viagra ® has been extensively researched in over 13,000 patients in more than 100 clinical trials. Viagra ® has been studied in a broader patient population than any other PDE5 inhibitor, including those with cardiovascular disease, spinal cord injury, taking antidepressant and antihypertensive medications and following the treatment of prostate cancer. In evaluating the comparative efficacy of PDE5 agents, it is difficult to draw conclusions about similar effectiveness based on randomized placebo controlled trials since these studies were conducted in different patient populations and may have used different measures of effectiveness. For example, exclusion of prior PDE5 nonresponders, as required in a number of competitor studies, would significantly increase the efficacy rates. In addition, contrary to the P&T Committee's conclusion, Padma-Nathan et al.[2] confirmed that ***head to head trials were conducted and submitted for Cialis®*** [3,4] ***and Levitra®*** [5] ***to the Food and Drug Administration and European Agency for Evaluation of Medicinal Products (EMEA). These studies failed to demonstrate that Cialis® and Levitra® were not inferior*** *to Vlagra®.*

The cardiovascular safety profile of Viagra® is well established. Neither Viagra® nor Cialis® have a precaution for QT prolongation or use with antiarrhythmic agents whereas Levitra® does. Additionally sildenafil citrate has shown

---

Cialis ® is a registered trademark of Lillylcos. Viagra ® is a registered trademark of Pfizer, Levitra ® is a registered trademark of Bayer and GlaxoSmithKline. Revatio ® is a registered trademark of Pfizer.

significant benefit in improving lung oxygenation and exercise tolerance in pulmonary arterial hypertension (PAH) patients and has recently been approved by the FDA as Revatio ® for the treatment of PAH.

Limiting access to Viagra ® may introduce additional costs to the DoD System associated with patients continuing utilization or switching back to Viagra® after trying a competitor. In a recent analysis of PDE5 inhibitor prescribing patterns using the NDCHealth's Intelligent Health Repository, only 6% of patients switched from Viagra ® to a competitor and 22-27% switched back.[6]

In sum, we respectfully disagree with the P&T Committee's conclusions that the three PDE5 agents are comparable. The role of Viagra® as the preferred PDE5 agent for DoD beneficiaries is supported by existing head to head studies, a more established cardiovascular safety profile and the current dominant share of PDE5 prescriptions in the DoD. Left unchallenged, the P&T Committee's recommendations will place additional monetary and access burdens on the
majority of DoD beneficiaries who are treated for ED and receive Viagra ®. Thus, we are requesting that members of the BAP and Dr. Winkenwerder disagree with the P&T Committee's recommendations. Hopefully you will be successful in sending a positive message to Dr. Winkenwerder and the DoD P&T that preserving access to beneficial therapies is of critical importance. This was demonstrated in the March 2005 decision to maintain access to six of the seven angiotensin receptor blockers (ARBs) that were evaluated. We urge a similar consideration for Viagra® that will set the precedence for future medication class reviews.

Thank you for your consideration of this matter.

Sincerely,

Bob Sikora, RPh
Vice President - Clinical Education Consultants Pfizer Global Pharmaceuticals
LTC, USA, MSC (Ret)

Evelyn L. Lewis, MD, MA
Director, Government Regional Medical Research Specialist pfizer Global Pharmaceuticals
CDR, MC, USN (Ret)

REFERENCES

[1]Anon. Vardenafil (Levitra) for Erectife Dysfunction The Medical Letter, Vol. 45, pg 77-78 September 29, 2003.

[2] Padma-Nathan H, MoCuliough A, Forest C.Erectile dysfunction secondary to nerve-sparing radical retropubic prostatectomy: comparative phosphodiesterase-5 inhibitor efficacy for therapy and novel prevention strategies. Curr Urol Rep. 2004 Dec;5(6):467-71.

[3] European Agency for the Evaluation of Medicinal Products (EMEA). Committee for Proprietary Medicinal Products European Public Assessment Report:Clalis-Intemational Non-Proprietary Name: tadalafil (CPMPI3960/02). London: European Agency for the Evaluation of Medicinal Products, 2002. Available at: http://www.emea.eu.intlhumandocslHumanslEPARlcialis/cialis.htm. 14. European Agency for the Evaluation of Medicinal Products (EMEA). Committee for Proprietary

[4] Cialis summary basis for approval. U.S. Food and Drug Administration. Available at: http://www.fda.gov/cder/foilnda/2oo3l21-368_Cialis.htm.

[5] European Agency for the Evaluation of Medicinal Products (EMEA). Committee for Proprietary Medicinal Products European Public Assessment Report: Levitra-Intemational Non-Proprietary Name: vardenafil (CPMP/621 0/02). London: European Agency for the Evaluation of Medicinal Products, 2003. Available at: http://www.emea. eu.intlhumandocs/HumanslEPARllevitra/levitra. htm.

[6] Harnett J, Mclaughlin T, Burhani 5, Scott B. Evaluation of tadalafil and vardenafil treatment patterns in prior sildenafil users. Value in Health [abstract PIH17] 2005; 8(3): 258

Letter No. 2

My name is (redacted). I'm a retired Lieutenant Colonel from the United States Air Force. I've been married twenty-two years and have an eleven-year old daughter. I have twenty-one years of active service. I spent fourteen of those twenty-one years with Multiple Sclerosis (MS). After completing my Master's Degree requirements in 1988, my MS symptoms began. No treatments were available.

The first medication available was Betaseron, which I started in February of 1995. When Avonex became available, my doctor suggested I consider changing medications because Avonex seemed to meet my needs better. In September of 1996, I started using Avonex. I had very few side effects and the once-a-week injection was more convenient for travel.

The FDA approved another medication for treating relapsing-remitting MS: Rebif. Being a former intelligence officer with an investigative mind, I thought I would try Rebif. My doctor reluctantly gave me his blessings. I experienced some rather severe side effects and quickly returned to Avonex.

I have always been an extremely active person. I played varsity basketball at VA Tech, ran track and have enjoyed a variety of other sports. I even played basketball for Peterson Air Force Base's Women's Basketball team following my first MS exacerbation.

Multiple Sclerosis is a chronic, progressive disease. It attacks our central nervous system, the core of our bodies and the core of our beings. Everyone is vulnerable! Yes, being told you have MS can send you into a tailspin, but in the same breath, the doctor can tell you about a variety of medications that you can have at "no cost" or "very little cost."

These medications are essential to maintaining a quality force. Without this medicine, the money the American people invested in me would have been lost. My career would have ended abruptly. We owe it to the American people to seek every opportunity to capitalize on their investments. It is a win-win situation. Military members must know their country is behind them 100 percent. That 100 percent includes the medications to treat relapsing-remitting MS. Avonex must be part of the survival kit.

Thank you
(name redacted)
LtCol, USAF (retired)

Letter Number 3

Martel, Richard, CTR; OASD(HA)/TMA
From: [*redacted*]
Sent: Friday, June 24,200510:49 AM
To: Martel, Richard, CTR, OASD(HA)/TMA
Subject: DoD Viagra Formulary Review

Dear Mr. Martel - I understand the Department of Defense is reviewing the coverage of erectile dysfunction products (Viagra, Levitra,Cialis) under Tricare.

As a 64-year old Viet Nam era Naval veteran and father of a Navy pilot currently on active duty (who had testicular cancer), we are both ED patients who have benefited from Viagra, **I'm writing to request your support to ensure that this medication continues to remain available** for those members of the military and veteran patients with erectile dysfunction.

Over the past 10 years, the clinical efficacy and safety ofViagra® has been extensively researched in over 13,000 patients in more than 100 clinical trials. Viagra® has been studied in a broader patient population than any other products for ED, including those with cardiovascular disease, spinal cord injury, taking antidepressant and antihypertensive medications and following the treatment of prostate cancer.

My son, LT. [*name redacted*] USNR, a veteran of Operation Iraqi Freedom, and a cancer survivor,
has used and continues to use Viagra successfully. To deny him, other US Armed Forces personnel and veterans like myself with erectile dysfunction, would be a travesty and could have a negative impact on their sexual relations and morale. **These men who have already sacrificed much for our country, deserve our support in ensuring that this vital treatment option continues to remain available to those who need it.**

Please don't let our veterans and military down, sir. Thank you!

"Any man who may be asked what he did to make his life worthwhile, can respond with a great deal of pride, I served in the United States Navy"! President John F. Kennedy

Letter Number 4

Martel, Richard, CTR, OASD(HA)/TMA

From: [*name redacted*]
Sent: Friday, June 24,200512:09 PM

To: Martel, Richard, CTR, OASD(HA)/TMA
Cc: Dyott, Steve
Subject: Viagra

Richard Martel, first of all I am a retired Marine of thirty years of service to this great country, I had prostate cancer due to agent orange. Please do not stop putting VIAGRA in the inventory of medicines for military men active and retired.
I haved tried other simular products but VIAGRA is the only one that I trust. I am on tricare and will be on tricare for life next month on my 65th birthday. There are a lot of men in the prostate cancer support group that I am in, in Jacksonville, NC that swear by this great product, PLEASE DO NOT LET US VETS DOWN.
[*name redacted*]
Msgysgt USMC Retired