Uniform Formulary Beneficiary Advisory Panel

Meeting Summary
June 21, 2007
Washington, D.C.

Panel Members Present:

- Robert Washington, Fleet Reserve Association, Chairman
- Kathryn Buchta, Health Net Federal Services
- John Class, Military Officers Association of America
- Deborah Fryar, Military Coalition
- Rance Hutchings, Uniformed Services Family Health Plan
- Lisa Le Gette, Express-Scripts, Inc.
- Jeffrey Lenow, Medical Professional
- Charles Partridge, National Military and Veterans Alliance
- Marissa Schlaifer, Medical Professional

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.

MAJ Watson indicated this meeting of the Panel has been convened to discuss and review the recommendations of the Department of Defense (DOD) Pharmacy and Therapeutic (P&T) Committee meeting held during May, 2007 in San Antonio, TX.

Agenda

The agenda for this meeting of the Panel is:

- Opening remarks and public comments
- Review and discussion of P&T Committee recommendations for drugs in the following drug classes:
  - Antilipidemics II (LIP-2s)
  - 5-Alpha Reductase Inhibitors (5-ARIs)
  - Proton Pump Inhibitors (PPIs)
  - Angiotensin Receptor Blockers (ARBs)
- Wrap-up comments

Opening Remarks

MAJ Watson stated that Title 10 United States Code (U.S.C.) section 1074g requires the Secretary of Defense to establish a DOD Uniform Formulary (UF) of pharmaceutical agents, review the formulary on a periodic basis and make additional recommendations regarding the formulary as the Committee deems necessary and appropriate.

10 U.S.C. section 1074g also requires the Secretary to establish a Uniform Formulary Beneficiary Advisory Panel (BAP) to review and comment on the development of the Uniform

Formulary. The Panel shall include members that represent non-governmental organizations and associations that represent the views and interests of a large number of eligible covered beneficiaries. Comments of the Panel must be considered before implementing changes to the Uniform Formulary. The Panel's meetings are conducted in accordance with the Federal Advisory Committee Act (FACA).

The duties of the Uniform Formulary Beneficiary Advisory Panel are:

- To review and comment on the recommendations of the P&T Committee concerning the establishment of the Uniform Formulary and subsequent recommended changes. Comments to the Director, TMA, regarding recommended formulary status, pre-authorizations, and suggested dates for changing from "formulary" to "non formulary" status must be reviewed by the Director before making a final decision.
- To hold quarterly meetings in an open forum. The Panel may not hold meetings except at the call of or with the advance approval of the Chairman of the Panel.
- To prepare minutes of the proceedings and prepare comments for the Secretary or his designee regarding the Uniform Formulary or changes to the Formulary. The minutes will be available on the website and comments will be prepared for the Director, TMA (Dr. Cassell).

As guidance to the Panel regarding this meeting, MAJ Watson said the role of the Beneficiary Advisory Panel is to comment on the Uniform Formulary recommendations made by the P&T Committee at their last meeting. While the Department appreciates that the BAP may be interested in the drug classes selected for review, drugs recommended for the basic core formulary (BCF) or specific pricing data, these topics do not fall under the purview of the BAP.

The P&T Committee met for approximately 20 hours to consider the class review recommendations presented today. Since this meeting is considerably shorter, the Panel will not receive the same extensive information that is presented to the P&T Committee members. However, the BAP will receive an abbreviated version of each presentation and its discussion. The materials provided to the Panel are available on the TRICARE website.

Detailed minutes of this meeting are being prepared. The BAP minutes, the DOD P&T Committee meeting minutes and Dr. Cassell's decisions will be available on the TRICARE website in approximately four weeks.

MAJ Watson next reviewed the ground rules for conducting the meeting:

- All discussion takes place in the open public forum. There is to be no committee discussion outside the room, during breaks or at lunch.
- Audience participation is limited to private citizens who signed up to address the Panel.
- Members of the Pharmacoeconomic Center (PEC) and the P&T Committee are available to answer questions related to the BAP's deliberations. Should a misstatement be made, these individuals may interrupt to ensure that the minutes accurately reflect relevant facts, regulations or policy.

MAJ Watson introduced the new Chair of the Beneficiary Advisory Panel, Mr. Robert Washington, and the other Panel members present. He then briefly reviewed housekeeping considerations.

Private Citizen Comments

MAJ Watson opened the meeting for private citizen comments. There was no response.

Presentation of Drug Class Reviews

Maj Wade Tiller, Deputy Director of the Pharmacoeconomic Center (PEC) began the agenda presentation with introductory remarks.

[Insert script page 1]

Review of the Antilipidemic II (LIP-2) Drug Class

Clinical Effectiveness Review

CPT Josh Napier of the PEC presented the P&T Committee's clinical effectiveness review of the Antilipidemic II (LIP-2) drug class.

[Insert script, pages 2-5]

Cost Effectiveness Review

Major Tiller next discussed the cost effectiveness review for this drug class.

[Insert script, page 6, paragraph 1]

P&T Committee Action and Recommendations

Major Tiller then detailed the P&T Committee's recommendations in the Antilipidemic II (LIP-2) drug class.

[Insert script, page 6, section 2 through page 8, first full paragraph].

P&T Committee Physician Perspective

CPT Napier provided the Panel with the physician's perspective on the P&T Committee's actions. He informed the Panel that recommendations in this drug class went over smoothly with the P&T Committee. The long history of use with fibric acid derivatives and the generally low usage of bile acid sequestrants is reflected in the results.

Panel Questions

Mr. Partridge said he has the impression from the briefing that Omacor is different from the other drugs in this class. CPT Napier said the impression is correct; Omacor uses the active ingredient of Omega-3 fatty acids in nutritive fish oil. Its main clinical effect is to lower triglycerides. But Omacor, while different in how it works, is no different in its clinical effect than the fibric acid derivatives. Mr. Partridge then noted that Omacor was the only drug of its kind approved by FDA and asked whether this situation wouldn't argue for being cautious about removing it from the formulary. Also, the data show that the use of this drug is increasing. CPT Napier said the variety of fibric acid derivatives available in the class provide good triglyceride lowering effects and that Omacor and other fish oil supplements can increase a patient's LDL – the bad cholesterol. Providers know they can get equal or better triglyceride-lowering effects with fibric acid derivatives without having to worry about raising LDL levels. Additionally, good fish oil supplements are available over the counter and Omacor was not as cost effective as other agents.

Mr. Class asked about the reasoning behind the one "opposed" vote on the P&T Committee. Major Tiller said the vote was an expression of concern that Omacor was being made "non formulary" under the UF. A small number of MTFs currently provide over-the-counter fish oil supplements as part of their formulary. The concern was the Committee action might affect this practice. Major Tiller said the Committee felt strongly about not endorsing either Omacor or OTC fish oil products for triglyceride lowering.

Regarding the implementation recommendation, Mr. Hutchings asked whether there would be any DoD communication with the patients using drugs that are being moved to non-formulary. He said he is especially concerned about Tricor, which has about 35,000 users. His organization —the Uniformed Family Services Health Plan — will send letters to their patients notifying them of their options for Tricor but the 90-day turnaround time for implementation is very tight. Major Watson replied that there wouldn't be any DoD communication with patients. Mr. Hutchings asked whether there was a budget for patient notification. He expressed the view that an effective communications program would save the DoD more money than moving drugs to non-formulary status. Major Watson replied that he has no budget for external patient communications. Mr. Hutchings followed up by asking if there was anything in motion to get a budget for that. Major Watson replied that there might be something included in the next round of pharmacy contracts. Mr. Hutchings noted that if there is no communication with the patients, all they know is that their co-pay went up; they won't necessarily switch to the formulary drugs.

Panel Discussion of P&T Committee LIP-2 Formulary Recommendations

The Chairman opened the meeting for Panel discussion of the P&T Committee's recommendations regarding the Antilipidemic II drug class:

"Taking into consideration the conclusions from the relative clinical effectiveness and the relative cost effectiveness determinations for the LIP-2s, and other relevant factors, the P&T Committee recommended (13 for, 1 opposed, 1 abstained, 2 absent) that:

1) Fenofibrate (lofibra, generics), IDD-P fenofibrate (Triglide), cholestyramine/aspartame (Questran Light, generics), cholestyramine/sucrose

(Questran, generics), colestipol (Colestid, generics), and gemfibrozil (Lopid, generics) be maintained as formulary on the Uniform Formulary;

2) Micronized fenifibrate (Antara), nanocrystallized (Tricor), prescription omega-3 fatty acids (Omacor), and colesevelam (Welchol) be classified as non-formulary under the UF; and

3) The normal brand formulary cost-share of $9.00 for IDD-P fenofibrate (Triglide) be Lowered to the generic formulary cost-share of $3.00.

The authority for the last recommendation is codified in 32 CFR 199.21(j)(3), which states that 'when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the Pharmacy and Therapeutics Committee may also designate the drug be cost-shared at the generic rate.' The objective is the maximize the use of IDD-P fenofibrate (Triglide) in the retail network and mail order, given its significantly lower cost relative to other fenofibrate products. Lowering the cost-share for brand name IDD-P fenofibrate (Triglide) will provide a greater incentive for beneficiaries to use the most cost-effective fenofibrate formulation in the purchased care arena."

Mr. Class expressed approval of the recommendation to lower the co-pay for Triglide from $9.00 to $3.00. However, he doesn't see how that action will bring about the change envisioned unless it is communicated to beneficiaries.

Ms. Fryar also commented on the number of discussions that the Committee has had in the past regarding implementation time and communication with the beneficiaries — who would send the message, how it would get out and how the beneficiaries would actually know what was happening and understand the process involved. She also said that lowering the co-pay to $3.00 would be a good thing, but if the beneficiaries don't understand the overall process it doesn't look good.

Mr. Hutchings said that there are other instances where branded drugs have a generic co-pay, so the action isn't really a departure from the norm and he favors it.

Panel Vote on Formulary Recommendation for the LIP-2 Drug Class

Mr. Washington called for the Panel vote on the LIP-2 drug class formulary recommendations. The Panel vote was:

8 Concur, 1 Non-Concur, 0 Abstentions.

Mr. Class commented that his non-concur vote was based on the absence of Omacor from the Uniform Formulary recommendation. Omacor is a different mechanism of action and is the only one of its kind in the class.

Panel Discussion of P&T Committee LIP-2 Implementation Recommendations

Mr. Washington read the P&T Committee's implementation period recommendations for the LIP-2 drug class:

"The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) an effective date no later than the Wednesday following a 90-day implementation period. The implementation period will begin immediately following approval by the Director, TMA."

Mr. Partridge voiced his agreement with Mr. Hutching's earlier concern regarding the 90-day implementation period. He noted that the implementation period can be as much as 180 days and expressed the view that the implementation date should be changed to a date that the pharmacists are comfortable with.

Mr. Hutchings also asked what the MTF turnaround time is — how long it will take to get Tricor off the shelf and replace it with Triglide and whether 90 days is enough time to do that. Major Tiller said that with the other classes, the PEC experience has been that the MTFs begin converting even before the implementation date. The MTFs haven't expressed any difficulty in moving patients off non-formulary medications. Mr. Hutchings said that his organization's perspective is that it takes 120 days to convert and that 90 days is a little tight. Accordingly, he would prefer 120 days in this case, especially because of the high volume.

Mr. Class agreed, noting that it is what the Panel has been saying all along. Communication is dependent on the Associations and their publications, which means that 120 days is a minimum time for implementation. Mr. Hutchings added that his organization's experience is that they reach 60 percent of patients in 90 days with the remaining 40 percent in the last month.

Panel Vote on Implementation Period Recommendation for the LIP-2 Drug Class

Mr. Washington called for the Panel vote on the LIP-2 drug class implementation period recommendation. The BAP vote was :

0 Concur, 9 Non-Concur, 0 Abstentions.

Panel Comment: The Panel officially commented that the implementation period should be a minimum of 120 days.

Review of the 5-Alpha Reductase Inhibitors (5-ARIs) Drug Class

Clinical Effectiveness Review

CPT Napier presented the results of the P&T Committee's review of the 5-Alpha Reductase Inhibitors (5-ARIs) drug class.

[Insert script, pages 9 and 10]

Cost Effectiveness Review

Major Tiller next discussed the cost effectiveness review for the 5-ARI drug class.

[Insert script, page 11, paragraphs 1 and 2]

P&T Committee Action and Recommendations

Major Tiller then informed the Panel of the P&T Committee's recommendations in this drug class.

[Insert script, page 11, paragraphs 3,4 and 5 and page 12, paragraphs 1 and 2].

P&T Committee Physician Perspective

CPT Napier provided the BAP with a physician's perspective on the P&T Committee recommendations. He said the discussion was similar to that for the LIP-2 class in that MHS has had years of successful use of Finasteride for treating BPH symptoms and reducing the risk of surgery. Along with the data that showed that Avodart and Finasteride were very similar in terms of their outcomes, the Committee was comfortable with the PEC's conclusions and there wasn't a lot of discussion about the recommendations.

Panel Questions

Ms. Buchta asked what period of time was covered by the cost effectiveness study of Finasteride for averting surgery. Major Tiller answered that the cost effectiveness analysis was based on clinical trial data that was available for both agents and four years of data were available. Proscar had one study that went four years and they used the data from that trial. Avodart had two years of RCP trial followed by two years observational. The cost effectiveness analysis was based on the two years of data. Differences between the two were incorporated into the model.

Panel Discussion of P&T Committee 5-Alpha Reductase Inhibitor (5-ARI) Recommendations

The Chairman read the Uniform Formulary recommendations for the 5-ARI drug class:

"In view of the conclusion from the relative clinical effectiveness and relative cost effectiveness determinations of the 5-ARIs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that finasteride (Proscar, generics) be maintained as formulary on the UF and that dutasteride (Avodart) be classified as non-formulary."

The Panel had no further discussion of the formulary recommendations in this drug class.

Panel Vote on 5-Alphareductase Inhibitor Drug Class Formulary Recommendations

The Beneficiary Advisory Panel vote on the recommendations in this drug class was:

8 Concur; 1 Non-Concur; 0 Abstain.

Mr. Class commented that his vote to non-concur was based on the fact that there are only two drugs in this class. He believes that it would be prudent to have a choice between them.

CPT Napier replied that Avodart would be available for the non-formulary co-pay through the retail network as well as at MTFs with a medical necessity justification.

Mr. Hutchings commented that his organization has encountered a similar situation in another drug class (alpha blockers) and that patients had successfully qualified for the non-formulary agent.

Panel Discussion of 5-Alphareductase Inhibitor Drug Class Implementation Period

Mr. Washington read the P&T Committee's implementation recommendation for this drug class:

"The P&T Committee recommended an effective date of the first Wednesday following a 90-day implementation period. The implementation period will begin immediately following approval by the Director, TMA."

There was no discussion of the recommendation.

Panel Vote on 5-Alphareductase Inhibitor Drug Class Implementation Period Recommendations

The Beneficiary Advisory Panel vote on the implementation period recommendations was:

4 Concur; 5 Non-Concur; 0 Abstain.

The Panel again commented that a 120-day period is the minimum necessary for the Associations to provide adequate communication to beneficiaries.

Major Tiller noted that the Committee takes into account the usage growth rate when making its implementation period recommendations. He pointed out that since generics are available for Proscar, there is no longer marketing support for it. However, with Avodart, the opposite is true. This means that a longer implementation period will result in the non-formulary drug having more users by the end date. The Committee hopes to avoid having more patients on the drug unnecessarily.

Discussion of Implementation Period Alternatives

Mr. Hutchings asked if there is a way to start the new co-pay arrangement before the end of the implementation period. For example, could the new $22 co-pay for Avodart be implemented immediately to avert starting new patients on it? He used Ambien-CR as an example of the difficulties of having new patients start up during the implementation period and then have to switch to another agent in a short period of time. He would prefer to put new starts on the third tier right away and switch other patients after the implementation date. MAJ Watson replied that there is nothing in the regulation that would allow MHS to apply a $22 co-pay to anything that is not non-formulary. Mr. Hutchings asked if there is anything in the regulations that would prohibit doing what he suggests. The General Counsel, Mr. Burleson, agreed with MAJ Watson that the regulation as written defines when certain things occur. However, he agreed to look into the matter. He said the Program Office might even want to consider changing the regulation.

Dr. Lenow asked about the formulary status of new releases. Mr. Burleson replied that under the regulation, new issuances have formulary status until there is action by the P&T Committee to move it to non-formulary.

Mr. Hutchings said that he would like to see the rule be that 15 or 30 days after signature, all new starts would be third tier. That would use the implementation time period to notify folks that are already on the drug. Mr. Burleson noted that the effect would be a two-step implementation period.

Mr. Class said he would like to have more discussion of this idea from a beneficiary standpoint. It seems to him that beneficiaries will be hit with the $22 co-pay even quicker and will not know anything about it until they show up at the pharmacy and there will be even less time to communicate changes to people. Mr. Hutchings said that most people, including him, don't find out what their co-pay will be until they go to the pharmacy. Mr. Class said that may be true but it isn't right.

Ms. Fryar commented that in a standard plan, you notify people who are on the drug, not people who aren't on the drug. Mr. Class asked whether any notification is made to physicians or those who are writing the medications. He said it sounds like the whole country doesn't know about the changes until they go to the pharmacy and get hit with a higher co-pay, and he doesn't accept that on behalf of beneficiaries. Mr. Hutchings said that is the case.

Review of the Proton Pump Inhibitors (PPI) Drug Class

Clinical Effectiveness Review

CPT Napier next briefed the Beneficiary Advisory Panel on the P&T Committee's review of the Proton Pump Inhibitors (PPI) drug class.

[Insert script, pages 13-15]

Cost Effectiveness Review

Major Tiller next discussed the cost effectiveness review for the PPI drug class.

[Insert script, page 16, paragraphs 1 and 2]

P&T Committee Action and Recommendations

Major Tiller detailed the P&T Committee's recommendations in this drug class.

[Insert script, page 16, paragraphs 3 and 4 and pages 17 and 18].

P&T Committee Physician Perspective

Presenting the DoD P&T Committee's perspective on the UF recommendation for the Proton Pump Inhibitor class, CPT Napier noted that the P&T Committee is made up of physicians and pharmacists who are treating patients every day. They are also in leadership positions where they represent larger groups of physicians and pharmacists who are treating beneficiaries on a daily basis. They are familiar with the evidence. All agree that the agents in this class are highly interchangeable. There are no are very few reasons why one should be preferred over another. They are also charged with managing the outpatient benefit and with looking at the hundreds of thousands of prescriptions that are dispensed monthly in this class and the hundreds of millions of dollars that are spent annually on this drug class alone. The Committee expressed overwhelming support for and agreement with the changes proposed in this class, as reflected in the vote.

Panel Questions

Referring to the schematic representation of the prior authorization (PA) process found on page 7 of the handout, Dr. Schlaifer asked about the automated prior authorization process for patients who have a history of non-formulary PPI use in the last 180 days. Specifically, she asked whether the notation "Prescription covered patient pays co-pay" means "non-formulary co-pay." The answer provided was that it does mean non-formulary co-pay. Dr. Schlaifer asked for a further explanation of what this process adds. Major Tiller explained that a patient who had a prescription for any proton pump inhibitor within a 180-day period would see no difference in getting a prescription refilled unless the prescription is for a non-formulary agent. In that case, the co-pay will increase from $9.00 to $22.00.

Dr. Schlaifer asked whether the same process would apply to a new start. Major Tiller answered that a new start (a patient who has not had a proton pump inhibitor prescription during the 180-day look back period) would be required to have a trial of either omeprazole or esomeprazole before they can get access to the other drugs. It is standard practice to require that patients meet certain criteria before they can have access to a non-formulary drug at the formulary cost share.

Ms. LeGette commented on the 180 day period in the prior authorization. She noted that anyone taking a PPI right now is "grandfathered" in terms of continuing to receive their medication. She agreed they will not be "grandfathered" in terms of their co-pay once the implementation period is in effect, but said that the co-pay is a secondary part of the prior authorization process.

Dr. Schlaifer said she understands that from a clinical and cost effectiveness standpoint this is an easy decision, but asked how much time the Committee spent discussing the implementation issue. CPT Napier answered that most of the discussion took place around the prior authorization process. There were also some comments on the history of the drug class and the changes that have been made, particularly the large numbers of switchovers that have taken place at the MTFs.

Ms. Buchta, noted that Aciphex used to be on the formulary and now won't be and that a patient on Aciphex will still have to pay a higher co-pay even though they don't have to go through a prior authorization. She asked whether the cost evaluation conducted considered the option of keeping Aciphex on the formulary so that patients wouldn't have to incur a higher co-pay and, without divulging specific price data, what was the magnitude of the cost differential of taking Aciphex off the formulary. She noted that the recommendation amounts to a reduction in cost to the system for the inconvenience of the patient. Major Tiller replied that the cost model includes direct medical costs incurred by the MHS, including the drug acquisition costs, the number of beneficiaries who are likely to be required to switch from a non-formulary to a formulary agent, additional physician visits and increased work at the pharmacy. But the analysis does not consider patient convenience as a direct medical cost.

In response to a question from Mr. Hutchings, Major Tiller said that the ability to migrate patients from non-formulary agents to formulary agents varies by point of service. The MTFs are the "champions" of what has been accomplished with the UF so far. They can always be counted on to deliver a very aggressive migration off non-formulary agents. In contrast, the other points of service deliver only 20-30 percent of market share. Mr. Hutchings said being blind to the pricing and the cost advantage is a really difficult thing for him. He noted, for example, that one of his organization's plans has a Nexium utilization of less than one percent. They have fought hard for five years to keep people from being on Nexium. Another plan has over 75 percent utilization of third tier agents. If they lose all the discount pricing and can't migrate patients, costs are going to triple in this drug class. He acknowledged that there has been pretty good migration so far, but wants to be sure that the program isn't adopting a perfect scenario only to find out later that it winds up increasing costs substantially. His quick tally indicates that 65 percent of patients in this class will be on drugs being moved to the third tier. Major Tiller indicated that the upper and lower boundaries of the migration had been taken into account in the analysis and said PEC feels pretty confident that they will do quite well.

Mr. Partridge asked how many of the PPI drugs were on the formulary before the review. Major Tiller replied that the only PPI that was non-formulary before was esomeprazole (Nexium), which is now one of only two agents that will remain on the UF. The previous non-formulary designation resulted from the P&T Committee action in February 2005. At that time, the Committee was very conservative in its recommendations in the absence of clear direction about how aggressively the UF was to be managed.

Mr. Partridge asked for an estimate of how much of the savings would result from simply reducing the number of agents on the formulary from its previous total to only two. Major Tiller

said that since the statin drug class decision in August, the PPI class, which is huge, is the system's most expensive class. Its $475 million in expenditures last year equates to approximately seven to eight percent of total MHS expenditures. He believes that the changes will be able to reduce that sum by over $100 million.

Ms. Fryar, noting the large number of beneficiaries to be affected by the changes, asked how the changes will be communicated with them, especially with Prilosec being put on the formulary. Major Watson replied that communications will vary by point of service. The program will be trying a new approach for the Sedative Hypnotics (SED-1) changes approved at the last meeting that might also be used for the Proton Pump Inhibitors. If the prescription come through TMOP, the provider will be faxed back a form that contains a prescription blank with the qualifying prescription indicated. The form will also include the criteria needed to meet the prior authorization requirements. If the provider doesn't want to switch and there is some qualifying reason why the patient can't be on the preferred agents, the prescription can be faxed back to TMOP with the criteria noted. In the Retail Pharmacy, there will also be messaging back to the pharmacy. The messaging will say something like, "Patient must try (name of qualifying agents)." It will also include a phone number that the pharmacist can give the patient for the provider to call if the qualifying agents are not appropriate for the patient. Based on experience, the program thinks the pharmacist will act on behalf of the patient right at the counter and contact the provider to try to make the switch. That is a routine pharmacy practice that is not new to the retail pharmacy industry. MAJ Watson repeated that the program does not have the funds to notify patients by letter, so they have tried to place the communication along the pathway of getting the prescription filled so the patient won't be delayed unduly in getting their medication.

Mr. Class asked what the authority is for prior authorizations. Without citing specific chapter and verse, MAJ Watson said that, in general, the regulation directs MHS to promote the use of generic medications and provides the authority to implement prior authorization. MAJ Watson said he would provide the Panel with a more precise answer.

Mr. Class noted that the recommendation here includes a mix of actions — moving agents to non-formulary combined with a prior authorization process. A lot of different things are going on at the same time. Looking at things from the patients' perspective, Mr. Class said he would like to know what criteria are used to determine when and how the various approaches are used and if there is a flow chart for the decision process. Major Tiller said there is no flow chart for the prior authorization decision process. There are many criteria. The extent to which there is a high degree of therapeutic interchangeability among the agents in the class is one of the main things the P&T Committee considers. Another consideration is the degree of market competitiveness. The Committee also considers whether requiring a PA will benefit the migration to formulary agents. Where it takes a longer time to know whether the drug is going to work, as with the 5-ARIs, prior authorizations are not appropriate

Mr. Class explained that the Panel is being asked to concur in recommendations about a process without knowing what goes into the process. And it changes from one class to another. Major Tiller asked if it would help to have the presentation provide more information on why prior authorizations are recommended in the section on justification for the non-formulary recommendations. Mr. Class said that it all comes down to some kind of a process that the P&T Committee uses; all he is asking for is an explanation of that process. Major Tiller replied that the decision of whether or not to require a prior authorization is made on a case-by-case basis.

Ms. Buchta followed up by asking how much of the projected savings would be achieved if the recommendation was for removal of agents from the formulary alone, i.e., without the prior authorization requirement. If the effect of the prior authorization requirement on savings is negligible, the question becomes why the patient has to go through the hassle of the PA process. Major Tiller said he doesn't have exact figures to provide.

Dr. Schlaifer said she assumes that just moving the agents to the third tier would result in a significant saving and asked if this was the case. Major Tiller said the Committee weighed the costs and benefits associated with each decision and ultimately decided that the recommended course of action — both non-formulary and PA — would be the best one. Dr. Schlaifer asked if one of the options looked at was going to non-formulary without the PA and Major Tiller replied that it was, along with a number of other options.

Mr. Class said again that he would like to know what criteria are applied to the decision when agents are looked at on a case-by-case basis. Major Tiller said the question would be taken under consideration.

Ms. Fryar expressed concern about putting Nexium back on the formulary. She said it is likely to be confusing to beneficiaries, especially those using TMOP or the retail network. Mr. Class added he has been asked several times about Nexium going generic. Ms. Fryar said her concern is with the message that is being sent to beneficiaries: first it was taken off and now we're switching it back. That's why it is so important to have an adequate communication plan; to explain why the drug is changing tiers.

CPT Napier said the change won't completely occur in the dark for beneficiaries. Physicians will have to write a new script. If asked, they should be able to explain why they are switching patients from one agent to another. Most are also aware of formulary management. There are a lot of good reasons for making the change.

Mr. Class said he thinks MTF formulary management is a lot different. The computer can tell the provider exactly what is and is not on the formulary. He doesn't know that same thing occurs is private practice. CPT Napier said any provider can get information about the DoD formulary. Mr. Class asked if every physician that writes a script for DoD checks the formulary first. CPT Napier said that network physicians have connections with the pharmacy. Mr. Class said one quarter of the beneficiaries use TRICARE standard, not network providers, and this is where the issue is. There is no communication out to the 25 percent of TRICARE patients who do not use network providers. CPT Napier said his experience has been that non-MTF physicians are much more accessible by pharmacists. It can be really hard for a pharmacist to get in touch with an MTF physician. Dr. Lenow said he gets calls every day from the pharmacy at Jefferson with feedback about coverage and co-pay. He said residents are told to ask patients about drug coverage. There is also electronic support; Epocrates has formulary information. So sensitivities to these kinds of issues are growing. The Accreditation Council for Graduate Medical Education (ACGME), which accredits residencies, promulgated new efficiency standards in 1999 that require hospitals to show that residents have been trained and have become proficient in these kinds of issues — practice management and system based issues. So it's starting to infiltrate the way we learn and train.

Mr. Hutchings said he is in favor of the PA in this class from a beneficiary standpoint. This will oblige physicians who do not know what is on the formulary to go to $3.00 co-pay Nexium rather than use a non-formulary drug at a higher co-pay from now until eternity.

Mr. Class reiterated that he is looking at things from the standpoint of the patient presenting a prescription at the pharmacy. He is hearing that there is a lot of common practice out there. However, as was said earlier, patient inconvenience or time is not taken into account in the numbers. But there is a cost associated with that. Unless the pharmacist actually informs the patient of the lower co-pay alternatives and offers to call the physician to see if it is okay to switch, the patient is inconvenienced. He acknowledged that sometimes things like that are in the new contract and problems go away. But not under the current structure.

Ms. Legette asked if Major Tiller had an estimate of the number of new users coming onto PPI by point of service. He replied that they do have an estimate and will provide it to the Panel.

Ms. Legette asked if the Committee considered OTC Prilosec as part of the demonstration project. A lot of commercial clients are using it. MAJ Watson said it wasn't considered by the Committee but it will be an option once the process is completed. People who will be affected by the $22 co-pay will also be eligible for the Prilosec OTC demonstration program. That will be an option for them. It's available right now through mail. By implementation time, it will probably also be available through retail.

Ms. Legette asked, in reference to the mandatory generic program, if the option was considered to drive toward generic omeprazole before Nexium secondarily and then to non-formulary products. To date, the messages to beneficiaries have been pushing generics. Major Tiller said that the scenario outlined by Ms. LeGette was considered and evaluated. Although more dollars were projected to be saved under such a scenario, the Committee felt that it would affect too many beneficiaries.

Mr. Hutchings asked if Major Tillers answer meant that it would be more cost effective to switch patients to generic omeprazole rather than Nexium. Major Tiller replied that it would. There has been a very significant reduction in the price of generic omeprazole. Mr. Hutchings asked what will be the most cost effective agent. Major Tiller answered that the PEC doesn't know. Two or three years from now, it looks like omeprazole will be the most cost effective agent if there is increased competition in the generic market.

Ms. LeGette commented that, since this is a Beneficiary Advisory Panel, and it has reviewed quite a few drug classes, she would find it helpful to have a one page listing of what is on the formulary. The situation is becoming more confusing now, with branded drugs in the first tier and generics in the third tier. Beneficiaries need information about what's what and what costs what. A one-page summary highlighting the therapeutic classes would be very useful. It could just be put on the web; it wouldn't have to be printed. Providers could get it there, too. Major Watson agreed to consider the suggestion.

Mr. Hutchings asked if we know how long the contract will be. His concern is that the action will create a huge utilization of Nexium and if the contract is only good for a year and then the price goes up eight-fold, that will be a problem. In this class, we have gone through four major interchanges in six years. He wants to make sure that we aren't creating a problem. Major Tiller answered that PPIs are a very significant drug class accounting for a large percentage of MHS

expenditures. He said it will be actively managed until it is a generic-dominated class. He said he would not get hopes up for not making more changes. The Committee will monitor the class and make recommendations for additional action when appropriate. Regarding the contract, MHS does blanket purchase agreements with 120-day termination clauses.

Mr. Hutchings also commented that we are going to try to incentivize patients to use Nexium, it will be impossible to do that until the co-pay drops to $3.00. Because this class has been flipped on its head, the system will already be losing a significant amount of money by the implementation date. The cost saving occurs with the signing of the BPA a month from now whereas implementation won't occur for another two months afterwards. It is a Catch-22 situation. He again asked if there was a way to drop the co-pay of Nexium early to promote the use of it over Aciphex and get the benefits earlier. Major Tiller asked Mr. Hutchings to call the PEC about the conversion plan after the meeting. However, he said that nothing could be done about the co-pay at this time.

Mr. Partridge commented that the most cost effective scenario would be to restrict the formulary to two drugs. But there were also savings if the formulary were restricted to four drugs. He asked what the difference would be between two and four drugs. Major Tiller answered that he is unable to provide that level of cost information to the Advisory Panel. The Panel can request it, however, and the request would be taken under consideration. In response to a follow up question, Major Tiller answered that the difference was "significant," not only in terms of cost but also in terms of the number of beneficiaries affected.

Dr. Schlaifer asked if it would be possible to do a spilt implementation with part of the action (the lower co-pay) taking effect in 90 days and the rest in 120 days. MAJ Watson answered that right now that is not possible. But the program has agreed to look into what might be done under the regulation.

Panel Discussion of P&T Committee Proton Pump Inhibitor (PPI) Formulary Recommendations

Mr. Washington read the P&T Committee's formulary recommendation for the PPI drug class:

"In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the PPIs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that: 1) omeprazole (Prilosec, generics) and esomeprazole (Nexium) be maintained as formulary on the UF with a prior authorization requiring a trial of either agent for new patients; 2) that rabeprazole (Aciphex), lansoprazole (Prevacid), pantoprazole (Protonix), and omeprazole/sodium bicarbonate (Zegerid) be classified as non-formulary with a PA requiring a trial of either omeprazole (Prilosec, generics) or esomeprazole (Nexium) for new patients; and 3) that the normal brand formulary cost-share of $9.00 for esomeprazole (Nexium) be lowered to the generic formulary cost-share of $3.00.

The authority for the last recommendation is codified in 32 CFR 199.21(j)(3), which states that 'when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the Pharmacy and Therapeutics Committee may also designate the drug be cost-shared at the generic rate.' Lowering the cost-share for brand name esomeprazole

(Nexium) will provide a greater incentive for beneficiaries to use esomeprazole rather than the less cost effective branded products — rabeprazole (Aciphex), lansoprazole (Prevacid), pantoprazole (Protonix), or omeprazole/sodium bicarbonate (Zegerid) — in the purchased care arena.

PPIs — PA Criteria

The P&T Committee agreed that the following PA criteria should apply to PPIs other than) omeprazole (Prilosec, generics) and esomeprazole (Nexium). Coverage would be approved if a patient met any of the following criteria:

1) Automated PA criteria:

   a) The patient has received a prescription for any PPI agent at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2) PA criteria if automated criteria are not met:

   a) The patient has tried omeprazole (Prilosec, generics) or esomeprazole (Nexium) and had an inadequate response or was unable to tolerate treatment due to adverse effects.

   b) Treatment with omeprazole (Prilosec, generics) or esomeprazole (Nexium) is contraindicated.

The P&T Committee noted that in order for a patient to receive a non-formulary PPI agent at the formulary cost-share, both the PA and MN criteria must be met. If the PA criteria are met without an approved MN determination, the patient cost-share will be at the non-formulary level. In other words, patients obtaining an approved PA for rabeprazole (Aciphex),), lansoprazole (Prevacid), pantoprazole (Protonix), or omeprazole/sodium bicarbonate (Zegerid) would NOT automatically receive it at the formulary cost-share."

There was no further Panel discussion of the formulary and PA recommendations.

Panel Vote on Proton Pump Inhibitor (PPI) Drug Class Formulary Recommendations

The vote on the P&T Committee recommendations was:

5 Concur; 4 Non-concur; 0 Abstentions.

No comments were appended.

Panel Discussion of P&T Committee Proton Pump Inhibitor (PPI) Implementation Recommendations

The Chair read the Committee's implementation recommendations:

"The P&T Committee recommended an effective date of the first Wednesday following a 90-day implementation period. The P&T Committee believed the considerable cost avoidance associated with this recommendation warranted a more aggressive implementation period. Furthermore, the P&T Committee was anxious to extend the $3.00 cost-share for esomeprazole (Nexium) to beneficiaries as soon as possible. The implementation period will begin immediately following approval by the Director, TMA."

Ms. LeGette said her organization will implement whatever is decided upon, but believes that 90-days is a bit too aggressive. She said over one-third of the beneficiaries are affected. In the next class (ARBs) reservations were expressed about the difficulties of handling a 120-day implementation period.

Mr. Washington read into the record a portion of a letter he received from the U.S. Family Health Plan regarding the 90-day implementation:

"We are concerned about the 90-day implementation period recommended by the P&T Committee. We understand the need to take advantage of cost savings as soon as possible, but there is a right way and wrong way to roll these initiatives out. There will be many beneficiaries and providers who need to be contacted with detailed information. There needs to be a commitment from the PEC that PA and medical necessity criteria will be available immediately upon approval to allow for enough time to implement."

He said he agrees with this comment. Previously, a brand product was put on the formulary and now we are switching back in only 90 days. He agrees with other Panel members that 90 days is not long enough. People are being forced to switch in just a very short period of time.

Ms. Fryar said that a lot of the concern centers around the issue of communication, and the need for a communication plan, which the Panel has frequently addressed.

Mr. Hutchings said that, as with the earlier classes, a minimum of 120 days is what his organization needs to get all of the scripts switched.

Mr. Partridge said his previous views about the inadequacy of the 90 days apply here as well.

Panel Vote on Proton Pump Inhibitor (PPI) Drug Class Implementation Recommendations

The Panel vote of the PPI implementation recommendations was:

0 Concur; 9 Non-Concur; 0 Abstentions.

The Beneficiary Advisory Panel comments on this class are that a period of 120 days should be allowed for implementation.

In addition, the Panel requests additional information about the decision process used for recommending third tier and PA determinations.

Review of the Angiotensin II Receptor Blocker (ARB) Drug Class

Clinical Effectiveness Review

CPT Napier presented the P&T Committee's review of the Angiotensin II Receptor Blocker (ARB) drug class.

[Insert script, pages 19-21]

Cost Effectiveness Review

Major Tiller then discussed the cost effectiveness review for this drug class.

[Insert script, page 22, paragraphs 1 and 2]

P&T Committee Action and Recommendations

Major Tiller next briefed the Panel on the P&T Committee's recommendations in this drug class.

[Insert script, page 22, paragraphs 3 and 4 and page 23 through first two full paragraphs].

P&T Committee Physician Perspective

CPT Napier provided the Panel with the physician's perspective on the P&T Committee's evaluation. He said there was a lot of feeling among the members of the P&T Committee that ARBs are relatively interchangeable in a lot of their uses. But there are data and specific indications among the members of the class. That was what compelled the Committee to decide to retain certain agents on formulary. Additionally, there are other agents, particularly ACEs, that will treat certain conditions.

Panel Questions

Dr. Lenow observed that the assertion that "an ARB is an ARB is an ARB" is probably true. It would be hard for him to argue that one is superior to another. Even so, part of the review is an evidence based analysis. For the most part the reviews have been right on point and have dealt with the issues fairly and objectively using the best available literature. There isn't always a lot of best evidence so you have to go with what you've got. Several sessions ago, he recused himself with the issue of ACEs, ramapril in particular (which did not survive even though evidence-based trials would indicate it deserved to stay on formulary). He believes there is a similar situation with the ARBs. He respects the companies who spent the time, money and effort to do evidence-based trials. However, it seems to him that one agent in this class has survived the formulary cut that hasn't done its fair share. He is surprised that Micardis is still listed when Avapro and Diovan will be non-formulary. Unless there is a really huge cost advantage, it seems to him as though the ARBs that are knee-deep in evidence-based trials

deserve to remain. It appears to be an arbitrary choice unless the financial benefit is that much greater.

Major Tiller observed that Micardis was on the UF from the February 2005 decision. Moreover, it was DoD's basic core formulary drug, which has special status in the Military Treatment Facilities. The thought process of the DoD P&T Committee was that they recognized that the other drugs had indications that Micardis did not have. But a retrospective analysis of current beneficiaries who are using drugs in this therapeutic class showed that most of them are using the drug for hypertension and not for diabetic kidney disease or chronic heart failure. The Committee's view was that if there is an ARB agent that is more cost effective for hypertension, it should be made available. Micardis clearly fits that criterion.

Mr. Hutchings said his organization is concerned that one of the drugs being moved to third tier is one of its workhorse drugs. Patients using this drug would only bring their hypertension under control if prescribed a higher dosage and a longer half-life drug. He asked if the cost analysis was based on dosing all of the medications once a day. Major Tiller said the calculation takes into account daily consumption.

Ms. Buchta asked for clarification regarding whether all of the agents in this class were formulary to begin with. Major Tiller said that eprosartan was the only agent that was non-formulary prior to this.

Panel Discussion of P&T Committee Angiotensin II Receptor Blocker (ARB) Formulary Recommendations

Mr. Washington read the P&T Committee's formulary recommendations for this drug class:

"In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the ARBs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that candesartan (Atacand), candesartan/HCTZ (Atacand HCT) losartan (Cozaar), losartan/HCTZ (Hyzaar), telmisartan (Micardis), and telmisartan/HCTZ (Micardis HCT) be maintained as formulary on the UF and that eprosartan (Teveten), eprosartan/HCTZ (Teveten HCT), irbesartan (Avapro), irbesartan/HCTZ (Avalide), olmesartan (Benicar), olmesartan/HCTZ (Benicar HCT), valsaratn (Diovan) and valsartan/HCTZ (Diovan HCT) be classified as non-formulary."

Mr. Hutchings said he is concerned that 60 percent of the patients on his plan, and 85 percent of others, will be on agents that are non-formulary. The class has blood pressure medications that, unlike the PPIs, will require a physician visit, and probably multiple physician visits to give the new drugs time to titrate.

Dr. Lenow asked if equivalencies have been looked at, i.e., what is the Diovan to Cozaar equivalency? He doesn't know of any studies that exist, and thinks it is really titration based on patient response. CPT Lanier agreed that physicians select an agent and look at what it does. This means extra doctor visits will be required to make a change. Major Tiller said that one doctor visit is included in the cost factor.

Panel Vote on ARB Drug Class Formulary Recommendations

The Beneficiary Advisory Panel vote on the Committee recommendations in this drug class was:

2 Concur; 7 Non-Concur; 0 Abstentions.

The Panel's comment was that the significance of the proposed cost saving has not been articulated well enough for the Panel to understand why the most commonly used agent is being taken off formulary. Additionally, this recommendation will result is a huge burden to switch patients over and titrate them. Additionally, there are concerns about quality and the appropriateness of indications.

Panel Discussion of P&T Committee Angiotensin Receptor Blocker (ARB) Implementation Recommendations

Mr. Washington read the P&T Committee's implementation recommendations:

"The P&T Committee recommended an effective date of the first Wednesday following a 120-day implementation period. The implementation period will begin immediately following approval by the Director, TMA."

Mr. Hutchings asked what period of time physicians would be comfortable with for making a switch in medications in this class. Dr. Lenow answered that it takes three to four weeks to tell if a change is effective or not.

Panel Vote on Angiotensin Receptor Blocker (ARB) Drug Class Implementation Recommendations

The Panel vote on the implementation recommendations was:

8 Concur; 1 Non-Concur; 0 Abstentions.

Mr. Partridge commented that he hoped the money saved would be used to improve the notification process, noting that the Panel is clearly not comfortable with the formulary recommendations. A lot of patients who are doing fine now are being moved to a different medication just based on cost.

In answer to an earlier Panel question, MAJ Watson said that the authority for prior authorizations is found in 32 CFR 199, 21(k).

Additional Information and Discussion

Major Tiller provided the Panel with additional information on the re-evaluation of non-formulary agents.

[Insert script , page 23, third paragraph ("Amlodipine (Norvasc) was designated non-formulary...") through page 24]

Mr. Class said that he is getting a lot of calls about Norvasc. Patients know that it has been generic, but when they get to the pharmacy they are being told they have to pay the $22.00 co-pay. He asked if there is the potential here for $9.00 drugs to go generic without a reduction in co-pay. If so, he will get the same questions from his membership. The answer provided was that only the co-pay would change. Mr. Class observed that is a big assumption. Mr. Hutchings noted that once a drug goes generic, the branded version is no longer covered and the generic version is provided automatically.

Ms. Buchta asked to have information included in the discussion of the drug class when the P&T Committee knows that a drug will be going generic in the next year. It would be a valuable piece of information. Mr. Class agreed, noting that he would like to avoid situations where drugs that are on the formulary get "flipped" in a short period of time. He understands the cost considerations but also wants to avoid confusion among patients. Ms. Fryar noted that there have been cases when a drug was going generic and said that the information was provided in the briefings. Major Tiller said the PEC tries to include that information where there is a sufficient amount of certainty. Generally, it is an unpredictable event.

Ms. Fryar asked about the use of the term "Prior Authorization" in relation to the process shown on the diagram in the handout. She would like to see it flagged as "step therapy." Mr. Hutchings agreed and asked if it could be labeled "step therapy" because that it what it is, and not really "prior authorization." MAJ Watson agreed. He said they had struggled in the past with terminology, such as "tier one, tier two and tier three" and "preferred and non-preferred." He said the program's marketing communications try to use what people will understand. But officially in the minutes and referencing back to the CFR, they try to stick to the terms that are in the regulations.

Mr. Class provided views and comments on a number of different subjects. The first subject is communications, which is an issue that the Panel has been pushing all along. Communicating program changes to beneficiaries — giving people a chance to react before the change goes into place, reaching out to physicians (through medical society training programs, for example) to let them know where they can find the TRICARE formulary. Even better would be letters to non-network physicians who have submitted network claims.

He also noted that a new set of contracts are coming in. He understands that they can't be discussed yet, but customer service is a big concern. There may be common practices, such as pharmacists calling physicians, and he believes it is important that the new contracts have more requirements for pharmacist interaction with patients and discussion of cheaper alternatives. What is happening now is that patients are being charged $22 without being told that cheaper alternatives, such as generics, are available. Mr. Hutchings said there is no way the pharmacist can give the patient that information, because they don't know that. Mr. Class said they should. It isn't only the cost to the beneficiary that's at stake, it's also cost to the plan. The system should be committed to reducing both beneficiary costs and program costs. The pharmacy point of service is most important. If the pharmacist just charges $22 and doesn't provide any other information, then everything the Panel is doing is worthless. The stats show that third tier usage is going up in retail and TMOP.

Mr. Class also said he would like to have the reasons for dissenting votes on the P&T Committee included in the read ahead materials. It is important to have that information ahead of time as it isn't practical to absorb it at the meeting.

He repeated that he would like to see some sort of flow chart or criteria for the decision process used to determine when to require a prior authorization (or step therapy).

As a non-clinician, he doesn't necessarily know, when a drug class is being discussed, what other classes of drugs may be used to treat whatever the class is used for. With ARBs, for example, he has the impression that there may be two other classes of drugs that are the first and second line for treatment of that disease. It would be very helpful to know that information when considering the recommendations. Dr. Lenow asked why this information was important. Mr. Class responded that, for him, it would lessen the impact of sometimes putting so many drugs in the non-formulary category in a given drug class by letting him know that there are other drugs available to deal with the disease. Dr. Lenow said that the Committee report did address the issue, as with the use of ARBs for heart failure and the availability of other drugs. Ms. Buchta suggested that simply adding a sentence to the presentation noting what other drugs are available for treatment might be sufficient.

Mr. Class said there is still a need to deal with the lack of cost information. He would like to have a legal opinion in writing stating why the Panel can't be provided with the data in any form. He would like to see what is the basis for that decision. Mr. Burleson, the General Counsel, said the answer is straightforward. The manufacturers have said that the information is proprietary and not for public distribution in a public forum. Mr. Class asked if there is anything in FACA that would allow the Panel as "special government employees" to be provided with information. Mr. Burleson said he would go back to the Office of the General Counsel and try to get approval to issue a written legal opinion on this subject and give it to the Designated Federal Officer. But he said if that happens he can guarantee that it will say the same thing. He said he has looked at the FACA statute and what is available for public distribution. FACA is very clear. This committee has to operate in the public domain. That being the case, the government cannot disclose in a public forum information that the manufacturers specifically label as "proprietary." Mr. Class said he sees a lot of committees that operate under FACA hold closed door meetings. He asked if the BAP could possibly do that. Mr. Burleson said he has also investigated that to see if there was a way the Panel could get information through side-bar conversations. It simply is not allowed under the regulation. Whether or not other committees do it.

Ms. Buchta asked if there might not be an answer in between no information and detailed information. She said "millions of dollars" to her means a "significant" cost saving. Perhaps there is a way to use terms like "significant" or "moderate" to designate rough approximations of the amount of dollars being discussed. Some rough order of magnitude of cost savings would be helpful.

Mr. Class said he also found it very troubling to hear that beneficiary and patient inconvenience is not something that is taken into account in the deliberations. Major Tiller replied that the number of beneficiaries affected is considered. But a dollar cost is not assigned to that.

Mr. Washington asked if, under its charter, the BAP can hold closed meetings. MAJ Watson said he would confer with Mr. Burleson to see whether and under what conditions that might occur. Mr. Washington asked, for example, about a conference call after the read ahead

materials are distributed. MAJ Watson said that would have to be publicly available. Mr. Burleson again stated that he has really looked into this, including the possibility of a closed "administrative meeting." He has yet to find any authority for it.

MAJ Watson announced that the next meeting would be September 19, 2007 at the Naval Heritage Center in Washington, D.C.

The meeting was adjourned at 12:00 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.

- ACE inhibitors — Angiotensin-converting Enzyme inhibitors (a drug class)
- 5-ARI — 5-Alpha Reductase Inhibitor (a drug class)
- ARB — Angiotensin Receptor Blocker (a drug class)
- BAK — Benzalkonium chloride (a preservative used in ophthalmic drugs)
- BAP — Uniform Formulary Beneficiary Advisory Panel (the "Panel" referred to above)
- BAS — Bile Acid Sequestratnts
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- BPA — Blanket Purchase Agreement
- CEA — Cost-effectiveness analysis
- C.F.R — Code of Federal Regulations
- CHD — Coronary Heart Disease
- CMA — Cost-Minimization Analysis
- CR — Controlled Release (a drug formulation)
- DEA — U.S. Drug Enforcement Administration
- DFO — Designated Federal Officer
- DOD — Department of Defense
- ECF – Extended Core Formulary
- ER — Extended Release (a drug formulation)
- ESI — Express-Scripts, Inc.
- FACA — Federal Advisory Committee Act
- FDA — U.S. Food and Drug Administration
- GI — Gastrintestinal
- HDL — High Density Lipoprotein
- HMO — Health Maintenance Organization
- IOP — Intraocular pressure
- IR — Immediate Release (a drug formulation)
- LIP-2 — Antilipidemic II (a drug class)
- LDL — Low Density Lipoprotein
- MHS — Military Health System
- MI — Myocardial Infarction
- MN — Medical Necessity
- MTF — Military Treatment Facility
- NNH — Number Needed to Harm
- NNT — Number Needed to Treat

- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DOD Pharmacy and Therapeutics Committee
- PDTS — Pharmacy Data Transaction Service
- PEC — DOD Pharmacoeconomic Center
- POS — Point of Service
- PPI — Proton Pump Inhibitor (a drug class)
- RCTs — Randomized Control Trials
- TG — Triglycerides
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TRRx — TRICARE Retail Pharmacy Program
- UF — DOD Uniform Formulary
- U.S.C. — United States Code
- VA — U.S. Department of Veterans Affairs

21 June 2007 BAP Meeting Script

(Major Tiller) Good Morning,

I'm Major Wade Tiller, Deputy Director of the PEC. Joining me today from the PEC Clinical Operations staff are CPT Josh Napier, who is our army internist physician, and LTC Brett Kelly, the PEC Director. CPT Napier will also give the physician perspective from the P&T Committee meeting, to comment on the recommendations made by the Committee. Also joining us today from TMA are RADM McGinnis, the Director of Pharmaceutical Operations, CAPT Blanche, Director of Pharmacy Programs and CAPT Patricia Buss, Chairman of the DoD P&T Committee.

The DoD Pharmacoeconomic Center (PEC) supports the DoD P&T Committee by conducting the relative (relative meaning in comparison to the other agents defined in the same class) clinical-effectiveness analyses and relative cost-effectiveness analyses of drug classes under review and consideration by the DoD P&T Committee for the Uniform Formulary (UF).

CPT Napier and I are here to present an overview of the analyses presented to the DoD P&T Committee. 32 Code of Federal Regulation (C.F.R.) establishes procedures for inclusion of pharmaceutical agents on the Uniform Formulary based upon both the relative clinical-effectiveness and the relative cost-effectiveness. The goal of this presentation is not to provide you with the same in-depth analyses presented to the DoD P&T Committee but a summary of the processes and analyses presented to the DoD P&T Committee which include:

1) A brief overview of the relative clinical-effectiveness analyses considered by the DoD P&T Committee.
2) A brief general overview of the relative cost-effectiveness analyses. This overview will be general in nature since we are unable to disclose the actual costs used in the economic models. This overview will include the factors used to evaluate the costs of the agents in relation to the safety, effectiveness, and clinical outcomes.
3) The DoD P&T Committee's Uniform Formulary recommendation based upon its collective professional judgment when considering the analyses from both the relative clinical and relative cost-effectiveness evaluations of the Antilipdemic II Agents, the 5-Alpha Reductase Inhibitors, the Proton Pump Inhibitors, or PPIs, and the Angiotensin II Receptor Blockers, or ARBs.
4) The DoD P&T Committee's recommendation as to the effective date of the agents being changed from formulary tier to the non-formulary tier of the Uniform Formulary. Based on 32 C.F.R. 199.21, such change will not be longer than 180 days from the final decision date but may be less.

We've given you a handout which includes the Uniform Formulary recommendations for all the drugs discussed today; this is found in Table 1, on pages two and three. There are tables and utilization figures for all the drug classes. We'll be using trade names as much as possible, so you can refer to your handout throughout the presentation.

CPT Napier will now present the Antilipidemic II Agents, or LIP-2s, relative clinical effectiveness evaluation.

ANTILIPIDEMIC IIs (LIP-2s) CLINICAL EFFECTIVENESS

***(CPT Napier)*: Background and members in the class:** The clinical effectiveness review for the Antilipidemic II (LIP-2) agents was conducted by Lt Col Jim McCrary, an Air Force family medicine physician stationed at the PEC, along with Harsha Mistry, a PEC clinical pharmacist. If you will refer to Table 1 on page 2 of your handout, you will see the three subclasses that the LIP-2 agents were divided into, based on their mechanism of action. These categories are fibric acid derivatives, prescription omega-3 fatty acids, and bile acid sequestrants. The omega-3 fatty acids, or fish oil supplements, are widely available over the counter in grocery stores and pharmacies. There is only one prescription omega-3 fatty acid available, under the trade name Omacor, thus Omacor was the only omega-3 fatty acid reviewed in the class.

The agents in the LIP-2 class have effects such as lowering triglycerides, low-density lipoprotein (or LDL, the "bad cholesterol"), and total cholesterol concentrations. The fibric acid derivatives and prescription omega-3 fatty acid are used clinically to reduce triglyceride concentrations, while the bile acid sequestrants are used clinical to reduce LDL levels. For the purpose of the clinical effectiveness evaluation, drugs within each subclass were compared to each other with regards to efficacy, safety and tolerability, and clinical outcomes.

Relevance to MHS and Utilization: The LIP-2 agents accounted for $63 million in Military Health System (or MHS) expenditures in Fiscal Year 2006, ranking in the top 20 in terms of total expenditures during that time period. Figure 1 on page 4 shows the breakdown in utilization among the LIP-2 drugs. The fibric acid derivative Tricor (or nanocrystallized fenofibrate) has the highest utilization of the class, at about 35,000 prescriptions dispensed monthly in the MHS, followed by Lopid (or gemfibrozil) with about 15,000 prescriptions dispensed monthly. The remaining categories (omega-3 fatty acids and bile acid sequestrants) have less than 10,000 prescriptions dispensed monthly.

Conclusion: I'll first give you some background and then give the relative clinical effectiveness conclusion for each of the three drub subclasses. Let's start with the fibric acid derivatives.

Clinical Effectiveness Conclusion

1) ***Fibric acid derivatives*** –

Background and Class Members - If you'll turn to figure 2 on page 4 of the handout, it shows the utilization of the fibric acid derivatives. There are two fibric acid derivatives, Lopid, or gemfibrozil, which is available generically, and fenofibrate. However, there are several different formulations of fenofibrate marketed. The original fenofibrate product became available in 1998, but was difficult to dissolve in water. Therefore, pharmaceutical companies have come up with new technologies to make the product easier to dissolve (or more soluble) in water. The products all have different brand names, and as a new product becomes available, earlier versions are removed from the market.

The fenofibrate products included in the LIP-2 class are:

- Tricor, which we'll refer to as nanocrystallized fenofibrate;
- Antara, which is micronized fenofibrate. Micronized refers to making the drug molecule size small, which also enhances its solubility;

- Triglide, which is called IDD-P micronized fenofibrate, for "insoluble drug delivery microparticle", which is the company's patented technology for reducing drug molecule size and enhancing solubility;
- And Lofibra, which is available in either a micronized or nonmicronized formulation. Only Lofibra is available in generic formulations.

Fenofibrate formulations - These newer formulations of fenofibrate, regardless of dosage strength or particle size, are bioequivalent to 200 mg of the original fenofibrate formulation marketed back in 1998. By changing the particle size and increasing solubility, three of the products (Antara, Tricor, and Triglide) can be dosed once a day and be taken without regard to meals. The DoD P&T Committee agreed that there was insufficient evidence to conclude that the newer fenofibrate formulations offer improved efficacy, safety, or tolerability compared to each other, or to older formulations.

Fenofibrate Utilization - If you look back at Figure 2 on page 4, Tricor and Lopid have the highest utilization of all the fibric acid derivatives. Antara, Triglide and Lofibra have less than 5,000 prescriptions dispensed monthly in the MHS, and are at the bottom of the Figure.

Efficacy – Next we're going to discuss how the fibric acid derivatives affect cholesterol levels. If we compare Lopid with fenofibrate, regardless of the formulation, both drugs reduce triglycerides by 20-50% and raise high density lipoprotein (HDL, or the "good" cholesterol) by 10-20%. There is insufficient evidence to conclude that Lopid and the fenofibrates differ in their ability to reduce triglyceride concentrations and raise HDL.

Efficacy for outcomes: Both Lopid and fenofibrate have been evaluated in clinical trials to determine whether they have a benefit on not only reducing lipid lab values, but also reducing cardiovascular events, such as death and myocardial infarction, or heart attack. Two placebo-controlled trials with Lopid have shown a benefit in reduction of cardiovascular events in the primary prevention setting (where patients don't have pre-existing heart disease), and in the secondary prevention setting (where patients have pre-existing heart disease, and the goal is to prevent another cardiovascular event). Lopid treatment resulted in a reduction in nonfatal myocardial infarction and death due to coronary heart disease.

In contrast, mixed results were demonstrated with fenofibrate (Tricor) in a large outcomes trial in a setting including both primary and secondary prevention. Treatment with Tricor did not result in a statistically significant benefit in reducing coronary heart disease death or nonfatal myocardial infarction when they were evaluated together as a group, but Tricor was associated with significant reductions when nonfatal myocardial infarction and coronary revascularization (or bypass, angioplasty or cardiac stent surgery) were evaluated alone.

Safety – Minor Adverse Events: In terms of minor adverse effects, gastrointestinal (or GI) adverse effects, including nausea, stomach ache, and diarrhea are the most frequent complaints of the fibric acid derivative. GI complaints occur in fewer than 5% of patients taking either Lopid or fenofibrate. GI complaints appear to occur more frequently in patients taking Lopid than those taking the fenofibrates, based on data from the package

inserts. Lopid must be taken twice daily prior to meals, in contrast to Antara, Triglide and Tricor, which can be taken once daily either with or without food.

Major Adverse Events - In terms of major adverse events, treatment with either the fibric acid derivatives or the statins as monotherapy (used alone by themselves) has been associated with a group of symptoms referred to as myalgia, myositis, and rhabdomyolysis. These symptoms range from muscle aches and pains, to elevated lab values, breakdown of the muscle, kidney failure, and sometimes death.

There is some evidence to suggest that Lopid may have a higher risk of causing muscle adverse events, or myotoxicity, when combined with a statin, compared to fenofibrate, however, the data is based on reports spontaneously submitted to the FDA. There are no head-to-head trials supporting a lower risk of myotoxicity with fenofibrate than with Lopid, either given alone or in combination with a statin. Additionally, professional organizations have not favored Lopid or fenofibrate over the other. The most recent 2003 joint guidelines from the American College of Cardiology, the American Heart Association, and the National Heart Lung and Blood Institute conclude that there is a risk with all the fibric acid derivative/statin combinations, not just Lopid plus statins.

2) ***Omacor*** –

Background and Utilization- Let's move on to the prescription omega-3 fatty acid product, Omacor. In Figure 1 on page 4 you can see the steady rise in Omacor utilization, to about 10,000 prescriptions dispensed monthly in the MHS. As we mentioned earlier, Omacor is the only prescription omega-3 fatty acid product approved by the FDA. FDA oversight of the manufacturing process for Omacor offers increased assurance of its omega-3 fatty acid content and purity. In contrast, some fish oil supplements available over the counter have shown variation in their content and purity.

Efficacy - In terms of efficacy, overall, Omacor decreases triglycerides by 20-45%. However, Omacor has also been associated with increases in LDL, which may offset the beneficial reductions seen in triglycerides.

Efficacy of Omacor compared to other lipid drugs- If you take a look at Table 2 on page 5, this shows how several antilipidemic drugs compare in their ability to reduce triglycerides, raise HDL, and affect LDL levels. Omacor reduces triglycerides to about the same extent as that seen with Lopid, fenofibrate, and Niaspan. Niaspan is a lipid lowering drug that was reviewed with the statins back in August 2006. Niaspan and Lopid both have clinical trial evidence supporting long-term benefits on cardiovascular outcomes. In contrast, the omega-3 fatty acid formulation found in Omacor does not have outcomes studies that demonstrate beneficial cardiovascular effects, such as reductions in cardiovascular death, myocardial infarction or stroke.

Safety and tolerability – Omacor appears to be safe and well tolerated. Patients most commonly complain of fishy-smelling breath, and taste perversion, which may limit compliance.

3) ***Bile acid sequestrants*** –

Background and members in the class - The third subclass of the LIP-2 drugs is the bile acid sequestrants. These drugs work in the GI tract by binding up cholesterol, and removing it from the circulation. There are three products in the subclass; cholestyramine

powder, which is available in a both a sucrose and non-sucrose, or aspartame, formulation (Questran, or Questran Light); colestipol or Colestid tablets; and colesevelam or Welchol. Welchol is the only one in the subclass that is not available generically.

Utilization - Figure 3 on page 5 shows the utilization of the bile acid sequestrants. Welchol utilization is steadily increasing, and is now up to about 4,000 prescriptions dispensed monthly in the MHS. The remaining products cholestyramine / sucrose or Questran, colestipol or Colestid, and cholestyramine / aspartame or Questran Light remain below 2,000 prescriptions a month in MHS utilization.

Efficacy- In terms of efficacy for lowering LDL, the bile acid sequestrants reduce LDL by 15-30%. This subclass has largely been replaced by the statins, which decrease LDL to a greater extent, by 18% to 55%. There is insufficient evidence to conclude that the three bile acid sequestrants, Welchol, Questran/Questran Light, and Colestid differ in their ability to lower LDL. Cholestyramine or Questran is the only bile acid sequestrant to show beneficial effects on cardiovascular outcomes in a clinical trial.

The manufacturer of Welchol, or colesevelam, claims that due to its structure, it has enhanced capacity to bind to bile acids, compared to Questran and Colestid. However this enhanced binding has not translated into greater reductions in LDL in the clinical setting.

Safety and Tolerability - For the bile acid sequestrants, there are issues with palatability of the Questran and Questran Light powder formulations, as they have a gritty texture. Additionally, there is the need for large tablet burdens, up to 7 tablets daily with Welchol and up to 16 tablets daily for Colestid. As a result, patient compliance may be affected with all the products. Welchol may cause less constipation than Questran and Colestid, which may be clinically relevant in patients with a previous history of GI obstruction.

In terms of special populations, Welchol does have a more favorable pregnancy category rating, as it has a category B rating, vs. a C rating with Questran and Colestid.

Finally, the bile acid sequestrant agents have a high degree of therapeutic interchangeability.

Overall Relative Clinical Effectiveness Conclusion: Based on clinical issues alone, there are no compelling reasons to classify any of the LIP-2 agents as non-formulary under the UF.

Major Tiller will now discuss cost-effectiveness for the LIP-2 agents.

ANTILIPIDEMIC-IIs (LIP-2) COST EFFECTIVENESS

(Major Tiller) The relative cost-effectiveness evaluation for this class was conducted by Eugene Moore, Pharm D. Both cost-minimization analyses (CMAs) and a cost-effectiveness analysis (CEA) were performed to determine the relative cost-effectiveness of the agents within each subclass. The CMAs and CEA compared the agents based on their weighted average cost per day of therapy.

Relative Cost Effectiveness Conclusion: Based on the results of the pharmacoeconomic analyses and other clinical and cost considerations, the DoD P&T Committee voted (15 for, 0 opposed, 0 abstained, and 2 absent) that:

1) Gemfibrozil (Lopid and generics) was the most cost-effective fibric acid derivative evaluated. Of the various fenofibrate formulations, Triglide (insoluble drug delivery microparticle, or IDD-P fenofibrate) demonstrated the best cost effectiveness profile.
2) Colesevelam(Welchol) was recognized as not cost effective in the treatment of hyperlipidemia compared to other bile acid sequestrants.
3) In the management of hypertriglyceridemia, prescription omega-3 fatty acids (Omacor) was identified as not cost-effective compared to gemfibrozil (Lopid, generics), fenofibrate (Triglide, Tricor, Antara, Lofibra), and niacin (Niaspan).
4) The UF scenario that maintained fenofibrate (Lofibra, generics), IDD-P fenofibrate (Triglide), cholestyramine/aspartame (Questran Light, generics), cholestyramine/sucrose (Questran, generics), colestipol (Colestid, generics), and gemfibrozil (Lopid, generics) on the UF was the most cost effective UF scenario.

COMMITTEE ACTION: UF RECOMMENDATION- Taking into consideration the conclusions from the relative clinical effectiveness and the relative cost effectiveness determinations for the LIP-2s, and other relevant factors, the P&T Committee recommended (13 for, 1 opposed, 1 abstained, 2 absent) that:

1) Fenofibrate (Lofibra, generics), IDD-P fenofibrate (Triglide), cholestyramine/ aspartame (Questran Light, generics), cholestyramine/sucrose (Questran, generics), colestipol (Colestid, generics), and gemfibrozil (Lopid, generics) be maintained as formulary on the Uniform Formulary;
2) Micronized fenofibrate (Antara), nanocrystallized fenofibrate (Tricor), prescription omega-3 fatty acids (Omacor), and colesevelam (Welchol) be classified as non-formulary under the UF; and
3) The normal brand formulary cost-share of $9.00 for IDD-P fenofibrate (Triglide) be lowered to the generic formulary cost-share of $3.00.

The authority for the last recommendation is codified in 32 CFR 199.21(j)(3), which states that "when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the Pharmacy and Therapeutics Committee may also designate that the drug be cost-shared at the generic rate." The objective is to maximize use of IDD-P fenofibrate (Triglide) in the retail network and mail order, given its significantly lower cost

relative to other fenofibrate products. Lowering the cost-share for brand name IDD-P fenofibrate (Triglide) will provide a greater incentive for beneficiaries to use the most cost effective fenofibrate formulation in the purchased care arena.

NF Justification:

The P&T Committee recommended that nanocrystallized fenofibrate (Tricor), micronized fenofibrate (Antara), prescription omega-3 fatty acids (Omacor), and colesevelam (Welchol) be classified as non-formulary under the UF. The Committee's recommendation was based on the following factors:

With regard to the fibric acid derivatives:

- Nanocrystallized fenofibrate (Tricor) and micronized fenofibrate (Antara) were not cost-effective relative to Triglide. Moreover, the DoD P&T Committee members felt that that based on the clinical needs of our patient population in DoD, providers should be able to adequately treat patients with gemfibrozil (Lopid and generics) and two fenofibrate products, Triglide and Lofibra. There is no data to suggest that the efficacy or safety profiles of Tricor or Antara offer a clinical advantage over Triglide and Lofibra.

With regard to prescription omega-3 fatty acids:

- Omacor was not cost-effective in the treatment of hypertriglyceridemia relative to gemfibrozil (Lopid, generics), fenofibrate (Triglide, Tricor, Antara, Lofibra), and niacin (Niaspan). Furthermore, the current FDA-approved indication for Omacor, which is to treat triglycerides greater than 500 mg / deci-liter, affects only a small percentage of the DoD population. For triglyceride lowering ability, the fibric acid derivatives and Niaspan can also decrease triglycerides by 20 to 50%, which is similar to that achieved with Omacor, as shown back in Table 2 on page 5. Additionally, Niaspan, which is currently included on the UF, has data to show improvement in cardiovascular outcomes, including myocardial infarction. There is no evidence for Omacor to reduce cardiovascular outcomes.

With regard to the bile acid sequestrants:

- The clinical effectiveness review did not suggest a compelling clinical advantage for Welchol, over Questran, Questran Light and Colestid to justify its increased cost. Based on indirect comparisons of placebo-controlled trials, all the bile acid sequestrants show comparable efficacy in lowering LDL by 15-30%. No direct comparisons of all three bile acid sequestrants were available. Statins offer the greatest LDL reduction (up to 55%), thus leading to the overall decline in clinical use of the bile acid sequestrants in general.
- Although Welchol may have benefits over the other bile acid sequestrants in women considering pregnancy who require lipid lowering therapy, and in patients with a history of GI obstruction, the medical necessity process should adequately allow for these patients to obtain Welchol.

COMMITTEE ACTION: IMPLEMENTATION PERIOD: The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) an effective date no later than the first

Wednesday following a 90-day implementation period. The implementation period will begin immediately following approval by the Director, TMA.

MTFs will not be allowed to have Tricor, Antara, Omacor, and Welchol 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) Medical necessity is established. MTFs may (but are not required) to fill a prescription for non-formulary LIP-2 agents written by a non-MTF provider to whom the patient was referred, as long as medical necessity was established.

CPT Napier will now provide the physician perspective from the meeting.

(CPT Napier) *(Whatever you're going to say)* That concludes the LIP-2 therapeutic class presentation. Major Tiller and I will gladly answer any questions that you may have.

(Major Tiller) Next, let's move on to the 5-alpha reductase inhibitors clinical effectiveness review.

5-ALPHA REDUCTASE INHIBITORS (5-ARIs) CLINICAL EFFECTIVENESS

(CPT Napier) **Background:** The relative clinical effectiveness evaluation was conducted by Julie Liss, one of the PEC clinical pharmacists, and Dr. McCrary. The drugs in this class are finasteride (Proscar, generics) and dutasteride (Avodart). Finasteride was the first 5-ARI on the market, and it recently became available in a generic formulation. The class review did not include the 1 mg low dosage strength of finasteride, which is marketed under the brand name Propecia for alopecia (hair loss), since this indication is not covered by TRICARE.

Relevance to MHS and Utilization: The 5-ARIs accounted for $31.2 million in MHS expenditures in fiscal year 2006, which places them at #50 in terms of cost. If you turn to Figure 4 on page 6 of the handout, you'll see the 5-ARI utilization graph. Approximately 281,000 prescriptions for the 5-ARIs were filled in the MHS during calendar year 2006. The breakdown was that 59% of the prescriptions were for Proscar with 41% for Avodart, however, Avodart is rapidly increasing in utilization.

Disease Symptoms: Both Proscar and Avodart are indicated for the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate. In BPH, the prostate becomes enlarged, which can lead to complaints of urinary frequency, urgency, nocturia (need to get up at night to void), a decreased or intermittent force of urine stream, sensation of incomplete bladder emptying, increased risk of acute urinary retention and increased risk of BPH-related surgery. 5-ARIs reduce prostate size, thus decreasing urinary complaints and increased risk of acute urinary retention (AUR) and BPH-related surgery. Acute urinary retention is considered a medical emergency.

Proscar is approved for use in combination with the alpha blocker doxazosin (Cardura and generics) to reduce the risk of progression of BPH symptoms. The Avodart package insert does not include an indication for combination therapy with Cardura. Both Proscar and Avodart are dosed once daily without regard to meals.

Clinical Conclusion – I'm not going to read the full clinical conclusion, just summarize the points that compare 5-ARI agents to each other.

With respect to efficacy:

- Based upon long-term placebo-controlled trials, there is insufficient evidence to conclude that there are clinically significant differences in efficacy between Proscar and Avodart. Both agents showed a similar degree of significant reduction in subjective symptom scores, maximum urinary flow rate, total prostate volume, risk of acute urinary retention, and risk of BPH-related surgery, compared to placebo.
- The only fully published head-to-head trial suggests that Avodart therapy reduces serum dihydrotestosterone levels, or DHT, a male hormone, about 20% more than Proscar after six months, but the clinical significance of this finding has yet to be determined. A large but as yet unpublished head-to-head trial (called EPICS) reported no differences in efficacy outcomes with Proscar vs. Avodart after one year of treatment.
- There is insufficient evidence to compare Proscar vs. Avodart when they are used in combination with an alpha-blocker, such as doxazosin (Cardura) or terazosin (Hytrin). A large, randomized, controlled trial reported that Proscar plus doxazosin or terazosin combination therapy was superior to Proscar alone in improving urinary symptoms, risk of

acute urinary retention, or BPH-related surgery. There are no published long-term combination trials with Avodart.

- There is limited evidence concerning the potential use of 5-ARIs for prostate cancer prevention, and the overall effect of 5-ARIs on prostate cancer prevention is unclear.

With respect to safety and tolerability:

- The 5-ARI agents appear to have similar adverse effect profiles. The most common adverse effects are related to sexual dysfunction. The incidence of sexual dysfunction is generally higher during the first six to twelve months of treatment and diminishes with chronic dosing. In clinical trials, Avodart and Proscar show similar rates of discontinuation due to adverse events
- Proscar and Avodart appear similar with regard to potential drug interactions and use in special populations. Both drugs are contraindicated in women and children, and carry special warnings against exposure of women who are or may become pregnant, due to the potential risk of fetal harm.
- Neither agent appears to interfere with prostate cancer detection.

Overall Relative Clinical Effectiveness Conclusion - There is insufficient evidence to conclude that there are significant differences in efficacy between Proscar (finasteride) and Avodart (dutasteride). Both 5-ARIs have been shown to have a positive effect on the symptoms of BPH, as well as to reduce the risk of acute urinary retention and need for BPH-related surgery. There appears to be no significant difference between the agents in terms of safety and tolerability. Neither drug offers a unique benefit over the other, nor is it likely that a patient who did not have an adequate response with one 5-ARI would have a better response with the other. Either Proscar or Avodart could be expected to meet the needs of the majority of DoD patients with BPH. Overall, based on clinical issues alone, there is no compelling reason to classify any of the 5-ARIs as non-formulary under the Uniform Formulary.

Major Tiller now will discuss the relative cost effectiveness of the 5-ARIs.

5-ALPHA REDUCTASE INHIBITORS (5-ARIs) COST EFFECTIVENESS

(Major Tiller) The relative cost effectiveness evaluation was conducted Major Josh Devine. Given the overall clinical conclusion that the agents within the 5-ARI class have similar relative clinical effectiveness, a cost-minimization analysis (CMA) was employed to assess the relative cost-effectiveness of Avodart and Proscar. The agents were evaluated on their weighted average cost per day of therapy across all three points of service. In addition, a cost effectiveness analysis was conducted evaluating the cost per BPH surgery avoided for each of the 5-ARIs. Also, a budget impact analysis (BIA) of various formulary scenarios was conducted to estimate the influence of other factors associated with a UF decision (i.e., market share migration, switch costs, and non-formulary cost shares). The goal of the BIA was to aid the Committee in determining which group of 5-ARIs best met the majority of the clinical needs of the DoD population at the lowest expected cost to the MHS.

Relative Cost Effectiveness Conclusion - Based on the results of the CMA and other clinical and cost considerations, the P&T Committee concluded that:

- Finasteride (Proscar and generics) was the most cost effective agent with a lower cost per day of treatment than Avodart (dutasteride) across all conditions sets evaluated. In addition, Proscar was the preferred choice in the cost effectiveness analysis with a lower expected cost per BPH surgery averted than Avodart.

COMMITTEE ACTION: UF RECOMMENDATION - Taking into consideration the conclusions from the relative clinical effectiveness and the relative cost effectiveness determinations for the 5-alpha reductase inhibitor drug class, and other relevant factors, the P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) that finasteride (Proscar, generics) be designated formulary under the UF; with dutasteride (Avodart) designated as non-formulary on the Uniform Formulary.

NF Justification: The P&T Committee recommended that dutasteride (Avodart) be classified as non-formulary under the UF. The Committee's recommendation was based on the following:

1) The results of the cost-effectiveness analysis showed that Avodart (dutasteride) was not cost-effective relative to Proscar (finasteride), which is generically available.
2) Based on the clinical needs of our population in DoD, providers should be able to adequately treat patients with Proscar. There is no data to suggest that the efficacy or safety profile of Avodart offers a clinical advantage over Proscar.

Implementation Plan: The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) an effective date no later than the first Wednesday following a 90-day implementation period. The implementation period will begin immediately following approval by the Director, TMA.

MTFs will not be allowed to have Avodart on their local formularies. MTFs will be able to fill non-formulary requests for this medication only if both of the following conditions are met:

1) The prescription must be written by a MTF provider, and
2) Medical necessity is established. MTFs may (but are not required to) fill a prescription for a non-formulary 5-alpha reductase inhibitor written by a non-MTF

provider to whom the patient was referred, as long as medical necessity has been established.

CPT Napier will now present the DoD P&T Committee's perspective on the UF recommendation for the 5-alpha reductase inhibitor class.

(CPT Napier) *(Whatever you're going to say)* That concludes the 5-alpha reductase inhibitor therapeutic class presentation, Major Tiller and I will now gladly answer any questions you may have.

(Major Tiller) Next we'll move on to the Proton Pump Inhibitors clinical effectiveness section.

PROTON PUMP INHIBITORS (PPIs) CLINICAL EFFECTIVENESS

(CPT Napier) The relative clinical effectiveness evaluation was conducted by Dr. Dave Meade, one of the PEC clinical pharmacists, and me. The PPI drug class includes the following agents: Aciphex, Prevacid, Prilosec and generics, Zegerid, which is a combination of omeprazole immediate release and sodium bicarbonate, Protonix, and Nexium. Nexium is the newest agent in the class and is a derivative of Prilosec.

Mechanism of Action: PPIs work by suppressing the final step in gastric acid production in the stomach's acid producing cells. These cells begin to produce acid just as food is entering the stomach, and the amount of acid that is produced in a given day is mainly accounted for by how much these cells are stimulated by the day's first meal. Therefore, for the medication to be most effective, it must be taken at least ½ hour prior to the first meal, so that it is circulating in the bloodstream by the time the first meal is consumed. PPIs have become standard of care for treatment of acid-related disorders, particularly treatment of erosive or ulcerative diseases which will be discussed further.

Relevance to MHS and Utilization: As of March 07, about 350,000 PPI prescriptions are dispensed monthly in the MHS. This drug class has now taken over the #1 spot in terms of MHS expenditures: more than $485 million spent over the 12 months from April 2006 to March 2007, compared to about $350 million spent in FY 2005. Military Treatment Facility (MTF) pharmacies dispense 47% of all PPI tablets or capsules, compared to 36% dispensed by retail network pharmacies, and 17% dispensed by the TMOP. If you look at figure 5 on page 6 of your handout, Aciphex is the most commonly prescribed PPI across the MHS, due mainly to its favorable previous formulary status and high utilization at MTFs. The next four most-prescribed PPIs - Nexium, Protonix and Prilosec - have similar utilization patterns. Of the PPIs, only Prilosec is generically available.

Disease Symptoms: Proton pump inhibitors are used to treat a wide variety of acid related disorders. Dyspepsia or sour stomach is very common. Its main symptom is pain or discomfort in the upper middle region of the stomach, sometimes associated with burping, or a sensation of fullness in the stomach. Gastroesophageal reflux disease or GERD has the predominant symptom of heartburn and acid indigestion, with the acidic content of the stomach regurgitating into the back of the throat. GERD is often associated with erosive esophagitis, a condition where erosions or ulcers develop on the lining of the esophagus due to the constant presence of stomach acid..

PPIs are also used to treat ulcer disease, with ulcers either in the stomach or in the upper part of the small intestine. In certain cases, ulcers can be caused by a bacterium called H. pylori. A combination of PPI's and antibiotics are used to eradicate the bacterium and heal the ulcer.

In most cases a PPI is initially prescribed for four to eight weeks, but can be continued for a longer period of time if clinically needed. GERD is often a disease that comes and goes over time, which requires long-term medical maintenance therapy; therefore PPIs will be continued for an extended period of time.

In reviewing in the clinical literature most of the outcomes are healing rates at the four and eight week. Some studies looked at symptom scores.

P&T Timeline: Before I discuss the PPI clinical conclusions, I'd like to take a minute and discuss the history of this particular drug class in terms of previous P&T Committee formulary decisions. If you skip over to figure 7 on page 8 of your handout, you see on the far left that prior to September of 2001, the DoD had an exclusive contract with the manufacturers of Prilosec(before it was available in a generic formulation) and this was a closed class, meaning that no other PPIs could be on the formulary. In September of 2001 that contract was not renewed, and the makers of Aciphex bid a significantly lower price than what had previously been paid for Prilosec. Aciphex replaced Prilosec as the preferred PPI in the DoD. In January of 2003, the class was re-bid because the makers of Aciphex raised prices. Aciphex and Prevacid were named as the preferred PPIs.

If you fast forward to February of 2005, the PPI class was one of the first classes reviewed under the rules of the uniform formulary. You can see that Aciphex and Prilosec, which by then was available generically, remained as the preferred agents. At that time only Nexium was designated as non-formulary; all the other PPIs were available at the discretion of the MTFs and were available in the mail and retail networks. And that brings us up to May of 2007 which is when our current review was done. The reason I'm presenting this timeline is to show that the preferred agent in the PPI class has varied, and we have moved a number of unique utilizers in this class to the preferred PPI. This decision as you can see in table 3 on page 9, has the potential to impact over 450,000 unique utilizers. A large percentage of these unique utilizers are in the MTFs which are very experienced at switching over patients taking proton pump inhibitors.

Clinical Conclusion-let me summarize the salient points from the clinical review.

With respect to efficacy:

1. Proton pump inhibitors are more effective in treating acid related disorders than the histamine-2 blockers (Zantac, Pepcid, Tagamet) previously reviewed in August 2006.
2. Based on head-to-head and other controlled trials, PPIs have similar efficacy in a wide range of acid related disorders and are highly therapeutically interchangeable.
3. There been many studies recently looking at the use of PPIs in the treatment of erosive esophagitis. Some of these studies have been used to claim one drug is better than the other. When reviewing the studies, we found the actual differences are small and inconsistent among trials, and not likely to be clinically significant. Evidence for clinical efficacy is similar enough to consider all PPIs equally effective in healing of erosive esophagitis.
4. There is sufficient evidence to support the use of PPIs for maintenance of initial healing and symptomatic relief of erosive esophagitis when used for as long as 5 years. However, the evidence is insufficient to conclude that one PPI is superior to others for maintenance of EE healing.
5. There appear to be no comparative differences among PPIs for healing, maintenance of healing, or symptom improvement in peptic ulcer disease (PUD). According to the published literature, they all seem to work equally well.
6. *H. pylori* eradication rates appear similar among PPIs when differing doses of antibiotics and treatment duration are taken into account.

With regards to safety and tolerability:

For Special Populations:

1. There are insufficient data to suggest superiority of one PPI over the others for treatment of pediatric patients. Prilosec, Prevacid, and Nexium have FDA indications for use in pediatric patients. Prevacid is indicated for patients one year and older. Prilosec is indicated for patients two years and older. Nexium is indicated for patients 12 years and older, even though its parent compound Prilosec is indicated for younger patients.
2. Nexium, Prevacid, Prilosec, and Zegerid are available in liquid dosage forms, which is useful in the pediatric setting or in patients with swallowing difficulties due to a stroke.
3. Nexium, Protonix, Aciphex and Prevacid are FDA pregnancy category B, meaning human studies have not revealed risk to the baby. Prilosec and Zegerid are pregnancy category C, indicating there have been no human studies to test the drug in pregnancy.
4. Minor differences include the lack of a requirement to adjust the dose of Protonix in patients with severe liver disease, unlike other PPIs, which do require a dosage adjustment.

And finally, with respect to Adverse Events and Tolerability:

The class as a whole is well tolerated, with an adverse effect profile similar to placebo. Most drug interactions are minor in nature. In general, the PPIs appear very similar with respect to safety and tolerability.

Overall Clinical Effectiveness Conclusion: In conclusion, the agents in the proton pump inhibitor class are similar in efficacy and are highly interchangeable. Overall, based on clinical issues alone, there are no compelling reasons to classify any of the PPI agents as non-formulary under the Uniform Formulary.

This concludes the proton pump inhibitor clinical effectiveness discussion. Major Tiller will now discuss the cost effectiveness section for the PPIs.

With regards to safety and tolerability:

For Special Populations:

1. There are insufficient data to suggest superiority of one PPI over the others for treatment of pediatric patients. Prilosec, Prevacid, and Nexium have FDA indications for use in pediatric patients. Prevacid is indicated for patients one year and older. Prilosec is indicated for patients two years and older. Nexium is indicated for patients 12 years and older, even though its parent compound Prilosec is indicated for younger patients.
2. Nexium, Prevacid, Prilosec, and Zegerid are available in liquid dosage forms, which is useful in the pediatric setting or in patients with swallowing difficulties due to a stroke.
3. Nexium, Protonix, Aciphex and Prevacid are FDA pregnancy category B, meaning human studies have not revealed risk to the baby. Prilosec and Zegerid are pregnancy category C, indicating there have been no human studies to test the drug in pregnancy.
4. Minor differences include the lack of a requirement to adjust the dose of Protonix in patients with severe liver disease, unlike other PPIs, which do require a dosage adjustment.

And finally, with respect to Adverse Events and Tolerability:

The class as a whole is well tolerated, with an adverse effect profile similar to placebo. Most drug interactions are minor in nature. In general, the PPIs appear very similar with respect to safety and tolerability.

Overall Clinical Effectiveness Conclusion: In conclusion, the agents in the proton pump inhibitor class are similar in efficacy and are highly interchangeable. Overall, based on clinical issues alone, there are no compelling reasons to classify any of the PPI agents as non-formulary under the Uniform Formulary.

This concludes the proton pump inhibitor clinical effectiveness discussion. Major Tiller will now discuss the cost effectiveness section for the PPIs.

PROTON PUMP INHIBITORS (PPIs) COST EFFECTIVENESS

(Major Tiller) The relative cost-effectiveness evaluation for this class was conducted by Eugene Moore, Pharm D. Given the overall clinical conclusion that the agents within the PPI class have similar relative clinical effectiveness, a series of cost-minimization analyses (CMA) were employed to assess the relative cost-effectiveness of the agents within this therapeutic class. The agents were evaluated on their weighted average cost per day of therapy across all three points of service, based on individual condition sets for inclusion on the UF/BCF.

Relative Cost Effectiveness Conclusion: Based on the results of the cost minimization analyses (CMAs) and other clinical and cost considerations, the P&T Committee voted (14 for, 0 opposed, 0 abstained, 3 absent) that:

1) The cost minimization analysis of each potential UF scenario showed that, as expected, the more restrictive the UF scenario, the lower the cost per day of treatment.
2) Among UF scenarios with two agents on the UF, omeprazole (Prilosec and generics) and esomeprazole (Nexium) were the most cost effective option.
3) Among UF scenarios with three to four agents on the UF, omeprazole (Prilosec), esomeprazole (Nexium), pantoprazole (Protonix), and rabeprazole (Aciphex) were the most cost effective agents.
4) The UF scenario that maintained omeprazole (Prilosec and generics) and esomeprazole (Nexium) as the only two agents on the UF in conjunction with a prior authorization requiring a trial of either agent for new patients was the most cost effective scenario.

COMMITTEE ACTION: UF RECOMMENDATION – Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the PPIs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (14 for, 0 opposed, 1 abstained, and 2 absent) to recommend that: 1) omeprazole (Prilosec, generics) and esomeprazole (Nexium) be maintained as formulary on the UF with a prior authorization requiring a trial of either agent for new patients; 2) that rabeprazole (Aciphex), lansoprazole (Prevacid), pantoprazole (Protonix), and omeprazole/sodium bicarbonate (Zegerid) be classified as non-formulary under the UF with a PA requiring a trial of either omeprazole (Prilosec, generics) or esomeprazole (Nexium) for new patients; and 3) that the normal brand formulary cost-share of $9.00 for esomeprazole (Nexium) be lowered to the generic formulary cost-share of $3.00.

The authority for the last recommendation is codified in 32 CFR 199.21(j)(3), which states that "when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the Pharmacy and Therapeutics Committee may also designate that the drug be cost-shared at the generic rate." Lowering the cost-share for brand name esomeprazole (Nexium) will provide a greater incentive for beneficiaries to use esomeprazole rather than the less cost effective branded products—rabeprazole (Aciphex), lansoprazole (Prevacid), pantoprazole (Protonix), or omeprazole/sodium bicarbonate (Zegerid)—in the purchased care arena.

MTFs will not be allowed to have Aciphex, Prevacid, Protonix, or Zegerid 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) Medical necessity is established. MTFs may (but are not required to) fill a prescription for non-formulary PPI agents written by a non-MTF provider to whom the patient was referred, as long as medical necessity was established.
3) In addition, MTFs will be able to fill prescriptions for Aciphex, Prevacid, Protonix, and Zegerid for patients newly starting PPI therapy only if the patient has tried and failed, been unable to tolerate, or has contraindications to treatment with omeprazole or Nexium.

CPT Napier will now present the DoD P&T Committee's perspective on the UF recommendation for the PPI class.

(CPT Napier) *(Whatever you're going to say)* That concludes the PPI therapeutic class presentation, Major Tiller and I will now gladly answer any questions you may have.

(Major Tiller) Next we'll move on to the Angiontensin II Receptor Blockers clinical effectiveness conclusion.

ANGIOTENSIN II RECEPTOR BLOCKERS (ARBs) CLINICAL EFFECTIVENESS

(CPT Napier): **Background and members in the class:** There are seven angiotensin receptor blockers (ARBs) marketed in the U.S. The ARBs include losartan (Cozaar), irbesartan (Avapro), valsartan (Diovan), candesartan (Atacand), telmisartan (Micardis), eprosartan (Teveten), and olmesartan (Benicar). All of the drugs are available in a combination tablet with the diuretic hydrochlorothiazide (or HCTZ). None of the ARBs are available in a generic formulation yet; generics aren't expected for about 3 years.

Utilization: If you look on Figure 8 on page 8 of the handout, each line shows utilization of the parent ARB, along with the diuretic combination. ARB utilization has been steadily increasing in the MHS. This class was one of the first classes reviewed when the Uniform Formulary was started back in February 2005. Overall, Diovan is the most frequently prescribed ARB at all three points of service, at about 60,000 prescriptions dispensed monthly. Its followed next by Cozaar, at about 50,000 prescriptions dispensed monthly, and Avapro, at about 35,000 prescriptions dispensed monthly.

The ARB drug class accounted for $137 million in MHS expenditures in FY 2006, and is ranked #10 in terms of total expenditures during that time period. The increasing utilization and expenditures prompted the DoD P&T Committee to reevaluate the class.

Indications: All the ARBs are approved for treatment of hypertension, or high blood pressure. Additionally, four of the ARBs have additional FDA approvals. Both Diovan and Atacand are approved for use in treating chronic heart failure. Avapro and Cozaar are approved for treatment of diabetic patients who have developed kidney disease. Diovan has an additional approval for use in patients who have experienced a myocardial infarction, to prevent death and development of heart failure. Cozaar also has an approval for a subset of patients with hypertension who have an enlarged left side of the heart (left ventricular hypertrophy), however, the benefit was not seen with African Americans.

Outcomes: The P&T Committee focused on efficacy differences with respect to labeled indications, particularly in those areas where a benefit in clinical outcomes was demonstrated. In other words, do the ARBs show benefits not only in reducing blood pressure, but also reducing the risk of death, hospitalization for heart failure, need for kidney dialysis or need for renal transplantation. The primary areas evaluated by the P&T Committee were efficacy for hypertension, chronic heart failure, and type 2 diabetic nephropathy, or diabetic kidney disease.

Once again, I'll go over the clinical efficacy conclusions first, followed by the overall clinical conclusion.

With respect to efficacy for treating hypertension:

- There is no evidence that any one ARB is more efficacious than the others for lowering blood pressure. All seven ARBs are effective at treating hypertension. When the diuretic HCTZ is added on to the ARB, additional reductions in blood pressure are seen.
- Cozaar is the only ARB labeled to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy (LVH). However, guidelines from Joint National Commission, a well-respected group, support use of other antihypertensive drugs (e.g., ACE inhibitors, diuretics) in this setting.

- Some trials with the ARBs in patients with hypertension have also shown benefits in reducing death and stroke. However, these benefits were due to the fact that the ARB lowered blood pressure to a greater extent than the comparator antihypertensive drug or placebo. Several studies have shown that reducing blood pressure with any antihypertensive drug, not just the ARBs, translates into stroke reduction and reduced mortality in patients with hypertension.

With respect to efficacy for treating chronic heart failure:

- Hospitalization for heart failure is one of the highest costs that the government pays in its Medicare program. Thus in patients with heart failure, one of the goals is to avoid unnecessary hospital admissions for shortness of breath and leg swelling.
- As we mentioned earlier, both Diovan and Atacand are approved for use in heart failure, and have been shown to reduce the risk of death and hospital admissions for heart failure. The P&T Committee agreed that there is no evidence to support clinically significant differences in efficacy between Atacand and Diovan in patients with chronic heart failure.

With respect to efficacy for treating diabetic kidney disease:

- Patients with diabetes frequently develop kidney disease, which starts with protein spilling into the urine, and can progress to patients requiring dialysis or a kidney transplant. A drug that can slow the progression of kidney disease in diabetic patients is useful, to avoid the complications and cost of dialysis and organ transplants.
- Both Avapro and Cozaar are approved for use in diabetic kidney disease. They have shown benefits in reducing the risk of doubling of serum creatinine (which is a lab marker for renal function), and development of end stage renal disease (where patients require dialysis or renal transplant to prevent death). The DoD P&T Committee agreed that there is no evidence to support clinically significant differences in efficacy between Avapro and Cozaar in improving clinical outcomes in patients with type 2 diabetic nephropathy.

With respect to efficacy for treating patients following a myocardial infarction:

- Diovan is the only ARB approved by the FDA to reduce death and development of heart failure in patients following a myocardial infarction (or MI) who have diminished heart function (left ventricular systolic dysfunction). However, other drugs have shown proven benefits in this setting. The ACE inhibitors (Zestril, Capoten, Altace) have a larger body of evidence supporting a mortality benefit in post-MI patients with left ventricular systolic dysfunction than Diovan. Additionally, two other drugs, the aldosterone antagonists spironolactone (Aldactone, generics) and eplerenone (Inspra) are also labeled for use, or have shown efficacy in the post-MI setting.

With respect to safety and tolerability:

- Overall, the ARBs are well tolerated, and there are no clinically significant differences between the seven products in their risk of adverse events. Major adverse events include increases in serum creatinine; angioedema, which can be a life-threatening swelling of the throat; and risk of fetal harm in pregnant women. There are no clinically significant differences in their drug interactions profiles. There is no evidence that the ARBs differ significantly with regard to safety and tolerability profiles.

Overall clinical effectiveness conclusion:

- Based on clinical issues alone, there are no compelling reasons to classify any of the ARBs as non-formulary under the UF.

This concludes the ARB clinical effectiveness discussion. Major Tiller will now discuss the cost effectiveness section for the ARBs.

ANGIOTENSIN II RECEPTOR BLOCKERS (ARBs) COST EFFECTIVENESS

(Major Tiller) Several cost minimization analyses (CMAs) were performed to determine the relative cost effectiveness of the ARBs. The cost effectiveness evaluation was completed by Major Joshua Devine. The CMAs compared the weighted average cost per day of treatment for each condition set. In conjunction with the clinical review, the results were reported by indication. The indications considered during the analysis included hypertension, chronic heart failure, and diabetic kidney disease.

Relative Cost Effectiveness Conclusion: Based on the results of the CMA, and other clinical and cost considerations, the P&T Committee concluded that:

1) A UF scenario with 3 or fewer agents on the UF was more cost effective than scenarios that included additional agents on the Uniform Formulary.
2) Telmisartan (Micardis) was the most cost effective agent for the management of hypertension; candesartan (Atacand) was more cost effective for management of chronic heart failure than valsartan (Diovan). Losartan (Cozaar) and irbesartan (Avapro) had similar cost effectiveness profiles for treatment of diabetic kidney disease.
3) The Uniform Formulary scenario that included candesartan (Atacand), candesartan/HCTZ (Atacand HCT), losartan (Cozaar), losartan/HCTZ (Hyzaar), telmisartan (Micardis), and telmisartan/HCTZ (Micardis HCT) was the most cost effective UF scenario evaluated.

COMMITTEE ACTION: UF RECOMMENDATION – In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the ARBs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (14 for, 0 opposed, 1 abstained, and 2 absent) to recommend that candesartan (Atacand), candesartan/HCTZ (Atacand HCT), losartan (Cozaar), losartan/HCTZ (Hyzaar), telmisartan (Micardis), and telmisartan/HCTZ (Micardis HCT) be maintained as formulary on the UF and that eprosartan (Teveten), eprosartan/HCTZ (Teveten HCT), irbesartan (Avapro), irbesartan/HCTZ (Avalide), olmesartan (Benicar), olmesartan/HCTZ (Benicar HCT), valsartan (Diovan) and valsartan/HCTZ (Diovan HCT) be classified as non-formulary under the UF

NF Justification:

The P&T Committee recommended that eprosartan (Teveten), eprosartan/HCTZ (Teveten HCT), irbesartan (Avapro), irbesartan/HCTZ (Avalide), olmesartan (Benicar), olmesartan/HCTZ (Benicar HCT), valsartan (Diovan) and valsartan/HCTZ (Diovan HCT) be classified as non-formulary under the UF. The Committee's recommendation was based on:

1) A UF scenario with 3 or fewer ARBs on the UF was the most cost effective UF scenario and the products selected for UF status provided the most cost effective mix of drugs available to treat patients with hypertension, chronic heart failure, or diabetic kidney disease.
2) The clinical effectiveness review did not show evidence of a compelling therapeutic advantage for the non formulary agents for hypertension (Teveten, Avapro, Benicar,

Diovan), chronic heart failure (Diovan) and diabetic kidney disease (Avapro), compared to the UF candidates.

3) There is no evidence to suggest that a patient with heart failure who did not respond to Atacand would have an improved response to Diovan. Likewise, for patients with diabetic kidney disease, there is no evidence to suggest that a patient who did not respond to Cozaar would have an improved response to Avapro.

4) Although Diovan is also labeled for use in patients following a myocardial infarction, other antihypertensive drugs, including the ACE inhibitors, are approved for this use. The use of the ARBs for myocardial infarction would reflect only a small number of patients in the MHS. The medical necessity process should adequately allow for patients with myocardial infarction to receive Diovan.

(CPT Napier) *(Whatever you're going to say)* That concludes the ARB therapeutic class presentation, the PEC staff and I will now gladly answer any questions you may have.

Amlodipine (Norvasc) was designated non-formulary at the August 2005 P&T Committee Meeting. In early 2007, the FDA approved Mylan Pharmaceutical's first-time generic for Norvasc (Amlodipine, Pfizer). The price of Amlodipine remains high enough that the Committee felt that even the generic was not cost-effective relative to the other drugs in the Calcium Channel Blocker Class. However, as part of its re-evaluation of the non-formulary UF status of Amlodipine, the P&T Committee recognized that there will be situations in the future in which it would be helpful if a procedure were in place that allowed reclassification of such a drug from non-formulary to generic in a more expeditious manner than can be accomplished through the normal quarterly P&T Committee cycle. Such a procedure would be advantageous for both the MHS and it's beneficiaries. The P&T Committee proposed the following process to more expeditiously reclassify non-formulary agents:

1) For each drug class in which such a reclassification is a possibility, the P&T Committee will recommend criteria under which non-formulary agents will be reclassified as generic agents under the UF. These criteria will be reviewed and adopted as a recommendation of the Committee. The recommendation will be subject to comment by the BAP and final decision by the Director, TMA (see recommended criteria below).

2) When the pre-established criteria for reclassification are met, the Chairperson of the P&T Committee will call for an electronic vote by the members of the P&T Committee on the matter.

3) Upon a majority vote affirming that the non-formulary drug should be reclassified as generic, that agent will be changed from non-formulary status to formulary status as a generic.

4) Committee members will be briefed on any reclassification of a non-formulary agent at the next meeting of the P&T Committee. This information will be recorded as an information-only item in the Meeting Minutes. The item will be included in information provided for the BAP's next week; however, since the BAP will have already made any comments on the subject, the item will normally not be subject to further BAP comment.

The DoD P&T Committee recommended the following criteria for the re-evaluation of non-formulary agents for UF status. These criteria would apply only to drug classes in which UF status was NOT awarded based on condition sets that specified the number of similar agents on the UF (i.e., agents in the same class or subclass). All three criteria must be met for the reclassification of a non-formulary agent:

1) The P&T Committee had concluded previously that the non-formulary agent had similar relative clinical effectiveness (i.e., similar efficacy, safety, and tolerability) compared to similar agents on the UF, and that the drug had not been excluded from the UF based on clinical issues alone.

2) The non-formulary agent becomes generically available and:

   a) The generic product is "A-Rated" as therapeutically equivalent to the brand name product according to the FDA's classification system.

   b) The generic market supply is stable and sufficient to meet DoD MHS supply demands.

3) The non-formulary agent is cost-effective relative to similar agents on the UF. A non-formulary agent become cost-effective when:

   a) The non-formulary agent's total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the UF class to which they are compared.

   b) The non-formulary agent's total weighted average cost based on an alternate measure used during the previous review is less than or equal to that for the UF class to which they were compared. For example, antibiotics may be compared on the cost per course of therapy used to treat a particular condition.

(Major Tiller) *(concluding remarks)*