Uniform Formulary Beneficiary Advisory Panel

Meeting Summary
September 18, 2007
Washington, D.C.

Panel Members Present:

- Robert Washington, Fleet Reserve Association, Chairman
- Kathryn Buchta, Health Net Federal Services
- Barbara Cahoon, Military Families Association
- John Class, Military Officers Association of America
- John Crum, Humana Military Healthcare Services, Inc.
- Deborah Fryar, Military Coalition
- Rance Hutchings, Uniformed Services Family Health Plan
- Lisa Le Gette, Express-Scripts, Inc.
- Kimberly Owens, Military Alliance
- 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 8:50 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 August 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:
  - Leukotriene Modifying Agents (LMAs)
  - Growth Stimulating Agents (GSAs)
  - Second Generation (Newer) Antihistamines (SGAs)
  - Designated Newly Approved Drugs
- 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 by the Director, TMA 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 Beneficiary Advisory Members present, including two new members: Barbara Cahoon, representing the National Military Families Association; and Kimberly Owens, an active duty military spouse.

MAJ Watson briefly reviewed housekeeping considerations pertaining to the meeting.

Opening Comments by the Chairman

Chairman Washington welcomed the two new Panel members. He also thanked Dr. Cassells for the recent changes made to the notification process that has resulted in beneficiaries being notified on time of the changes being made to the formulary status of drugs.

Private Citizen Comments

MAJ Watson next opened the meeting for private citizen comments. There was no response from individuals present at the meeting. However, Chairman Washington read into the record two letters that private citizens had sent to the Panel for their consideration. The letters, both dealing with decisions to move medications to non-formulary status, are included in full as Appendix 2 and Appendix 3.

Presentation of Drug Class Reviews

LTC Brett Kelly, Director of the Pharmacoeconomic Center (PEC) began the agenda presentation with introductory remarks. He began by saying that he appreciates hearing from beneficiaries who are having difficulty with the system, such as the individuals whose letters were read by the Chairman, and noted that mechanisms are available to help them. He introduced the members of the Clinical Operations Staff who will be making the presentations: CPT Josh Napier, an Army internal medicine physician, and Major Josh Devine, an Air Force Pharmacy Officer on the PEC staff. CPT Napier will also provide the Panel with the physician's perspective on the recommendations made by the P&T Committee. Other TMA staff members present were also introduced and additional PEC participation in the meeting took place via telephone conference call.

[Insert script, page 1]

Review of the Newer Antihistamines (NAs) Drug Class

Clinical Effectiveness Review

CPT Josh Napier of the PEC presented the P&T Committee's clinical effectiveness review of the Newer Antihistamines (NAs) drug class.

[Insert script, pages 2 through first paragraph, page 4]

Cost Effectiveness Review

Major Josh Devine next discussed the cost effectiveness review conducted for this drug class.

[Insert script, page 4 second paragraph]

P&T Committee Action and Recommendations

Major Devine then detailed the P&T Committee's recommendations regarding the Newer Antihistamines (NAs) drug class.

[Insert script, page 4 third paragraph through page 5 third paragraph].

P&T Committee Physician Perspective

CPT Napier told the Panel that the prevailing feeling among the P&T Committee members was there was a lot of good clinical experience with using these agents and that physicians were familiar with their benefits, side effects and overall effectiveness. He noted that the majority of the products in the class would remain on formulary and that beneficiaries who could only get relief using the Clarinex products would be able to get them through the Medical Necessity process.

Panel Questions

Mr. Hutchings asked if the Committee's recommendation would change at all if Loratadine (Claritin) were available through the Retail and Mail Order pharmacies. Major Devine replied that Claritin and Claritin-D, which are available over-the-counter and so do not require a prescription, are far and away the most effective products available and are the preferred products within this group. Accordingly, TMA finds it appropriate to encourage the use of these products as first line for a patient that's going to initiate therapy within this class. Additionally, there is some uncertainty in the market for this class. Zyrtec, for example, is scheduled to become over-the-counter during the coming year, Allegra will also become available generically and some new products are scheduled to enter the market. Major Devine's view is that if Claritin were available through TMOP and TRXX, it might not have changed the recommendation, it would just have helped put patients on the most cost-effective product.

Mr. Class asked about the date when Clarinex and Clarinex D would become generic and be cost-effective so that the will be reclassified and added to the formulary. Ms. Le Gette said the scheduled date is October 2008 or early 2009. Mr. Class said his concern is that if it happens quickly, the result will be that beneficiaries will be moved from one product to another and then back again in rapid succession.

Panel Discussion of P&T Committee Formulary Recommendations for the Newer Antihistamines (NAs) Drug Class

The Chairman read the P&T Committee's recommendations regarding the Newer Antihistamines (NAs) drug class:

> "In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the NAs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that:

1) Fexofenadine (Allegra, generics), Fexofenadine/Pseudoephedrine (Allegra D), Cetirizine (Zyrtec), Cetirizine/Pseudoephedrine (Zyrtec D), and Acrivastine/Pseudoephedrine (Semprex-D) should be maintained as formulary on the UF.
2) Desloratadine (Clarinex) and Desloratadine/Pseudoephedrine (Clarinex D) should be classified as non-formulary.
3) Loratadine (Claritin, generics) and Loratadine/Pseudoephedrine (Claritin D) should be added to the UF for purposes of the TRICARE OTC Pilot Program.
4) At such time as Cetirizine (Zyrtec) and Cetirizine/Pseudoephedrine (Zyrtec D) are made available over-the-counter, both products should be maintained on the UF for purposes of the TRICARE OTC Pilot Program.

Desloratadine -/+ Pseudoephedrine (Clarinex and Clarinex D) should be reclassified as formulary on the UF when the generic products are available and cost effective relative to similar agents in the newer antihistamine class.

There was no further Panel discussion of the recommendation.

Panel Vote on Formulary Recommendation for the Newer Antihistamines (NAs) Drug Class

Mr. Washington called for the Panel vote on the Newer Antihistamine drug class formulary recommendations. The Panel vote was:

11 Concur, 0 Non-Concur, 0 Abstentions.

Panel Discussion of P&T Committee Newer Antihistamines (NAs) Drug Class Implementation Recommendations

The Chairman read the implementation plan for the Newer Antihistamines (NAs) 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."

Mr. Class asked about implementing the new notification procedures and whether they would apply to this drug class. He said he didn't want to agree with the recommendation and have there be no notification. MAJ Watson said he believed there was a commitment to continue the notification. A staff member added that funding was available for it through the first quarter. MAJ Watson said he was 99.8 percent confident that the notification procedures would be used in this class. Mr. Class said he would interpret that statement to mean that the BAP couldn't assume that the procedure would be used for this drug class.

Mr. Hutchings said his organization has been able to reduce the 120 days previously required to 90 days now. Mr. Class said that the Associations still require 120 days to get the decisions publicized in their magazines and newsletters.

Dr. Schlaifer noted that this was one class where the change would not mean that someone wouldn't be able to get a drug because of the over-the-counter availability of Claritin. Mr. Hutchings said Clarinex will also be available over-the-counter by the implementation date.

Panel Vote on Implementation Period Recommendation for the Newer Antihistamines (NAs) Drug Class

The Panel vote on the implementation recommendations for the NA drug class was:

10 concur, 1 non-concur, 0 abstain.

Review of the Leukotriene Modifier (LM) Drug Class

Clinical Effectiveness Review

CPT Napier presented the results of the P&T Committee's review of the Leukotriene Modifier (LM) drug class.

[Insert script, pages 6 through 7]

Cost Effectiveness Review

Major Devine reviewed the cost effectiveness considerations for the Leukotriene Modifier (LM) drug class.

[Insert script, page 8, paragraphs 1 and 2]

P&T Committee Action and Recommendations

Major Devine presented and explained the P&T Committee's recommendations in this drug class.

[Insert script, page 8 through page 9, paragraph 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 Committee considered the recommendations in this drug class to be a straightforward decision. The number of beneficiaries that will be affected by moving Zyflo

to non-formulary is small and easy to account for with medical necessity. Similarly, the large number of Singulair users made it seem reasonable to make that a formulary agent.

Panel Questions

The Beneficiary Advisory Panel had no questions regarding the Committee's decisions in this drug class.

Panel Discussion of P&T Committee Leukotriene Modifier (LM) Drug Class Recommendations

Chairman Washington read the P&T Committee's formulary recommendations for the Leukotriene Modifier (LM) drug class:

> "In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the LMs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that Zafirlukast (Accolate) and Montelukast (Singulair) be maintained as formulary on the UF and that Zileuton (Zyflo) be classified as non-formulary."

Dr. Schlaifer asked about the provision that prior authorization would be required to use Accolate and Singulair for allergic rhinitis and what this means for patients with asthma. Major Devine replied that there is no prior authorization required for using the drugs in this class for allergic rhinitis. He said there was consideration of a prior authorization policy, but the Committee recommended not to enact a prior authorization step therapy program. Instead, it will take a pragmatic approach and gather data about the decisions that have been implemented thus far.

Dr. Schlaifer asked about the following statement included in the background information:

> "The Committee concluded that the Uniform Formulary scenario that placed Zafirlukast (Accolate) and Montelukast (Singulair) on formulary with a prior authorization required for use in allergic rhinitis was the scenario that resulted in the lowest expected expenditures in the LM class."

Major Devine explained that the conclusion was as stated, but that the recommendation did not include a prior authorization.

Panel Vote on Leukotriene Modifier (LM) Drug Class Formulary Recommendations

The Beneficiary Advisory Panel Vote on the Leukotriene Modifier (LM) drug class formulary recommendations was:

11 concur; 0 non concur; 0 abstain.

Panel Discussion of Leukotriene Modifier (LM) Drug Class Implementation Period

The Chairman read the recommendation regarding the implementation period 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."

Mr. Class referred to the letter which was read at the beginning of the meeting from the person who said they were not being told in advance of changes to the formulary. He reminded the group that it is a beneficiary panel.

Ms. Owens said she would like to make sure that the very small number of beneficiaries affected by the switch are notified because it will require a medical necessity determination for them to keep receiving Zyflo. She noted that retirees on a fixed income might be unable to come up with the required $22 co-pay on the spot if they don't know about it beforehand. She thinks 90-days is too short a period.

Panel Vote on Leukotriene Modifier (LM) Drug Class Implementation Period Recommendations

The Beneficiary Advisory Panel vote on the Leukotriene Modifier (LM) drug class implementation period recommendations was:

8 concur; 3 non-concur; 0 abstain.

Review of the Growth Stimulating Agents (GSAs) Drug Class

Clinical Effectiveness Review

CPT Napier briefed the Beneficiary Advisory Panel on the P&T Committee's review of the clinical effectiveness of the Growth Stimulating Agents (GSAs) drug class.

[Insert script, page 10 through page 12, second full paragraph]

Cost Effectiveness Review

Major Devine next discussed the cost effectiveness review for the GSA drug class.

[Insert script, page 12, paragraph 3 through page 13, bullet number 4]

P&T Committee Action and Recommendations

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

[Insert script, page 13, first full paragraph through end of page].

P&T Committee Physician Perspective

CPT Napier said one unique thing about this class of medications is that it is a very costly class of therapy so patients have always been required to fill out a lot of different medical necessity forms to ensure that they were getting appropriate treatment. He said that the process wouldn't change, although the medications that the patients get may be different that what they have been using in the past. The P&T Committee and the specialists they consulted with in the field all agreed that the important thing was to be able to meet such beneficiaries' needs as the type delivery mechanism (i.e., the pen device) available and storage requirements. Other than that, all of the medications in this class are essentially the same product: recombinant growth hormones.

Panel Questions

Ms. Cahoon asked about MHS expenditures in this drug class. CPT Napier said that for individuals the cost is very high, but the overall use is small. He wasn't sure where it ranked in terms of overall MHS expenditures.

Dr, Schlaifer asked who the prescribers in this drug class are, i.e., are they military physicians or outside physicians. CPT Napier said that in larger areas, such as Washington D.C. and San Antonio, where there are pediatric endocrinologists, the beneficiaries go to outside physicians, but there are a lot of areas where there are no pediatric endocrinologists. Dr. Schlaifer also noted that the number of beneficiaries affected by the change in this drug class is small — about 400 individuals — and asked if there was any chance that the notification could be 100 percent. MAJ Watson said again that every effort would be made, but that 99.8 percent was all he was willing to commit to.

Mr. Partridge asked about the significance of the drugs being preservative free. CPT Napier said there are some instances in which some kinds of preservatives may be contra-indicated. For example, benzyl alcohol is fine for older children and adults but not for infants or neo-nates. The important thing is that those without preservatives require refrigeration. Mr. Partridge also asked whether the fact that most prescriptions in this class are written by non-military physicians imposed an unusually heavy burden on medical necessity determinations. CPT Napier agreed that medical necessity forms would be required to have the prescriptions filled at an MTF, but that prior authorization forms would be sufficient for the other points of service.

Mr. Class asked about the criterion used for the 60-day implementation period other than the low number of beneficiaries affected. The answer was that prior authorizations are already in place for this whole drug class.

Ms. Owens asked if a beneficiary has a prior authorization based on medical necessity for a drug being made non-formulary whether the co-pay would now be $22. She said her concern is that the mothers of the children who are receiving this type of drug are young, active-duty spouses. They may not have an understanding of how the system work and may not know about medical necessity process that they are going to have to go through and may be dealing with doctors who are also not completely familiar with it. She acknowledged that the numbers are small, but said

that these are the wives whose husbands are overseas. She said she doesn't think 60 days will be enough if TMA can't guarantee that everybody will be notified on time.

CPT Napier agreed with the concern, but said that everybody on these medications knows about the forms because they are already filling them out. Ms. Owens said that the problems are compounded for wives whose husbands are deployed are who are worried about their kids. CPT Napier said that one of the added features the companies provide is that there is a lot of support for the paperwork and have staff dedicated to help that are available through a 1-800 number. The problem is unique to this class. Ms. Owens said that she doesn't think it is up to the drug companies to walk people through the paperwork; it's up to TMA.

Mr. Hutchings said he isn't concerned about the physicians and paperwork, because they know the drill. But he agrees that 60 days is too short an implementation period for this class. One reason is that the pens for administering the drugs are different, so there will have to be new training on how to use the new pen. Also, by the time the letters get mailed, there may only be a week left and the chances of getting in to see a pediatric endocrinologist in that time frame are small.

Panel Discussion of P&T Committee Formulary Recommendations in the Growth Stimulating Agents (GSA) Drug Class

The Chairman read the P&T Committee's formulary recommendations for the Growth Stimulating Agents (GSA) drug class:

> "The P&T Committee, based upon its collective professional judgment, voted to recommend that Tev-tropin, Nutropin, Nutropin AQ, Norditropin, Nortropin Nordiflex, Serostim, Zorbtive, and Increlex be maintained as formulary on the UF and that the Genotropin, Humatrope, Saizen and Omnitrope brands of Somatropin be classified as non-formulary. Currently, prior authorization criteria apply to both growth hormone (Somatropin products) and Mecasermin (Increlex). The P&T Committee voted that the following PA criteria should apply to growth hormone and Mecasermin (Increlex). Changes from previous growth hormone (Somatropin) criteria are the addition of Noonan's Syndrome and SHOX Deficiency as covered uses; no changes were recommended to Mecasermin criteria."

Mr. Partridge commented that he disagrees with the requirement that the doctor has to be an MTF provider if another doctor recommends the treatment and has sufficient justification. He agrees with what Ms. Owens said about the young active duty wives and their concerns.

Mr. Hutchings added that a lot of times it just seems like that a hoop that has to be jumped through and the beneficiary gets sent to a primary care physician who just writes the prescription. He asked if the requirement regarding MTF providers was part of the law.

MAJ Watson said that if a non-MTF physician writes a prescription based on a referral that is brought to the MTF, it is the option of the MTF whether or not to fill it. If the prescription was not the result of a referral, the regulation states that MTF may not fill the prescription for a non-formulary drug. In other words, if a patient is referred by an MTF to a physician in the community network and the doctor writes a prescription for a non-formulary agent and provides

the proper documentation for a medical necessity, then the regulation permits the MTF, at their discretion, to go ahead and fill the prescription.

Ms. Buchta asked whether the prescription would still be approved if the primary care physician was a civilian not part of the network and the patient was not enrolled through the MTF. MAJ Watson said in that case, the prescription would not be filled. That requirement is written in the regulations.

Panel Vote on Growth Stimulating Agents (GSA) Drug Class Formulary Recommendations

The vote on the P&T Committee recommendations was:

9 concur; 2 non-concur; 0 abstentions.

Panel Discussion of P&T Committee Growth Stimulating Agents (GSA) Implementation Recommendations

The Chair read the Committee's implementation recommendations:

> "The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period at the TMOP and TRRx, and at the MTFs no later than a 60-day implementation period. The implementation period will begin immediately following approval by the Director, TMA."

Mr. Hutchings said he believes the time period should definitely be extended, but would like to have a discussion about how long it should be. Half of the prescriptions are filled in retail, so the Government won't realize any cost savings there. He said, he would push the implementation out to four months.

Major Devine said that some companies did submit voluntary agreements for retail rebates which would not begin until implementation, so there are retail considerations. LTC Kelly said that the products involved in this class are all the same products and that every day's delay costs the chance to reduce expenses. He said the Committee was very, very liberal in product inclusion.

Mr. Class said the Panel understands and agrees with the cost implications, but it is concerned with what happens when the patient goes in to the point of service to pick up the med. If the time is insufficient, the patient gets surprised by the change, because the doctor is going to write a prescription for whatever he is writing for already. The BAP is responsible for looking at the process from the beneficiaries' side. Notification is the key to the whole thing — telling the 653 people who will be affected by the change that there will be a change and they will need to do something about it.

Ms. Owens said she wasn't arguing about moving the drug to the third tier, only that 60 days might not be enough time for the moms who are affected to be adequately notified.

Mr. Hutchings said his plan would have no problem with 60 days because they probably have about three patients who are affected and the plan will call them the day after the implementation

decision is made. This will give the patient two months to make an appointment. But if there is no way to notify patients, there could be a problem with the $13 co-pay difference. He sees that there could well be issues arise from it.

Dr. Schlaifer said she is still looking for a reason to concur because she understands the cost issue. She asked if patients that have been going through the prior authorization process will already have paperwork going on because they have to do it anyway. The answer provided was that the paperwork for prior authorization only needs to be done once and the medical necessity is only needed once, 30 days in advance of the change. So a provider can get the form and send it in advance of the actual implementation period. Ms. Trice commented by phone from San Antonio, indicating that the growth hormones don't require the regular authorization form and there are two different forms for prior authorization and medical necessity. Patients who are just starting on growth hormones will get forms that provide them information about which products will cost $9.00 and which will cost $22.00. Additionally, patients on this drug need to be checked at least once a year by a pediatric endocrinologist and the prior authorizations need to be renewed every year, which will expose patients to the changes.

Ms. Buchta noted that most implementation plans call for a 90-day period and asked what was different about this drug class that triggered the 60-day recommendation. CPT Napier said it stemmed from the numbers involved and the fact that new patients are required to get a PA and will receive the appropriate information then.

Mr. Hutchings asked if it is possible to change the PA requirement before changing the co-pay in order to facilitate information transfer. CPT Napier said that the PA form will be changed right away and made available on the website.

Ms. Owens explained that the problem, from her viewpoint, is that the beneficiaries in this case are mostly young mothers with sick children who walk in to get their renewal and find that it's now $22.00 and they can't afford it. Under these circumstances, she doesn't think that it's right to make the notification period 60 days just because the group is so small.

A member asked how long a prescription lasts and how often they have to be refilled. CPT Napier answered that the prescription lasts for a year but is probably dispensed in one-month increments because of the nature of the drug and the fact that it has to be kept in a refrigerator.

Panel Vote on Growth Stimulating Agents (GSA) Drug Class Implementation Recommendations

The Panel vote on the GSA implementation period recommendations was:

0 concur; 11 non-concur; 0 abstentions.

The Panel comment was that if TMA can give the patient 60 days notice, then a 90-day implementation period would be acceptable; otherwise, the implementation period should be 120 days.

Review of Recently Approved Agents: Veramyst

CPT Napier said the next items to be discussed would concern two new drugs in previously reviewed drug classes: a nasal steroid and a new antihypertensive agent.

Clinical Effectiveness Review

CPT Napier presented the P&T Committee's review of the recently approved agent, Veramyst.

[Insert script, page 14, paragraphs 1-5]

Cost Effectiveness Review

Major Devine then discussed the cost effectiveness review for Veramyst.

[Insert script, page 14, paragraph 6 and page 15, paragraph 1]

P&T Committee Action and Recommendations

Major Devine also informed the Panel of the P&T Committee's Veramyst recommendations.

[Insert script, page 15, paragraph 2 through end].

P&T Committee Physician Perspective

CPT Napier provided the Panel with the physician's perspective on the P&T Committee's evaluation of Veramyst. He said the Committee determined that was Veramyst offered was not really different from what the current Uniform Formulary products, particularly Flonase, already offered. The Committee strongly agreed with the recommendations to classify Veramyst as non-formulary under the Uniform Formulary.

Panel Questions

MAJ Watson informed the Panel that the operational feasibility portion of the recommendation, which would begin the $22 co-pay for new users immediately upon approval, was found not to be operationally feasible. A $22 co-pay can't be made effective for new users only. The idea was to keep too many people from getting on the new drug before the implementation date, after which it would be non-formulary.

Mr. Class asked if that was why the provision was not included in the final recommendation. MAJ Watson agreed that was the reason.

Panel Discussion of P&T Committee Formulary Recommendations for Veramyst

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

> "Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations of Fluticasone Furoate (Veramyst), and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that Fluticasone Furoate (Veramyst) be classified as non-formulary."

Mr. Partridge asked about members of the P&T Committee who were opposed to this recommendation. CPT Napier said there were none; the vote was 12 for, 0 opposed, 0 abstain and 4 absent.

Panel Vote on Formulary Recommendations for Veramyst

The Beneficiary Advisory Panel vote on the Committee's formulary recommendations for Veramyst was:

11 concur; 0 opposed; 0 abstain.

Panel Discussion of P&T Committee Veramyst Implementation Recommendations

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

> "The P&T Committee voted to recommend an effective date of the first Wednesday following a 60-day implementation period in the TMOP and TRRx, and at the MTFs no later than a 60-day implementation period."

Mr. Hutchings expressed the view that in this case, the implementation period is too long. He would suggest that a week would be sufficient. Just a couple of months ago, there were no patients on this medication. Now there are over 600. The longer we wait, the more people will get on the medication and will not receive the initial mailing. He asked if a week would be possible. MAJ Watson said that the earliest date would be when they get a decision from Dr. Cassells, but there may be operational considerations that would come into play. Ms. LeGette said her organization could do a 30-day implementation because of the coordination and forms required.

Mr. Class asked about the timing of the notification letters. Specifically, what is the effective date of when they go out. For example, would new people put on the drug after the first letters go out also be notified; what is the cut-off date. The answer provided was that TMA goes back 120 days to identify patients to be notified, but only one mailing is sent out 60 days prior to implementation. Anyone who is put on after that would not automatically receive a notice.

Mr. Hutchings asked again whether the reason why the co-pay for new users can't be changed immediately is operation or whether it comes from the regulation. MAJ Watson said the reasons are operational. Mr. Hutchings said that if TMA set a 30-day "grandfather" period, after which all new users would have to pay the $22 co-pay, it could guarantee that all users would be included in the 60-day notification.

Mr. Crum suggested that a solution would be to return a message to pharmacists about the change after the decision is made but prior to implementation. CPT Napier said that would done in any event; the PEC provides advisory messaging back to pharmacists.

Ms LeGette suggested that the Automated Profile Review (APR) could be used to identify and advise patients who would be going on to the new drug.

Dr. Schlaifer said she assumes that the recommendation represents the quickest way to get the formulary recommendation implemented. The Panel can say it would like it to be sooner, but if the P&T Committee had the same discussion and came up with this recommendation, she wonders if contrary Panel views would be accomplishing much. CPT Napier said that feedback of this kind is always helpful to the P&T Committee in its future deliberations.

Ms. LeGette also reminded the Panel that 30 days was the time needed to get letters out. There will still be a need for patients to have time after that to make the adjustment.

Panel Vote on Veramyst Implementation Recommendations

The Panel vote on the Veramyst implementation recommendations was:

3 concur; 8 non-concur; 0 abstain.

Two panelists said they would prefer a 30 day implementation period; one said 120 days.

The Panel commented that its preference would be to prevent more people from getting on this product, which is going non-formulary, during the implementation period.

Review of Recently Approved Agents: Tekturna

Clinical Effectiveness Review

CPT Napier presented the P&T Committee's review of a second recently approved agent, Tekturna.

[Insert script, page 16, paragraphs 1-4]

Cost Effectiveness Review

Major Devine then discussed the cost effectiveness review for Tekturna.

[Insert script, page 15, paragraph 5 through page 17 paragraph 1]

P&T Committee Action and Recommendations

Major Devine also briefed the Panel on the P&T Committee's Tekturna recommendations.

[Insert script, page 17 paragraph 2 through end].

P&T Committee Physician Perspective

CPT Napier provided the Panel with the physician's perspective on the P&T Committee's evaluation of Tekturna. He noted that there was some opposition to including this drug on the formulary. He said what was important is that this is a brand new drug on the market that uses a mechanism that hasn't previously been clinically proven. He said some people were uncomfortable with it without more clinical testing. Otherwise, it doesn't seem to offer much more for the cost, which is high compared with other hypertension agents and that there are plenty of agents on the angiotensin receptor blocker (ARB) class for physicians to use to keep their patients' blood pressure under control.

Panel Questions

Ms. Buchta asked whether a new drug has to meet the "hierarchy of evidence" test. CPT Napier said it does and in this case there are a sufficient number of adequately controlled trials to show that it does lower blood pressure.

In response to further panel discussion, Major Devine said that because the drug is relatively new, it is still on its uptake and there is no real feeling for how widely it's going to be adopted in practice.

Mr. Hutchings commented that it sounds like we're leaving it on the formulary because of its novel mechanism.

Ms. Buchta asked whether TMA is putting the product on formulary or leaving it on. The answer provided was that new drugs are automatically included on the formulary, so the Committee is voting to leave it on.

Mr. Class said he didn't think going to medical necessity should be the answer to everything. Major Devine commented that the alternative would be going to step therapy.

Mr. Class said he understands the product involves a different mechanism and gives the providers a choice, but there doesn't seem to be enough evidence here.

Mr. Hutchings commented that the majority of medications taken off the market are brand new medications that we know nothing about. From a safety standpoint, he wouldn't want his mother using such a product, for example. Mr. Hutchings also said he wasn't sure TMA should automatically grant formulary status to new drugs. Mr. Class observed that this drug product has been approved for use by FDA. Mr. Hutchings replied by saying we don't know anything about the long-term outcomes in the case of this drug. When we do know the long-term outcomes of medications that are in a similar category and have a similar effect on blood pressure, he is hesitant to say "yes" to a new product with unknown or limited safety effects. Also the drug is

not cost effective. He thinks it would be safer for the patient and more cost effective to wait for more information.

A PEC member from San Antonio commented by phone that there was a cardiologist at the meeting who also raised questions about the safety. Clinical trials of Tekturna so far — about ten thousand patients — have resulted in studies out to one year. One reason why the Committee decided in favor of formulary placement was that there are several large clinical trials underway that are looking at mortality, with initial results expected in November at a very large American Heart Association meeting. Part of the rationale for the decision was that if the Committee recommended non-formulary placement and there was a positive clinical outcome study in November showing either a reduction in heart failure, hospitalization and mortality, then TMA would have to back-pedal and have another vote on the decision.

Mr. Hutchings asked if there was any reason why consideration of this drug wasn't tabled. Mr. Class observed that it's already on the formulary because it has been approved. Major Devine said the key consideration is the outpatient pharmacy benefit of FDA-approved drugs that require physicians' prescriptions. When a new drug is introduced into the market, the Committee takes it up at the next meeting. Under the regulation, the options are to make it unavailable through formulary until evaluated or to make it formulary until the next meeting when it can be evaluated. This was a drug that had to be evaluated. The next step was to decide whether it belongs in a class already looked at or one not already looked at. This one fell into a class already looked at, and PEC did a clinical and cost effectiveness evaluation to compare it to the other drugs in that class. In this case, regarding the issue of long-term effects and safety, the statute requires the presumption that all drugs in the class are clinically effective unless there is evidence to the contrary. With the trials ongoing, the jury is still out so the tie goes to the statutory presumption that the product is as clinically effective as every other drug in the class and safety concerns haven't been proven yet. The question then boils down to the issue of cost effectiveness versus the drug being a new mechanism of therapy. The Committee decision was to give providers the new method of therapy until we get more information on the clinical effectiveness.

MAJ Watson reminded the Panel that the Director, TMA cannot designate an agent non-formulary without the recommendation of the P&T Committee. So, the recommendation to include it on the formulary will be what goes forward and the Director of TMA does not have the authority to then make it a non-formulary drug. If the Panel wants to non-concur, it can do so, but the Director cannot make the drug non-formulary as a result of the non-concurrence. MAJ Watson noted, however, that the Director TMA can send the recommendation back to the P&T Committee for consideration at their next meeting.

Mr. Partridge said it makes sense to him to come down on the side of supporting the recommendation. FDA approval is in place, trials are coming up and cardiologists are going to be looking at the drug before they prescribe it.

Dr. Schlaifer asked if anything special would be required for the Committee to re-review its decision once the November data are available. i.e., does the Committee have to wait for some period of time. Major Devine answered that the Committee would not have to wait. He said that the PEC would more than likely review a class if a negative aspect comes forth, from the FDA for example. Dr. Schlaifer asked what would happen if the November data showed the

medication to be perfectly safe but doesn't offer added benefits. Would there be an opportunity to review the decision sooner rather than later.

Major Devine said the PEC wouldn't look at just one drug, it would re-review the entire class. It sounds like the decision is stacked against this product to say that there is no long term case information about it. Unfortunately, the same is true about all new products that come on the market. Similarly, this drug doesn't seem cost effective compared to other agents in the class because the majority of the agents in the class (angiotensin converting enzyme inhibitors — ACEs) are generic. When the PEC compared the product to ARBs, it found that there is not a significant cost effectiveness gap.

Another PEC member said his perspective on this drug is that it depends on what you're using it for. If you are using Tekturna just for what it is indicated for, which is to manage blood pressure, and compare it to all the other drugs in this class, you will find that all the drugs in this class have indications for blood pressure. But there is also a separation between drugs that are just indicated for hypertension and that are lower cost and products that have additional clinical outcomes data and are used for indications like prevention of kidney disease, patients with diabetes or treatment of congestive heart failure. Because of these additional clinical outcomes, there is sometimes a premium attached in the form of a higher cost. That's where the decision comes in when you're comparing these products and accounts for the difference between the price of Tekturna and the price of uniform formulary ARBs.

Panel Discussion of P&T Committee Formulary Recommendations for Tekturna

Mr. Washington read the P&T Committee's formulary recommendations for Tekturna:

> "Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations of Aliskiren, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that Aliskiren (Tekturna) be maintained as formulary on the UF."

There was no additional Panel discussion of the Tekturna formulary recommendations but one Panelist asked how long the trials have been going on. A PEC staff member replied by phone that some clinical trails such as this take three to five years. Some safety data was presented at a meeting last month and the data to be released in November will add to that.

Panel Vote on Tekturna Formulary Recommendations

The Beneficiary Advisory Panel vote on the Committee's Tekturna formulary recommendations was:

8 concur; 3 non-concur; 0 abstain.

The comment provided regarding the non-concurring votes was that the members would be more comfortable if this decision were tabled and sent back to the P&T Committee for reconsideration.

Panel Discussion Tekturna Implementation Plan

No implementation plan was required for the Tekturna recommendation because the drug is to remain on formulary.

Closing Remarks

Chairman Washington again expressed the Panel's appreciation for the new TMA notification process and hoped it will continue to be used for future drug classes.

MAJ Watson announced that the next meeting would be January 10, 2008 at the Naval Heritage Center in Washington, D.C.

The meeting was adjourned at 11:40 A.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)
- APR — Automated Profile Review
- ARB — Angiotensin Receptor Blocker (a drug class)
- BAP — Uniform Formulary Beneficiary Advisory Panel (the "Panel" referred to above)
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- BPA — Blanket Purchase Agreement
- CEA — Cost-effectiveness analysis
- C.F.R — Code of Federal Regulations
- CIU — Chronic idiopathic urticaria
- 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
- GHD — Growth hormone deficiency
- GSA — Growth Stimulating Agents (a drug class)
- HMO — Health Maintenance Organization
- IR — Immediate Release (a drug formulation)
- LIP-2 — Antilipidemic agents (a drug class)
- LM — Leukotriene Modifiers (a drug class)
- MHS — Military Health System
- MN — Medical Necessity
- MTF — Military Treatment Facility
- NA — Newer Antihistamines (a drug class)
- NOH — National Institutes of Health
- NNH — Number Needed to Harm
- NNT — Number Needed to Treat
- OTC — Over the counter
- PA — Prior Authorization

- PAR — Perennial allergic rhinitis
- P&T Committee — DOD Pharmacy and Therapeutics Committee
- PDTS — Pharmacy Data Transaction Service
- PEC — DOD Pharmacoeconomic Center
- POS — Point of Service
- RCTs — Randomized Control Trials
- SAR — Seasonal allergic rhinitis
- SGA — Second generation newer antihistimines
- SHOX — Short stature homeobox containing gene deficiency
- 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

18 September 2007 BAP Meeting Script

(LTC Kelly) Good Morning,

I'm LTC Brett Kelly, Director of the PEC. Joining me today from the PEC Clinical Operations staff are CPT Josh Napier, who is our army internist physician and Major Josh Devine, our Air Force pharmacy officer. 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, Major Devine 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 Newer Antihistamines, Leukotriene Modifiers, Growth Stimulating Agents, and two new drugs in previously reviewed classes.
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 Newer Antihistamines or NAs, relative clinical effectiveness evaluation.

NEWER ANTIHISTAMINES (NAs) CLINICAL EFFECTIVENESS

***(CPT Napier)*: Background and members in the class:** The relative clinical effectiveness evaluation was conducted by Dr. Dave Meade, a PEC clinical pharmacist and Dr. Jim McCrary, Lt. Colonel, United States Air Force, a PEC family practice physician. Please look at Table 1 on page 2 of your handout for the drugs in the newer antihistamine class, which include Claritin, Claritin-D, Clarinex, Clarinex D, Allegra, Allegra D, Zyrtec, Zyrtec D, and Semprex D. The products with D in the name are antihistamine products combined with the decongestant pseudoephedrine, or Sudafed. The newer antihistamines decrease the body's histamine response which results in a runny nose, itchy eyes, and hives. The newer agents are more specific for the histamine receptors in the respiratory track and can cause less sedation than some of the older antihistamines such as Benadryl and Atarax. The older antihistamines are not part of this review. We expect a new product Xyzal, which is a derivative of Zyrtec, to enter the market in September or October of 2007.

Relevance to MHS and Utilization: As of July 07, about 265,000 newer antihistamine prescriptions are dispensed monthly in the MHS. This drug class is number five in terms of MHS expenditures, with more than $178 million dollars spent over the 12 month period ending in July 2007. Military treatment facilities or MTF pharmacies dispensed 49% of all newer antihistamine prescriptions, compared to 43% dispensed by the retail network pharmacies and 8% dispensed by the Mail Order.

If you look at figure 1 on page 5 of your handout, Zyrtec is the most commonly prescribed antihistamine across the entire MHS. In the Retail Network Zyrtec and Allegra are most frequently prescribed newer antihistamines. Claritin is available over-the-counter and does not require a written prescription, and is not covered in the Retail Network or Mail Order. At the MTFs, Claritin and Zyrtec are prescribed at about the same rate, with Allegra as the third most used newer antihistamine. Utilization over the next year will change dramatically due to some of the newer antihistamines, including Zyrtec moving to over-the-counter status.

Indications: The newer antihistamines are indicated for the treatment allergic rhinitis, or the runny nose and puffy eyes, that is caused when a person is exposed allergens. Allergic rhinitis is split up into two different diagnoses, depending on what type of allergen the patient is exposed to. Seasonal allergic rhinitis, which is also known as SAR, intermittent allergic rhinitis, or hayfever, is usually caused by outdoor allergens such as tree of grass pollen. Perennial allergic rhinitis, also known as persistent allergic rhinitis, is usually caused by indoor allergens such as dust mites and cockroaches. It is estimated that 20% of patients with allergic rhinitis suffer from SAR, 40% from PAR, and 40% have a mix of PAR with seasonal-exacerbations.

The newer antihistamines are also indicated for the treatment chronic idiopathic urticaria, or CIU, which is when hives form with no apparent cause. To be considered chronic urticaria, the hives must persist for at least six weeks. The incidence of chronic urticaria is very low; occurring in less than one tenth of 1% of the population. While CIU is usually short term in nature, some patients with CIU can have symptoms for more than 20 years.

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

With respect to efficacy:

1. The literature for the treatment of allergic rhinitis is sparse and does not consistently measure the same outcomes.

2. For the treatment of adults with seasonal allergic rhinitis, Zyrtec, Allegra, Claritin, and Clarinex are all superior to placebo in relieving allergic symptoms, such as runny noses and sneezing. Zyrtec, Allegra, Claritin and Clarinex show similar efficacy between agents in relieving symptoms.
3. For the treatment of adults with perennial allergic rhinitis, there is insufficient evidence to suggest that the agents within the class differ in regards to efficacy in the treatment of PAR.
4. In the treatment of chronic idiopathic urticaria, there is very limited evidence. The evidence that is available suggests that Claritin may be more efficacious than Zyrtec, and that Zyrtec may be more efficacious than Allegra. Again, this is based on very limited data.
5. In the treatment of children with seasonal allergic rhinitis and chronic idiopathic urticaria, there insufficient evidence to suggest that the agents differ in efficacy.
6. In the treatment of perennial allergic rhinitis in children ranging between two and six years of age, there is some evidence that shows Zyrtec may be more efficacious than Claritin, however the data are limited.

With respect to safety and tolerability:

7. All the newer antihistamines have similar adverse effect profiles, and are regarded as generally safe and very well tolerated. Claritin is now available over the counter and Zyrtec is expected to be available OTC in a year. OTC status supports the fact that the class is safe.
8. The major advantage of this class over older antihistamines is that in general, the new antihistamines cause less sedation. When given at normal doses, Allegra, Claritin, and Clarinex are less sedating than Zyrtec. When given in the higher doses needed to treat CIU, Claritin and Clarinex are more sedating than Allegra.
9. The addition of pseudoephedrine to the combination products can cause problems for patients with heart conditions, such as coronary heart disease and hypertension, as this ingredient can raise blood pressure.
10. Most drug interactions with the newer antihistamines are minor in nature and do not require dosing changes.
11. With regard to special populations, in pregnant patients, Clarinex and Allegra are rated FDA pregnancy category C. Zyrtec, Claritin and Semprex D are pregnancy category B, which is considered a "safer" pregnancy rating.
12. In lactating patients, Claritin has been deemed compatible with breast-feeding. Infant risk cannot be ruled out when the other newer antihistamines (Zyrtec, Clarinex and Allegra) are used.
13. In pediatric patients, Zyrtec, Allegra, and Clarinex are indicated for use in patients 6 months and older. Claritin can be used in patients two years and older. None of the products that contain pseudoephedrine are indicated for use in children. All the agents, except combination products with pseudoephedrine, are available in several different pediatric dosage forms, such as syrups or suspensions.

Overall Relative Clinical Effectiveness Conclusion: The agents in the newer antihistamine class are similar with regard to clinical efficacy and safety, and are considered to be highly interchangeable. Overall, based on clinical issues alone, there are no compelling reasons to classify any of the newer antihistamine agents as non-formulary under the Uniform Formulary. The P&T Committee concluded (14 for, 0 opposed, 1 abstained, 2 absent) to accept the clinical effectiveness conclusions stated above.

Major Devine will now discuss cost-effectiveness for the newer antihistamines.

NEWER ANTIHISTAMINE (NAs) COST EFFECTIVENESS

(Maj Devine) I conducted the relative cost-effectiveness evaluation for the Newer Antihistamine or NA class. Based on the overall clinical conclusion that the agents within the NA class have similar relative clinical effectiveness, a cost-minimization analysis (CMA) was 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.

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

1) Loratadine (Claritin, generics) was the most cost effective agent with a lower cost per day of treatment than the other newer antihistamines however, the product is OTC and not available in the Retail network
2) Desloratadine (Clarinex) and desloratadine/pseudoephedrine (Clarinex D) were recognized as not cost effective compared to other newer antihistamines.

COMMITTEE ACTION: UF RECOMMENDATION – Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the NAs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstention, and 2 absent) to recommend that loratadine (Claritin, generics), loratadine/pseudoephedrine (Claritin D, generics), fexofenadine (Allegra, generics), fexofenadine/pseudoephedrine (Allegra D), cetirizine (Zyrtec), cetirizine/pseudoephedrine (Zyrtec D), and acrivastine/pseudoephedrine (Semprex-D) be classified as formulary on the UF while desloratadine (Clarinex) and desloratadine/pseudoephedrine (Clarinex D) be classified as non-formulary under the UF

NF Justification:

The P&T Committee recommended that desloratadine (Clarinex) and desloratadine/pseudoephedrine (Clarinex D) be classified as non-formulary under the UF. The Committee's recommendation was based on:

1) The recommended UF agents provide sufficient clinical coverage to manage the needs of the MHS patient population. There is not data to suggest that the efficacy or safety profile of Clarinex or Clarinex D offers a clinical advantage over the UF agents.
2) In addition, the recommended UF products are more cost effective than the products identified for non-formulary placement.

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

MTFs will not be allowed to have Clarinex or Clarinex-D on their local formularies. MTFs will be able to fill non-formulary requests for Clarinex or Clarinex-D 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 Newer Antihistamine 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 Newer Antihistamine therapeutic class presentation. Major Devine and I will gladly answer any questions that you may have.

(CPT Napier) Now we'll move on to the Leukotriene Modifiers clinical effectiveness review.

LEUKOTRIENE MODIFIERS CLINICAL EFFECTIVENESS

(CPT Napier) **Background:** The relative clinical effectiveness evaluation for the Leukotriene Modifiers was conducted by myself, and Dr. Angela Allerman, one of the PEC clinical pharmacists. If you look on Table 1 on page 2 of the handout, you'll see that the class is comprised of three different agents, montelukast (Singulair), zafirlukast (Accolate) and zileuton (Zyflo). All of these drugs are FDA approved for treatment of asthma in adults and children, but Singulair is also approved for the treatment of seasonal and perennial allergic rhinitis, as well as exercise induced asthma.

Relevance to MHS and Utilization: For FY 2006, drug expenditures for the Leukotriene Modifiers were $101 million dollars for the entire Military Health System (MHS), and ranked #16 among therapeutic classes in terms of drug expenditures. The highest utilization of the LM occurs at the MTFs, where over 895,000 prescriptions were dispensed at a cost of $50.3 million in Fiscal Year 2006. The Tricare Retail Network accounted for 506,000 prescriptions dispensed at a cost of $41.6 million, and the Tricare Mail Order Pharmacy had 172,000 prescriptions dispensed at a cost of $9.1 million in FY 06.

On page 5 of your handout, Figure 2 shows the utilization of the Leukotriene Modifiers. Singulair has about 95% of the market share in DoD. There were over 300,000 unique users of Singulair in FY 06, compared to only 3,000 Accolate unique users, and only 300 Zyflo unique users.

Clinical Efficacy: In regard to place in therapy, particularly in asthma therapy, according to the latest guidelines from the NIH's National Heart, Lung, and Blood Institute, leukotriene modifiers are alternative, but not preferred, therapy for the treatment of mild persistent asthma. These agents can also be used as adjunctive (or add-on) therapy with inhaled steroids. However, for youths $\geq$12 years of age and adults, they are not the preferred adjunctive therapy compared to the addition of long acting beta agonists. Zileuton can be used as an alternative, but not preferred adjunctive therapy in adults, due to issues we will discuss later.

In regard to place in therapy for the treatment of allergic rhinitis, specifically the place in therapy of the FDA approved agent Singulair, there is less clarity from available clinical practice guidelines. It is suggested that Singulair has a place as an adjunctive medication, secondary to an nasal corticosteroids such as Flonase or Nasonex, and perhaps secondary to newer antihistamine agents such as Claritin and Zyrtec.

Now I would like to briefly discuss the clinical evidence that is available to support the use of leukotriene modifiers as a treatment for asthma, allergic rhinitis and exercise induced asthma. Published clinical trials support that in the treatment of asthma, leukotriene modifiers are more effective than placebo in controlling asthma symptoms, but are less effective than an inhaled corticosteroid, like Flovent. When added to a long acting beta agonist (like Serevent), the combination was found to be less effective than the combination of an inhaled corticosteroid plus a long acting beta agonist. Evidence shows that addition of a leukotriene modifier to an inhaled corticosteroid provides a modest increase to the benefit of an inhaled corticosteroid therapy alone. There is insufficient evidence to determine whether one leukotriene modifier is more effective at controlling asthma symptoms when compared to another.

As mentioned previously, Singulair is the only leukotriene modifier that is FDA approved to treat allergic rhinitis. There is some limited published data in regard to the use of Accolate in

allergic rhinitis treatment, but the evidence as published is inconclusive and will not be further discussed here. There is no data published to support the use of Zyflo for treatment of allergic rhinitis.

In the treatment of allergic rhinitis, clinical trials demonstrate that Singulair is superior to placebo; however the size of the treatment effect is modest. When compared to newer antihistamines, (Zyrtec and Claritin), Singulair shows relatively similar efficacy. Across the studies, it is demonstrated however, that nasal corticosteroids such as Flonase and Nasonex are clinically superior to both Singulair, and the newer antihistamines in all endpoints studied. Studies also demonstrated that combination therapy consisting of Singulair plus a newer antihistamine was more effective than either agent alone, but still not superior to nasal corticosteroids therapy alone.

In children, Singulair is approved for use in seasonal allergic rhinitis in children age 2 years and older, and in perennial allergic rhinitis for children older than 6 months of age. There is very little clinical effectiveness data published that focuses on children as young as 6 months or 2 years of age, but approval for use among this age group was granted by the FDA based on extrapolation of safety data in older children and based on laboratory evaluation of drug concentrations and drug elimination in younger children.

Singulair is also FDA-approved for the treatment of exercise-induced asthma and studies showed that daily use of monoluekast reduced the airway constriction brought on by exercise. However, other drugs are widely considered as first-line therapy for exercise induced asthma, primarily the short acting beta-agonists, (inhaled drugs like albuterol). Clinical trials have been performed with Singulair versus placebo, and versus a long acting beta agonist (salmeterol), but there are no studies comparing Singulair with albuterol. Singulair may have a unique clinical role in this setting among patients who cannot physically manipulate an inhaler (such as young children) or those who do not get satisfactory improvement from a beta-agonist alone.

In regard to safety and tolerability of the leukotriene modifiers, Zilueton has been associated with liver toxicity, and requires periodic monitoring of labs associated with liver function. This drug is not to be used in patients with active liver disease. Accolate has also been associated with liver toxicity, including liver failure and death. This data, however, comes from spontaneously reported adverse events reports to the FDA and must be interpreted cautiously. Both Accolate and Zyflo are associated with more clinically significant drug-drug interactions than montelukast.

In regard to other important factors, Singulair has a clinical advantage over the other leukotriene modifiers in that it has a greater number of FDA approved indications, including pediatric indications; and it has a less frequent dosing requirement (once daily versus twice daily and four-times-daily for Accolate and Zyflo. In addition, Singulair has alternative dosage formulations such as a chewable tablet, and granules for mixing with soft foods.

Overall Relative Clinical Effectiveness Conclusion - In conclusion, the P&T committee voted (14 for, 0 opposed, 0 abstained, 3 absent) that based on these noted clinical issues alone, Singulair is preferred over Accolate, which in turn is preferred over Zyflo.

Major Devine now will discuss the relative cost effectiveness of the leukotriene modifiers.

LEUKOTRIENE MODIFIERS COST EFFECTIVENESS

(Major Devine) I conducted the relative cost effectiveness evaluation for the LM class. Given the overall clinical conclusion that there was evidence of differences among the LM agents in regard to both safety and efficacy, a cost minimization analysis (CMA) and cost effectiveness analysis (CEA) were performed to determine the relative cost effectiveness of the agents in the class. The CMA 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 P&T Committee voted (14 for, 0 opposed, 1 abstention, and 2 absent) that:

1) Zafirlukast (Accolate) was the most cost effective agent with a lower cost per day of treatment than the other products in this class.
2) Montelukast (Singulair) was more costly than Accolate, but provided additional FDA-approved indications, an improved adverse event profile, multiple dosage forms, and more studies in pediatric patients.
3) Zileuton (Zyflo) was not cost effective compared to the other LM products.

COMMITTEE ACTION: UF RECOMMENDATION – In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the LMs, 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 zafirlukast (Accolate) and montelukast (Singulair) be maintained as formulary on the UF and that zileuton (Zyflo) be classified as non-formulary under the UF.

NF Justification:

The P&T Committee recommended that zileuton (Zyflo) be classified as non formulary under the UF. The Committee's recommendation was based on the following:

1) There is no evidence that Zyflo has a clinical advantage over the products recommended for the UF. Furthermore, Zyflo requires additional monitoring and has concerns of hepatotoxicity.
2) The results of the cost effectiveness analysis showed that Zyflo was not cost effective relative to the other agents in the class.
3) Providers should be able to adequately treat patients with the drugs selected for the UF as they provide sufficient coverage to meet the clinical needs of our patient population.

COMMITTEE ACTION: IMPLEMENTATION PERIOD – The P&T Committee recommended (13 for, 1 opposed, 1 abstained, 2 absent) an effective date of the first Wednesday following a 90-day implementation period at the TMOP and TRRx, and at the MTFs no later than a 90-day implementation period. The implementation period will begin immediately following the approval by the Director, TMA. The one opposing vote cast was that a 60 day implementation period was rationale, due to the low numbers of beneficiaries affected (145 patients).

Approximately 145 (0.07%) beneficiaries will be affected by the UF decision. MTFs will not be allowed to have zileuton (Zyflo) on their local formularies. MTFs will be able to fill non-formulary requests for zileuton (Zyflo) 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 present the DoD P&T Committee's perspective on the UF recommendation for the newer antihistamine class.

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

(CPT Napier) Next on the agenda is the Growth Stimulating Agents (of GSA) clinical effectiveness section.

GROWTH STIMULATING AGENTS (GSAs) CLINICAL EFFECTIVENESS

(CPT Napier) **Background:** The P&T committee evaluated the relative clinical effectiveness of the growth stimulating agents. The clinical review was conducted by me, along with two clinical pharmacists, Drs. Harsha Mistry and Julie Liss. Please turn back to page 2 of your handout, and look at the bottom of Table 1. This class is divided into two subclasses: growth hormone agents (somatropin products), and insulin-like growth factor-1 or IGF-1 agents, of which there is currently only one product called mecasermin. Both somatropin and mecasermin are primarily used for treatment of growth deficiencies in children, however, both the two products differ from each other, and there is also a use for somatropin in adults, which I will discuss.

As you can see from the table, there are multiple somatropin products marketed under different brand names. However, all of them have the exact same active ingredient; human growth hormone, which is derived from a widely used process called recombinant DNA technology. Due to evolving federal regulations regarding this type of drug therapy, known as "biologics" it is permissible that there be multiple brand-name products of essentially the same entity—there are none that are considered "generic".

Relevance to MHS and Utilization: This class of drugs accounted for about $23 million in military health system expenditures in FY 2006. If you look on page 6 of the handout, Figure 3 shows the MHS utilization of the GSAs. The somatropin products Nutropin AQ, Humatrope, and Genotropin have the highest utilization in the MHS at over 150 prescriptions dispensed monthly. The mecasermin product Increlex doesn't show up on the graph, since there were only 12 prescriptions for it in the entire MHS for Y 2006.

Next I'm going to discuss the efficacy and safety of the somatropin products first, and then briefly discuss the information for increlex.

FDA Indications: The largest portion of utilization for somatropin is for childhood growth hormone deficiency. Within the MHS, over 67% of the GSA utilization is in children younger than 17 years of age, and the majority of the pediatric usage is in children 5-14 years of age. The goal of treatment here is to improve the profound short stature that results.

Somatropin is also FDA-approved for the treatment of adult growth hormone deficiency. Since final adult height is attained usually in late adolescence, increasing height is not the goal of treatment. In adults with growth hormone deficiency there is an increase in body fat and a decrease in lean body tissue, which can increase the risk of developing cardiovascular disease. In clinical trials, somatropin treatment resulted in improved metabolic factors such as improved cholesterol profiles, reduced levels of C-reactive protein, a marker of inflammation, improved bone mineral density of the skeleton, and improvements in blood pressure.

Somatropin is FDA approved for a variety of other conditions including Turner Syndrome, small for gestational age, the short stature associated with chronic renal insufficiency, and Prader-Willi syndrome. Recently somatropin received approval for two new growth disorders, short stature homeobox containing gene deficiency or SHOX deficiency, and Noonan syndrome. All of these

conditions have the hallmark clinical feature of short stature, and the primary reason to use somatropin is to increase in growth.

Two other conditions where somtatropin is approved are in AIDS wasting and in short bowel syndrome. For these two conditions, a reduction in lean body mass is the problem, not short stature. Somatropin has proved useful in improving lean body mass in AIDS wasting, and increasing nutrient absorption in for short bowel syndrome.

Efficacy: In terms of clinical efficacy, although there are several branded products from several different companies, somatropin is the active ingredient for all of them. When used at the appropriate doses for the FDA-approved indications, there is no evidence that one product would be more effective than another.

Safety: In regard to safety of somatropin, common adverse events include injection site reactions, hypothyroidism, headaches, fatigue, nausea/vomiting, and fluid retention. Fluid retention can cause problems such as edema of the extremities, pain in the joints or muscles, and even carpal tunnel syndrome. These adverse effects may become severe enough to warrant discontinuation of therapy. Growth hormone therapy is often associated with insulin resistance, which results in an increase in blood sugar. This should be monitored by the physician to avoid the complications of the development of diabetes.

There are rare, yet serious adverse events associated with its use. Because of this, usually only physicians experienced with the use of growth hormone should prescribe somatropin. Traditionally there had been a concern that the overall risk of malignancy is increased with the use of growth hormone products, but over recent years, data has tended to show that this is not the case.

Other Factors: Please turn to the table at the bottom of page 6. There were other important factors considered by the P&T committee. The Committee evaluated the added features that the different manufacturers provide, including educational support to patients and clinicians, as well as product support for refills and technical problems with the delivery mechanisms. These different features are shown in the table.

Differences in the delivery mechanism were an important factor in the clinical efficacy determination. Somatropin is an injection, and is supplied as a liquid in a vial that is withdrawn and then injected with a syringe by the patient, or in a pre-filled syringe ready for injection, or a pen-like device in which the drug can be loaded and delivered with the push of a button. In discussing these issues with physicians in the field, the pen device was the most popular. Additionally, providers felt that to meet the needs of the majority of the MHS patients, a somatropin product that was available in a pen device was considered essential.

Mecasermin: Lastly, we are going to briefly discuss mecasermin, or Increlex. Mecasermin was approved by the FDA in 2005 to treat severe primary deficiency of insulin like growth factor-1. Mecasermin is used only rarely, as this condition affects approximately 6,000 individuals in the United States, and in the MHS there are approximately 7 users. The drug is produced by a single manufacturer.

Mecasermin has unique safety concerns as well that require careful monitoring by an experienced physician. Due to its insulin-like effects, mecasermin can cause low blood sugar in many of the patients who use it. For these reasons, it must be administered around mealtime.

This was the most common adverse event reported in trials of mecasermin, and probably the most serious.

Overall Clinical Effectiveness Conclusion: The P&T Committee voted (15 for, 0 opposed, 0 abstained, 2 absent) to accept the following clinical effectiveness conclusions:

1. Somatropin products appear to be safe and efficacious for the treatment of various growth-related conditions and for a few specialized non-growth related conditions.
2. There are no studies comparing any somatropin product to another for any given indication. Given that all of the products contain the same concentration of bioidentical recombinant human growth hormone, they are unlikely to differ in efficacy for the treatment of growth-related or other disorders.
3. There are potential differences between somatropin products with respect to delivery devices, formulations, and stability/storage requirements. Differences that may favor particular products include availability of a pen device (preferably along with a vial/syringe product); the ability to use the pen device without having to do dose conversions, and the ability to store products at room temperature before or after initial use.
4. Mecasermin is safe and efficacious for severe IGF-1 deficiency, a much rarer condition than growth hormone deficiency. It is the only product available for the treatment of this condition.
5. Based on clinical issues alone, there are no compelling reasons to classify any of the GSA agents as non-formulary under the UF.

This concludes the growth stimulating agents clinical effectiveness discussion. Major Devine will now discuss the cost effectiveness section for the GSAs.

(Major Devine) **GROWTH STIMULATING AGENTS COST-EFFECTIVENESS**

(Maj Devine) The relative cost-effectiveness evaluation for this class was conducted by Eugene Moore, Pharm D. Given the overall clinical conclusion that the somatropin agents within the GSA class have similar relative clinical effectiveness, a cost-minimization analysis (CMA) was employed to assess the relative cost-effectiveness of agents within this therapeutic class. The agents were evaluated on their estimated average annual cost of treating growth hormone deficiency (GHD) weighted across all three points of service.

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

1) Mecasermin (Increlex) and the two somatropin products (Zorbtive and Serostim) have a specific niche in therapy and are offer sufficient value on a cost/mg basis relative to the other agents within the therapeutic class.
2) Tev-Tropin was the most cost-effective somatropin agent based on cost-minimization analysis. However, the product offers fewer features than most other growth stimulating agent product lines.
3) Two product lines of somatropin (Norditropin and Nutropin) offered more features (pen dosage forms, storage at room temperature, and ease of use) at a middle range of cost.

4) The Budget Impact Analysis results showed that the most cost-effective formulary strategy for the somatropin agents was the combination of the Tev-tropin and the Norditropin and Nutropin product lines.

COMMITTEE ACTION: UF RECOMMENDATION – Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations of the GSA agents, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (13 for, 0 opposed, 1 abstained, 3 absent) to recommend that:

1) Tev-tropin, Nutropin, Nutropin AQ, Norditropin, Nortropin Nordiflex, Serostim, Zorbtive, and Increlex be maintained as formulary on the UF, *and*

2) That the Genotropin, Humatrope, Saizen and Omnitrope brands of somatropin be classified as non-formulary under the UF.

NF Justification:

The P&T Committee recommended that the Genotropin, Humatrope, Saizen and Omnitrope brands of somatropin be classified as non-formulary under the UF. The Committee's recommendation was based on:

1) The clinical effectiveness review did not suggest differences in clinical outcomes for the Genotropin, Humatrope, Saizen and Omnitrope, compared to the UF candidates Tev-tropin, Nutropin, Nutropin AQ, Norditropin, Nortropin Nordiflex, Serostim, Zorbtive, and Increlex.

2) A survey of MTF pediatric endocrinology providers suggested that DoD patients with growth hormone deficiency could be successfully treated with the least costly agents, so long as the mix of products included multiple dosage forms.

3) The cost-effectiveness analysis showed that the UF scenario that employed the combination of the Tev-tropin and the Norditropin and Nutropin product lines to be more cost-effective relative to other UF scenarios considered.

COMMITTEE ACTION: IMPLEMENTATION PERIOD – The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period at the TMOP and TRRx, and at the MTFs no later than a 60-day implementation period. The implementation period will begin immediately following approval by the Director, TMA.

MTFs will not be allowed to have the somatropin products Genotropin, Humatrope, Saizen and Omnitrope 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) MN is established. MTFs may (but are not required to) fill a prescription for a non-formulary Somatropin agent written by a non-MTF provider to whom the patient was referred, as long as MN has been established.

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

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

(CPT Napier): Now we will discuss the clinical and cost effectiveness for two new drugs that fall into classes that were previously reviewed for UF placement. First we'll discuss a new nasal steroid, and then a new antihypertensive agent. Please turn to page 3 of your handout, and look at Table 2.

FLUTICASONE FUROATE (VERAMYST) CLINICAL EFFECTIVENESS

(CPT Napier): **Background:** The nasal corticosteroids were originally reviewed at the November 2005 P& T Committee meeting. The UF products are fluticasone propionate (Flonase, generics), mometasone furoate (Nasonex) and flunisolide (Nasarel). The non-formulary nasal corticosteroid agents are beclomethasone dipropionate (Beconase AQ, Vancenase AQ), budesonide (Rhinocort AQ), and triamcinolone (Nasacort AQ, Nasacort HFA). We now have one new product, Veramyst (fluticasone furoate).

Utilization: There have been approximately 650 prescriptions for Veramyst in the MHS, all in the TRRx, since market introduction.

Veramyst: Veramyst is a new nasal corticosteroid marketed by the same manufacturer of fluticasone propionate (or Flonase). Flonase has been available in a generic formulation since February 2006. Both Veramyst and Flonase are FDA-approved for treating symptoms of seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) in adults and children. Veramyst and mometasone (Nasonex) are approved for use in children down to the age of 2 years, compared to 4 years with Flonase. Nasonex is approved for the treatment of nasal polyps, but Veramyst currently does not have that indication.

There is insufficient evidence to determine if there are clinically relevant differences between Veramyst and Flonase. One head-to-head trial in patients older than 12 years of age with SAR showed that Veramyst was not inferior to Flonase in terms of changes from baseline in treating nasal symptoms. Veramyst's adverse effect profile appears similar to Flonase and the other nasal corticosteroids. The P&T Committee also evaluated differences in the delivery device, ease of administration, and particle size of Veramyst compared to other nasal corticosteroids, but did not find a unique advantage or disadvantage relative to fluticasone propionate (Flonase, generics) or mometasone furoate (Nasonex).

Clinical effectiveness Conclusion: The P&T Committee voted (15 for, 0 opposed, 0 abstained, 2 absent) that Veramyst has no clinically significant differences with respect to safety, efficacy, or tolerability, when compared to other nasal corticosteroids included on the UF.

This concludes the Veramyst clinical effectiveness discussion. Major Devine will now discuss the cost effectiveness section for Veramyst.

VERAMYST COST EFFECTIVENESS

(Major Devine) The relative cost-effectiveness evaluation for this drug was conducted by Eugene Moore, Pharm D. A cost minimization analysis (CMA) was employed to evaluate the cost effectiveness of fluticasone furoate (Veramyst) relative to the UF nasal corticosteroids. The results of the CMA showed that the projected weighted average daily cost of fluticasone furoate (Veramyst) was significantly higher than weighted average daily cost of the UF nasal corticosteroids.

Relative Cost Effectiveness Conclusion: The P&T Committee voted (12 for, 0 opposed, 1 abstained, and 4 absent) that fluticasone furoate (Veramyst) was not cost-effective relative to the UF nasal corticosteroids.

COMMITTEE ACTION: UF RECOMMENDATION – Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of Fluticasone furoate (Veramyst), and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (12 for, 0 opposed, 1 abstained, and 4 absent) to recommend that fluticasone furoate (Veramyst) be classified as non-formulary under the UF.

NF Justification:

1. There are no clinically significant differences in the efficacy and safety profiles of the nasal corticosteroids. There was no evidence to suggest that Veramyst offered clinical advantages over the UF nasal corticosteroids.
2. The results of the cost effectiveness analysis showed that Veramyst was not cost effective relative to the other agents in the class.
3. Providers should be able to adequately treat patients with the drugs selected for the UF as they provide sufficient coverage to meet the clinical needs of our patient population

COMMITTEE ACTION: IMPLEMENTATION PERIOD: There have been approximately 650 prescriptions for Veramyst in the MHS, all in the TRRx, since market introduction. The P&T Committee voted (14 for, 0 opposed, 1 abstained, 2 absent) to recommend an effective date of the first Wednesday following a 60-day implementation period in the TMOP and TRRx, and at the MTFs no later than a 60-day implementation period. The implementation period will begin immediately following approval by the Director, TMA. If determined to be operationally feasible, the $22 co-pay would start immediately upon signing of the minutes for new users; the $22 co-pay would go into effect after the 60-day implementation date for current Veramyst users.

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

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

(CPT Napier) Let's move on to our last newly approved drug, aliskiren of Tekturna.

ALISKIREN (TEKTURNA) CLINICAL EFFECTIVENESS

(CPT Napier) **Background:** Aliskiren, or Tekturna, is a new antihypertensive agent with a new mechanism of action. Technically it is defined as a direct renin inhibitor, and it affects the Renin Angiotensin System in the body, which regulates blood pressure. Aliskiren is classified as a renin angiotensin antihypertensive agent (or RAA). The RAA drug class was defined at the May 2007 DoD P&T Committee meeting, and combines three categories of cardiovascular drugs that have already been reviewed for UF placement. These subcategories are described pages 3 and 4 of your handout. The RAAs now includes the direct renin inhibitors, the ACE inhibitors (which were originally reviewed in August 2005), the Angiotensin Blockers or ARBs (which were discussed at the May 2007 meeting), and combinations of ACE inhibitors with calcium channel blockers (which were discussed in February 2006). This new drug classification, RAAs, will encompass any newly approved drug that works via the renin angiotensin system.

With regards to the efficacy and safety of Tekturna, the Committee voted (14 for, 1 opposed, 0 abstained, 2 absent) the following:

a) Tekturna is a new antihypertensive agent with a novel mechanism of action as a direct renin inhibitor.

b) Tekturna's blood pressure lowering effects are similar to those achieved with other antihypertensives, but it does not show improved efficacy compared to other classes of antihypertensive agents.

c) Combination therapy of Tekturna with ACE inhibitors, diuretics and ARBs has shown additive BP lowering effects compared to monotherapy with other antihypertensive agents.

d) Several other safe, once-daily, less costly antihypertensive drugs are available that have proven clinical outcomes (e.g., ACE inhibitors, ARBs, and diuretics).

e) The long-term adverse event profile of Tekturna is unknown; diarrhea is the most commonly reported adverse event and the discontinuation rate is similar to placebo.

f) Clinical outcomes of Tekturna are unknown. Trials are underway, with initial results anticipated in November 2007.

The one opposing vote to the clinical effectiveness conclusion was due to the opinion that there was insufficient clinical experience with Tekturna at this time.

Major Devine will now discuss the cost effectiveness evaluation.

ALISKIREN (TEKTURNA) COST EFFECTIVENESS

(Major Devine): The relative cost-effectiveness evaluation for this drug was conducted by Eugene Moore, Pharm D. A cost minimization analysis (CMA) was employed to evaluate the cost effectiveness of aliskiren (Tekturna). The cost-effectiveness of Tekturna was evaluated relative to ARBs, which were recently evaluated at the May 2007 DoD P&T Committee meeting.

The results of the CMA showed that the projected weighted average daily cost of Tekturna was higher than the weighted average daily cost of the ARBs designated as formulary on the UF.

Cost Effectiveness Conclusion – The P&T Committee concluded (14 for, 0 opposed, 1 abstained, 2 absent) that although Tekturna was somewhat more costly relative to the ARBs designated as formulary on the UF, the P&T Committee was reluctant to designate Tekturna non-formulary at this time given its novel mechanism of action and the anticipated availability of clinical outcomes data that would enable the P&T Committee to more definitively asses its value relative to other antihypertensives. Additionally the Committee recognized the BP control is often inadequate and that often more than one antihypertensive drug is needed.

COMMITTEE ACTION – UF RECOMMENDATION: Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations of aliskiren, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (10 for, 4 opposed, 1 abstained, 2 absent) to recommend that aliskiren (Tekturna) be designated as formulary on the UF.

The four opposing votes were cast due to the opinion that there was insufficient evidence to recommend formulary placement, and that Tekturna was more costly compared to the ARBs.

Since Tekturna was recommended for UF placement, there was no need for an implementation date.

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

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