Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
July 24, 2008
Washington, D.C.

Panel Members Present:

- Robert Washington, Fleet Reserve Association, Chairman
- Morgan Brown, Military Coalition
- Kathryn Buchta, Health Net Federal Services
- Barbara Cohoon, Military Families Association
- John Class, Military Officers Association of America
- 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. Lt Col Thomas Bacon, the Designated Federal Officer (DFO), called the proceedings to order at 8:30 A.M.

Lt Col Bacon indicated this meeting of the Panel has been convened to review and comment on the recommendations of the Department of Defense (DOD) Pharmacy and Therapeutic (P&T) Committee meeting held June 12-13, 2008 in San Antonio, TX.

Agenda

The agenda for this meeting of the Panel is:

- Opening remarks
- Public citizen comments
- Selection of Chairperson for the September 2008-June 2009 Term
- Review and discussion of P&T Committee recommendations for drugs in the following therapeutic classes:
  - 5-Hydroxytriptamine Agonists (Triptans)
    Osteoporosis Agents
  - Designated Newly Approved Drugs
- Wrap-up comments

Opening Remarks

Lt Col Bacon stated that Title 10 United States Code (U.S.C.) section 1074g requires the Secretary of Defense to establish a DOD 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, TRICARE Management Activity (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 the effective dates for changing drugs 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. Casscells).

As guidance to the Panel regarding this meeting, Lt Col Bacon said the role of the BAP 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 chartered functions 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. Casscells's decisions will be available on the TRICARE website in approximately four – six weeks.

Lt Col Bacon 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.

Lt Col Bacon briefly reviewed housekeeping considerations pertaining to the meeting, introduced the presenters from the Pharmacoeconomic Center – CDR Matt Carlberg, Dr. Dave Meade and CDR James Ellzy -- and also introduced the Beneficiary Advisory Panel Members present, including a new member: Morgan Brown, Senior Legislative Assistant for the National Association for Uniformed Services, representing the Military Coalition.

As the first order of business, Lt Col Bacon distributed ballots to Panel members for the election of a new Chairperson for the coming year. The person receiving the most votes is elected Chair of the Panel for a one –year term. In the event of a tie, all ties are voted again. In case of a second tie, the DFO will select a Chair. The results of the vote were announced later in the meeting: after a tie on the first vote, Deborah Fryar was elected Chairperson on the second vote.

Private Citizen Comments

Lt Col Bacon opened the meeting for private citizen comments. There was no response from individuals present at the meeting.

Presentation of Drug Class Reviews

CDR Matt Carlberg, Navy physician consultant to the PEC, then began the presentation of drug class reviews and recommendations from the June meeting of the P&T Committee.

[Insert script, page 1 through first full paragraph on page 2]

REVIEW OF THE TRIPTANS DRUG CLASS

Clinical Effectiveness Review

CDR Carlberg provided the BAP with a summary of the P&T Committee's clinical effectiveness review of the agents in the triptans drug class.

[Insert script from page 2 at "Triptans – Relative Clinical Effectiveness" through end of page]

Cost Effectiveness Review

Dr. Dave Meade then provided the Panel with the results of the cost-effectiveness review.

[Insert script, page 3, "Relative Cost Effectiveness" subsection]

P&T Committee Action and Recommendations

Dr. Meade also presented the P&T Committee's formulary and implementation plan recommendations.

[Insert script, page 3 "Triptans – Uniform Formulary Recommendation" through end of page 4]

Committee Physician Perspective

CDR Ellzy, Vice Chair of the P&T Committee, presented the physician's perspective. He said that the inferior clinical effectiveness of two agents (Frova and Amerge) meant that their non-formulary status was not an issue. In the case of Axert, the Committee found no significant advantages in providing pain relief from migraine headaches. These factors, combined with the fact that all three of these agents were at the bottom of the class in terms of cost effectiveness resulted in the "non formulary" recommendation.

Panel Discussion of P&T Committee Formulary Recommendations for the Triptans Drug Class

Mr. Robert Washington, the Chair of the Beneficiary Advisory Panel, read the P&T Committee's formulary recommendations for this drug class:

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the Triptans, and other relevant factors, the P&T Committee voted to recommend that:

1) Sumatriptan (Imitrex), sumatriptan/naproxen (Treximet), eletripan (Relpax), rizatriptan (Maxalt), and zolmitriptan (Zomig) be classified as formulary on the UF.

2) Almotriptan (Axert), frovatriptan (Frova), and naratriptan (Amerge) be designated as non-formulary under the UF, based on cost effectiveness.

Panel Member Cohoon asked whether or not Axert had been found to be effective for migraine headache. CDR Carlberg replied that the Committee determined that Axert scored well for one of the common measures and that all of the drugs in this class are adult migraine medications. Ms. Cohoon noted that the Committee also found Axert to be most favorable in terms of safety and tolerability and said she believes physicians might want to have such a drug available for those who might have difficulty with the other drugs in the class. Her view is that removing the drug from the formulary is not warranted on the basis of cost alone.

Mr. Hutchings also asked about the analyses supporting safety and tolerability. CDR Carlberg replied that the most substantive meta analysis on efficacy of triptans was performed by Ferrari in 2002. One of the pluses of the analysis was a detailed comparison of adverse events. In terms of the adverse event profile, compared to Imitrex 100 mg, Axert and Amerge were consistently lower in terms of adverse events. However, the confidence intervals were very wide and actually cross zero. They do well in terms of safety and tolerability. However, both were much less side-effects prone than the placebo, so interpreting the data is difficult. Amerge consistently brings up the rear in terms of efficacy.

Mr. Partridge said he agreed with not pulling the drugs off the formulary based on the adverse event profile findings.

Mr. Hutchings commented that if the drug had fewer side effects than the placebo, i.e. less than nothing, that is a statistical anomaly. That makes no sense. There may be a safety and tolerability issue but, if so, it is not statistically significant. Additionally, removing the agents from the formulary doesn't mean that beneficiaries can't get the drug.

Ms. Cohoon noted that it does seem to be considered superior to the others in terms of being pain free for 24 hours. The decision was presented as being based on cost alone. However, the drug seems to be high safety and high efficiency with lower adverse events. If she were a physician, she would be more likely to choose this particular medication.

Panel Vote on Formulary Recommendation for the Triptan Drug Class

Mr. Washington called for the Panel vote on the Triptan drug class. The vote was:

7 Concur, 4 Non-Concur, 0 Abstentions.

Panel Comment on the Formulary Recommendations

Ms. Fryar noted that she appreciates having the detailed minutes and information from the P&T Committee available on the website.

Ms. Cohoon asked that the reasons for the non-concurrence votes be included in the record of Panel actions. The non-concurrence vote was based on the recommendation that Axert be made non-formulary based on cost effectiveness alone. The safety and tolerability factors as well as its apparent efficiency for migraine headaches suggest that it should remain on formulary.

Panel Discussion of P&T Committee Implementation Recommendations for the Triptans Drug Class

Mr. Washington read the implementation recommendations for the Triptan drug class:

> The P&T Committee recommended an effective date of the first Wednesday following a 90-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and in the TRICARE Retail Network Pharmacy Program (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.

Mr. Class asked whether the Panel could assume that for all of the classes being looked at the beneficiaries will be notified individually. The answer provided by the staff present was "yes."

Ms. Fryar said she is not so sure that is the case. She is hearing that physicians are feeling "stuck in the middle" on several of the drug class changes. Patients come back to them when they go to get their prescriptions at retail and find out that their medications have been made non-formulary. So they feel like they are in the middle. Lt Col Bacon said he appreciates the comment and acknowledged that there have been some difficulties. TMA is working to fix them.

Mr. Class noted that there will always be some beneficiaries who won't get notified. There are the people who get their prescriptions during that period of time when approval of the change is pending final approval.

Ms. Fryar noted that physicians, not beneficiaries, are the people doing the calling. They feel as though the system has put them in the middle between the patient and the system without adequate notification. She thinks the problem might lie with the implementation process.

Lt Col Bacon indicated that TMA's intent is to notify those beneficiaries who are affected by having medications removed from the formulary. He will try to track down the source of this issue and resolve it.

Panel Vote on P&T Committee Implementation Recommendations for the Triptans Drug Class

The Panel vote on the 90-day implementation plan was:

11 concur; 0 non-concur.

REVIEW OF THE OSTEOPOROSIS AGENTS DRUG CLASS

Clinical Effectiveness Review

CDR Carlberg provided the BAP with a summary of the P&T Committee's clinical effectiveness review of the agents in the osteoporosis agents drug class.

[Insert script, pages 5, "Osteoporosis Agents -- Relative Clinical Effectiveness" through bottom of page 6]

Cost Effectiveness Review

Dr. Meade next provided the Panel with the results of the cost-effectiveness review for this drug class.

[Insert script, page 7, ""Osteoporosis Agents -- Relative Cost Effectiveness" through first full paragraph on page 8: "Committee Action."]

P&T Committee Action and Recommendations

Dr. Meade presented the P&T Committee's formulary and implementation plan recommendations.

[Insert script, page 8: ""Osteoporosis Agents – Uniform Formulary Recommendations" through bottom of page 8: "Osteoporosis Agents – Implementation Plan" subsection]

Committee Physician Perspective

CDR Ellzy began the physician's perspective on the recommendations in this class by saying that the P&T Committee's discussion was lively and lengthy. The discussion centered around what was proven to be effective or not and on misuses of the drug agents. Moreover, the varied scales used for the analysis caused the Committee to try to compare and contrast different things. He also corrected the report on the Committee vote, saying it was 14 for, 1 opposed, 0 abstain and 0 absent. CDR Ellzy explained that the one person who voted to oppose did so because he wanted to include an additional drug as non-formulary, saying that the medical necessity procedure would cover the niche market for the drug.

Panel Discussion of P&T Committee Formulary Recommendations for the Osteoporosis Agents Drug Class

Mr. Washington read the Committee's formulary recommendations for the osteoporosis agents drug class:

> Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations and other relevant factors, the P&T Committee, based on its professional judgment, voted to recommend that alendronate (Fosamax), alendronate/vitamin D (Fosamax plus D), risedronate (Actonel), risedronate with calcium (Actonel with calcium) ibandronate (Boniva), raloxifene (Evista), teriparatide (Forteo), and recombinant calcitonin (Fortical) be maintained as formulary on the UF, and that salmon-calcitonin (Miacalcin) be designated as non-formulary on the UF.

Dr. Schlaifer said she thinks of Forteo as being somewhat of a niche – third or fourth tier – agent with a very specific patient population. She asked if there was discussion about the formulary being left open for this drug to be prescribed for anyone. CDR Ellzy replied that Forteo was the agent that had been the additional candidate for non-formulary and that the reason was just as Dr. Schlaifer had described. But the Committee, looking at the whole situation, decided to leave it on formulary. Dr. Schlaifer asked for a sense of the discussion. CDR Ellzy said that it took 20-30 minutes just for the vote alone and he is unable to adequately summarize the long discussion that took place.

Mr. Hutchings asked if the Committee discussed using a PA (prior authorization). He said the situation seems the same as for Enbrel or any other really expensive agent. The retail cost difference for Forteo is staggering. He asked why a PA or step therapy wouldn't be more appropriate. Dr. Meade said most of the Committee members were scared of the drug and didn't want to touch it, even those who had prescribed it before.

CDR Ellzy added that most of the physicians on the Committee – who are a very diverse group -- indicated that the drug was not something they would ever consider putting a patient on unless there was a very good reason to do so.

Dr. Schlaifer commented that when physicians say things like that about a drug, it indicates to her that it is the type of drug for which a PA is appropriate. CDR Ellzy replied that the drug would only be used in the event other drugs failed and the Committee questioned the advisability of adding an extra step then for people to move to that drug. Why add a barrier if no one is going to prescribe the drug initially? Mr. Hutchings asked if step therapy wouldn't automatically take care of that issue.

Mr. Hutchings also asked about the statement that Alendronate with vitamin D is generic. Dr. Meade confirmed the statement. Mr. Hutchings asked if a lot of weight in the cost analysis was given to Boniva because of its monthly dosage in terms of better outcome. The answer given was that the cost analysis was based on an external study of the class as a whole and that outcome was not a factor. Mr. Hutchings asked about the statement that improved persistence on bisphosphonate therapy has been shown to be associated with a reduced risk of fracture. CDR Carlsberg replied that observational studies do demonstrate that is the case. Mr. Hutchings asked if the comparison was based on daily versus weekly rather than weekly versus monthly. CDR Carlsberg replied that most of the data available is based on daily dosing and has been translated into standard interval dosing. Mr. Hutchings commented that the material provided makes it seem like Boniva wasn't cost effective until the extended cycle dosing was taken into consideration. Dr. Meade indicated that the manufacturer came in with a pretty good price for Boniva which put it right in the mix. Mr. Hutchings asked if the situation in this class was the same as for the first class presented where, when the price for generics drops below 70 percent of the current price the agent becomes the most cost effective. Dr. Meade replied that it is getting close right now. The retail network is being asked to give generic prices; the price is lower at TMOP.

Mr. Hutchings commented that in this class there are new drugs coming out which add calcium and vitamin D. He wonders if taxpayers should be spending extra money just to give somebody calcium on a daily basis. Patients starting on a brand name product are actually paying a higher co-pay; it costs the beneficiary extra money not to be given a generic.

Panel Vote on Formulary Recommendation for the Osteoporosis Agents Drug Class

Mr. Washington called for the Panel vote on the osteoporosis agents drug class. The vote was:

11 Concur, 0 Non-Concur.

Panel Discussion of P&T Committee Implementation Plan Recommendations for the Osteoporosis Agents Drug Class

The Chair read the implementation plan recommendations for this drug class:

> The P&T Committee recommended an effective date of the first Wednesday following a 90-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and in the TRICARE Retail Network Pharmacy Program (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.

Ms. Owen asked how many people are actually on Miacalcin. The answer given is about 2,900.

Panel Vote on Implementation Plan Recommendation for the Osteoporosis Agents Drug Class

Mr. Washington called for the vote on the implementation plan recommendations. The vote was:

11 Concur, 0 Non-Concur.

REVIEW OF NEWLY APPROVED DRUGS

After the break, CDR Carlberg presented the P&T Committee's recommendations regarding newly-approved drugs in previously reviewed drug classes.

REVIEW OF FENOFIBRATE MELTDOSE (FENOGLIDE)

Clinical Effectiveness Review

CDR Carlberg presented the clinical effectiveness review of Fenoglide.

[Insert script, page 9, first paragraph through subsection titled "Fenofibrate Meltdose (Fenoglide) – Relative Clinical Effectiveness"]

Cost Effectiveness Review

Dr. Meade provided the cost-effectiveness review.

[Insert script, page 9 "Fenofibrate Meltdose (Fenoglide) – Relative Cost Effectiveness" subsection]

P&T Committee Action and Recommendations

Dr. Meade also presented the P&T Committee's formulary recommendations.

[Insert script, page 9, "Fenofibrate Meltdose (Fenoglide) – Uniform Formulary Recommendations" subsection to page 10, "Fenoglide – Committee Physician Perspective"]

Committee Physician Perspective

CDR Ellzy, providing the physician's perspective, said there wasn't a lot of discussion about this drug. The Committee looked at the effectiveness and the packaging advantages and was in agreement with the conclusions.

Panel Discussion of Formulary Recommendation for Fenoglide

The Chair read the Committee's recommendation:

> The P&T Committee, based on its professional judgment, voted to recommend that fenofibrate meltdose (Fenoglide) be maintained as formulary on the Uniform Formulary.

Dr. Schlaifer asked how many drugs have already been changed from a $9.00 co-pay to a $3.00 co-pay under the regulation cited by Dr. Meade in his presentation. The answer was that there are two, one being Triglide.

Panel Vote on Formulary Recommendation for Fenoglide

Mr. Washington called for the Panel vote on the Fenoglide recommendation. The vote was:

11 Concur, 0 Non-Concur.

REVIEW OF NEBIVOLOL (BYSTOLIC)

Clinical Effectiveness Review

CDR Carlberg presented the clinical effectiveness review of Bystolic.

[Insert script, page 11, "Nebivolol (Bystolic) – Relative Clinical Effectiveness" subsection]

Cost Effectiveness Review

Dr. Meade presented the cost-effectiveness review for Bystolic.

[Insert script, page 11, "Bystolic – Relative Cost Effectiveness" subsection]

P&T Committee Action and Recommendations

Dr. Meade next presented the P&T Committee's formulary and implementation plan recommendations.

[Insert script, page 11, "Bystolic – Uniform Formulary Recommendations" subsection through page 12, "Bystolic – Implementation Plan" subsection]

Committee Physician Perspective

CDR Ellzy said the key question in regard to Bystolic was whether it offered anything different or special compared to the many other drugs in the class (Adrenergic Beta Blocking Agents) already on formulary. After comparing Bystolic to the other agents, the Committee concluded it wasn't really different from what MHS already has on formulary and that its cost was significantly higher.

Panel Discussion of Formulary Recommendation for Bystolic

Chairman Washington read the Committee's formulary recommendation for Bystolic:

> The P&T Committee, based on its professional judgment, voted to recommend that nebivolol (Bystolic) be classified as non-formulary on the Uniform Formulary.

Ms. Fryar asked when Bystolic was approved by the FDA. CDR Carlberg said it was approved December 17, 2007 but it didn't launch in time for consideration at the February P&T Committee meeting. It has about 2,500 users so far, all in the retail point of service.

Panel Vote on Bystolic Formulary Recommendation

On the matter of the Bystolic formulary recommendation, the BAP vote was:

11 concur; 0 non-concur.

Panel Discussion of Implementation Plan Recommendation for Bystolic

The Chair then read the Committee's implementation plan recommendation for Bystolic:

> The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and in the TRICARE Retail Network Pharmacy Program (TRRx), and at the MTFs no later than a 60-day implementation period. The implementation period will begin immediately following the approval by the Director, TMA.

There was no Panel discussion of this recommendation.

Panel Vote on Implementation Plan Recommendation for Bystolic

The panel vote on the Bystolic implementation plan recommendation was:

11 concur; 0 non-concur.

REVIEW OF LEVOCETIRIZINE (XYZAL)

Clinical Effectiveness Review

CDR Carlberg provided the BAP with the results of the clinical effectiveness review of Xyzal.

[Insert script, page 13: "Levocetirizine (Xyzal) – Relative Clinical Effectiveness" subsection]

Cost Effectiveness Review

Dr. Meade presented the cost-effectiveness review for Xyzal.

[Insert script, page 13: "Xyzal – Relative Cost Effectiveness" subsection]

P&T Committee Action and Recommendations

Dr. Meade also presented the P&T Committee's formulary and implementation plan recommendations.

[Insert script, page 13: "Xyzal – Uniform Formulary Recommendations" subsection through page 14, "Xyzal – Implementation Plan" subsection]

Committee Physician Perspective

CDR Ellzy informed the Panel that there wasn't much discussion on this recommendation. The Committee looked at the clinical and cost effectiveness. When compared with the other drugs on the formulary and available over the counter in this class the Committee could find no significant advantage for Xyzal.

Panel Discussion of Formulary Recommendation for Xyzal

Chairman Washington read the Committee's implementation plan recommendation for Xyzal:

> The P&T Committee, based on its professional judgment, voted to recommend that Levocetirizine (Xyzal) be classified as non-formulary on the Uniform Formulary.

Ms. Cohoon noted that Xyzal can be used for children up to age six and asked whether there are other drugs in this class that would be available for this age group. The staff indicated that several formulations of available drugs in this class, including Zyrtec, which is OTC, that can be used for children.

Panel Vote on Formulary Recommendation for Xyzal

The Chair called for a Panel vote on the formulary recommendation for Xyzal. The vote was:

11 concur; 0 non-concur.

Panel Discussion of Implementation Plan Recommendation for Xyzal

The Chair read the Committee's implementation plan recommendation for Xyzal:

> The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and in the TRICARE Retail Network Pharmacy Program

(TRRx), and at the MTFs no later than a 60-day implementation period. The implementation period will begin immediately following the approval by the Director, TMA.

Dr. Schlaifer commented that the drug has only been available for a short time and there are already 2000 patients using it. She asked if the 60 days was necessary to inform all of the beneficiaries. Dr. Meade explained that this drug has the utilization that it does because it took the P&T Committee longer than normal to review it. The drug was actually launched last fall.

Mr. Class noted that most of the use comes through the retail point of service, which makes it more difficult to implement quickly.

Mr. Hutchings asked if there was a way MHS could have a two-tiered implementation process under which current users get 60 days but the non-formulary status would be effective immediately for all new users. The concern is with new users who get started in the lag period and that the number of such patients might skyrocket during that time. Dr. Meade answered that such a recommendation would have to go back to the Committee for reconsideration, which would take even more time.

Panel Vote on Implementation Plan Recommendation for Xyzal

The Panel vote on the implementation recommendation for Xyxal was:

11 concur; 0 non-concur.

REVIEW OF ZILEUTON EXTENDED RELEASE (ZYFLO CR)

Clinical Effectiveness Review

CDR Carlberg presented the clinical effectiveness review of Zyflo CR.

[Insert script, page 15, "Zileuton Extended Release (Zyflo CR) -- Relative Clinical Effectiveness" subsection]

Cost Effectiveness Review

Dr. Meade presented the cost-effectiveness review for Zyflo CR.

[Insert script, page 15, "Zyflo CR -- Relative Cost Effectiveness" subsection]

P&T Committee Action and Recommendations

Dr. Meade next provided the BAP with the P&T Committee's formulary and implementation plan recommendations on Zyflo CR.

[Insert script, page 15, "Zyflo CR – Uniform Formulary Recommendations" subsection through page 16, "Zyflo CR – Omplementation Plan" subsection]

Committee Physician Perspective

CDR Ellzy said that, once again, there was very little discussion of this recommendation. The main advantage of the formulation is that it is dosed twice daily instead of four times a day for Zyflo. However, it is still not cost effective.

Panel Discussion of Formulary Recommendation for Zyflo CR

The Chair read the Committee's formulary recommendation for Zyflo CR:

> The P&T Committee, based on its professional judgment, voted to recommend that Zileuton Extended Release (Zyflo CR) be classified as non-formulary on the Uniform Formulary.

Ms. Owen asked was the daily dosage is for Singulair and Accolate. The answer provided was once a day.

Mr. Hutchings commented that immediately after Zyflo IR went third tier, you couldn't get it anymore. All that was available was Zyflo CR and there were a few patients who paid the $22 co-pay that had to change to it. Acknowledging that this is a special case, he asked if there is a way the decision to make Zyflo IR non-formulary could have been carried over into the follow-on CR formulation. The answer provided was that if the formulation is changed, the P&T Committee probably has to look at it anew. Only if the changes are for minor things like packaging could the non-formulary decision be extended. Mr. Hutchings noted this also happened with Benicar and patients were forced to switch to a combination drug with the higher co-pay. Dr. Meade assured the Panel that MHS is catching up with the new drugs, which should alleviate the problem in the future.

Panel Vote on Formulary Recommendation for Zyflo CR

The Chair called for a Panel vote on the formulary recommendation for Zyflo CR. The vote was:

11 concur; 0 non-concur.

Panel Discussion of Implementation Plan Recommendation for Zyflo CR

The Chair read the Committee's implementation plan recommendation for Zyflo CR:

The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and in the TRICARE Retail Network Pharmacy Program (TRRx), and at the MTFs no later than a 60-day implementation period. The implementation period will begin immediately following the approval by the Director, TMA.

There was no further discussion of the recommendation.

Panel Vote on Zyflo CR Implementation Plan Recommendation

The BAP vote on the implementation plan recommendation was:

11 concur; 0 non-concur.

REVIEW OF SIMVASTATIN / NIACIN EXTENDED RELEASE (SIMCOR)

Clinical Effectiveness Review

CDR Carlberg once again presented the results of the clinical effectiveness review for Simcor.

[Insert script, page 17, "Simvastatin / Niacin Extended Release (Simcor) – Relative Clinical Effectiveness" subsection]

Cost Effectiveness Review

The cost-effectiveness review results for Simcor were provided by Dr. Meade.

[Insert script, page 17, "Simcor – Relative Cost Effectiveness" subsection]

P&T Committee Action and Recommendations

Dr. Meade also presented the P&T Committee's formulary recommendations on Simcor.

[Insert script, page 17, "Simcor – Uniform Formulary Recommendations" subsection]

Committee Physician Perspective

CDR Ellzy informed the Panel that this was an easy decision because both of the drugs components – niacin and simvastatin – are already on the Uniform Formulary and the combination was cheaper than the two individual drugs.

Panel Discussion of Formulary Recommendation for Simvastatin/Niacin ER (Simcor)

The Chair of the BAP read the P&T Committee's recommendation:

> The P&T Committee, based upon its collective professional judgment, voted to recommend that simvastatin/niacin ER (Simcor) be classified as formulary on the UF.

Mr. Hutchings asked when niacin will go generic. The answer provided was "not soon." There was no further discussion.

Panel Vote on Formulary Recommendation for Simcor

The Panel vote on the formulary recommendation for Simcor was:

11 concur; 0 non-concur.

REVIEW OF BRIMONIDINE / TIMOLOL MALEATE (COMBIGAN)

Clinical Effectiveness Review

CDR Carlberg presented the results of the clinical effectiveness review for Combigan.

[Insert script, page 18, "Brimonidine / Timolol Maleate (Combigan) – Relative Clinical Effectiveness" subsection]

Cost Effectiveness Review

Dr. Meade presented the cost-effectiveness review.

[Insert script, page 18, "Combigan – Relative Cost Effectiveness" subsection]

P&T Committee Action and Recommendations

Dr. Meade also presented the P&T Committee's recommendations on Combigan.

[Insert script, page 18, "Combigan – Uniform Formulary Recommendations" subsection]

Committee Physician Perspective

Dr. Ellzy said that once again the individual agents were already included on the Uniform Formulary and the combination was offered at a lower price so the Committee agreed it should be on the UF as well.

Panel Discussion of Formulary Recommendation for Brimonidine / Timolol Maleate (Combigan)

The Chair of the BAP read the P&T Committee's recommendation regarding Combigan:

> The P&T Committee, based upon its collective professional judgment, voted to recommend that brimonidine / timolol maleate (Combigan) be classified as formulary under the UF.

Mr. Class asked about the entry on Table 6 of the handout, which shows Combigan being recommended for non-formulary status. CDR Carlberg replied that the table was in error.

There was no further discussion.

Panel Vote on Formulary Recommendation for Brimonidine / Timolol Maleate (Combigan)

The Chair called for the Panel vote on Combigan. The vote was:

11 concur; 0 non-concur.

REVIEW OF OLMESARTAN / AMLODIPENE (AZOR)

Clinical Effectiveness Review

CDR Carlberg next discussed the review of Azor.

[Insert script, p.19, "Olmesartan / Amlodipine (Azor) – Relative Clinical Effectiveness" subsection]

Cost Effectiveness Review

Dr. Meade presented the results of the relative cost effectiveness review

[Insert script, p. 19, "Azor – Relative Cost Effectiveness" subsection]

P&T Committee Action and Recommendations

Dr. Meade also presented the P&T Committee's recommendations on Azor.

[Insert script, page 19, "Azor – Uniform Formulary Recommendation" subsection through page 20, "Azor – Implementation Plan" subsection]

Committee Physician Perspective

CDR Ellzy noted that the individual agents are already on formulary and that an ACE calcium channel blocker combination drug is also already on formulary, although there is no ARB calcium channel blocker. The problem in the case of this drug was that it is not cost effective relative to the other drugs in its category or the individual agents taken separately.

Panel Discussion of Formulary Recommendation for Olmesartan / Amlodipine (Azor)

Chairman Washington read the formulary recommendation for Azor:

> Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of olmesartan / amlodipine (Azor) and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that olmesartan / amlodipine be designated as non-formulary under the UF.

There was no discussion of this recommendation.

Panel Vote on Formulary Recommendation for Olmesartan / Amlodipine (Azor)

The BAP vote on the formulary recommendation for Azor was:

11 concur; 0 non-concur.

Panel Discussion of Implementation Plan Recommendation for Olmesartan / Amlodipine (Azor)

The Chair read the implementation plan recommendation:

The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and in the TRICARE Retail Network Pharmacy Program (TRRx), and at the MTFs no later than a 60-day implementation period. The implementation period will begin immediately following the approval by the Director, TMA.

There was no discussion of the implementation plan recommendation.

Panel Vote on Implementation Plan Recommendation for Olmesartan / Amlodipine (Azor)

The Panel vote on the implementation plan was:

11 concur; 0 non-concur.

REVIEW OF ALISKIREN / HYDROCHLOROTHIAZIDE (TEKTURNA HCT)

Clinical Effectiveness Review

CDR Carlberg presented the results of the clinical effectiveness review of Tekturna HCT.

[Insert script page 21, "Aliskiren / Hydrochlorothiazide (Tekturna HCT) – Relative Clinical Effectiveness" subsection]

Cost Effectiveness Review

Dr. Meade provided the BAP with the results of the cost effectiveness review for Tekturna HCT.

[Insert script page 21, "Tekturna HCT – Relative Cost Effectiveness" subsection]

P&T Committee Recommendations

Dr. Meade presented the P&T Committee's recommendations.

[Insert script p. 21, "Tekturna HCT – Uniform Formulary Recommendation" subsection through page 22]

Committee Physician Perspective

CDR Ellzy said the Committee's discussed the methodology used by this drug to achieve its outcome and that the decision was based mainly on the fact that it uses the same process as Tekturna, which is already on the UF.

Panel Discussion of Formulary Recommendation for Aliskiren / Hydrochlorothiazide (Tekturna HCT)

Chairman Washington read the formulary recommendation for Tekturna HCT:

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

There was no further discussion of this recommendation.

Panel Vote on Formulary Recommendation for Aliskiren / Hydrochlorothiazide (Tekturna HCT)

The Panel vote on the Tekturna HCT recommendations was:

11 concur; 0 non-concur.

Closing Remarks

Lt Col Bacon thanked the Panel for its efforts and commended it on the questions asked. He especially thanked Mr. Robert Washington for his service as Chair of the Panel for the past year.

He noted that MHS has just gone through the process of re-chartering the Beneficiary Advisory Panel. He asked to be notified when events occur – job changes, etc. -- that might change the Panel members' status so that appropriate adjustments can be made to the Panel.

The meeting was adjourned at 10:30 A.M.

Appendix 1

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.

- ABAs — Adrenergic Blocking Agents (a drug class)
- ABs — Alpha blockers
- 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
- BMD — Bone Mineral Density
- BPA — Blanket Purchase Agreement
- CCBs — Calcium Channel Blockers (a drug class)
- CEA — Cost-effectiveness analysis
- C.F.R — Code of Federal Regulations
- 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
- FCP — Federal Ceiling Price
- FDA — U.S. Food and Drug Administration
- HCTZ — Hydrochlorothiazide
- HMO — Health Maintenance Organization
- IR — Immediate Release (a drug formulation)
- IV — Intravenous
- 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)
- NIH — National Institutes of Health
- NNH — Number Needed to Harm
- NNT — Number Needed to Treat
- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DOD Pharmacy and Therapeutics Committee
- PDTS — Pharmacy Data Transaction Service
- PEC — DOD Pharmacoeconomic Center
- POS — Point of Service
- PTH — Parathyroid Hormone (a drug class)
- RAAs — Renin Angiotensin Antihypertensives (a drug class)
- RCTs — Randomized Control Trials
- SERMs — Selective Estrogen Receptor Modulators (a drug class)
- TIBs — Targeted Immunomodulatory Biologics (a drug class)
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TNF — Tumor necrosis factor
- TRRx — TRICARE Retail Pharmacy Program
- UF — DOD Uniform Formulary
- U.S.C. — United States Code
- VA — U.S. Department of Veterans Affairs
- VARR — Voluntary Agreement on Retail Rebates

1 August 2008

Executive Summary

UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL COMMENTS
24 July 2008

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy & Therapeutics (P&T) Committee June 2008 meeting.

1. **5-Hydroxytriptamine Agonists (Triptans) Drug Class:** The P&T Committee recommended the following:

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

1) Sumatriptan (Imitrex), sumatriptan/naproxen (Treximet), eletriptan (Relpax), rizatriptan (Maxalt), and zolmitriptan (Zomig) be classified as formulary on the UF.

2) Almotriptan (Axert), frovatriptan (Frova), and naratriptan (Amerge) be designated as non-formulary under the UF, based on cost effectiveness.

All triptan drugs recommended for inclusion on the UF were covered by Uniform Formulary Voluntary Agreement for Retail Refunds (UF VARR) submissions at or below the Federal Ceiling Price (FCP). (One of the triptan drugs recommended for non-formulary status was also covered by a UF-VARR at or below the FCP, but was not considered cost-effective.)

The P&T Committee recommended that Amerge, Axert, and Frova be classified as non formulary under the UF. The Committee's recommendation was based on the following:

1) Results of the clinical effectiveness evaluation did not support clinically significant advantages to almotriptan (Axert) in providing pain relief from migraine headache compared to the other triptans; and the clinical evaluation found that frovatriptan (Frova) and naratriptan (Amerge) were clinically inferior to the other triptans at providing pain relief, and

2) These three drugs were not cost effective relative to the other triptans.

The P&T Committee recommended an effective date of the first Wednesday following a 90-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and in the TRICARE Retail Network Pharmacy Program (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.

Summary of Panel Vote/Comments:

The Panel voted 7 Concur, 4 Non-Concur regarding the recommendations for formulary and non-formulary agents.

The non-concurrence vote was based on the recommendation that Axert be made non-formulary based on cost effectiveness alone. The safety and tolerability factors as well as its apparent efficiency for migraine headaches suggest that it should remain on formulary.

- The Panel voted 11 Concur, 0 Non-Concur regarding the recommended implementation period of 90 days.

Director, TMA:

☑ These comments were taken under consideration prior to my final decision.

2. **Osteoporosis Agents:** The P&T Committee, based upon its collective professional judgment, voted to recommend that:

1) Alendronate (Fosamax), alendronate/vitamin D (Fosamax plus D), risedronate (Actonel), risedronate with calcium (Actonel with calcium), ibandronate (Boniva), raloxifene (Evista), teriparatide (Forteo), and recombinant calcitonin (Fortical) be maintained as formulary on the UF.
2) Salmon-calcitonin (Miacalcin) be designated as non-formulary on the UF.

All osteoporosis drugs recommended for inclusion on the UF were covered by Uniform Formulary Voluntary Agreement for Retail Refunds (UF VARR) submissions at or below the Federal Ceiling Price (FCP), with the exception of raloxifene, teriparatide, and recombinant calcitonin. These three osteoporosis agents were recommended for inclusion on the UF without UF VARR quotes, due to their unique indications and place in therapy.

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

1) Results of the clinical effectiveness evaluation did not support clinically significant differences in efficacy or incidence of adverse effects between the two calcitonin products, Miacalcin and Fortical.
2) Results from the CMA revealed that recombinant calcitonin (Fortical) is significantly more cost effective than salmon-calcitonin (Miacalcin).

The P&T Committee recommends an effective date of the first Wednesday following a 90-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and TRICARE Retail Pharmacy (TRRx), and at the Military Treatment Facilities (MTF) no later than a 90-day

implementation period. The implementation period will begin immediately following the approval by the Director, TMA.

Summary of Panel Vote/Comments:

- The Panel voted 11 Concur, 0 Non-Concur regarding the recommendations for formulary and non-formulary agents.
- The Panel voted 11 Concur, 0 Non-Concur regarding the recommended implementation period of 90 days.

Director, TMA:

☐ These comments were taken under consideration prior to my final decision.

3. **Recently Approved Agents in Classes Reviewed for the Uniform Formulary:**

Fenofibrate meltdose (Fenoglide): Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (13 for, 0 opposed, 1 abstained, 1 absent) that:

1) fenofibrate meltdose (Fenoglide) be classified as formulary on the UF; and

2) the normal brand cost-share of $9.00 for fenofibrate meltdose (Fenoglide) be lowered to the generic formulary cost share of $3.00 in the retail and mail order points of service.

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

Fenofibrate meltdose (Fenoglide) was covered by the UF VARR submission at or below the FCP.

Nebivolol (Bystolic): The P&T Committee recommended that nebivolol (Bystolic) be classified as non-formulary.

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

1) The relative clinical effectiveness conclusion did not support clinically significant differences in the efficacy or safety profile of Bystolic compared to the other ABA drugs on the Uniform Formulary, and

2) The cost effectiveness evaluation determined that atenolol (Tenormin, generics), carvedilol extended release (Coreg CR) and metoprolol succinate extended release (Toprol XL, generics) remain the most cost effective ABA agents on the UF compared to nebivolol.

The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and TRICARE Retail Pharmacy Network (TRRx), and at the Military Treatment Facilities (MTFs) no later than a 60-day implementation period. The implementation period will begin immediately following approval by the Director, TMA.

Levocetirizine (Xyzal): The P&T Committee recommended that levocetirizine (Xyzal) be classified as non-formulary.

1) The relative clinical effectiveness conclusion did not support clinically significant differences in the efficacy or safety profile of Xyzal compared to the other Newer Antihistamine drugs on the Uniform Formulary, and
2) The cost effectiveness evaluation determined that Xyzal was not cost effective relative to the other Newer Antihistamines.

The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and TRICARE Retail Pharmacy Network (TRRx), and at the Military Treatment Facilities (MTFs) no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Zileuton extended release (Zyflo CR): The P&T Committee recommended that zileuton extended release (Zyflo CR) be classified as non-formulary.

1) The relative clinical effectiveness conclusion did not support clinically significant differences in the efficacy of Zyflo CR compared to the other Leukotriene Modifiers, and that the safety profile of Zyflo CR was inferior to the other drugs in the class, and
2) The cost effectiveness evaluation determined that Zyflo CR was not cost effective relative to the other Leukotriene Modifiers.

The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and TRICARE Retail Pharmacy Network (TRRx), and at the Military Treatment Facilities (MTFs) no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Simvastatin / niacin extended release (Simcor): The P&T Committee recommended that simvastatin / niacin extended release (Simcor) be classified as formulary.

Simvastatin/niacin ER was covered by a UF VARR submission at or below the FCP.

Brimonidine / timolol maleate (Combigan): The P&T Committee recommended that brimonidine / timolol maleate (Combigan) be classified as formulary.

Brimonidine/timolol maleate was covered by a UF VARR submission at or below the FCP.

Olmesartan / amlodipine (Azor): The P&T Committee recommended that olmesartan/amlodipine (Azor) be classified as non-formulary.

1) The relative clinical effectiveness conclusion did not support clinically significant differences in the efficacy of Azor compared to the other RAAs, and
2) The cost effectiveness evaluation determined that Azor was not cost effective relative to the other RAAs or taking the components separately.

The P&T Committee recommended an effective date of the first Wednesday following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and TRICARE Retail Pharmacy Network (TRRx), and at the Military Treatment Facilities (MTFs) no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Aliskiren / Hydrochlorothiazide (Tekturna HCT): The P&T Committee recommended that aliskiren/hydrochlorothiazide (Tekturna HCT) be classified as formulary.

Aliskiren/hydrochlorothiazide was covered by a UF VARR submission at or below the FCP.

Summary of Panel Vote/Comments:

- **Fenofibrate meltdose (Fenoglide):** The Panel voted 11 Concur, 0 Non-Concur regarding the recommendation of formulary status for Fenoglide.
- **Nebivolol (Bystolic):** The Panel voted 11 Concur, 0 Non-Concur regarding the recommendation of non-formulary status for Bystolic.
- The Panel voted 11 Concur, 0 Non-Concur regarding the recommended implementation period of 60 days.
- **Levocetirizine (Xyzal):** The Panel voted 11 Concur, 0 Non-Concur regarding the recommendation of non-formulary status for Xyzal.
- The Panel voted 11 Concur, 0 Non-Concur regarding the recommended implementation period of 60 days.

- **Zileuton extended release (Zyflo CR):** The Panel voted 11 Concur, 0 Non-Concur regarding the recommendation of non-formulary status for Zyflo CR.
- The Panel voted 11 Concur, 0 Non-Concur regarding the recommended implementation period of 60 days.
- **Simvastatin / niacin extended release (Simcor):** The Panel voted 11 Concur, 0 Non-Concur regarding the recommendation of formulary status for Simcor.
- **Brimonidine / timolol maleate (Combigan):** The Panel voted 11 Concur, 0 Non-Concur regarding the recommendation of formulary status for Combigan.
- **Olmesartan / amlodipine (Azor):** The Panel voted 11 Concur, 0 Non-Concur regarding the recommendation of non-formulary status for Azor.
- The Panel voted 11 Concur, 0 Non-Concur regarding the recommended implementation period of 60 days.
- **Aliskiren / Hydrochlorothiazide (Tekturna HCT):** The Panel voted 11 Concur, 0 Non-Concur regarding the recommendation of formulary status for Tekturna.

***Director, TMA*:**

☑ These comments were taken under consideration prior to my final decision.

24 JULY 2008 BENEFICIARY ADVISORY PANEL MEETING

Script

(CDR Carlberg): I'm CDR Matt Carlberg, Navy physician consultant to the PEC. Joining me today from the PEC Clinical Operations staff is Dr. Dave Meade, a civilian clinical pharmacist. Also joining us today is CDR James Ellzy, the Vice DoD P&T Committee chair, who will provide the physician perspective and comment on the recommendations made by the 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).

Dave Meade 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 relative clinical effectiveness and 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. These 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 adrenergic beta-blocking agents, alpha blockers for BPH, and the targeted immunomodulatory biologics; and three 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.
5) The DoD P&T Committee's recommendation regarding UF status of amlodipine (Norvasc), a currently non-formulary medication that recently became generically available at a substantially reduced cost.
6) The DoD P&T Committee's recommendation concerning a process to be followed to facilitate reclassification of non-formulary medications when they become generically available and cost effective relative to similar drugs on the UF.

We've given you a handout which includes the Uniform Formulary recommendations for all the drugs discussed today; this is found in Table 1, pages 2 through 8. 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.

I will now present the 5-hydroxytryptamine drugs (triptans) relative clinical effectiveness evaluation.

TRIPTANS – RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg) The triptan clinical effectiveness review was conducted by me. If look at the top half of Table 1 on page 2 of your handout, you'll see that the P&T Committee evaluated the relative clinical effectiveness of the eight marketed 5-hydroxytryptamine agonists (triptans) in the US, almotriptan (Axert), eletriptan (Relpax), frovatriptan (Frova), naratriptan (Amerge), sumatriptan (Imitrex), sumatriptan/naproxen (Treximet), rizatriptan (Maxalt), and zolmitriptan (Zomig). None of the triptans are available in generic formulations, although generic formulations of sumatriptan are expected in early 2009.

If you turn to Figure 1 found on page 9 of the handout, you'll see the utilization for the triptan class. MHS expenditures for the triptans were approximately $70 million for the time period of May 2007 to April 2008. In terms of total quantity dispensed between May 2007 and April 2008, sumatriptan is the highest utilized triptan in the MHS (~150,000 tablets dispensed/month), followed by zolmitriptan (~60,000 tablets/month), and rizatriptan (~45,000 tablets/month).

Relative Clinical Effectiveness Conclusion

a) With regards to efficacy at providing pain relief at 2 hours, 1) rizatriptan 10 mg (Maxalt) appears superior to the other triptans; 2) almotriptan (Axert), eletriptan (Relpax), sumatriptan (Imitrex) and zolmitriptan (Zomig) have comparable relative effectiveness; 3) frovatriptan (Frova) appears inferior to the other triptans, although these results are based on limited data; 4) naratriptan (Amerge) appears inferior to the other triptans; and 5) sumatriptan/naproxen (Treximet) appears superior to sumatriptan 85 mg, but there is insufficient evidence to suggest clinically relevant differences between Treximet and the other triptans.

b) With regards to other efficacy endpoints, 1) rizatriptan 10 mg (Maxalt) and almotriptan 12.5 mg (Axert) are superior to the other triptans for pain free response at 24 hours; and 2) rizatriptan 10 mg is superior to the other triptans for pain-free response at 2 hours.

c) With regards to safety and tolerability, almotriptan (Axert) and naratriptan (Amerge) had the most favorable adverse event profiles compared to the other triptans. There is only limited data for frovatriptan from the product labeling.

COMMITTEE ACTION: The P&T Committee voted (15 for, 0 opposed, 0 abstained, 0 absent) to accept the clinical effectiveness conclusion.

TRIPTANS – RELATIVE COST EFFECTIVENESS

(Dave Meade) The triptan relative cost effectiveness evaluation for the triptans was conducted by me. In considering the relative cost-effectiveness of pharmaceutical agents in this class, the P&T Committee evaluated the costs of the agents in relation to the efficacy, safety, tolerability, and clinical outcomes of the other agents in the class. Information considered by the P&T Committee included but was not limited to sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost Effectiveness Conclusion:

The cost effectiveness of the triptan agents was evaluated by cost minimization analysis (CMA), cost effectiveness analysis (CEA), and by budget impact analysis (BIA). Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded:

a) Results from the triptan CMA revealed that sumatriptan/naproxen (Treximet) was the most cost effective agent overall. However, sumatriptan (Imitrex) is expected to become the most cost-effective triptan when generic formulations reach the market in early 2009.

b) Results from the 2 hour pain response CEA revealed that 1) sumatriptan/naproxen (Treximet), eletriptan (Relpax) and rizatriptan (Maxalt) formed the efficiency frontier and are the most cost-effective agents; and 2) when the price for generic formulations of sumatriptan (Imitrex) drops below 70% of the current price, sumatriptan and rizatriptan will become the most cost-effective agents.

c) Results from the 2 hour pain-free response CEA yielded results similar to the 2 hour pain response.

d) The BIA evaluated the potential impact of scenarios with selected triptans designated formulary or non-formulary on the UF. Results from the BIA revealed that the scenario that designated almotriptan (Axert), frovatriptan (Frova), and naratriptan (Amerge) as non-formulary under the UF was more favorable to the MHS.

COMMITTEE ACTION: The P&T Committee voted (14 for, 0 opposed, 0 abstained, 1 absent) to accept the cost effectiveness conclusion.

TRIPTANS – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the Triptans, and other relevant factors, the P&T Committee voted (13 for, 0 opposed, 1 abstained, and 1 absent) to recommend that:

1) Sumatriptan (Imitrex), sumatriptan/naproxen (Treximet), eletriptan (Relpax), rizatriptan (Maxalt), and zolmitriptan (Zomig) be classified as formulary on the UF.

2) Almotriptan (Axert), frovatriptan (Frova), and naratriptan (Amerge) be designated as non-formulary under the UF, based on cost effectiveness.

All triptan drugs recommended for inclusion on the UF were covered by Uniform Formulary Voluntary Agreement for Retail Refunds (UF VARR) submissions at or below the Federal Ceiling Price (FCP). (One of the triptan drugs recommended for non-formulary status was also covered by a UF-VARR at or below the FCP, but was not considered cost-effective.)

NF JUSTIFICATION:

The P&T Committee recommended that Amerge, Axert, and Frova be classified as non formulary under the UF. The Committee's recommendation was based on the following:

1) Results of the clinical effectiveness evaluation did not support clinically significant advantages to almotriptan (Axert) in providing pain relief from migraine headache compared to the other triptans; and the clinical evaluation found that frovatriptan (Frova) and naratriptan (Amerge) were clinically inferior to the other triptans at providing pain relief, and

2) These three drugs were not cost effective relative to the other triptans.

TRIPTANS – IMPLEMENTATION PLAN

(Dave Meade) The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday following a 90-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) program and in the TRICARE Retail Network Pharmacy Program (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.

TRIPTANS – COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy):

OSTEOPOROSIS AGENTS RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg) The P&T Committee evaluated the relative clinical effectiveness of the osteoporosis agents currently marketed in the US. The clinical effectiveness review was conducted by CAPT Josh Napier, the former Army physician consultant to the PEC, and Dr. Harsha Mistry, a PEC clinical pharmacist. The bottom part of table 1 on page 2 has the individual drugs in the class, which include the following:

- *Bisphosphonates*: alendronate (Fosamax), alendronate/vitamin D (Fosamax plus D), ibandronate (Boniva), risedronate (Actonel), and risedronate/calcium (Actonel with calcium). Intravenous (IV) zoledronic acid (Reclast) and IV ibandronate (Boniva) were not part of the UF review, as they are not included as a TRICARE pharmacy benefit.
- *Selective estrogen receptor modulators (SERMs)*: raloxifene (Evista)
- *Parathyroid hormone(PTH) 1-34 amino acids:* teriparatide (Forteo)
- *Calcitonin nasal sprays:* calcitonin-salmon (Miacalcin) and recombinant calcitonin (Fortical)

Generic formulations of alendronate and alendronate/vitamin D 2800 IU (Fosamax) became commercially available in 2008. There are no generic formulations of any of the other osteoporosis agents. All the agents are approved for treating osteoporosis; raloxifene (Evista) is also approved for the reduction in risk of invasive breast cancer in postmenopausal women with osteoporosis or those at high risk of invasive breast cancer.

Figure 2 on page 10 of the handout shows the utilization of the osteoporosis drugs. As you can see, Fosamax by far has the highest utilization of the class, at about 20,000 prescriptions dispensed monthly. The 2nd most utilized osteoporosis drug in the MHS is Actonel, at about 40,000 prescriptions dispensed monthly, followed by Evista, at just under 40,000 prescriptions dispensed monthly.

Relative Clinical Effectiveness Conclusion: The P&T Committee concluded that:

a) With regard to changes in bone mineral density (BMD), all the drugs in the bisphosphonates, SERMs, PTH derivative, and calcitonin subclasses increase BMD, but superiority of one drug over another cannot be determined by BMD changes alone.

b) With regard to fracture risk reduction, 1) the supporting evidence for the bisphosphonates is stronger than that available for raloxifene (Evista), teriparatide (Forteo) and the calcitonin nasal sprays (Fortical and Miacalcin); and 2) there is insufficient evidence to determine if there are clinically relevant differences between the drugs in each osteoporosis subclass.

c) With regard to the orally administered bisphosphonates, 1) the bisphosphonates reduce the risk of vertebral fractures to a similar degree, but the data is limited to daily dosing and there is insufficient evidence to determine if there are clinically relevant differences in fracture risk reduction with extended interval dosing regimens; 2) risedronate (Actonel) and IV zoledronic acid have evidence from adequately powered clinical trials that they reduce the risk of non-vertebral and

hip fractures compared to the other bisphosphonates; and 3) there is insufficient evidence to suggest clinically relevant differences between the orally administered bisphosphonates in preventing fractures.

d) With regard to the SERM raloxifene (Evista) and the calcitonin nasal sprays, 1) both subclasses reduce the risk of vertebral fractures, but the data is more limited than that available with the bisphosphonates; and 2) there is no data to suggest clinically relevant efficacy differences between calcitonin-salmon (Miacalcin) and recombinant calcitonin (Fortical).

e) With regard to the PTH derivative teriparatide (Forteo), 1) there is evidence from one clinical trial supporting vertebral and non-vertebral fracture risk reduction; and 2) teriparatide is potentially beneficial in reducing fracture risk in patients experiencing fractures despite bisphosphonate therapy.

f) With regard to safety of the oral bisphosphonates, 1) there is no evidence to suggest that there are clinically relevant differences between alendronate (Fosamax), risedronate (Actonel) and ibandronate (Boniva) in the incidence of gastrointestinal complaints; 2) the overall incidence of osteonecrosis of the jaw with the oral agents is low; and 3) long-term safety data extending out to 10 years is available with alendronate (Fosamax).

g) With regard to tolerability of the oral bisphosphonates, a retrospective observational cohort analysis of 23,044 DoD beneficiaries performed by the Pharmacy Operations Outcomes Team (PORT) compared medication persistence between weekly vs. monthly dosing regimens, based on prescription claims during the year following the initial prescription. The study included all DoD beneficiaries filling initial prescriptions for bisphosphonates at the retail and mail order points of service from 1 Aug 06 to 31 Jan 07. Results of the multivariate logistic regression model were adjusted for age, gender, point of service, TRICARE region, and number of concomitant maintenance medications. The odds of a patient being persistent with treatment (≥80% of days covered based on cumulative days supply) were 18% higher among monthly users compared to weekly users of bisphosphonates (OR 1.18; 95% CI 1.12-1.25). Improved persistence on bisphosphonate therapy has been shown to be associated with a reduced risk of fracture based on observational data, although data from randomized controlled trials supporting a causal relationship are not yet available.

h) With regard to safety and tolerability of the other osteoporosis subclasses, each subclass (SERM, calcitonin and PTH derivative) has unique adverse event profiles.

i) With regard to other factors of the calcitonin nasal sprays, there are no clinically relevant differences between calcitonin-salmon (Miacalcin) and recombinant calcitonin (Fortical), with the exception of differences in the preservative and ease of administration.

COMMITTEE ACTION: The P&T Committee voted (15 for, 0 opposed, 0 abstained, 0 absent) to accept the clinical effectiveness conclusion.

OSTEOPOROSIS AGENTS– RELATIVE COST EFFECTIVENESS

(Dave Meade) The relative cost effectiveness evaluation for the osteoporosis agents was conducted by Dr. Eugene Moore, one of the PEC civilian pharmacists. The relative clinical effectiveness evaluation for the osteoporosis drugs concluded that:

1) the bisphosphonates Fosamax, Actonel and Boniva are highly clinically interchangeable with each other for the treatment of osteoporosis;
2) there is evidence that the extended dosing interval (monthly) bisphosphonates may yield greater rates of persistence than the weekly formulations;
3) the two calcitonin products Fortical and Miacalcin are formulated with identical molecules and are highly clinically interchangeable for their osteoporosis indications; and,
4) teriparatide (Forteo) and raloxifene (Evista) occupy treatment niches for selected patients.

As a result, CMAs were conducted for the bisphosphonate and calcitonin subclasses to compare the relative cost effectiveness of these agents. Additionally a CEA was performed to evaluate the extended dosing interval bisphosphonates. The SERM (Evista) and parathyroid agents (Forteo) were compared to the other subclasses in a further cost analysis.

Relative Cost Effectiveness Conclusion: The P&T Committee concluded the following:

a) Results from the bisphosphonate CMA revealed that ibandronate (Boniva) was the most cost effective agent overall. However, generic formulations of alendronate (Fosamax) have recently become available, and alendronate is expected to become the most cost effective oral bisphosphonate when the generic exclusivity period ends in the third quarter, 2008.

b) Results from the nasal calcitonin CMA revealed that recombinant calcitonin (Fortical) is significantly more cost effective than salmon-calcitonin (Miacalcin).

c) Results from the extended dosing interval bisphosphonate CEA revealed: 1) based on available published literature, improved persistence with extended cycle bisphosphonates would likely result in a small decrease in the risk of fractures; 2) the incremental annual cost per patient using extended dosing interval bisphosphonates is modest; and 3) while extended dosing interval products are slightly more costly, these agents remain cost effective for the treatment of osteoporosis.

d) The cost comparison of teriparatide (Forteo) and raloxifene (Evista) to the other osteoporosis subclasses concluded that 1) raloxifene is slightly more costly than the bisphosphonates and calcitonin; and 2) teriparatide is significantly more costly than bisphosphonates and calcitonin.

e) The BIA evaluated the potential impact of scenarios with selected bisphosphonates, teriparatide (Forteo), and calcitonin products designated formulary or non-formulary on the UF. The BIA results showed that the scenario

that designated the salmon-calcitonin (Miacalcin) as non-formulary on the UF was more favorable to the MHS.

COMMITTEE ACTION: The P&T Committee voted (14 for, 1 opposed, 0 abstained, 0 absent) to accept the cost effectiveness conclusion.

OSTEOPOROSIS AGENTS – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) The P&T Committee, based upon its collective professional judgment, voted (12 for, 1 opposed, 2 abstained, and 0 absent) to recommend that:

1) Alendronate (Fosamax), alendronate/vitamin D (Fosamax plus D), risedronate (Actonel), risedronate with calcium (Actonel with calcium), ibandronate (Boniva), raloxifene (Evista), teriparatide (Forteo), and recombinant calcitonin (Fortical) be maintained as formulary on the UF.

2) Salmon-calcitonin (Miacalcin) be designated as non-formulary on the UF.

All osteoporosis drugs recommended for inclusion on the UF were covered by Uniform Formulary Voluntary Agreement for Retail Refunds (UF VARR) submissions at or below the Federal Ceiling Price (FCP), with the exception of raloxifene, teriparatide, and recombinant calcitonin. These three osteoporosis agents were recommended for inclusion on the UF without UF VARR quotes, due to their unique indications and place in therapy.

NF JUSTIFICATION:

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

1) Results of the clinical effectiveness evaluation did not support clinically significant differences in efficacy or incidence of adverse effects between the two calcitonin products, Miacalcin and Fortical.

2) Results from the CMA revealed that recombinant calcitonin (Fortical) is significantly more cost effective than salmon-calcitonin (Miacalcin).

OSTEOPOROSIS AGENTS – IMPLEMENTATION PLAN

(Dave Meade) The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday following a 90-day implementation period in 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.

OSTEOPOROSIS AGENTS - COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy):

NEWLY APPROVED DRUGS

(CDR Carlberg) – There are 8 newly approved drugs that fall into classes previously reviewed for the Uniform Formulary. We'll start with Fenoglide, and go in the order starting on page 3 of your handout

FENOFIBRATE MELTDOSE (FENOGLIDE) – RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg) The clinical effectiveness evaluation was conducted by Dr. Angela Allerman, one of the civilian pharmacists at the PEC. Fenoglide is a new formulation of fenofibrate that is FDA-approved for treating hyperlipidemia and mixed dyslipidemia. As shown in Table 2 of page 3 of your handout, Fenoglide is part of the Antilipidemic-part 2, or LIP-2, drug class.

Relative Clinical Effectiveness Conclusion: The P&T Committee concluded that 1) there is no evidence to suggest that there are clinically relevant differences in the efficacy, safety and clinical outcomes of Fenoglide compared to other fenofibrate formulations, as they all contain the same active ingredient. 2) In terms of packaging and storage requirements, Fenoglide has advantages over fenofibrate insoluble drug delivery microparticle (Triglide) in that it is available in 90 count bottles and does not require dispensing in moisture-proof containers.

COMMITTEE ACTION: The P&T Committee voted (14 for, 0 opposed, 0 abstained, 1 absent) to accept the clinical effectiveness conclusion.

FENOGLIDE – RELATIVE COST EFFECTIVENESS

(Dave Meade) The Fenoglide relative cost effectiveness evaluation was conducted by LTC Chris Conrad, the Army pharmacy consultant. A cost CMA was employed to evaluate the cost effectiveness of fenofibrate meltdose (Fenoglide). The cost effectiveness of Fenoglide was evaluated relative to the following agents: Triglide (currently the most cost effective UF fenofibrate) and Tricor. The results of the CMA showed that the projected weighted average daily cost of Fenoglide was significantly lower than the weighted average daily cost of Triglide or Tricor.

Relative Cost Effectiveness Conclusion: The P&T Committee concluded that fenofibrate meltdose (Fenoglide) is cost effective relative to the evaluated agents in the LIP-2 class. The weighted average cost of Fenoglide is more cost effective relative to Triglide or Tricor.

COMMITTEE ACTION: The P&T Committee voted (14 for, 0 opposed, 0 abstained, 1 absent) to accept the cost effectiveness conclusion.

FENOGLIDE – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (13 for, 0 opposed, 1 abstained, 1 absent) that:

1) fenofibrate meltdose (Fenoglide) be classified as formulary on the UF; and

2 the normal brand cost-share of $9.00 for fenofibrate meltdose (Fenoglide) be lowered to the generic formulary cost share of $3.00 in the retail and mail order points of service.

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

Fenofibrate meltdose (Fenoglide) was covered by the UF VARR submission at or below the FCP.

FENOGLIDE - COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy)....

NEWLY APPROVED DRUGS – NEBIVOLOL (BYSTOLIC) – RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg) The Bystolic clinical effectiveness evaluation was conducted by me. Nebivolol (Bystolic) is an Adrenergic Beta-Blocking Agent (ABA) that is FDA-approved for treatment of hypertension. Table 3 on page 4 of your handout shows the entire ABA class.

Relative Clinical Effectiveness Conclusion - The P&T Committee concluded that nebivolol (Bystolic) does not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over other ABA agents currently included on the UF.

COMMITTEE ACTION: The P&T Committee voted 15 for, 0 opposed, 0 abstained, 0 absent) to accept the clinical effectiveness conclusion.

BYSTOLIC – RELATIVE COST EFFECTIVENESS

(Dave Meade) The Bystolic relative cost effectiveness evaluation was evaluated by LTC Chris Conrad. P&T Committee evaluated the relative cost effectiveness of nebivolol in relation to efficacy, safety, tolerability, and clinical outcomes of the other agents in the class, particularly to the following ABA medications: atenolol (Tenormin, generics), carvedilol extended release (Coreg CR) and metoprolol succinate extended release (Toprol XL, generics).

A CMA was employed to determine the cost effectiveness of nebivolol (Bystolic) relative to atenolol, Coreg CR and metoprolol succinate ER. Results of the CMA showed that the projected weighted average daily cost of nebivolol was significantly higher than its ABA comparators.

Relative Cost Effectiveness Conclusion: P&T Committee, based upon its collective professional judgment, voted that the weighted average daily cost of nebivolol (Bystolic) was significantly higher than the weighted average daily cost of atenolol (Tenormin, generics), carvedilol extended release (Coreg CR), or metoprolol succinate extended release (Toprol XL, generics).

COMMITTEE ACTION: The P&T Committee voted 15 for, 0 opposed, 0 abstained, 0 absent) to accept the cost effectiveness conclusion stated.

BYSTOLIC – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness of nebivolol, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (14 for, 0 opposed, 1 abstained, 0 absent) to recommend that nebivolol (Bystolic) be designated as non-formulary on the UF.

NF Justification

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

1) The relative clinical effectiveness conclusion did not support clinically significant differences in the efficacy or safety profile of Bystolic compared to the other ABA drugs on the Uniform Formulary, and
2) The cost effectiveness evaluation determined that atenolol (Tenormin, generics), carvedilol extended release (Coreg CR) and metoprolol succinate extended release (Toprol XL, generics) remain the most cost effective ABA agents on the UF compared to nebivolol.

BYSTOLIC – IMPLEMENTATION PLAN

(Dave Meade) The P&T Committee voted (14 for, 0 opposed, 1 abstained, 0 absent) to recommend an effective date of the first Wednesday following a 60-day implementation period in TMOP and TRRx, and at MTFs no later than a 60-day implementation period. The implementation period will begin immediately following approval by the Director, TMA.

BYSTOLIC – COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy)…

NEWLY APPROVED DRUGS – LEVOCETIRIZINE (XYZAL) - RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg) The next new drug, levocetirizine, Xyzal is found in the top part of Table 4 on page 5 of the handout. The relative clinical effectiveness evaluation was conducted by Lt Col Jim McCrary, the Air Force physician consultant. Xyzal is a Newer Antihistamine (NA) that is the R-enantiomer of cetirizine. It is FDA-approved in adults and in children as young as six years of age for the treatment of seasonal and perennial allergic rhinitis, and chronic idiopathic urticaria.

Relative Clinical Effectiveness Conclusion - The Committee voted that levocetirizine (Xyzal) did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness or clinical outcome over other NAs included on the UF.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the clinical effectiveness conclusion.

XYZAL – RELATIVE COST EFFECTIVENESS

(Dave Meade): The relative cost effectiveness evaluation of Xyzal was conducted by LTC Chris Conrad. The P&T Committee evaluated the relative cost effectiveness of levocetirizine (Xyzal) in relation to efficacy, safety, tolerability, and clinical outcomes of other agents in the class.

A CMA was employed to determine the cost effectiveness of levocetirizine relative to other NAs: loratadine (OTC Claritin, generics), cetirizine (OTC Zyrtec, generics), fexofenadine (Allegra, generics), and desloratadine (Clarinex). The results of the CMA revealed that the weighted average cost per day of levocetirizine is significantly higher than loratadine, cetirizine, and fexofenadine, but is significantly lower than the non-formulary NA desloratadine (Clarinex).

Relative Cost Effectiveness Conclusion: The Committee voted that levocetirizine (Xyzal) is not cost effective relative to the other UF Newer Antihistamines.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 0 absent to accept the cost effectiveness conclusion.

XYZAL – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of levocetirizine (Xyzal) and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (13 for, 0 opposed, 0 abstained, 2 absent) to recommend that levocetirizine be designated as non-formulary under the UF.

NF Justification

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

1) The relative clinical effectiveness conclusion did not support clinically significant differences in the efficacy or safety profile of Xyzal compared to the other Newer Antihistamine drugs on the Uniform Formulary, and

2) The cost effectiveness evaluation determined that Xyzal was not cost effective relative to the other Newer Antihistamines.

XYZAL – IMPLEMENTATION PLAN

(Dave Meade): The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to recommend an effective date of the first Wednesday following a 60-day implementation period in the TMOP and TRRx, and no later than a 60-day implementation period at MTFs. The implementation period will begin immediately following approval by Director, TMA.

XYZAL – COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy)…….

NEWLY APPROVED DRUGS – ZILEUTON EXTENDED RELEASE (ZYFLO CR) - RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg) Please look at the bottom of table 4 on page 5 of your handout, where you will see Zyflo CR and the remainder of the Leukotriene Modifier class. The relative clinical evaluation of Zyflo CR was conducted by Lt Col Jim McCrary. Zileuton extended release (Zyflo CR) is a new formulation of zileuton immediate release (Zyflo) that is dosed twice daily, rather than four times daily. It is FDA-approved for the treatment of asthma in adults and in children as young as 12 years of age.

Relative Clinical Effectiveness Conclusion - The Committee voted that zileuton extended release (Zyflo CR) did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness or clinical outcome over other Leukotriene Modifiers (LMs) included on the UF.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the clinical effectiveness conclusion.

ZYFLO CR – RELATIVE COST EFFECTIVENESS

(Dave Meade) The relative cost effectiveness evaluation for Zyflo CR was conducted by LTC Chris Conrad. The Committee evaluated the relative cost effectiveness of zileuton extended release (Zyflo CR) in relation to efficacy, safety, tolerability, and clinical outcomes of the other agents in the LM class.

A CMA was employed to evaluate the cost effectiveness of zileuton extended release (Zyflo CR) relative to montelukast (Singulair), zafirlukast (Accolate), and zileuton immediate release (Zyflo). The results of the CMA demonstrated that the projected weighted average daily cost of zileuton extended release was significantly higher than the weighted average daily cost of the comparators within the LM class.

Relative Cost Effectiveness Conclusion: The Committee voted that zileuton extended release (Zyflo CR) is not cost effective relative to the other agents in the LM class. The weighted average cost of montelukast (Singulair), zafirlukast (Accolate) and zileuton immediate release (Zyflo) is more cost effective relative to zileuton extended release

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the cost effectiveness conclusion.

ZYFLO CR – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of zileuton extended release (Zyflo CR) and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (13 for, 0 opposed, 0 abstained, 2 absent) to recommend that zileuton extended release be designated as non-formulary under the UF.

NF Justification

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

1) The relative clinical effectiveness conclusion did not support clinically significant differences in the efficacy of Zyflo CR compared to the other Leukotriene Modifiers, and that the safety profile of Zyflo CR was inferior to the other drugs in the class, and
2) The cost effectiveness evaluation determined that Zyflo CR was not cost effective relative to the other Leukotriene Modifiers.

ZYFLO CR – IMPLEMENTATION PLAN

(Dave Meade) The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to recommend an effective date of the first Wednesday following a 60-day implementation period in the TMOP and TRRx, and no later than a 60-day implementation period at MTFs. The implementation period will begin immediately following approval by Director, TMA.

XYZAL – COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy)

NEWLY APPROVED DRUGS – SIMVASTATIN / NIACIN EXTENDED RELEASE (SIMCOR) - RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg): Simcor is s part of the Antilipidemic part 1 (or LIP-1) class, found in Table 5 on page 6 of your handout. Simcor is the combination of 40 mg simvastatin (Zocor, generics) with 500-, 750- or 1000- mg of niacin extended release (Niaspan). The clinical effectiveness evaluation of Simcor was conducted by Lt Col Jim McCrary.

Simcor is approved by the FDA for patients with hyperlipidemia to raise HDL concentrations, and to lower LDL, triglyceride, non-HDL, and total cholesterol concentrations, when monotherapy is inadequate.

Relative Clinical Effectiveness Conclusion -The Committee voted that there is insufficient evidence to suggest if there are clinically relevant differences between simvastatin/niacin extended release Simcor) and the other statins and niacin in terms of efficacy, and that in terms of safety and tolerability, Simcor appears comparable to giving the simvastatin and niacin components separately.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the clinical effectiveness conclusion.

SIMCOR – RELATIVE COST EFFECTIVENESS

(Dave Meade): The relative cost effectiveness evaluation for Simcor was conducted by LTC Chris Conrad. The P&T Committee evaluated the relative cost effectiveness of simvastatin/niacin ER (Simcor) in relation to efficacy, safety, tolerability, and clinical outcomes of other agents in the Antilipidemic-I (LIP-1) class.

A CMA was employed to evaluate the cost effectiveness of simvastatin/niacin ER relative to simvastatin (Zocor, generics), niacin ER (Niaspan), lovastatin/niacin ER (Advicor) and the combination of the individual components of Simcor (simvastatin plus Niaspan). The results of the CMA showed that the projected weighted average daily cost of Simcor was significantly less than the weighted average daily cost of its comparators.

Relative Cost Effectiveness Conclusion: The Committee voted that simvastatin/niacin ER (Simcor) is cost effective relative to the evaluated agents in the LIP-1 class.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the cost effectiveness conclusion.

SIMCOR – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of simvastatin/niacin ER (Simcor) and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (13 for, 0 opposed, 0 abstained, 2 absent) to recommend that simvastatin/niacin ER be classified as formulary on the UF.

Simvastatin/niacin ER was covered by a UF VARR submission at or below the FCP.

SIMCOR – COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy)…..

NEWLY APPROVED DRUGS – BRIMONIDINE / TIMOLOL MALEATE (COMBIGAN) - RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg): Table 6 on page 7 of your handout contains Combigan and the other Glaucoma Agents. The relative clinical effectiveness evaluation was conducted by Lt Col Jim McCrary. Combigan is a combination ophthalmic product that contains the alpha-2 adrenergic agonist brimonidine 0.02% (Alphagan, generics) with the beta blocker timolol maleate 0.05% (Timoptic, generics). Combigan is approved for twice daily use for the reduction of elevated intraocular pressure in patients with ocular hypertension or glaucoma who require adjunctive or replacement therapy.

Relative Clinical Effectiveness Conclusion - The Committee voted that while brimonidine/timolol (Combigan) offers a convenience to the patient in terms of ease of administration, there is currently insufficient evidence to suggest if there are clinically relevant differences between Combigan and the other Glaucoma Agents in terms of efficacy. In terms of safety and tolerability, Combigan appears comparable to administering brimonidine and timolol as separate products dosed twice daily.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the clinical effectiveness conclusion.

COMBIGAN – RELATIVE COST EFFECTIVENESS

(Dave Meade) The P&T Committee evaluated the relative cost effectiveness of brimonidine/timolol ophthalmic solution (Combigan) in relation to efficacy, safety, tolerability, and clinical outcomes of the other agents in the class. The cost effectiveness evaluation was conducted by LTC Chris Conrad.

A CMA was employed to evaluate the cost effectiveness of Combigan relative to timolol maleate (Timoptic, generics), brimonidine (Alphagan, generics), dorzolamide/timolol (Cosopt), and the single ingredient agents of Combigan (timolol maleate and brimonidine). The results of the CMA showed that the projected weighted average daily cost of Combigan was significantly lower than its comparators.

Relative Cost Effectiveness Conclusion: The Committee voted that the projected weighted average daily cost of Combigan was significantly lower than the weighted average daily cost of dorzolamide/timolol (Cosopt), or the pairings of the individual brimonidine and timolol components.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the cost effectiveness conclusion.

COMBIGAN – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade): Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of brimonidine/timolol maleate (Combigan) and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (13 for, 0 opposed, 0 abstained, 2 absent) to recommend that brimonidine/timolol maleate (Combigan) be classified as formulary under the UF.

Brimonidine/timolol maleate was covered by the UF VARR submission at or below the FCP.

COMBIGAN – COMMITTEE PHYSICIAN PERSPECTIVE *(CDR Ellzy)*

NEWLY APPROVED DRUGS – OLMESARTAN / AMLODIPINE (AZOR) RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg): The next drug, Azor is part of a large class of drugs, the Renin Angiotensin Antihypertensive agents (RAAs) that is comprised of several subclasses which are found on Table 7 on page 8 of your handout. The Azor clinical effectiveness evaluation was done by Angela Allerman.

Azor is the combination of the angiotensin receptor blocker (ARB) olmesartan with the dihydropyridine calcium channel blocker (DHP CCB) amlodipine. It is FDA-approved for treating hypertension.

Relative Clinical Effectiveness Conclusion - The Committee voted that while olmesartan/amlodipine (Azor) offers a convenience to the patient in terms of decreased tablet burden and simplified medication regimen, it does not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness or clinical outcome over other Renin Angiotensin Antihypertensives (RAAs) included on the UF.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the clinical effectiveness conclusion.

AZOR – RELATIVE COST EFFECTIVENESS

(Dave Meade) The P&T Committee evaluated the relative cost effectiveness of olmesartan/amlodipine (Azor) in relation to efficacy, safety, tolerability, and clinical outcomes of the other agents in the RAA class, particularly the ARBs. LTC Chris Conrad conducted the Azor relative cost effectiveness evaluation.

A CMA was employed to evaluate the cost effectiveness of olmesartan/amlodipine relative to telmisartan (Micardis), the most cost-effective UF ARB; generic amlodipine (Norvasc), a UF DHP-CCB; valsartan/amlodipine (Exforge); and to the combination of the individual components of telmisartan plus generic amlodipine. The results of the CMA demonstrated that the projected weighted average daily cost of Azor was significantly higher than the weighted average daily cost of combined individual agents (telmisartan plus generic amlodipine).

Relative Cost Effectiveness Conclusion: The Committee voted that olmesartan/ amlodipine (Azor) is not cost effective relative to the other UF agents in the RAA class. The weighted average cost of combined individual agents (the most cost-effective ARB telmisartan and the UF generic DHP CCB amlodipine) is more cost effective relative to Azor.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the cost effectiveness conclusion.

AZOR – UNIFORM FORMULARY RECOMMENDATION

(Dave Mead) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of olmesartan/amlodipine (Azor) and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (13 for, 0 opposed, 0 abstained, 2 absent) to recommend that olmesartan/amlodipine be designated as non-formulary under the UF.

NF Justification

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

1) The relative clinical effectiveness conclusion did not support clinically significant differences in the efficacy of Azor compared to the other RAAs, and
2) The cost effectiveness evaluation determined that Azor was not cost effective relative to the other RAAs or taking the components separately.

AZOR – IMPLEMENTATION PLAN

The P&T Committee voted 13 for, 0 opposed, 0 abstained, 2 absent) to recommend an effective date of the first Wednesday following a 60-day implementation period in the TMOP and TRRx, and no later than a 60-day implementation period at MTFs. The implementation period will begin immediately following approval by Director, TMA.

AZOR –COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy)

NEWLY APPROVED DRUGS – ALISKIREN / HYDROCHLOROTHIAZIDE (TEKTURNA HCT) - RELATIVE CLINICAL EFFECTIVENESS

(CDR Carlberg): The second row of Table 7 on page 8 lists Tekturna HCT and the other direct renin inhibitors, which are part of the RAA class. The clinical effectiveness evaluation for Tekturna HCT was conducted by Angela Allerman.

Tekturna HCT contains the renin inhibitor aliskiren with the diuretic hydrochlorothiazide (HCTZ). It is FDA-approved for treating hypertension. Preliminary results of clinical outcomes trials with aliskiren evaluating benefits in addition to blood pressure reduction have been positive.

Relative Clinical Effectiveness Conclusion: The Committee voted that while aliskiren/HCTZ offers a convenience to the patient in terms of decreased tablet burden and simplified medication regimen, there is insufficient evidence to suggest that the blood pressure lowering effect of aliskiren/HCTZ would be significantly greater than that achieved with other antihypertensive fixed-dose combinations. In terms of safety and tolerability, Tekturna HCT appears comparable to administering the aliskiren and HCTZ components separately

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the clinical effectiveness conclusion.

TEKTURNA HCT – RELATIVE COST EFFECTIVENESS

(Dave Meade) The P&T Committee evaluated the relative cost effectiveness of aliskiren/HCTZ (Tekturna HCT) in relation to efficacy, safety, tolerability, and clinical outcomes of the other agents in the RAAs class, particularly the ARBs. LTC Chris Conrad conducted the relative cost effectiveness evaluation.

A CMA was employed to evaluate the cost effectiveness of aliskiren/HCTZ relative to the renin inhibitor aliskiren (Tekturna) and the angiotensin receptor blockers (ARBs), which were evaluated at the May and August 2007 DoD P&T Committee meetings. The results of the CMA showed that the projected weighted average daily cost of aliskiren/HCTZ (Tekturna HCT) was higher than the weighted average daily cost of the ARBs designated as formulary on the UF, but similar to the UF agent aliskiren (Tekturna).

Relative Cost Effectiveness Conclusion: The Committee voted that the projected weighted average daily cost of aliskiren/HCTZ (Tekturna HCT) was comparable to the renin inhibitor aliskiren (Tekturna), and higher than the weighted average daily cost of ARBs designated as formulary within the RAAs class on the UF.

COMMITTEE ACTION: The P&T Committee voted (13 for, 0 opposed, 0 abstained, 2 absent) to accept the cost effectiveness conclusion.

TEKTURNA HCT – UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of aliskiren/HCTZ (Tekturna HCT) and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (13 for, 0 opposed, 0 abstained, 2 absent) that although aliskiren/HCTZ was somewhat more costly relative to the ARBs designated as formulary in the RAA class, Tekturna HCT was

recommended to be classified as formulary on the UF, due to the novel mechanism of action of the aliskiren component and preliminary positive outcomes data.

Aliskiren/hydrochlorothiazide was covered by the UF VARR submission at or below the FCP.

AZOR – COMMITTEE PHYSICIAN PERSPECTIVE

(CDR Ellzy)