

27 January 2009

## Executive Summary

### UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL COMMENTS 8 January 2009

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

**1. Nasal Allergy 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 Nasal Allergy Drugs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that:

- 1) Fluticasone propionate (Flonase, generics), flunisolide (Nasarel, generics), mometasone (Nasonex), azelastine (Astelin), and ipratropium nasal spray (Atrovent, generics) be classified as formulary on the UF.
- 2) Beclomethasone dipropionate (Beconase AQ), budesonide (Rhinocort Aqua), ciclesonide (Omnaris), fluticasone furoate (Veramyst), olopatadine HCl (Patanase), and triamcinolone acetonide (Nasacort AQ) be designated as nonformulary under the UF, based on cost effectiveness.

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

#### ***Summary of Panel Vote/Comments:***

- The Panel voted 10 Concur, 0 Non-Concur, 2 Absent regarding the recommendations for formulary and non-formulary agents.
- The Panel voted 10 Concur, 0 Non-Concur, 2 Absent regarding the recommended implementation period of 60 days.
- There was no Panel discussion of the P&T Committee's recommendations or implementation plan recommendations.

***Director, TMA:***

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



**2. Short-Acting Beta Agonists (SABAs) 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 SABA agents, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted to recommend that:

- 1) Albuterol HFA inhaler (Ventolin HFA, Proventil HFA, Proair HFA), levalbuterol inhaler (Xopenex HFA), albuterol inhalation solution (Accuneb, generics), and levalbuterol inhalant solution (Xopenex inhalation solution) be classified as formulary on the UF; and
- 2) Pirbuterol CFC inhaler (Maxair) and metaproterenol inhalation solution (Alupent, generics) be designated as nonformulary on the UF, based on cost effectiveness.

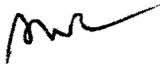
The P&T Committee recommended an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) and TRICARE Retail Network Pharmacy Program (TRRx), and in the MTFs, no later than a 60-day implementation period.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

***Summary of Panel Vote/Comments:***

- The Panel voted 9 Concur, 1 Non-Concur, 2 Absent regarding the recommendations for formulary and non-formulary agents.
- The one non-concur vote was based on the view that, from a health care perspective, when you have three similar brand name drugs vying for formulary status, choosing one or two of those should lead to better results for the MHS. At least that would be the case in a commercial environment.
- The Panel voted 10 Concur, 0 Non-Concur, 2 Absent regarding the recommended implementation period of 60 days.

***Director, TMA:***

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



## Uniform Formulary Beneficiary Advisory Panel (BAP)

### Meeting Summary

January 8, 2009

Washington, D.C.

#### Panel Members Present:

- Deborah Fryar, National Military Family Association, representing The Military Coalition, Chairperson
- Morgan Brown, National Association of Uniformed Services, representing the National Military and Veterans Alliance
- Kathryn Buchta, Medical Professional, Health Net Federal Services
- John Class, Military Officers Association of America, representing The Military Coalition
- John Crum, Medical Professional, Humana Military Healthcare Services, Inc.
- Rance Hutchings, Medical Professional, Uniformed Services Family Health Plan
- Lisa Le Gette, Medical Professional, Express-Scripts, Inc.
- Charles Partridge, National Military and Veterans Alliance
- Marissa Schlaifer, Medical Professional, Academy of Managed Care Pharmacy
- Robert Washington, Fleet Reserve Association, representing The Military Coalition

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 8:00 A.M.

Lt Col Bacon said the 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 on November 18-19, 2008 in San Antonio, TX.

#### Agenda

The agenda for this meeting of the Panel is:

- Opening remarks
- Public citizen comments
- Review and discussion of P&T Committee recommendations for drugs in the following therapeutic classes:
  - Nasal Allergy Drugs
  - Short-Acting Beta Agonists
- Informational Presentation on FY 08 Uniform Formulary Performance
- Wrap-up comments

## Opening Remarks

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

10 U.S.C. section 1074g (subparagraph d) 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 includes 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 considered 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 provided the ground rules for conducting the meeting:

- All discussions take 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 then introduced new TRICARE Management Agency officials present at the meeting (the Deputy Director of Pharmaceutical Operations), Pharmacoeconomic Center (PEC) Director LTC Stacia Spridgen and her staff, and the individual members of the BAP.

#### Private Citizen Comments

The DFO opened the meeting for private citizen comments. No individuals signed up in advance and there were no individuals present at the meeting who wished to address the Panel.

#### Chairperson's Opening Remarks

BAP Chair, Deborah Fryar, expressed the Panel's appreciation to the staff for the work done in preparation for today's meeting. She also extended congratulations to Panel Member Kimberly Owens on the birth of her new baby girl.

#### Presentation of Drug Class Reviews

LTC Spridgen, PEC Director, then began the presentation of drug class reviews and recommendations from the June meeting of the P&T Committee.

#### BAP Script – 8 January 2008

I'm LTC Stacia Spridgen, the PEC Director. Joining me today from the PEC are CDR Joe Lawrence, Deputy Director of the PEC, Dr. Dave Meade, and Dr. Angela Allerman, who are civilian clinical pharmacists. Also joining us today are CDR James Ellzy, the Vice DoD P&T Committee chair, and LTC Michael Wynn, 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).

The PEC staff 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 Nasal Allergy Drugs and the Short-Acting Beta Agonists.
- 4) The DoD P&T Committee's recommendation as to the effective date of the agents being changed from formulary tier to the non-formulary tier of the Uniform Formulary. Based on 32 C.F.R. 199.21, such change will not be longer than 180 days from the final decision date but may be less.

We've given you a handout which includes the Uniform Formulary recommendations for all the drugs discussed today. As usual, 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.

Angela will now present the Nasal Allergy Drugs relative clinical effectiveness evaluation.

## **NASAL ALLERGY DRUG CLASS REVIEW**

### Clinical Effectiveness Review

Dr. Angela Allerman of the PEC began the presentation of the analysis and evaluation of agents in the nasal allergy drug class.

BAP Script – 8 January 2009

Please turn to the handout on page 2, and look at Table 1. The Nasal Allergy Drugs are comprised of three subclasses:

- a) *Nasal corticosteroids*: beclomethasone (Beconase AQ), budesonide (Rhinocort AQ), ciclesonide (Omnaris), flunisolide (Nasarel, generics), fluticasone furoate (Veramyst), fluticasone propionate (Flonase, generics), mometasone furoate (Nasonex), and triamcinolone (Nasacort AQ); the
- b) *Nasal Antihistamines*: azelastine (Astelin) and olopatadine (Patanase) and the
- c) *Nasal Anticholinergics*: ipratropium (Atrovent, generics)

The nasal corticosteroids were previously reviewed for UF placement in November 2005 and August 2007.

- ***Expenditure and Utilization***: MHS expenditures for the Nasal Allergy Drug class exceeded \$63M in FY 2008. The breakdown by point of service is as follows: Military Treatment Facility [MTF]: \$18.6M, TRICARE Retail Network [TRRx], \$37.5M, and TRICARE Mail Order Pharmacy [TMOP] \$7M). If you turn to page 3 and look at Figure 1, you'll see that in terms of numbers of prescriptions dispensed, generic fluticasone propionate (Flonase) is the highest utilized nasal allergy drug at all three points of service, followed by mometasone furoate (Nasonex), and azelastine (Astelin). Page 4, Figure 2 shows the overall Military Health System utilization without generic Flonase. As shown here, the remaining Nasal Allergy Drugs have less than 200,000 prescriptions dispensed monthly.

*Relative Clinical Effectiveness Conclusion* – The relative clinical effectiveness conclusion is divided by subclass (nasal steroid, nasal antihistamine, nasal anticholinergic). The P&T Committee concluded (16 for, 0 against, 0 abstained, 0 absent) the following:

*Nasal corticosteroids*

- a) With regards to efficacy/clinical effectiveness of the nasal corticosteroids, the following conclusions were made:
  - FDA-approved indications – The Committee recognized that there were minor differences among the drugs with regard to FDA-approved uses for seasonal allergic rhinitis (SAR), perennial allergic rhinitis (PAR), prophylaxis of allergic rhinitis (AR) symptoms, nonallergic rhinitis, and nasal polyps. Additionally, the pediatric FDA-approved age ranges differ between the products.
  - Clinical Practice Guidelines – Evidence-based guidelines from the American Academy of Allergy, Asthma and Immunology (AAAAI) consider the nasal corticosteroids as the most effective drug class at reducing allergic rhinitis symptoms of sneezing, rhinorrhea, nasal congestion, and itching.
  - Pharmacodynamic/pharmacokinetic properties – The AAAAI guidelines concluded that despite differences in topical potency, lipid solubility,

receptor binding affinity, and systemic bioavailability, the overall clinical response does not appear to vary significantly between drugs.

- Efficacy for SAR/PAR – The Committee concluded there was no new data to change the previous conclusion from the 2005 meeting that there was no evidence of clinically relevant differences between beclomethasone (Beconase AQ), budesonide (Rhinocort AQ), flunisolide (Nasarel, generics), fluticasone propionate (Flonase, generics), mometasone (Nasonex), and triamcinolone (Nasacort) at relieving AR symptoms.
- Efficacy of newer agents – Fluticasone furoate (Veramyst) was non-inferior to fluticasone propionate (Flonase, generics) at relieving symptoms of SAR; there was no new data to change this conclusion. The newest nasal corticosteroid, ciclesonide (Omnaris) does not have published data comparing efficacy to other nasal corticosteroids. Placebo-controlled trials with ciclesonide report statistically significant improvements in patients with SAR and PAR.
- Relief of ocular symptoms - None of the nasal corticosteroids are FDA-approved for use in reducing ocular symptoms of itching, tearing or erythema. However, all of the agents, with the exception of ciclesonide (Omnaris), have shown efficacy at reducing ocular symptoms in placebo-controlled trials.
- Nasal polyps – Data from clinical trials conducted with beclomethasone (Beconase AQ), budesonide (Rhinocort AQ), and fluticasone propionate (Flonase, generics) report reductions in the size of nasal polyps. Both mometasone furoate (Nasonex) and beclomethasone (Beconase AQ) are FDA-approved for nasal polyps.

b) With regards to regards to safety and tolerability, the following conclusions were made:

- Local effects - Nasal irritation, epistaxis, and rhinorrhea are the most common local adverse effects and are equally likely to occur with any of the nasal corticosteroids.
- Pharmacodynamic/pharmacokinetic properties – Minor differences in binding affinity, lipophilicity, and bioavailability between the products have not correlated to clinically relevant differences in safety. Pharmacokinetic studies report that the newer agents would be expected to pose fewer risks than the older agents (flunisolide [Nasarel], beclomethasone [Beconase AQ], budesonide [Rhinocort AQ], and triamcinolone [Nasacort AQ]).
- Systemic effects- For systemic effects of hypothalamic pituitary adrenal-axis suppression, growth suppression, and cataract formation, there is insufficient evidence to determine whether one nasal corticosteroid is more likely to cause these effects than another. When given in recommended doses, the nasal corticosteroids are not generally associated with clinically significant systemic adverse effects. Providers and patients must assess the risks to benefits, if higher than recommended doses are required.

- Tolerability and patient preferences - Patient preferences may play a role in differentiating between the nasal corticosteroids. However, the available clinical data is poor, and no nasal corticosteroid has proven superior to the others in patient preference trials. More well-designed head-to-head trials are needed to support superiority of a nasal corticosteroid based on tolerability and compliance.
- c) With regards to differences in other factors, the following conclusions were made:
- Special populations – Budesonide (Rhinocort AQ) is the only nasal corticosteroid with a pregnancy category B rating by the FDA (low evidence of risk to humans), which was based on a retrospective review of data from three Swedish registries and one prospective study. All the nasal corticosteroids have a class labeling that these drugs should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
  - Provider survey – A survey of MTF providers found that the majority of prescribers (49%) preferred fluticasone propionate (Flonase, generics) as their first choice of nasal corticosteroid, followed by no preference (17%), and mometasone (15%). Providers showed no preference for differences in formulations between the products (e.g., hypotonic formulation, ergonomic design, prodrug active ingredient, scent-free product, or preservative-free product).

#### *Nasal antihistamines*

- a) With regards to efficacy/clinical effectiveness of the nasal antihistamines, the following conclusions were made:
- FDA-approved indications – The Committee recognized that there were minor differences between olopatadine (Patanase) and azelastine (Astelin) with regard to FDA-approved uses for seasonal allergy rhinitis (SAR) and nonallergic rhinitis (e.g., vasomotor rhinitis [VMR]), and pediatric approval.
  - Clinical Practice Guidelines – AAAAI guidelines state that nasal antihistamines are generally less effective than nasal corticosteroids for treating allergic rhinitis, but may be considered for use as first-line treatment for allergic rhinitis and nonallergic rhinitis. Nasal antihistamines are associated with a clinically significant effect on nasal congestion.
  - Efficacy for seasonal allergic rhinitis – Both nasal antihistamines are superior to placebo in relieving symptoms of SAR. Determining whether there are relevant clinical differences in efficacy between olopatadine (Patanase) and azelastine (Astelin) is difficult because different rating scores were used in the individual placebo-controlled trials.
  - Efficacy for vasomotor rhinitis (VMR): Only azelastine (Astelin) is FDA-approved for treating the symptoms of VMR, which consist of postnasal drip, sneezing, rhinorrhea, and nasal congestion. FDA-approval was based

on the results of two placebo-controlled studies in 200 patients that used a rating scale not previously seen in the literature.

- Head to head study - The one head-to-head trial comparing the use of olopatadine (Patanase) with azelastine (Astelin) was conducted in an allergen exposure unit, making applicability to the clinical setting difficult.
- b) With regards to safety and tolerability of the nasal antihistamines, the following conclusions were made:
- Local adverse effects: package insert data- For safety data, package insert data report a higher incidence of bitter taste and somnolence with azelastine (Astelin), while olopatadine (Patanase) has a higher incidence of epistaxis.
  - Local adverse effects: AAAAI guidelines – the AAAAI guidelines recognize that the two nasal antihistamines can cause sedation and can inhibit skin test reactions, due to systemic absorption.
  - Patient preferences and tolerability – There is insufficient evidence to determine whether clinically relevant differences exist between the nasal antihistamines with respect to patient preferences and tolerability. The available clinical data is sparse, and is limited to manufacturer-sponsored studies that are not yet available in peer-reviewed publications.
- c) With regards to other factors,
- Provider survey - A survey of MTF providers found that 37% of responders preferred a nasal corticosteroid over a nasal antihistamine for managing AR and nonallergic rhinitis.
  - Onset and duration of action – The Committee recognized that the onset of action to relieve allergic rhinitis symptoms was slightly faster with olopatadine (Patanase) compared to the package insert data for azelastine (Astelin); 0.5 - 1 hour vs. 2-3 hours. However, the onset of action with both nasal antihistamines is faster than that reported overall with nasal corticosteroids (2-3 days).

#### *Nasal anticholinergic agents*

- a) With regards to efficacy/clinical effectiveness, safety, tolerability and other factors of the ipratropium nasal spray (Atrovent, generics), the following conclusions were made:
- FDA-approved indications – Ipratropium is solely indicated for the relief of SAR in adults and children 12 years of age and older.
  - Clinical Practice Guidelines – AAAAI guidelines state that nasal anticholinergics may effectively reduce rhinorrhea, but have no effect on other nasal symptoms. Although adverse effects are minimal, dryness of the nasal membranes may occur.

- Efficacy - Further head-to-head trials are needed to prove the superiority of a nasal anticholinergic over a nasal antihistamine or nasal corticosteroid in the treatment of rhinorrhea.

#### Cost Effectiveness Review

Dr. Dave Meade of the PEC summarized the results of the relative cost effectiveness review of nasal allergy drugs.

#### BAP Script – 8 January 2009

In considering the relative cost-effectiveness of pharmaceutical agents in the Nasal Allergy Drug 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). Cost minimization analysis (CMA) and budget impact analysis (BIA) were used to evaluate the cost effectiveness of the NAD agents.

#### *Relative Cost Effectiveness Conclusion:*

Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded the following:

- a) Results from the CMA of nasal corticosteroid agents revealed that flunisolide (Nasarel, generics) was the most cost effective nasal corticosteroid agent overall.
- b) Results from the CMA of nasal antihistamines agents revealed that azelastine (Astelin) was the most cost effective nasal antihistamine agent overall.
- c) The potential impact of scenarios with selected NAD agents designated formulary or nonformulary on the UF was evaluated with the BIA. BIA results designated beclomethasone dipropionate (Beconase AQ), budesonide (Rhinocort Aqua), ciclesonide (Omnaris), fluticasone furoate (Veramyst), olopatadine HCl (Patanase), and triamcinolone acetonide (Nasacort AQ) nonformulary on the UF as the most favorable scenario for the MHS.

**COMMITTEE ACTION:** The P&T Committee voted (16 for, 0 against, 0 abstained, 0 absent) to accept the cost effectiveness conclusion stated above.

#### P&T Committee Recommendations

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

#### BAP Script – 8 January 2009

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the Nasal Allergy Drugs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (14 for, 1 against, 1 abstained, 0 absent) that:

- 1) Fluticasone propionate (Flonase, generics), flunisolide (Nasarel generics), mometasone (Nasonex), azelastine (Astelin), and ipratropium nasal spray (Atrovent, generics) be classified as formulary on the UF.
- 2) Beclomethasone dipropionate (Beconase AQ), budesonide (Rhinocort Aqua), ciclesonide (Omnaris), fluticasone furoate (Veramyst), olopatadine HCl (Patanase), and triamcinolone acetonide (Nasacort AQ) be designated as nonformulary under the UF, based on cost effectiveness.

#### **NON-FORMULARY JUSTIFICATION:**

The P&T Committee recommended that the Nasal Allergy Drugs listed as non-formulary on Table 1 on page 2 of the handout 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 between the nasal corticosteroids or nasal antihistamine recommended for non-formulary status, compared to those recommended for formulary status. The Nasal Allergy drugs selected for inclusion on the Uniform Formulary show existing high utilization in the MHS, and include products that are FDA-approved for treating SAR, PAR, nasal polyps and VMR.
- 2) The Nasal Allergy Drugs designated as non-formulary were not cost-effective relative to those drugs recommended for inclusion on the UF.

#### **NASAL ALLERGY DRUGS – IMPLEMENTATION PLAN**

The P&T Committee recommended (16 for, 0 against, 0 abstained, 0 absent) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) and TRICARE Retail Network Pharmacy Program (TRRx), and in the MTFs, no later than a 60-day implementation period. The implementation period will begin immediately following the approval by the Director, TMA.

#### P&T Committee Physician's Perspective

LTC Michael Wynn provided the Panel with a physician's perspective on the P&T Committee recommendations. LTC Wynn noted that the drug class has three subclasses: nasal corticosteroids, nasal antihistamines and nasal anticholinergics. Nasal steroids were first reviewed in November 2005; for the November 2008 meeting, all three subclasses were combined. All three subclasses have about the same indications and there was a new nasal antihistamine on the market to review (Patanase). For the nasal corticosteroid subclass, the recommendations are the same as those made in 2005 with the exception of

the new drug Omnaris, which was made non-formulary. Veramyst was first reviewed in August 2007 when it was a new drug. Also non-formulary, it has the same active ingredient as Flonase. Omnaris is the newest nasal drug to reach the market. The company has not conducted any head-to-head studies with other nasal steroids to show that it is superior to what is already on the market.

Flonase has been available in generic form since 2005; it was introduced as a brand-name drug in 1994 so physicians have over ten years' experience with it. Flonase has the highest utilization in the Military Health System (MHS) and has a wide range of U. S. Food and Drug Administration (FDA) indications, including approval for use with children as young as four. Clinically, nasal steroids all reduce nasal congestion and there are no large-scale studies that prove one is superior to another. Professional guidelines from a respected allergy group also agree that the overall clinical response is similar between the drugs. The nasal antihistamine subclass consists of only two products: Patanase and Astelin. Astelin was selected to be on the formulary with Patanase recommended for non-formulary. Professional guidelines state that nasal antihistamines are less effective than nasal steroids. Astelin has been on the market since 1996 while Patanase just came out in 2008. Their side-effect profiles are similar and there are some minor differences in their FDA-approved indications. Astelin has been approved for non-allergic rhinitis and is approved for use in children five and above.

For the nasal anticholinergics, there is only one drug on the market, Atrovent and generics. It has been available since 1995. It is less effective than the nasal steroids and antihistamines. It is approved only for use with a runny nose and has no efficacy for congestion or itching.

#### Panel Questions Regarding the Nasal Allergy Drug Class

The BAP had no questions or comments for the presenters regarding the P&T Committee recommendations in this drug class.

#### Panel Discussion of P&T Committee Formulary Recommendations for the Nasal Allergy Drug Class

The Panel Chair, Ms. Fryar, read the P&T Committee's formulary recommendations for the Nasal Allergy Drug Class:

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

1) Fluticasone propionate (Flonase, generics), flunisolide (Nasarel, generics), mometasone (Nasonex), azelastine (Astelin), and ipratropium nasal spray (Atrovent, generics) be classified as formulary on the UF.

2) Beclomethasone dipropionate (Beconase AQ), budesonide (Rhinocort Aqua), ciclesonide (Omnaris), fluticasone furoate (Veramyst), olopatadine HCl (Patanase), and triamcinolone acetonide (Nasacort AQ) be designated as nonformulary under the UF, based on cost effectiveness.

There was no further Panel discussion of the P&T Committee's recommendations.

Panel Vote on P&T Committee Formulary Recommendations for Nasal Allergy Drug Class Agents

The BAP vote on the Nasal Allergy Drug formulary recommendations was:

10 concur; 0 non-concur, 2 absent.

Panel Discussion of P&T Committee Implementation Plan Recommendations for Nasal Allergy Drug Class Agents

Ms. Fryar read the Committee implementation plan recommendations:

“The P&T Committee recommended an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TRICARE Mail Order Pharmacy (TMOP) and TRICARE Retail Network Pharmacy Program (TRRx), and in the Military Treatment Facility (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 the implementation recommendation.

Panel Vote on P&T Committee Implementation Plan Recommendations for Nasal Allergy Drug Class Agents

The vote on the Nasal Allergy Drug implementation plan recommendations was:

10 concur, 0 non-concur, 2 absent.

**SHORT-ACTING BETA AGONISTS (SABAs) DRUG CLASS REVIEW**

Clinical Effectiveness Review

Dr. Allerman next presented the clinical effectiveness review of the Short-Acting Beta Agonists drug class.

BAP Script – 8 January 2009

**Background** - The P&T Committee evaluated the clinical effectiveness of the inhaled Short-Acting Beta Agonists or SABAs. The SABAs' clinical effectiveness review was conducted by Lt Col James McCrary, the Air Force physician at the PEC. If you'll turn to page 2 of the handout, Table 1 shows the drugs in the class. There are two different dosage formulations – handheld devices, called pressurized metered dose inhalers (MDIs), and solutions that are inhaled via a mask, called inhalation solutions or nebulized solutions. The SABA inhaled solutions include albuterol (generic Accuneb), levalbuterol (Xopenex), and metaproterenol (generic Alupent). The manufacturing of generic Alupent inhalation solution was discontinued in Fall, 2008, but there could be remaining supply available.

For the MDIs, as of December 31, 2008, albuterol products that used a propellant called chlorofluorocarbon (CFC) were removed from the market. Albuterol products that use hydrofluoroalkane (HFA) have replaced the CFC-containing products. The MDIs on the market as of January 1, 2009 now include albuterol HFA, which is available under three different trade names – Proventil HFA, ProAir HFA, and Ventolin HFA; levalbuterol (Xopenex), metaproterenol (Alupent), and pirbuterol (Maxair). The three albuterol HFA products are not considered therapeutically interchangeable by the FDA. The manufacturer of the Alupent MDI voluntarily discontinued manufacture of the product at the end of December 2008, but there could be remaining stock on pharmacy shelves.

**Expenditures and Utilization:** In the past fiscal year, over \$43M was spent on the SABAs at all three points of service in the MHS, with \$30M spent in TRICARE Pharmacy Retail Network, \$10M in the Military Treatment Facilities, and \$3M in the TRICARE Mail Order Pharmacy.

If you turn to Figure 3 on page 5 of your handout, it shows utilization of the SABA metered dose inhalers throughout the entire MHS. The blue line shows the decline in albuterol CFC MDIs – as of the end of December 2008, this line will go to zero, due to FDA regulations. In terms of numbers of prescriptions dispensed, the highest utilization is Proventil HFA, followed by Xopenex, Ventolin HFA, and ProAir.

Figure 4 on page 6 of the handout shows utilization of the inhalation solution. The generic albuterol inhalation solution has the highest utilization over the Xopenex solution. The utilization of generic Alupent solution does not even appear on the graph, as there are only 5 unique utilizers of this product in the MHS.

Information regarding the safety, effectiveness, and clinical outcomes of the SABAs was considered by the Committee. The clinical effectiveness review for the SABAs was limited to the outpatient setting; emergency department (ED) use was evaluated only when pertinent.

**Relative Clinical Effectiveness Conclusion:** The P&T Committee concluded (16 for, 0 against, 0 abstained, 0 absent) that:

- a) In terms of efficacy/clinical effectiveness, there is little evidence to suggest there are clinically significant differences between agents for their FDA approved indications. Other conclusions regarding efficacy include the following:
  - Clinical Practice Guidelines – Evidence based guidelines from the VA/DoD Clinical Practice Group, Global Initiative for Asthma, National Heart, Lung

and Blood Institute/National Asthma Education & Prevention Program, and Global Initiative for Chronic Obstructive Lung Disease do not list a preference for one SABA over another for treating asthma, exercise-induced bronchospasm (EIB) or chronic obstructive pulmonary disease (COPD).

- Asthma
  - *MDI and inhalation solution administration – placebo-controlled studies:* For asthma, all the SABA agents were more efficacious than placebo at improving the change in forced expiratory volume in one second (FEV1)  $\geq 12\%$  from baseline, whether administered via MDI or inhalational solution.
  - *MDI administration – albuterol vs. levalbuterol:* There are no studies in adults or children assessing efficacy of albuterol vs. levalbuterol (Xopenex) when administered by metered-dose inhaler in the outpatient setting.
  - *Inhalation administration – albuterol vs. levalbuterol in adults:* For adults with asthma, there is little evidence to suggest there are clinically relevant differences between albuterol and levalbuterol (Xopenex) when administered via inhaled solutions (e.g., nebulized route) in either the outpatient or emergency department (ED) settings in terms of number of puffs of rescue medication used daily or hospitalization admission rates from the ED.
  - *Inhalation administration – albuterol vs. levalbuterol in children:* There are conflicting and inconclusive results as to whether there are efficacy differences between albuterol and levalbuterol (Xopenex) inhalation solution when administered in the outpatient or ED settings to children with asthma. Some studies reported no clinically significant differences in outcomes such as changes in asthma symptom score, symptom-free days, rescue medication use, and hospitalization rates between albuterol and levalbuterol. However, levalbuterol (Xopenex) treatment resulted in statistically significant results in terms of more asthma-controlled days, higher quality of life scores, and lower hospitalization admission rates from the ED compared to albuterol. Interpretation of the results of these studies is complicated by the low patient enrollment, varying definitions of criteria for hospitalization, and enrollment of patients as old as 18-21 years.
- EIB – Placebo controlled trials with albuterol administered via MDI 15 to 30 minutes before exercise reported statistically significant results in terms of preventing exercise-related symptoms compared to placebo. Although levalbuterol MDI (Xopenex) is not currently approved by the FDA for EIB, the results of placebo-controlled phase III trials do not suggest that the effect of levalbuterol at preventing EIB symptoms would differ from albuterol.

- COPD - There is insufficient evidence to compare the SABAs when used in COPD.
- CFC vs. HFA efficacy - HFA products were as effective as CFC products when evaluated in head-to-head studies. Placebo-controlled trials assessing efficacy of HFA albuterol with CFC albuterol have reported similar effects on percentage change in FEV1.

b) With regards to safety/tolerability, the following conclusions were made:

- *Discontinuation rates due to adverse events (AEs)* – All the SABAs are associated with similar systemic adverse effects. A systematic review found no clinically relevant differences in discontinuation rates due to changes in heart rate, blood pressure, palpitations, nervousness, anxiety, tremor, hyperglycemia or hypokalemia between albuterol and levalbuterol inhalation solution.
- *Rare but serious AEs* – There do not appear to be clinically relevant differences between the SABAs in terms of serious adverse effects (e.g., paradoxical bronchospasm, cardiac effects).
- *Inhalation solution administration – albuterol vs. levalbuterol* - In the outpatient setting, in both adults and children, the incidence of the withdrawal rates due to AEs and overall AE rates were similar between albuterol and levalbuterol (Xopenex) inhaled solutions. However, in children there is insufficient evidence from the outpatient studies to determine whether there are clinically relevant differences in the incidence of tachycardia, as conflicting results were reported. One study reported a lower incidence of tachycardia with albuterol compared to levalbuterol, while another reported that both drugs resulted in a change of heart rate of 4 beats per minute.
- *MDI administration – albuterol vs. levalbuterol* - There is insufficient data with the SABA MDI formulations to assess safety differences between albuterol and levalbuterol (Xopenex).
- *Drug-Drug interactions*- Drug-drug interactions between the SABAs are well-known and considered a class effect.
- *FDA Adverse Event Reporting System (AERS)* – FDA AERS data shows higher signals than expected with device malfunction/failure for Proair HFA MDI and Proventil HFA MDI. However, this is observational data only and these safety signals have not been validated.

c) With regards to differences between the SABAs in terms of other factors, the following conclusions were made:

- *Special populations* – The Committee recognized that the pediatric FDA-approved age ranges differ between the products. All four SABAs are labeled as category C drugs for pregnancy and breast feeding, and infant risk cannot be ruled out.

- *CFC Phase out* – As of 31 December 2008, all albuterol CFC metered-dose inhalers cannot be dispensed. Metaproterenol CFC MDIs (Alupent) ceased manufacturing at the end of 2008. It is likely that pirbuterol CFC MDIs (Maxair) will also be removed from the market.
- *HFA formulations* - There are only minor differences between the HFA formulations of albuterol and levalbuterol, including presence of a dose counter (Ventolin HFA is the only product with a dose counter), requirements for priming, storage conditions, and excipients (Ventolin HFA is the only SABA that does not contain alcohol). However, per FDA ruling, the HFA albuterol agents are not interchangeable.
- *Provider Survey* – A survey of MTF providers found that albuterol HFA MDI was preferred over levalbuterol HFA MDI (Xopenex) in the outpatient setting for relief of bronchospasm.

#### Cost Effectiveness Review

Dr. Meade presented the SABA relative cost effectiveness findings.

#### BAP Script – 8 January 2009

In considering the relative cost-effectiveness of pharmaceutical agents in the SABA drug 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). Cost minimization analysis (CMA) and budget impact analysis (BIA) were used to evaluate the cost effectiveness of the SABA agents.

*Relative Cost Effectiveness Conclusion:* Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 against, 0 abstained, 0 absent) the following:

- a) Results from the CMA of SABA MDIs revealed that Ventolin HFA was the most cost effective SABA MDI agent overall.
- b) Results from the CMA of SABA inhalant solutions revealed that albuterol inhalation solution (generic; 2.5 mg/3mL concentration) was the most cost effective agent overall.
- c) The potential impact of scenarios with selected SABA agents designated formulary or nonformulary on the UF was evaluated with the BIA. Generic albuterol CFC inhaler and metaproterenol inhaler (Alupent) were not included in the BIA as they are no longer being manufactured. BIA results designated pirbuterol (Maxair) CFC MDI and metaproterenol inhalant solution (Alupent, generic) nonformulary on the UF as the most favorable scenario for the MHS.

#### P&T Committee Recommendations

Dr. Meade next informed the Panel of the P&T Committee's formulary and implementation recommendations and reasons.

### BAP Script – 8 January 2009

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the SABA agents, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (14 for, 1 opposed, 1 abstained, 0 absent) that:

- a) Albuterol HFA inhaler (Ventolin HFA, Proventil HFA, Proair HFA), levalbuterol inhaler (Xopenex HFA), albuterol inhalation solution (Accuneb, generics), and levalbuterol inhalant solution (Xopenex inhalation solution) be classified as formulary on the UF; and
- b) Pirbuterol CFC inhaler (Maxair) and metaproterenol inhalation solution (Alupent, generics) be designated as nonformulary on the UF, based on cost effectiveness.

### **NON-FORMULARY JUSTIFICATION**

The P&T Committee recommended that the SABA agents listed as non-formulary on Table 1 on page 2 of the handout be classified as non formulary under the UF. The Committee's recommendation was based on the following:

- 1) The products selected for non-formulary status have existing low utilization in the MHS, the manufacturing of metaproterenol inhalation solution (generic Alupent) has already ceased, and the manufacturing of pirbuterol (Maxair) MDI is also likely to be discontinued, as it contains CFC.
- 2) The SABAs designated as non-formulary were not cost-effective relative to those drugs recommended for inclusion on the UF.

### **SABAs – IMPLEMENTATION PLAN**

The P&T Committee recommended (14 for, 0 against, 1 abstained, 1 absent) an effective date of the first Wednesday one week after the minutes are signed following a 60-day implementation period in the TMOP and TRRx, and at the MTFs no later than a 60-day implementation period.. The implementation period will begin immediately following the approval by the Director, TMA.

### P&T Committee Physician's Perspective

LTC Wynn again provided the BAP with a physician's perspective on the P&T Committee recommendations. He said the decision was straight forward as the only products selected for non-formulary placement were those that were already removed from the market (the generic albuterol inhaler that is no longer manufactured — Alupent) and the one that the Committee expects to be removed from the market soon (Maxair). He characterized the results as a win-win situation for DoD in that all three marketed albuterols are recommended for formulary placement and both formulations of Xopenex — the inhaler as well as the solution — are both recommended for formulary placement.

### Panel Questions Regarding SABA Recommendations

Dr. Crum asked why there is no generic albuterol Hydrofluoroalkane (HFA) metered dose inhaler (MDI). Dr. Allerman answered that FDA kept the generic Chlorofluorocarbon (CFC) inhaler on the market for so long that there would be more than one albuterol HFA product. All of the HFA products — the Proair, the Proventil and the Ventolin — contain albuterol and have just minor differences. She said it would be a good question for the FDA as to why these are not therapeutically interchangeable. She said she understands it is very difficult to manufacture an inhaler, which is why it takes so long for generics to come out.

Mr. Hutchings said he also believes that manufacturers were given extended patent rights on HFAs.

Dr. Crum said it is interesting that the products in this class have gone from being predominantly generic to mostly brand name drugs.

Dr. Allerman said she thinks it is likely that the regulations will be extended to other classes of drugs in the near future. Pulmonary drugs administered by inhalers that will be reviewed at the February meeting are one example.

Mr. Hutchings asked about the recommendations for third tier placement. Specifically, he asked whether we might not end up spending money notifying patients about drugs that will no longer be available in about a month. Because the drugs are being discontinued, very little money will be saved. He wonders if it's worth the bother making the agents third tier and notifying patients for something that won't exist. Dr. Meade replied that there are very few people on these drugs but he feels they should be notified that their product is being discontinued and it is time to start changing over to something else now. Otherwise they might show up at the pharmacy and be told that there is nothing at all for them.

Mr. Class asked for clarification regarding which drug is being talked about. Dr. Meade answered that the drug in question is the Alupent solution, which is no longer being manufactured (although there may be some still sitting on the shelf). Dr. Allerman added that the supply of the Alupent CFC inhaler has already been exhausted.

Dr. Crum asked whether consideration was given to selecting just one of the albuterol MDI agents for non-formulary placement. Dr. Meade answered that such a scenario was part of the budget impact analysis. Thirteen or fourteen different scenarios were looked at and it was determined that if one agent were to be taken off the formulary it would cost MHS more.

### Panel Discussion of P&T Committee Formulary Recommendations for the Short-Acting Beta Agonists (SABA) Drug Class

The Panel Chair, Ms. Fryar, read the P&T Committee's formulary recommendations for the Short-Acting Beta Agonists (SABA) drug class:

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

- a. Albuterol HFA inhaler (Ventolin HFA, Proventil HFA, Proair HFA), levalbuterol inhaler (Xopenex HFA), albuterol inhalation solution (Accuneb, generics), and levalbuterol inhalant solution (Xopenex inhalant solution) be classified as formulary on the UF; and
- b. Pirbuterol CFC inhaler (Maxair) and metaproterenol inhalation solution (Alupent, generics) be designated as nonformulary on the UF, based on cost effectiveness.

There was no further Panel discussion of the P&T Committee's recommendations.

Panel Vote on P&T Committee Formulary Recommendations for Short-Acting Beta Agonists Class Agents

The BAP vote on the Short-Acting Beta Agonists Drug formulary recommendations was:

9 concur; 1 non-concur, 2 absent.

Dr. Crum indicated that his vote to not concur with the recommendation was based on the view that, from a health care perspective, when you have three similar brand-name drugs vying for formulary status, choosing one or two of those should lead to better results for the MHS. At least that would be the case in a commercial environment.

Panel Discussion of P&T Committee Implementation Plan Recommendations for Short-Acting Beta Agonists Class Agents

The Chair read the P&T Committee implementation plan recommendations for the SABA drug class:

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

There was no Panel discussion of the implementation recommendation.

Panel Vote on P&T Committee Implementation Plan Recommendations for Short-Acting Beta Agonists Agents

The vote on the Short-Acting Beta Agonists Drug implementation plan recommendations was:

10 concur; 0 non-concur, 2 absent.

**INFORMATION PRESENTATION — FY 2008 UNIFORM FORMULARY PERFORMANCE (“TRENDS AND SPENDS”)**

Dr. Meade of the PEC presented an informational slide show to the BAP addressing trends in drug classes and MHS expenditures and savings resulting from establishment of the Uniform Formulary. He said he will review some of the drugs that were looked at last year, which is important because some of them are now coming up for re-review, as well as a couple of the classes that were done this year. This overview presentation is called “Trends and Spends.”

The slide captioned “TRICARE Eligible Beneficiaries” gives an overview of the beneficiary population by type of eligibility (active duty, dependents, retirees and their dependents and other). Overall there were 9.3 million beneficiaries in FY 2008, up from 8.6 million in FY 02 but stable for the last 2-3 years. The next slide indicates where these beneficiaries are getting their prescriptions filled by point of service. Dr. Meade pointed out that for the last year and a half, more beneficiaries have been utilizing the retail network than any other point of service (POS). Before then, the MTFs had been the most heavily used. Over the last six years, there has been steady growth in retail network use. There has also been growth in the TMOP, which MHS has promoted. The MTF are still the lowest cost point of service.

The next chart illustrates the mix of POS use by beneficiaries. Among those who use one point of service exclusively, the MTFs are used a little more than the retail network. Dr. Meade noted that a significant number of beneficiaries use both the MTF and the retail network, speculating that the reason is that the retail network is quicker if you’re in a rush but there is no co-pay at the MTFs. He also pointed out that only about 7 million of the 9.3 million beneficiaries use the pharmacy benefit — about three-quarters of those eligible. But even that number is up from what it was in 2002, when only 66 percent of eligible beneficiaries used the pharmacy benefit.

Dr. Meade’s next slide displayed overall growth expressed in “30-Day Equivalent Prescriptions” by point of service from fiscal 01 through fiscal 08. He explained that the

“30-day equivalent” measure is used to adjust for the different quantities of agents that are dispensed by the different POS. The retail POS normally dispenses a 30-day supply whereas the mail order and MTF points of service will dispense up to a 90-day supply. That means that there are a lot more prescriptions out in the retail network than in the TMOP and MTFs. The slide shows that, with the adjustment, the MTFs are still dispensing more 30-day equivalents than the retail network or the TMOP — 45 percent of the total in FY 08 compared to 39 percent for retail and 16 percent for TMOP. But the greatest growth has been in the retail network.

The next slide shows where the dollars are spent by point of service. The figures again show significant growth in the retail network while MTF drug spending has dropped slightly during that time. TMOP spending has also increased. Right now, the MTF is the most efficacious point of service for MHS. Because there is no co-pay, it should also be the most efficacious for beneficiaries.

The slide entitled “MHS Outpatient Drug Spend” displays MHS drug expenditures by point of service for FY 01 through FY 08 (exclusive of overhead costs and dispensing and processing fees). The numbers show that total MTF drug expenditures in FY 08 were the same as in FY 01 (\$1,388 million) and have actually gone down in each of the last 4 years. Retail POS drug expenditures have risen from \$1,278 million in FY 01 to \$4,537 million in FY 08) and TMOP expenditures have risen from \$347 million to \$954 million. The bottom line on the chart shown on this slide indicates that the cost per beneficiary has doubled over the last six years across all points of service. However, it appears that the increase is now beginning to slow.

The next slide summarizes the factors that affect utilization and cost. Dr. Meade listed the main ones as: formulary decisions, implementation of the Automatic PA (Prior Authorization) and drugs going generic. He said that a combination of all these factors had caused the changes, but mentioned that several “blockbuster” drugs going generic (including Zocor, the number one drug, Zoloft and Zyrtec, which went over-the-counter (OTC)) had a significant effect.

Four drug classes were selected for use as examples of what’s going on in the MHS: Proton Pump Inhibitors (PPIs), cholesterol lowering agents (LIP-1), newer antihistamines, and Benign Prostatic Hyperplasia (BPH) drugs.

In the PPI class, the first slide showed the effect of formulary decisions implemented in July 2007 and Automatic PA decisions implemented in October 2007 across all points of service. Prior to these decisions, the leading agents dispensed were Aciphex, Omeprazole, Prevacid, Nexium, Protonix and Zegerid. After the decision, Nexium rapidly grew to first place, followed by Omeprazole (whose use increased). The use of Aciphex and the other agents in the class designated non-formulary decreased. Overall, across all points of service, the preferred drugs now have 86 percent of the MHS market, which is good news. The slide showing just the retail sector also showed very significant growth in the use of formulary drugs, especially Nexium, after the placement decision. Today, use of formulary drug agents continues to grow while non-formulary agent use

has declined significantly. Overall, preferred drugs have 75 percent of the retail market in this class. USE of PPI agents in the MTFs shows similar results, with Nexium use skyrocketing, Omeprazole increasing and Aciphex dropping off sharply. Prior to 2007, Nexium had virtually no use at MTFs because it was non-formulary; by November 2007, it was the leading PPI drug dispensed at MTFs. Because of pricing, the MTFs have an incentive to make the change immediately, and they did. Dr. Meade said when the MTF pharmacists jump on something, they do it very quickly, as this case illustrates. Today (2008) preferred drugs have 98 percent of the market at MTFs and Nexium use is still increasing. The bottom line is that formulary decisions combined with automatic PAs can cause significant market movement. But he said that MHS also wants to make sure that it doesn't let people fall through the cracks by potentially leaving people without any drug available. A special group has been formed to track data down to the patient level in cases where decisions lead to a "hard stop" to make sure that nothing bad happens. The goal is to make sure that the PA is a good thing.

Dr. Meade next presented figures for agents in the cholesterol lowering (LIP-1) drug class, the statins. He said the data in this class are kind of like "apples and oranges" because it is such a big class. The first slide in this group shows data from May 06 through November 07. Zocor, the leading agent, went generic in 2007. Dr. Meade said that when drugs go generic, usage of the patented brand name drugs usually increases because industry is no longer promoting the generics. MHS was concerned that might happen with Zocor, which now costs only about three or four cents a tablet whereas some of the brand name agents are close to a dollar a tab, and wanted to keep track of how it was doing with the generic. When Zocor went generic, usage went down about 10 percent. For comparison purposes, MHS wanted to watch what happened with Lipitor, which is a very good drug for certain cases but which MHS didn't want people to go crazy with. The next slide shows what happened through August 2008 (in terms of percentages as opposed to 30-day equivalents). The figures show that Zocor hasn't lost any more users than the initial 10 percent. There has been growth in Vytorin, a high-potency lipid-lowering agent, which is acceptable because (a) it is the preferred high-potency lipid-lowering agent, and (b) it is probably being given to people who need it. The downturn at the start of 2008 resulted from the release of information about some unfavorable trials. The red line on the chart is Lipitor, which has grown about five percent in usage over the time period shown. Dr. Meade said this drug class is slated to come up for re-review later this year, probably at the August P&T Committee meeting. When it does come up, the Committee will discuss whether to push the generic a little bit further based on cost-effectiveness. The next slide, showing "Statin Utilization in the Retail Network" measured in 30 day equivalents illustrates the potential. In this POS, Zocor and generics have actually been gaining market share while Lipitor, the number one seller, has decreased. Dr. Meade said he has never seen a generic continue to grow as well as Zocor has done. The next slide, retail network market share percentages, shows that by August 2008, Zocor (the green line) has just about caught up with Lipitor (the red line). Although not shown on the chart, this trend has continued through October 2008. The bottom line is that the generic has taken over the market. One reason is that a significant number of plans require step therapy, under which the patient has to try generic Zocor for lipid lowering before being switched to a different agent. Because so

many plans have done this, doctors in the retail network have gotten used to writing prescriptions that way. MHS is benefiting from this practice. When the lipid agents are re-reviewed, Dr. Meade thinks the Committee will probably consider going to step therapy in MHS too.

The next group of agents presented were the newer antihistamines. The data in this category are interesting because Cetirizine, which was the market leader, not only went over-the-counter -- it went generic. Retail network figures following implementation (August 2007) show a sharp drop in Cetirizine, which is understandable because OTC products aren't covered in the retail network. The sales remaining represent what is left on the shelf, but once it's gone, that figure will drip to zero. This has led to a big drop in the total number of units prescribed in the newer antihistamines (the top line on the chart). Fexofenadine, the leading agent now, has been around quite a while and has generic products coming out. The remaining two agents are follow-on drugs for Claritin and for Zyrtec and haven't yet made much of an impact in the DoD retail network. In the MTF POS, utilization of the follow-on drugs has not gone down as it did in the retail network. One reason is that MTFs can cover OTC products. Dr. Meade pointed out that the March-April 2008 "hump" in the figures is due to allergy season. The final slide in this group is entitled "Newer Antihistamines, Price Per Tablet/Capsule." The two follow-in drugs on the formulary are more than \$2.00 per day. The graph shows nicely with a big drop-off exactly when Cetirizine went generic and went OTC, which impacted the class average price per tablet (the red line on the chart). Dr. Meade said there are still some things happening in the market as a whole that MHS doesn't know about, but even so, there has been a 40 percent drop in the class average price per tablet/capsule. Some groups have recommended that OTCs ought to be deliberated upon by the P&T Committee and be available at all three points of service. That idea may or may not be adopted.

The last group of agents presented were the BPH symptom relief drugs. This drug class has had two reviews. The 30-day equivalent figures show that making Tamsulosin non-formulary in December 2007 didn't have much of an impact, but implementing the automated PA in April of 2008 has resulted in Alfuzosin overtaking Tamsulosin in just eight months. Again, MHS is concerned that patients not be deprived of drugs when step therapy is implemented. The next slide, "BPH Drug Utilization" shows that there has been a slight increase in the use of BPH agents and that overall the market has been steady. Dr. Meade said that a lot of the agents in this class are affected by the Voluntary Agreement on Retail Rebates (VARR) (the retail refund), but those figures haven't yet been included in any of the reports because the information is sensitive. But MHS is getting significant refund dollars both here and in the PPI class — about \$200 million over the last couple of years.

In closing, Dr. Meade emphasized that the presentation had focused on a limited number of classes and that the figures covered the time period from three months prior to the decision up to the current time (December 2008). Most of the time, the figures represent conservative estimates, especially as VARR savings are not included. The conclusions to be drawn are that significant savings results from aggressive formulary management.

Moreover, there has been growth in the utilization of the classes, so formulary management techniques don't appear to be inhibiting use of the benefit. The initial results of step therapy appear very encouraging in guiding patients toward the most desirable products, but MHS is proceeding carefully here because it doesn't want to lose patients.

One Panel member asked a question about the average use by beneficiaries compared to non-MHS programs. Dr. Meade replied that the average use has gone from about 15 prescriptions for an average beneficiary to over 25, which is significantly higher than the national average. One reason is that a lot of programs don't cover OTCs, which MHS does, and there is no co-pay in one of the venues. Additionally, MHS co-pay amounts are very advantageous compared to other plans.

Another member asked whether the average cost per beneficiary of \$740 was annual or monthly. The answer provided was "annual." The figure is derived by dividing how much MHS spends by the number of beneficiaries who use the pharmacy program.

A member asked whether the dollar figures used are adjusted for inflation or "raw dollars." Dr. Meade said this presentation uses raw dollars, but adjustments are made for inflation later on as well as for intensity and market mix. The important thing is that MHS is only experiencing single digit increases in expenditures.

#### Closing Remarks

Lt Col Bacon thanked Dr. Meade and the staff for putting together the presentation on how the Panel's decisions are playing out and for its focus on the beneficiaries. He also thanked the Panel members for their time and interest, the presenters for their excellent work and the industry representatives for their interest in the work of the Panel.

Lt Col Bacon announced that the next meeting will be held March 26, 2009 at the Naval Heritage Center in Washington, DC.

The meeting was adjourned at 10:00 A.M.

Brief Listing of Acronyms Used in This Summary

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

- AAAAI — American Academy of Allergy, Asthma and Immunology
- AE — Adverse event
- APR — Automated Profile Review
- BAP — Uniform Formulary Beneficiary Advisory Panel (the “Panel” referred to above)
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- BPA — Blanket Purchase Agreement
- BPH — Benign Prostatic Hyperplasia (a drug class)
- CEA — Cost-effectiveness analysis
- CFC — Chlorofluorocarbon
- C.F.R — Code of Federal Regulations
- CMA — Cost-Minimization Analysis
- COPD — Chronic obstructive pulmonary disease
- CR — Controlled Release (a drug formulation)
- DEA — U.S. Drug Enforcement Administration
- DFO — Designated Federal Officer
- DHP — Dihydropyridine
- DOD — Department of Defense
- ECF — Extended Core Formulary
- EIB — Exercise-induced bronchospasm
- 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
- HFA — Hydrofluoroalkane
- HMO — Health Maintenance Organization
- IR — Immediate Release (a drug formulation)
- IV — Intravenous
- LIP-1 — Antilipidemic agents (a drug class)
- MDI — Metered dose inhalers
- MHS — Military Health System
- MN — Medical Necessity

- MTF — Military Treatment Facility
- NA — Newer Antihistamines (a drug class)
- NAD — Nasal allergy drugs (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
- PAR — Perennial allergic rhinitis
- P&T Committee — DOD Pharmacy and Therapeutics Committee
- PDTS — Pharmacy Data Transaction Service
- PEC — DOD Pharmacoeconomic Center
- POS — Point of Service
- RCTs — Randomized Control Trials
- SABA — Short-Acting Beta Agonists (a drug clas)
- SAR — Seasonal allergic rhinitis
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TRRx — TRICARE Retail Pharmacy Program
- UF — DOD Uniform Formulary
- U.S.C. — United States Code
- VA — U.S. Department of Veterans Affairs
- VARR — Voluntary Agreement on Retail Rebates
- VMR — Vasomotor rhinitis