8 July 2011

Executive Summary

UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL COMMENTS
23 June 2011

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy & Therapeutics (P&T) Committee May 2011 meeting.

1. ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — UF RECOMMENDATIONS

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 (9 for, 6 against, 2 abstained, 0 absent) clozapine (Clozaril, generics; Fazlaco), risperidone (Risperdal, Risperdal ODT, generics), aripiprazole (Abilify, Abilify Discmelt), olanzapine (Zyprexa, Zyprexa Zydis), olanzapine/fluoxetine (Symbyax), paliperidone (Invega), quetiapine (Seroquel; Seroquel XR), and ziprasidone (Geodon) remain formulary on the UF. The P&T Committee recommended iloperidone (Fanapt), asenapine (Saphris), and lurasidone (Latuda) be designated NF on the UF.

Summary of Panel Vote/Comments:

Dr. Cohoon noted that the information provided shows that Abilify is the third most utilized drug in this class and asked about the primary reason for that, considering its cost. Dr. Meade indicated it was provider preference.

Ms. Fryar asked about the six Committee members who opposed the UF recommendations, specifically whether they were in favor of putting all of the drugs on formulary. LTC Young replied that they were and that was the reason for their vote.

- Without further discussion/comments, the Panel voted on the atypical antipsychotic (AAP) drug class recommendation as follows: Concur: 7 Non-concur: 2 Abstain: 0 Absent: 2

No further comments from the Panel.

- Without further discussion the Panel votes as follows on the implementation plan as follows: Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

No further comments from the Panel.

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

2. NASAL ALLERGY DRUGS (NADS) — UF RECOMMENDATION

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the NADs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (16 for, 0 opposed, 1 abstained, and 0 absent) to recommend that:

a. Fluticasone propionate (Flonase, generics), flunisolide (generics), mometasone (Nasonex), azelastine 0.1% (Astelin, generic), olopatadine (Patanase), and ipratropium (Atrovent, generics) be classified as formulary on the UF.

b. Azelastine 0.15% (Astepro), beclomethasone (Beconase AQ), budesonide (Rhinocort Aqua), ciclesonide (Omnaris), fluticasone furoate (Veramyst), and triamcinolone (Nasacort AQ) remain designated as NF on the UF.

Summary of Panel Vote/Comments:

Dr. Cohoon asked what the backup agent would be if there were a shortage of flonase. Dr. Meade said none was selected. One of the purposes of the review was to enable a solicitation for an alternate. In the meantime, there are a lot of products already on the formulary that could be used.

- Without further discussion/comments, the Panel voted on NADS recommendations as follows: Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

No further comments from the Panel.

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

3. KOMBIGLYZE XR — UF RECOMMENDATION

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 (16 for, 0 opposed, 1 abstained, 0 absent) saxagliptin/metformin ER (Kombiglyze XR) remain formulary on the UF. Prior authorization/step therapy for the DPP-4s would require a trial of metformin or sulfonylurea prior to use of Kombiglyze XR for new patients.

Summary of Panel Vote/Comments:

Dr. Salom remarked that he was confused by the fact that one of the PA criteria for Kombiglyze was the patient having an adverse reaction to one of the components of the drug, namely metformin. LCDR Selvester agreed that there is an error in the PA criteria, which he believes were taken from Onglyza. Criteria "a" and "c" in the manual PA criteria noted above are not required and should be removed. Only criterion "b" -- the patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment – would apply. The PEC staff agreed that the record should be corrected to make this change.

Mr. Hutchings noted that Kombiglyze is not cost effective but remains on the UF. He asked if that is a function of the difference in dosage. Dr. Meade explained that the reason was more that the Committee didn't want to limit the MTFs if they wanted to use the combination drug.

Mr. Hutchings also asked whether, when applying the automated PA criteria, the requirement would be for both "a" and "b" or whether it would be for "a" or "b". The answer provided was that it would be "a" or "b".

Dr. Crum commented that he still doesn't understand why Kombiglyze is recommended for UF placement since it doesn't have significant therapeutic advantages and costs more. Dr. Meade replied that the question was whether the Committee wanted to limit what was available at the MTFs. If the drug is made non-formulary, it would be less available and also more costly in the retail network.

- Without further discussion/comments, the Panel voted on the Kombiglyze recommendation as follows: Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

No further comments from the Panel.

Corrected recommendation for PA Criteria:

The Chair read the **corrected recommendation** regarding the PA criteria for Kombiglyze.

1. Automated PA criteria:

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

    b. The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, or Onglyza) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual PA criteria, if automated criteria are not met:

    a. The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.

Note for the record: two additional manual PA criteria were removed from the original recommendation as being erroneous (see discussion above). The vote reflects the corrected recommendation.

- Without further discussion, the Panel voted on the PA criteria recommendations as follows: Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

No further comments from the Panel.

- Without further discussion, the Panel voted on the implementation plan as follows: Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

No further comments from the Panel.

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

4. BROMDAY — UF RECOMMENDATION

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 (15 for, 0 opposed, 1 abstained, 1 absent) bromfenac 0.09% ophthalmic solution (Bromday) remain formulary on the UF.

Summary of Panel Vote/Comments:

Ms. Fryar began the questioning. She asked whether she understood correctly that Bromday was actually more expensive and not as cost effective as other drugs that are available. Dave Meade said that there are generics available that are less cost effective but this product is comparable to the other branded products in this class.

Mr. Hutchings commented that ophthalmologists prefer to use branded products over generic. Ms. Fryar asked if that was due to a safety issue. Mr. Hutchings answered that it isn't a proven safety issue but is the kind of issue that impacts the perception of safety.

- The Panel vote was: Concur: 8 Non-concur: 1 Abstain: 0 Absent: 2

The non-concurring Panelist commented that his vote was due to the availability of alternatives and the fact that the manufacturer appears to have done nothing more than change the label and the dosing recommendation.

No further comments from the Panel.

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

5. JALYN — UF RECOMMENDATION

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 (14 for, 1 opposed, 1 abstained, 1 absent) tamsulosin/dutasteride (Jalyn) remain formulary on the UF, with automated PA/Step Therapy requiring generic tamsulosin or alfuzosin (Uroxatral) for new patients.

Summary of Panel Vote/Comments:

Dr. Cohoon asked why Committee members abstain when a drug is placed on the UF with a PA in place. Dr. Meade said there are various reasons.

Mr. Hutchings said he intends to vote to non-concur on this recommendation because he believes the combination is not necessary and there are less expensive alternatives available for the patient, citing an example. He also noted that changing to combination drugs tends to create chaos at the pharmacy. Dr. Meade noted that the patent expiration is coming up very quickly on Avodart, which will make the class largely generic. That will tend to curb the use of Jalyn. Mr. Hutchings said he would prefer to do that now rather than wait until there are a larger number of patients to deal with. Dr. Meade said he thought that the step therapy of the PA would tend to have that effect anyway.

Ms. Fryar asked for clarification about the wording of the PA criteria.

- Without further discussion/comment, the Panel voted on the Jaylin recommendation as follows: Concur: 7 Non-concur: 2 Abstain: 0 Absent: 2

  a. The non-concurring Panel members commented that this combination drug does not seem to be necessary and that less costly alternatives are available for patients.

No further comments from the Panel.

- Without further discussion, the Panel voted on the PA criteria recommendation as follows: Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

No further comments from the Panel.

- Without further discussion, the Panel voted on the implementation recommendations as follows: Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

No further comments from the Panel.

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

6. ITEMS FOR INFORMATION

A. Dabigatran (Pradaxa)—Potential Prior Authorization:

Summary of Panel Vote/Comments: The Panel had no questions regarding this matter.

B. Pharmacy Co-pay Changes:

At the May 11-12, 2011 meeting, the Pharmacy &Therapeutics Committee, based on experience with the Uniform Formulary, changes in economic circumstances, and other appropriate factors, voted (14 for, 0 against, 3 abstain, 0 absent) to recommend an

adjustment to the per prescription co-payments established in 32 C.F.R. §199.21(i)(2). The co-payment changes proposed in the President's FY 2012 budget for tiers 1 (generic)/2 (formulary)/3 (non-formulary) are $5/$12/$25 for up to a 30-day supply at the Retail Network and $0/$9/$25 for up to a 90-day supply at the Mail Order Pharmacy. These adjusted amounts maintain compliance with the requirements of 10 U.S.C. §1074g(a)(6).

Panel Questions

Dr. Crum asked when the changes would be effective. Dr. Meade said he didn't know yet. A staff member in the audience noted that the change was proposed in the President's budget for FY 2012, which means that it wouldn't take effect before October 1. Dr. Cohoon asked why three Committee members abstained. The answer given was that they saw it as a budget matter and didn't feel it was appropriate for the Committee to either support or not support such changes. There was also a brief discussion as to whether this should have been brought before the P&T Committee for discussion earlier. The staff member noted that the change will be included in the regulations and that such regulations are required to be reviewed by the P&T Committee.

One Panel member commented that the way the changes are structured there is the potential for families to be impacted by changes for medications that are not maintenance medications, for example an antibiotic or an ear infection medicine.

Another Panel member asked if the numbers were proposed by the White House.

This note is included to correct the following statement:

"The staff member noted that the change will be included in the regulations and that such regulations are required to be reviewed by the P&T Committee".

The P&T Committee is responsible for the development and maintenance of the uniform formulary. They make recommendations on the co-pay structure to the Assistant Secretary of Defense (Health Affairs) for final approval. The above statement is incorrect; this change will not be included in the regulations.

No further comments from the Panel.

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
June 23, 2011
Washington, D.C.

Panel Members Present:

- Deborah Fryar, National Military Family Association, representing The Military Coalition, Chairperson
- Kathryn Buchta, Medical Professional, Health Net Federal Services
- Barbara Cohoon, National Military Families Association, representing The Military Coalition
- Santiago Chavez, Association of Military Surgeons of the United States, 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.
- Katherine O'Neill-Tracy, Military Officers Association of America, representing The Military Coalition
- Ira Salom, Medical Professional, Clinical Associate Professor, Geriatrics and Medicine, Mount Sinai School of Medicine

Medical professional Panel members Brian Casull (TriWest Healthcare Alliance) and Marissa Schlaifer (Academy of Managed Care Pharmacy) were absent from the meeting.

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. LTC Stacia Spridgen, the Designated Federal Officer (DFO), called the proceedings to order at 9:00 A.M.

LTC Spridgen stated 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 May 11 and 12, 2011 in San Antonio, TX.

Agenda

The agenda for this meeting of the Panel is:

- Welcome and opening remarks
- Public citizen comments
- Review and Panel discussion of P&T Committee recommendations for the following therapeutic drug classes:

  - *Drug Class Reviews*
    - Atypical Antipsychotics (AAPs)
    - Nasal Allergy Drugs (NADs)

- Nasal corticosteroids
- Nasal antihistamines
- Nasal anticholinergic

- *Designated Newly Approved Drugs*

  - Dipeptidyl Peptidase-4 iInhibitor (dpp-4)/Biguanide fixed-dose combination FDC)—Saxagliptin/Metformin extended release tablets (Kombiglyze XR)
  - Ophthalmic-1s—Bromefenac 0.9% ophthalmic solution(Bromday)
  - Alpha Blockers for Benign Prostatic Hypertrophy—Tamsulosin/dutasteride capsules (Jalyn)

- *Items for Information —Darvon/Darvocet (propxyphene) withdrawal from the market*
  - Dabigatran (Pradaxa) potential prior authorization
  - Co-pay changes

Opening Remarks

LTC Spridgen began by indicating that Title 10 United States Code (U.S.C.) section 1074g subsection b requires the Secretary of Defense to establish a DoD Uniform Formulary (UF) of pharmaceutical agents, and establishes the P&T Committee to review the formulary on a periodic basis and make additional recommendations regarding the formulary as the Committee determines necessary and appropriate.

In addition, 10 U.S.C. section 1074g subsection c also requires the Secretary to establish a UF Beneficiary Advisory Panel (BAP) to review and comment on the development of the UF. 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 establishing the UF or implementing changes to the UF. The Panel's meetings are conducted in accordance with the Federal Advisory Committee Act (FACA).

The duties of the Uniform Formulary Beneficiary Advisory Panel include:

- To review and comment on the recommendations of the P&T Committee concerning the establishment of the UF 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 DFO in consultation with the Chairperson 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.

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

The P&T Committee met for approximately 20 hours conducting its reviews of the drug class 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 the Director's decisions will be available on the TRICARE website in approximately four to six weeks.

The DFO 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 the minutes accurately reflect relevant facts, regulations or policy.

After introducing the individual Panel members (see list above), LTC Spridgen then noted the housekeeping considerations pertaining to the meeting.

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

The DFO then turned the meeting over to the Panel Chairperson, Ms. Fryar, who welcomed the audience. She noted that a recent article in Consumer Reports May 2011 magazine showed that the Beneficiary Advisory Panel process is having a positive effect in holding down costs for beneficiaries. Before beginning the scheduled drug class review presentations, the Chair reminded the Panel that its function is to review the recommendations, ask questions, offer input, vote to concur or not and make comments as appropriate; however the Panel cannot make recommendations on its own. Those must come from the P&T Committee. She then asked Dr. Meade to begin the presentations.

DRUG CLASS REVIEW PRESENTATIONS

[PEC Script]

(Dave Meade)*:* I'm Dave Meade, Director of Clinical Operations at the Pharmacoeconomic Center. Joining me today from the PEC is LCDR Bob Selvester, our Navy physician consultant. Also joining us today is LTC Amy Young, one of the DoD P&T Committee members who will provide the physician perspective and comment on the recommendations made by the. Dr. Kugler, the chairmen of the P&T Committee and a retired Army Colonel and physician, is also here. Joining us from the TMA is Col George Jones, the TMA Deputy Director of the Pharmaceutical Operations Directorate.

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).

We 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 is based upon its collective professional judgment when considering the analyses from both the relative clinical and relative cost-effectiveness evaluations. The Committee reviewed two Uniform Formulary drug classes – the Atypical Antipsychotic Drugs, and the Nasal Allergy Drugs. The 3 newly approved drugs that were reviewed were Kombiglyze XR, Bromday and Jalyn. Lastly, one prior authorization will also be discussed.
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; these are found on pages 2 through 16. 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.

UNIFORM FORMULARY CLASS REVIEWS — ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS

(PEC Script)

(LCDR Selvester):

Background Relative Clinical Effectiveness— The P&T Committee evaluated the relative clinical effectiveness of the drugs in the atypical antipsychotics (AAP) Drug Class. The clinical review for the oral AAP drugs included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1). The injectable AAPs were not included in the review.

The class is comprised of the following agents listed in table 1 on page 2 of your handout.

The AAP Drug Class has not previously been reviewed for UF status, although quetiapine IR (Seroquel) and risperidone tablets were added to the Basic Core Formulary (BCF) in May 2003 (prior to implementation of the Uniform Formulary Rule). Clarifications were made in August 2007 to include quetiapine ER (Seroquel XR) on the BCF and to exclude risperidone ODT. Currently, risperidone is the only AAP drug available in a generic formulation. The anticipated generic entries in the class are Zyprexa, Geodon, Abilify, and Seroquel IR, with patents set to expire in 2011 to 2014.

The AAP Drug Class is associated with a significant cost within the Military Health System (MHS); expenditures exceed $200 million annually. In terms of MHS utilization, Figure 1 on page 2, quetiapine is the most utilized AAP, followed by generic risperidone. Aripiprazole is the third most utilized agent but accounts for most of the expenditures in the class.

The Pharmacy Outcomes Research Team (PORT) analyzed utilization and prescribing patterns in the MHS and noted that approximately 60% of AAP use in the MHS appears to be consistent with FDA-approved labeling. This estimate is higher than noted in the literature and may be overstated.

ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — RELATIVE CLINICAL EFFECTIVENESS

The P&T Committee recommended (16 for, 0 against, 0 abstained, 1 absent) the following conclusions for the AAPs:

1. Schizophrenia: All AAPs are efficacious in treating schizophrenia. Data from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) trial suggests that olanzapine is superior to the other AAPs in efficacy, but use is limited by adverse events. The four newest AAPs (asenapine, iloperidone, lurasidone, and paliperidone) are superior to placebo in treating schizophrenia, but the data is limited to small trials of short duration.

2. Bipolar Disorders: AAPs are used as adjunctive therapy to mood stabilizers in treating mania and mixed episodes. Six AAPs are FDA-approved for use in bipolar disorders (aripiprazole, asenapine, olanzapine, quetiapine, ziprasidone, and risperidone). Recommendations from the 2010 VA/DoD Clinical Practice Guideline (CPG) for bipolar disorder conclude olanzapine and quetiapine have more positive evidence than the other AAPs.
3. Major Depressive Disorder (MDD): For treatment-resistant MDD, AAPs are superior to placebo in augmenting antidepressant therapy. Three AAPs are FDA-approved for the treatment of MDD: aripiprazole, olanzapine/fluoxetine, and quetiapine ER. Data from systematic reviews suggests more positive evidence exists with quetiapine and aripiprazole for this indication. Risperidone also shows benefit in treating MDD, but is not FDA-approved.
4. Post-Traumatic Stress Disorder (PTSD): The available evidence from the 2010 VA/DoD CPG for PTSD and the American Psychiatric Association supports some benefit for the AAPs when used as adjunctive therapy to cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs) or selective norepinephrine reuptake inhibitors (SNRIs). The results of one meta-analysis show olanzapine and risperidone were more efficacious than placebo. None of the AAPs are FDA-approved for treating PTSD.
5. Dementia: There is evidence from systematic reviews that dementia symptoms of aggression and agitation are improved with AAPs (risperidone and olanzapine) but there is no benefit conferred in terms of cognition and functionality. Use of AAPs for psychiatric symptoms and behavioral disturbances in dementia patients is not approved by the FDA and is associated with significant risks of adverse events, including development of heart failure, cerebrovascular accident, and sudden cardiac death.
6. Insomnia: None of the AAPs are FDA-approved for treating insomnia. Current military guidance for deployment allows for the use of low-dose quetiapine (25 mg) for sleep with no waivers required. In the absence of other psychiatric comorbidities, the use of low-dose AAPs for primary insomnia should be discouraged due to the lack of supportive evidence, risk of adverse events (metabolic and cardiac), and lack of monitoring (e.g., EKG) for adverse events in-theatre. Other drug options to treat insomnia are available on the deployment formulary, which have a lower risk of adverse events than the AAPs.
    - The P&T Committee strongly recommends education of providers regarding the lack of evidence to support use of AAPs for primary insomnia and revision of current theater guidance.
7. With regards to safety, a black box warning applies to the entire class precluding use in elderly patients with behavioral and psychological symptoms of dementia due to increased mortality risk.
8. AAPs have different tolerability profiles as noted below:

- Extrapyramidal symptoms are most likely to occur with risperidone (higher doses), paliperidone, and asenapine; and are least likely to occur with quetiapine, ziprasidone, aripiprazole, iloperidone, and olanzapine.
- Diabetes and weight gain are most commonly associated with clozapine and olanzapine. These effects are less common with aripiprazole, lurasidone, and ziprasidone.
- Hyperprolactinemia has been most commonly associated with risperidone and paliperidone. Aripiprazole, iloperidone, and quetiapine have the lowest risk of this adverse event.
- QTc interval prolongation is a concern with ziprasidone and iloperidone, but is least likely to occur with aripiprazole and lurasidone.

9. Adverse events are usually dose dependent and can be potentiated by patient characteristics such as age and comorbid conditions. AAP receptor binding affinities are associated with individual adverse events. Overall, the benefits conferred by AAPs are offset by limiting adverse effects.
10. For the pediatric population, the AAPs differ in their FDA-approved indications and ages. Aripiprazole, olanzapine, risperidone, paliperidone, and quetiapine are approved for use in the pediatric population.
11. In a request for provider opinion, most respondents wanted 4 or more AAPs on their local formulary. In addition to risperidone, most respondents requested aripiprazole and quetiapine for inclusion on the BCF.
12. The clinician's choice for selecting an AAP should be influenced by the relationship between the efficacy and tolerability profile of the drug as well as individual patient characteristics.

(LCDR Selvester): Dr. Meade will now discuss the cost effectiveness conclusion and Uniform Formulary recommendations

ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — RELATIVE COST EFFECTIVENESS

(PEC Script)

(Dave Meade):

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the AAP Drug Class. Although there are differences within the drug class regarding safety and tolerability profiles, cost minimization analyses (CMA) and budget impact analyses (BIA) were conducted, since clinically relevant differences in efficacy for schizophrenia are not apparent. 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—Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained,

1 absent) BIA results for the AAP agents showed that all investigated scenarios resulted in lower cost estimates compared to current MHS expenditures. Overall cost analyses indicated the most cost-effective scenario and operationally-appropriate choice placed clozapine (Clozaril, generics; Fazaclo), risperidone (Risperdal, Risperdal ODT, generics), aripiprazole (Abilify, Abilify Discmelt), olanzapine (Zyprexa, Zyprexa Zydis), olanzapine/fluoxetine (Symbyax), paliperidone (Invega), quetiapine (Seroquel; Seroquel XR), and ziprasidone (Geodon) on the UF.

ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — UF RECOMMENDATIONS

(PEC Script)

(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 (9 for, 6 against, 2 abstained, 0 absent) clozapine (Clozaril, generics; Fazlaco), risperidone (Risperdal, Risperdal ODT, generics), aripiprazole (Abilify, Abilify Discmelt), olanzapine (Zyprexa, Zyprexa Zydis), olanzapine/fluoxetine (Symbyax), paliperidone (Invega), quetiapine (Seroquel; Seroquel XR), and ziprasidone (Geodon) remain formulary on the UF. The P&T Committee recommended iloperidone (Fanapt), asenapine (Saphris), and lurasidone (Latuda) be designated NF on the UF.

ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — UF IMPLEMENTATION PLAN

(PEC Script)

(Dave Meade):

The P&T Committee recommended (15 for, 0 against, 2 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

(Dave Meade) LTC Young will now provide the physician perspective for the AAP class.

ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — COMMITTEE PHYSICIAN'S PERSPECTIVE

(LTC Young)

LTC Young informed the Panel that there was a lot of discussion on the UF recommendations for this drug class related to the difficulty of the disorders involved. The majority of the P&T Committee agreed that the drugs recommended for non-formulary status did not have as much information available about them as the other agents in this class. They were also less cost effective and don't offer a significant advantage over the other drugs. Additionally, there are several drugs already available on the UF.

ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — PANEL QUESTIONS AND DISCUSSION

The Chair opened the floor for Panel questions and discussion of the recommendations.

Dr. Cohoon noted that the information provided shows that Abilify is the third most utilized drug in this class and asked about the primary reason for that, considering its cost. Dr. Meade indicated it was provider preference.

Ms. Fryar asked about the six Committee members who opposed the UF recommendations, specifically whether they were in favor of putting all of the drugs on formulary. LTC Young replied that they were and that was the reason for their vote.

ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — PANEL VOTE ON UF RECOMMENDATIONS

Without further Panel questions or discussion, Ms. Fryar read the P&T Committee's UF recommendations for the atypical antipsychotic (AAP) 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 upon its collective professional judgment, recommended clozapine (Clozaril, generics; Fazlaco), risperidone (Risperdal, Risperdal ODT, generics), aripiprazole (Abilify, Abilify Discmelt), olanzapine (Zyprexa, Zyprexa Zydis), olanzapine/fluoxetine (Symbyax), paliperidone (Invega), quetiapine (Seroquel; Seroquel XR), and ziprasidone (Geodon) remain formulary on the UF. The P&T Committee recommended iloperidone (Fanapt), asenapine (Saphris), and lurasidone (Latuda) be designated NF on the UF.

The Panel then voted as follows:

Concur: 7 Non-concur: 2 Abstain: 0 Absent: 2

The Panel comments offered were 1) it would be preferable to have all options readily available when dealing with this type of disorders; and 2) if six of the fifteen Committee members voted against the recommendation it is likely they had strong reasons for doing so.

ATYPICAL ANTIPSYCHOTIC (AAP) DRUGS — PANEL VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

There was no Panel discussion of the implementation plan recommendations, which the Chair read for the record.

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

The Panel vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

The Chair then called for the next briefing.

NASAL ALLERGY DRUGS (NADs)

NASAL ALLERGY DRUGS (NADS) — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(LCDR Selvester):

The P&T Committee evaluated the clinical effectiveness of the NADs. The nasal corticosteroids were previously reviewed in November 2005, August 2007, and November 2008. The class is comprised of three subclasses as listed on table 2 on page 3.

Information regarding the safety, effectiveness, and clinical outcomes of these drugs was considered. The clinical review included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

In terms of quantity dispensed (Figure 2 on page 3), fluticasone propionate (Flonase, generics) is the highest utilized nasal allergy drug , followed by mometasone (Nasonex), and azelastine 0.1% (Astelin). The current BCF drug for the NAD Drug Class is azelastine 0.1%; fluticasone propionate was removed from the BCF in May 2010 due to supply issues.

Relative Clinical Effectiveness Conclusion—The P&T Committee voted (17 for, 0 opposed, 0 abstained, 0 absent) to accept the following clinical effectiveness conclusions:

Nasal Corticosteroids:

With regards to efficacy/clinical effectiveness of the nasal corticosteroids, the following conclusions were made:

- FDA-approved indications—The P&T 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 2008 American Academy of Allergy, Asthma and Immunology (AAAAI) and 2010

Allergic Rhinitis and its Impact on Asthma (ARIA) 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—There was no compelling new data to change the conclusion from the 2008 P&T Committee Meeting review, which established there is no evidence of clinically relevant differences between the agents at relieving nasal or ocular symptoms of AR. However, ciclesonide lacks published evidence for reducing ocular symptoms.
- Nasal polyps—Mometasone and beclomethasone are FDA-approved for nasal polyps.
- There was no compelling new evidence to change previous conclusions.

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.
- Systemic effects—For systemic effects of hypothalamic pituitary adrenal-axis suppression, growth suppression, and ocular adverse events (cataracts/glaucoma), 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.
- 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. Nevertheless, flunisolide is poorly tolerated and must be dosed three or four times daily while the others are dosed once or twice daily. Budesonide (Rhinocort AQ) is the only nasal corticosteroid with a pregnancy category B rating by the FDA. 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.

Nasal Antihistamines:

With regards to efficacy/clinical effectiveness of the nasal antihistamines, the following conclusions were made:

- FDA-approved indications—The P&T Committee recognized that there were minor differences between olopatadine (Patanase), azelastine 0.1% (Astelin,

generic), and azelastine 0.15% (Astepro) with regard to FDA-approved uses for SAR and nonallergic rhinitis [e.g., vasomotor rhinitis (VMR)], and pediatric approval.

- Clinical Practice Guidelines—The 2010 ARIA guidelines suggest use of non-sedating oral antihistamines preferentially to nasal antihistamines. The 2008 AAAAI guidelines state that nasal antihistamines are generally less effective than nasal corticosteroids for treating AR, but may be considered for use as first-line treatment for AR and nonallergic rhinitis. Nasal antihistamines are associated with a clinically significant effect on reducing nasal congestion.
- Efficacy for SAR—Azelastine and olopatadine are superior to placebo in relieving symptoms of SAR. There is no new compelling clinical data to suggest one product is more efficacious than the others.
- Head-to-head study—One head-to-head trial comparing the use of olopatadine with azelastine found no difference in relief of nasal symptoms, but suggests that olopatadine may be better tolerated by patients, as shown by a lower incidence of bitter taste.

With regards to safety and tolerability of the nasal antihistamines, the following conclusions were made:

- Local adverse effects—Somnolence is considered a class effect (AAAAI guidelines). Bitter taste has a higher incidence with azelastine, while epistaxis occurred with roughly equal frequency between olopatadine and azelastine.
- Patient preferences and tolerability—The available clinical data is sparse and is limited to manufacturer-sponsored studies, but tends to favor olopatadine. However, there is insufficient evidence to definitively conclude that clinically relevant differences exist between the nasal antihistamines.

Nasal Anticholinergics:

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—2010 AAAAI guidelines state that nasal anticholinergics may effectively reduce rhinorrhea, but have no effect on other nasal symptoms. Although adverse events are minimal, dryness of the nasal membranes may occur.
- Efficacy and Safety—No new efficacy or safety data have been published since the prior review. Ipratropium is rated Pregnancy Category B by the FDA.

(LCDR Selvester) Dr. Meade will now discuss the cost effectiveness conclusion and Uniform Formulary recommendations

NASAL ALLERGY DRUGS (NADS) — RELATIVE COST EFFECTIVENESS

(PEC Script)

(Dave Meade):

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the NADs. CMAs and BIAs were performed based on findings that there were no clinically relevant differences in efficacy, safety, tolerability, and other factors among the NADs. 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—Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

BIA results for the NADs showed that six out of seven investigated scenarios resulted in lower cost estimates than current MHS expenditures. Scenarios where generic fluticasone propionate was selected as a BCF agent, with branded agents olopatadine (Patanase) and mometasone (Nasonex) on the UF were the most cost-effective scenarios overall. Sensitivity analysis results supported the above conclusion unless generic fluticasone propionate becomes unavailable for an extended period of time.

(Off script)

Dr. Meade explained that one of the reasons why this class was looked at was that several manufacturers were going to discontinue making generic Flonase. Additionally, many physicians were indicating that this is one of the worst allergy seasons on record. The aim of the review was to avoid possible shortages in this drug class.

NASAL ALLERGY DRUGS (NADS) — UF RECOMMENDATION

(PEC Script)

(Dave Meade):

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the NADs, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (16 for, 0 opposed, 1 abstained, and 0 absent) to recommend that:

1. Fluticasone propionate (Flonase, generics), flunisolide (generics), mometasone (Nasonex), azelastine 0.1% (Astelin, generic), olopatadine (Patanase), and ipratropium (Atrovent, generics) be classified as formulary on the UF.

2. Azelastine 0.15% (Astepro), beclomethasone (Beconase AQ), budesonide (Rhinocort Aqua), ciclesonide (Omnaris), fluticasone furoate (Veramyst), and triamcinolone (Nasacort AQ) remain designated as NF on the UF.

NASAL ALLERGY DRUGS (NADS) — IMPLEMENTATION PLAN

Not applicable; no products were moved from Uniform Formulary to Non-formulary.

(Dave Meade) LTC Young will now provide the physician perspective.

NASAL ALLERGY DRUGS (NADS) — COMMITTEE PHYSICIAN'S PERSPECTIVE

(LTC Young)

LTC Young told the Panel that there were no controversies in this class; there were no new drugs and no new clinical data to consider and no additional products were recommended for non-formulary placement. The only change from before is that Patanase is now on the UF.

NASAL ALLERGY DRUGS (NADS) — PANEL QUESTIONS AND DISCUSSION

Dr. Cohoon asked what the backup agent would be if there were a shortage of flonase. Dr. Meade said none was selected. One of the purposes of the review was to enable a solicitation for an alternate. In the meantime, there are a lot of products already on the formulary that could be used.

NASAL ALLERGY DRUGS (NADS) — PANEL VOTE ON UF RECOMMENDATION

The Chair read the UF recommendations for this drug class.

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

1. Fluticasone propionate (Flonase, generics), flunisolide (generics), mometasone (Nasonex), azelastine 0.1% (Astelin, generic), olopatadine (Patanase), and ipratropium (Atrovent, generics) be classified as formulary on the UF.

2. Azelastine 0.15% (Astepro), beclomethasone (Beconase AQ), budesonide (Rhinocort Aqua), ciclesonide (Omnaris), fluticasone furoate (Veramyst), and triamcinolone (Nasacort AQ) remain designated as NF on the UF.

Without further discussion, the Panel voted as follows:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

As no implementation plan was required for this drug class, the Chair called for the next presentation.

RECENTLY APPROVED U.S. FDA AGENTS

(PEC Script)

(LCDR Selvester):

For the Newly Approved Drugs, information considered by the Committee for the clinical and cost evaluations included, but were not limited to, the requirements stated in 32 Code of Federal Regulations (CFR) 199.21(e)(1).

NEWLY APPROVED DRUGS—DIPEPTIDYL PEPTIDASE-4 INHIBITOR (DPP-4)/BIGUANIDE FIXED-DOSE COMBINATION (FDC) —Saxagliptin/Metformin XR (Kombiglyze XR)

KOMBIGLYZE XR — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(LCDR Selvester):

Kombiglyze XR is a FDC product containing the DPP-4 inhibitor saxagliptin (Onglyza) and the biguanide metformin extended-release (ER) (generic Glucophage XR) in one tablet. This drug is the second FDA-approved DPP-4/metformin FDC product. The Non-Insulin Diabetes Drug Class, which included the DPP-4s and biguanides separately, as well as combinations, was reviewed during the November 2010 P&T Committee meeting. The drugs included in this class (Table 3 page 4) and DPP-4 utilization (Fig 3 page 5) are in your handout.

Kombiglyze XR is approved for use as adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate. In November 2010, sitagliptin (Januvia) and sitagliptin/metformin immediate-release (IR) (Janumet) were designated with BCF status and saxagliptin was designated with UF status. Automated Prior Authorization or Step Therapy applies to the DPP-4 subclass, which requires a trial of metformin alone or a sulfonylurea (SU) prior to use of sitagliptin, sitagliptin/metformin IR, or saxagliptin. The generic metformin ER component of Kombiglyze XR is available on the BCF as a single agent.

Clinical trials with sitagliptin and saxagliptin when used as monotherapy show reduction in hemoglobin A1C (HbA1C) of 0.4 - 0.79%. The saxagliptin/metformin FDC provides a 2.5% decrease in HbA1c from baseline. There are no head-to-head trials comparing saxagliptin/metformin ER (Kombiglyze XR) and sitagliptin/metformin IR (Janumet). However,

in a head-to-head non-inferiority trial, sitagliptin/metformin IR lowered HbA1c by approximately 0.1% more from baseline than saxagliptin/metformin IR. Saxagliptin was considered non-inferior to sitagliptin. While statistical significance was achieved, the difference between the two agents is not clinically significant. There are no clinically relevant differences between sitagliptin and saxagliptin when combined with metformin in terms of glycemic control, and changes in lipid profile, weight, or blood pressure.

The product labeling for Kombiglyze XR contains the same contraindications and warnings as metformin. Renal and hepatic impairment remains a concern as well as other conditions that increase the risk of developing lactic acidosis. Kombiglyze XR can be dosed once daily. To achieve the target dose of metformin, patients can take an additional dose of metformin or take two 2.5mg/1000mg Kombiglyze XR tablets together once daily.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) saxagliptin/metformin XR (Kombiglyze XR) offers no clinically meaningful therapeutic advantage over sitagliptin/metformin IR (Januvia) in terms of efficacy, safety, or tolerability.

(LCDR Selvester):

Dr. Meade will now discuss the cost effectiveness conclusion and Uniform Formulary recommendations

KOMBIGLYZE XR — RELATIVE COST EFFECTIVENESS

(PEC Script)

(Dave Meade):

CMA was performed to evaluate the cost of saxagliptin/metformin ER (Kombiglyze XR) in relation to the other UF DPP-4 inhibitor/biguanide FDC agent, sitagliptin/metformin IR (Janumet), and to generic metformin IR or ER in combination with sitagliptan (Januvia) or saxagliptan (Onglyza).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that saxagliptin/metformin ER (Kombiglyze XR) tablets were more costly, compared with the other DPP-4s currently designated with BCF or UF status.

KOMBIGLYZE XR — UF RECOMMENDATION

(PEC Script)

(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 (16 for, 0 opposed, 1 abstained, 0 absent) saxagliptin/metformin ER (Kombiglyze XR) remain formulary on the UF. Prior authorization/step therapy for the DPP-4s would require a trial of metformin or sulfonylurea prior to use of Kombiglyze XR for new patients.

KOMBIGLYZE XR — PA CRITERIA

(PEC Script)

(Dave Meade):

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to Kombiglyze XR. Coverage would be approved if the patient met any of the following criteria:

1. Automated PA criteria:

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

    b) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, or Onglyza) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual PA criteria, if automated criteria are not met:

    a) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.

    b) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.

    c) The patient has a contraindication to both metformin and a SU.

KOMBIGLYZE XR — UF AND PA IMPLEMENTATION PLAN

(PEC Script)

(Dave Meade):

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

(Dave Meade) LTC Young will now provide the physician perspective.

KOMBIGLYZE XR — COMMITTEE PHYSICIAN'S PERSPECTIVE

(LTC Young)

LTC Young noted again that this is a combination drug and said it is the second combination product available in this subclass. The first one – Janumet – is dosed twice daily whereas Kombiglyze can be dosed once daily. Regarding the PA criteria, she noted that the same criteria were adopted as are being used for Januvia, Janumet and Onglyza, i.e. that patients are required to have had a trial of metformin or a sulfonylurea first.

KOMBIGLYZE XR — PANEL QUESTIONS AND DISCUSSION

Dr. Salom remarked that he was confused by the fact that one of the PA criteria for Kombiglyze was the patient having an adverse reaction to one of the components of the drug, namely metformin. LCDR Selvester agreed that there is an error in the PA criteria, which he believes were taken from Onglyza. Criteria "a" and "c" in the manual PA criteria noted above are not required and should be removed. Only criterion "b" -- the patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment – would apply. The PEC staff agreed that the record should be corrected to make this change.

Mr. Hutchings noted that Kombiglyze is not cost effective but remains on the UF. He asked if that is a function of the difference in dosage. Dr. Meade explained that the reason was more that the Committee didn't want to limit the MTFs if they wanted to use the combination drug.

Mr. Hutchings also asked whether, when applying the automated PA criteria, the requirement would be for both "a" and "b" or whether it would be for "a" or "b". The answer provided was that it would be "a" or "b".

Dr. Crum commented that he still doesn't understand why Kombiglyze is recommended for UF placement since it doesn't have significant therapeutic advantages and costs more. Dr. Meade replied that the question was whether the Committee wanted to limit what was available at the MTFs. If the drug is made non-formulary, it would be less available and also more costly in the retail network.

KOMBIGLYZE XR — PANEL VOTE ON UF RECOMMENDATION

The Chair noted that she would read the corrected recommendations for the record as the Panel votes. She then read the UF recommendation.

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 saxagliptin/metformin ER (Kombiglyze XR) remain formulary on the UF. Prior authorization/step therapy for the DPP-4s would require a trial of metformin or sulfonylurea prior to use of Kombiglyze XR for new patients.

The Panel vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

KOMBIGLYZE XR — PANEL VOTE ON PA CRITERIA

The Chair read the **corrected recommendation** regarding the PA criteria for Kombiglyze.

1. Automated PA criteria:

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

   b. The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, or Onglyza) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual PA criteria, if automated criteria are not met:

   a. The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.

Note for the record: two additional manual PA criteria were removed from the original recommendation as being erroneous (see discussion above). The vote reflects the corrected recommendation.

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

KOMBIGLYZE XR — PANEL VOTE ON IMPLEMENTATION PLAN

The Chair then read the implementation plan recommendation.

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

Again the Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

NEWLY APPROVED DRUGS — OPTHALMIC-1 DRUG CLASS — Bromfenac 0.09% Ophthalmic Solution (Bromday)

BROMDAY — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(LCDR Selvester):

Relative Clinical Effectiveness—Bromfenac 0.09% ophthalmic solution (Bromday) is a non-steroidal anti-inflammatory drug (NSAID). It is the only ophthalmic NSAID approved for once daily dosing. Bromday is the same formulation of bromfenac (Xibrom) that was previously a twice daily dosed product. The branded formulation Xibrom was withdrawn from the market in February 2011 by the manufacturer. At the time of the May 2011 P&T Committee meeting, no generic formulations of Xibrom were approved. The Ophthalmic-1 Class was reviewed at the August 2010 P&T Committee meeting. All the ophthalmic NSAIDs are designated with formulary status on the UF; none are designated with BCF status. The drugs included in this class (Table 4 page 5) and ophthalmic NSAID utilization (Fig 4 page 6) are in your handout.

Bromday was approved under a Supplemental New Drug Application using the data from Xibrom to change the dosing regimen to once daily dosing. Two Phase III placebo-controlled studies concluded that bromfenac dosed once daily for 16 days is effective for treating inflammation and pain in patients who have undergone cataract extraction with intraocular lens implantation. There are no head-to-head clinical trials comparing the bromfenac once-a-day formulation with the twice-a-day formulation. There are no studies comparing the bromfenac once daily formulation with any other ophthalmic NSAIDs. The safety profile of bromfenac is consistent with the other ophthalmic NSAIDs. The most common adverse events in the Phase III clinical trials that led to drug discontinuation and which occurred in a higher incidence than placebo were eye inflammation, photophobia, and eye pain. Based on the safety data from two Phase III studies, there are no clinically relevant differences between bromfenac ophthalmic solution and other ophthalmic NSAIDs.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) there is no published evidence to suggest that bromfenac ophthalmic solution 0.09% (Bromday) has a compelling clinical advantage over other ophthalmic NSAID products currently included on the UF.

LCDR Selvester) Dr. Meade will now discuss the cost effectiveness conclusion and Uniform Formulary recommendations

BROMDAY — RELATIVE COST EFFECTIVENESS

(PEC Script)

(Dave Meade):

The P&T Committee evaluated the cost of bromfenac 0.09% ophthalmic solution (Bromday) in relation to the efficacy, safety, tolerability, and clinical outcomes of the other Ophthalmic-1 NSAIDs prescribed for postoperative pain and inflammation following cataract surgery. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of Bromday compared to other UF agents. CMA results showed the projected weighted average cost per day for Bromday is higher than generic ophthalmic NSAIDs, but comparable in price to brand name ophthalmic NSAIDs.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) bromfenac 0.09% ophthalmic solution (Bromday) is cost-effective relative to the other branded Ophthalmic-1 NSAIDs in this class.

BROMDAY — UF RECOMMENDATION

(PEC Script)

(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 (15 for, 0 opposed, 1 abstained, 1 absent) bromfenac 0.09% ophthalmic solution (Bromday) remain formulary on the UF.

BROMDAY — IMPLEMENTATION PLAN

Not applicable.

(Dave Meade) LTC Young will now provide the physician perspective.

BROMDAY — COMMITTEE PHYSICIAN'S PERSPECTIVE

(LTC Young)

LTC Young noted again that Bromday is the exact same product as the original formulation (Xibrom). The only change is the recommendation for a once-daily dose instead of two times a day.

BROMDAY — PANEL QUESTIONS AND DISCUSSION

Ms. Fryar began the questioning. She asked whether she understood correctly that Bromday was actually more expensive and not as cost effective as other drugs that are available. Dave Meade said that there are generics available that are less cost effective but this product is comparable to the other branded products in this class.

Mr. Hutchings commented that ophthalmologists prefer to use branded products over generic. Ms. Fryar asked if that was due to a safety issue. Mr. Hutchings answered that it isn't a proven safety issue but is the kind of issue that impacts the perception of safety.

BROMDAY — PANEL VOTE ON UF RECOMMENDATION

The Chair read the UF recommendation for Bromday.

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 bromfenac 0.09% ophthalmic solution (Bromday) remain formulary on the UF.

The Panel vote was:

Concur: 8 Non-concur: 1 Abstain: 0 Absent: 2

The non-concurring Panelist commented that his vote was due to the availability of alternatives and the fact that the manufacturer appears to have done nothing more than change the label and the dosing recommendation.

NEWLY APPROVED DRUGS — ALPHA BLOCKERS FOR BENIGN PROSTATIC HYPERPLASIA (BPH) — Tamsulosin/Dutasteride (Jalyn)

JALYN — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(LCDR Selvester):

Relative Clinical Effectiveness—Tamsulosin/dutasteride (Jalyn) is a FDC product containing tamsulosin (Flomax, generics), an uroselective alpha-1 blocker (A1B) and dutasteride (Avodart), a 5-alpha reductase inhibitor (5-ARI). Jalyn is the first combination product for BPH. The drug is indicated for treatment of symptomatic BPH in men who have an enlarged prostate (>30 mL prostate volume). Jalyn is classified in the A1B subclass of the BPH agents, which was last reviewed in May 2010. Automated PA/Step Therapy applies to the A1B subclass, which requires a trial of generic tamsulosin or alfuzosin (Uroxatral) for new patients. For the 5-ARI subclass, finasteride (Proscar, generics) is designated with BCF status, and dutasteride (Avodart)

is nonformulary on the UF. The drugs included in this class (Table 5 page 6) and BPH drug utilization (Fig 5 page 7) are in your handout.

FDA approval for Jalyn is based on the large randomized controlled four-year study, Combination of Avodart and Tamsulosin (CombAT), which evaluated the combination versus individual components. Results from the CombAT study showed the combination of dutasteride and tamsulosin (Jalyn) was not superior to dutasteride monotherapy for males with BPH with an enlarged prostate (>30ml), in terms of objective clinical progression to acute urinary retention (AUR) or BPH-related surgery. The combination was superior to both tamsulosin and dutasteride monotherapy in terms of improvement of BPH-related symptoms.

The safety and tolerability data from the ComBAT study did not show a clinically relevant difference with Jalyn as compared to monotherapy with tamsulosin or dutasteride. There was a numerical increase in the incidence of cardiac failure with combination tamsulosin/dutasteride, however the FDA determined that co-morbidities were more likely the cause than the drug effect. There was a higher incidence of sexual adverse events (e.g., erectile dysfunction, retrograde ejaculation) with Jalyn, but these did not lead to a higher discontinuation rate with Jalyn, compared to the single agents administered as monotherapy.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that the FDC tamsulosin/dutasteride (Jalyn) is superior to tamsulosin and dutasteride monotherapy in terms of delaying BPH symptoms. However, it was not superior to dutasteride in delaying clinical progression to AUR and BPH-related surgery. There were no clinically relevant differences for Jalyn as compared to tamsulosin or dutasteride monotherapy in terms of safety and tolerability. The P&T Committee also agreed there is a high degree of therapeutic interchangeability between Jalyn and other combinations of selective A1B and a 5-ARI (e.g., tamsulosin/finasteride).

(LCDR Selvester) Dr. Meade will now discuss the cost effectiveness conclusion and Uniform Formulary recommendations

JALYN — RELATIVE COST EFFECTIVENESS

(PEC Script)

(Dave Meade):

The P&T Committee evaluated the cost of tamsulosin/dutasteride (Jalyn) in relation to the efficacy, safety, tolerability, and clinical outcomes of the other uroselective A1Bs and 5-ARIs used for BPH. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of Jalyn compared to other UF agents. Results from the CMA showed the projected weighted average cost per day for Jalyn was higher than the most cost-effective combination—generic tamsulosin and generic finasteride. However, Jalyn was more cost-effective than its individual components taken separately.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) the combination of tamsulosin and finasteride administered together represents the most cost-effective combination of uroselective A1Bs and 5-ARIs for treatment of BPH. The FDC tamsulosin/dutasteride (Jalyn) is a cost-effective alternative relative to other combinations of A1Bs and dutasteride (Avodart).

JALYN — UF RECOMMENDATION

(PEC Script)

(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 (14 for, 1 opposed, 1 abstained, 1 absent) tamsulosin/dutasteride (Jalyn) remain formulary on the UF, with automated PA/Step Therapy requiring generic tamsulosin or alfuzosin (Uroxatral) for new patients.

JALYN — PA CRITERIA

(PEC Script)

(Dave Meade):

Prior authorization for the A1Bs requires a trial of a step-preferred drug [tamsulosin or alfuzosin (Uroxatral)] prior to a non-step-preferred A1B [silodosin (Rapaflo)]. Tamsulosin/dutasteride (Jalyn) would be designated non-step-preferred. The P&T Committee recommended (13 for, 1 opposed, 2 abstained, 1 absent) the following PA criteria apply to tamsulosin/dutasteride (Jalyn):

1. Automated PA criteria:
    a) The patient has received a prescription for a preferred agent in the A1B subclass at any MHS pharmacy point of service (MTFs, retail network pharmacies, or home delivery) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:
    a) The patient has received a trial of tamsulosin or alfuzosin and had an inadequate response and requires therapy with both an A1B and 5-ARI.
    b) The patient has received a trial of alfuzosin but was unable to tolerate it due to adverse effects but is expected to tolerate tamsulosin and requires therapy with both an A1B and 5-ARI.
    c) Treatment with alfuzosin is contraindicated for this patient (e.g., due to hypersensitivity) but tamsulosin is not contraindicated, and the patient requires therapy with both an A1B and 5-ARI.

d) The patient requires therapy with both an A1B and 5-ARI and requires a fixed-dose combination (e.g., swallowing difficulties).

JALYN — UF AND PA IMPLEMENTATION PLAN

(PEC Script)

(Dave Meade):

The P&T Committee recommended (14 for, 0 opposed, 2 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

(Dave Meade) LTC Young will now provide the physician perspective.

JALYN — COMMITTEE PHYSICIAN'S PERSPECTIVE

(LTC Young):

LTC Young noted that Jaylyn is the first combination product in this class for the treatment of BPH. Some committee members felt that Jalyn should be made non-formulary because its dutateride component is non-formulary. However, the combination product is more cost effective than its two components taken separately so the decision was to make Jalyn formulary. It was placed behind the step with a trial of tamsulosin or Uroxatral required first. She said most patients would be put on an alpha blocker first anyway. The whole alpha blocker class is scheduled to be reviewed again soon.

JALYN — PANEL QUESTIONS AND DISCUSSION

Dr. Cohoon asked why Committee members abstain when a drug is placed on the UF with a PA in place. Dr. Meade said there are various reasons.

Mr. Hutchings said he intends to vote to non-concur on this recommendation because he believes the combination is not necessary and there are less expensive alternatives available for the patient, citing an example. He also noted that changing to combination drugs tends to create chaos at the pharmacy. Dr. Meade noted that the patent expiration is coming up very quickly on Avodart, which will make the class largely generic. That will tend to curb the use of Jalyn. Mr. Hutchings said he would prefer to do that now rather than wait until there are a larger number of patients to deal with. Dr. Meade said he thought that the step therapy of the PA would tend to have that effect anyway.

Ms. Fryar asked for clarification about the wording of the PA criteria.

JALYN — PANEL VOTE ON UF RECOMMENDATION

The Chair read the P&T Committee's UF recommendation for Jalyn.

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 tamsulosin/dutasteride (Jalyn) remain formulary on the UF, with automated PA/Step Therapy requiring generic tamsulosin or alfuzosin (Uroxatral) for new patients.

The Panel vote was:

Concur: 7 Non-concur: 2 Abstain: 0 Absent: 2

The non-concurring Panel members commented that this combination drug does not seem to be necessary and that less costly alternatives are available for patients.

JALYN — PANEL VOTE ON PA CRITERIA

The Chair read the recommended PA criteria for Jalyn.

Prior authorization for the A1Bs requires a trial of a step-preferred drug [tamsulosin or alfuzosin (Uroxatral)] prior to a non-step-preferred A1B [silodosin (Rapaflo)]. Tamsulosin/dutasteride (Jalyn) would be designated non-step-preferred. The P&T Committee recommended the following PA criteria apply to tamsulosin/dutasteride (Jalyn):

1. Automated PA criteria:
   a) The patient has received a prescription for a preferred agent in the A1B subclass at any MHS pharmacy point of service (MTFs, retail network pharmacies, or home delivery) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:
   a) The patient has received a trial of tamsulosin or alfuzosin and had an inadequate response and requires therapy with both an A1B and 5-ARI, or
   b) The patient has received a trial of alfuzosin but was unable to tolerate it due to adverse effects but is expected to tolerate tamsulosin and requires therapy with both an A1B and 5-ARI, or
   c) Treatment with alfuzosin is contraindicated for this patient (e.g., due to hypersensitivity) but tamsulosin is not contraindicated, and the patient requires therapy with both an A1B and 5-ARI, or
   d) The patient requires therapy with both an A1B and 5-ARI and requires a fixed-dose combination (e.g., swallowing difficulties).

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

JALYN — PANEL VOTE ON IMPLEMENTATION PLAN

The Chair then read the implementation plan for Jalyn.

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

The Panel vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

ITEMS FOR INFORMATION

(PEC Script)

(Dave Meade):

A. Dabigatran (Pradaxa)—Potential Prior Authorization:

Dabigatran is the first oral anticoagulant to reach the market since warfarin (Coumadin). It is currently limited to use in patients with non-vavular atrial fibrillation to reduce the risk of stroke and systemic embolism. The P&T Committee reviewed the existing clinical data for dabigatran and its advantages and disadvantages versus warfarin. The P&T Committee also discussed whether prior authorization was required to ensure prescribing is consistent with the current FDA-approved indications. The P&T Committee agreed that Prior Authorization was not needed at this time. Dabigatran will be reviewed with the other anticoagulants at a future meeting.

(Dave Meade) LTC Young will now provide the physician perspective.

(LTC Young)

LTC Young said the Committee discussed the need for a PA but found that the majority of the time the drug was used within FDA-approved usage guidelines. Several new products are in the pipeline that are expected to be approved by FDA within the next year. Since the MHS utilization was found to be appropriate, a PA was deemed not to be required at this time.

Panel Questions

The Panel had no questions about this matter.

B. Pharmacy Co-pay Changes:

At the May 11-12, 2011 meeting, the Pharmacy &Therapeutics Committee, based on experience with the Uniform Formulary, changes in economic circumstances, and other appropriate factors, voted (14 for, 0 against, 3 abstain, 0 absent) to recommend an adjustment to the per prescription co-payments established in 32 C.F.R. §199.21(i)(2). The co-payment changes proposed in the President's FY 2012 budget for tiers 1 (generic)/2 (formulary)/3 (non-formulary) are $5/$12/$25 for up to a 30-day supply at the Retail Network and $0/$9/$25 for up to a 90-day supply at the

Mail Order Pharmacy. These adjusted amounts maintain compliance with the requirements of 10 U.S.C. §1074g(a)(6).

Panel Questions

Dr. Crum asked when the changes would be effective. Dr. Meade said he didn't know yet. A staff member in the audience noted that the change was proposed in the President's budget for FY 2012, which means that it wouldn't take effect before October 1. Dr. Cohoon asked why three Committee members abstained. The answer given was that they saw it as a budget matter and didn't feel it was appropriate for the Committee to either support or not support such changes. There was also a brief discussion as to whether this should have been brought before the P&T Committee for discussion earlier. The staff member noted that the change will be included in the regulations and that such regulations are required to be reviewed by the P&T Committee.

One Panel member commented that the way the changes are structured there is the potential for families to be impacted by changes for medications that are not maintenance medications, for example an antibiotic or an ear infection medicine.

Another Panel member asked if the numbers were proposed by the White House.

Closing Remarks

The Chair thanked the presenters and those in attendance for coming to the meeting.

The DFO, LTC Spridgen, closed the meeting by announcing that the next P&T Committee meeting is scheduled for August 10 and 11 and that the next BAP meeting is scheduled for September 22, 2011.

LTC Spridgen also announced that this is her last official function as the Designated Federal Officer (DFO) as she is retiring this summer. She said it has been a true pleasure to serve as DFO for the Advisory Panel. Ms. Fryar thanked LTC Spridgen for her work with the Panel and for her strong impact on beneficiaries.

The meeting was adjourned at 10:40 A.M.

Deborah Fryar

Ms. Deborah Fryar,
Chairperson, Uniform Formulary Beneficiary Advisory Panel

Appendix 1 06/23/2011 Meeting Minutes

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 commonly used as acronyms in Panel discussions 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
- AAP — Atypical Antipsychotic (a drug class)
- 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
- BP — Blood pressure
- BPA — Blanket Purchase Agreement
- CEA — Cost-effectiveness analysis
- CFR — Code of Federal Regulations
- CHD — Coronary heart disease
- CMA — Cost-Minimization Analysis
- COMBAT — Combination of Avodart and Tamsulosin (a study)
- COPD — Chronic obstructive pulmonary disorder
- CPG — Clinical Practice Guideline
- CR — Controlled Release (a drug formulation)
- CV — Cardiovascular
- DEA — U.S. Drug Enforcement Administration
- DFO — Designated Federal Officer
- DM — Diabetes mellitus
- 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
- IR — Immediate Release (a drug formulation)
- IV — Intravenous
- MHS — Military Health System
- MN — Medical Necessity

- MTF — Military Treatment Facility
- NADs — Nasal Allergy Drugs (a drug class)
- NDAA — National Defense Authorization Act
- NF — Non-formulary
- NIH — National Institutes of Health
- NNH — Number Needed to Harm
- NNT — Number Needed to Treat
- NSAID — Non-steroidal anti-inflammatory drug
- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DoD Pharmacy and Therapeutics Committee
- PAR — Perennial allergic rhinitis
- PDTS — Pharmacy Data Transaction Service
- PEC — DoD Pharmacoeconomic Center
- PORT — Pharmacy Outcomes Research Team
- POS — Point of Service
- PTSD — Post Traumatic Stress Disorder
- RCTs — Randomized Control Trials
- SAR — Seasonal allergic rhinitis
- SNRIs — Selective neopinephrine reuptake inhibitors
- SR — Sustained release (a drug formulation)
- SQ — Subcutaneously
- SSRIs — Selective serotonin reuptake inhibitors
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TPHARM — TRICARE Pharmacy Program
- TRRx — TRICARE Retail Pharmacy Program
- UF — DoD Uniform Formulary
- USC. — United States Code
- VA — U.S. Department of Veterans Affairs
- VARR — Voluntary Agreement on Retail Rebates