

1 February 2010

Executive Summary

UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL COMMENTS 14 January 2010

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy & Therapeutics (P&T) Committee November 2009 meeting.

1. **Phosphodiesterase Type-5 (PDE-5) Inhibitors for Pulmonary Arterial Hypertension (PAH) Class:** The P&T Committee recommended the following:

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, voted (14 for, 0 opposed, 1 abstained, 1 absent) to recommend that:

- 1) Sildenafil (Revatio 20 mg) remain classified as formulary on the UF.

- 2) Tadalafil (Adcirca 20 mg) be designated as non-formulary under the UF, based on cost effectiveness.

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent)

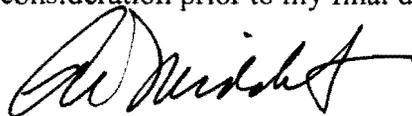
1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendations for formulary and non-formulary agents.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 60 days.

Director, TMA:

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



2. Disease-Modulating Drugs for Multiple Sclerosis — Interferon Beta-1b Injection (Extavia): The P&T Committee recommended the following:

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, 0 abstained, 1 absent) interferon beta-1b injection (Extavia) be designated non-formulary on the UF.

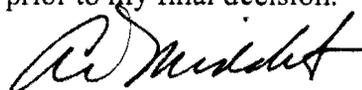
The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at Military Treatment Facilities (MTFs) no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation for interferon beta-1b injection (Extavia) be designated non-formulary on the UF.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 60days.

Director, TMA:

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



3. Bupropion Hydrobromide Extended Release (Bupropion HBr ER) Tablets (Aplenzin): The P&T Committee recommended the following:

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the AD-1s, and other relevant factors, the P&T Committee voted (14 for, 0 opposed, 2 abstained, 0 absent) to recommend bupropion HBr ER tablets (Aplenzin) be designated as non-formulary under the UF, based on cost effectiveness.

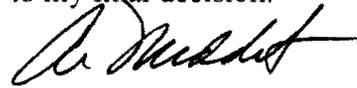
The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation for bupropion hydrobromide extended release tablets (Aplenzin) be designated as non-formulary on the UF.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 60days.

Director, TMA:

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



4. Antidepressant-1s (AD-1s) — Milnacipran Tablets (Savella): The P&T Committee recommended the following:

Taking into consideration the conclusions from the relative clinical effectiveness, 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, 0 absent) that milnacipran (Savella) be designated non-formulary on the UF.

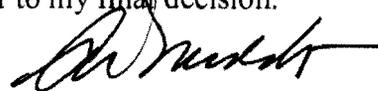
The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that milnacipran (Savella) be designated non-formulary on the UF.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 60days.

Director, TMA:

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



5. Overactive Bladder Drugs (OABs) — Oxybutynin Topical Gel (Gelnique): The P&T Committee recommended the following:

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, 0 abstained, 1 absent) oxybutynin 10% gel (Gelnique) be designated non-formulary on the UF.

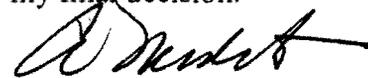
The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that oxybutynin 10% gel (Gelnique) be designated non-formulary on the UF.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 60days.

Director, TMA:

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



6. Narcotic Analgesics — Tapentadol Tablets (Nucynta): The P&T Committee recommended the following:

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, 0 absent) tapentadol (Nucynta) be designated non-formulary on the UF. This recommendation was based on the clinical effectiveness conclusion and the determination that morphine sulfate (MS-IR/generic; MS-Contin/generic) remains the most cost-effective narcotic analgesic on the UF compared to tapentadol (Nucynta).

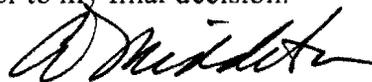
The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that tapentadol (Nucynta) be designated non-formulary on the UF.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 60days.

Director, TMA:

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



7. Narcotic Analgesics — Tramadol Extended Release Tablets (Ryzolt): The P&T Committee recommended the following:

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, 0 abstained, 1 absent) tramadol ER tablets (Ryzolt) be designated non-formulary on the UF. This recommendation was based on the clinical effectiveness conclusion and the determination that Ultram (tramadol IR) remains the most cost effective low-potency single narcotic agent on the UF compared to Ryzolt (tramadol ER).

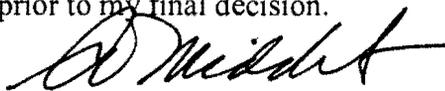
The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that tramadol ER tablets (Ryzolt) be designated non-formulary on the UF.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 60days.

Director, TMA:

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



~~7. Narcotic Analgesics~~ **8. Renin Angiotensin Aldosterone Antihypertensive Agents (RAAs) — Valsartan/Amlodipine/Hydrochlorothiazide (HCTZ) Tablets (Exforge HCT):** The P&T Committee recommended the following:

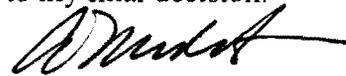
Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (4 for, 11 opposed, 0 abstained, 1 absent) to recommend that valsartan/amlodipine/HCTZ (Exforge HCT) be designated as non-formulary on the UF, thus Exforge HCT was recommended to be retained on the uniform formulary.

Summary of Panel Vote/Comments:

- The Panel voted 4 Concur, 6 Non-Concur, 0 Absent regarding the recommendation that Exforge HCT should remain as formulary on the UF.
- The BAP comment regarding this action was that increased compliance may not occur, but that the possibility exists that some patients will be forced to take extra and unneeded medication simply to obtain the agents they do need at formulary co-pay cost. Finances are also a motivator in regard to compliance.
- Based on the possibility that the Director, TMA may follow the BAP's recommendation to designate Exforge HCT as non-formulary on the UF, the Panel voted 8 Concur, 0 Non-Concur, 2 Abstain, 0 Absent regarding a BAP recommended implementation period of 60days.

Director, TMA:

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



9. Re-evaluation of Wellbutrin XL's Uniform Formulary Status: The P&T Committee recommended the following:

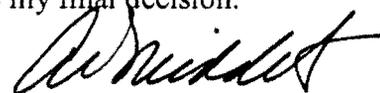
Taking into consideration the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 1 abstained, and 0 absent) that bupropion ER (Wellbutrin XL, generic) be immediately reclassified as generic on the UF. Wellbutrin XL was included on the "list of non-formulary drugs for re-evaluation of UF status" presented to the Beneficiary Advisory Panel in January 2008 and approved by the Director, TMA on 13 February 2008. No further approval is needed.

Summary of Panel Vote/Comments:

- The Panel voted 8 Concur, 0 Non-Concur, 2 Abstain, 0 Absent regarding the recommendation that bupropion ER (Wellbutrin XL, generic) be designated formulary on the UF.

Director, TMA:

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



10. Implementation of Federal Ceiling Price Regulation: The P&T Committee recommended the following:

- A. The following branded drugs with generic equivalents follow the standard TRICARE rules for brand-generic prior-authorization criteria.

| | | |
|----------|---------|-----------------------|
| Aclovate | Altace | Carnitor, Carnitor SF |
| Cutivate | Cytosan | Depakene |

| | | |
|------------|----------|-------------------|
| Kaon-CL | Mobic | Omnicef |
| Persantine | Pletal | Septra; Septra DS |
| Silvadene | Tapazole | Temovate |
| Viroptic | Zonegran | |

- B. The implementation date for the medical necessity criteria for the branded drugs will not be prior to 1 April 2010 and not later than 180 days after the minutes of this meeting are signed.
- C. The transition period at the MTF POS for the medical necessity criteria for the branded drugs as ending no later than 1 January 2011.
- D. The following drugs retain formulary status on the Uniform Formulary.

ARICEPT
 ARICEPT ODT
 DILANTIN
 EPIPEN
 EPIPEN JR
 FARESTON
 HEXALEN
 MENOPUR
 MESNEX
 QUALAQUIN
 TARGRETIN
 VANCOCIN HC

- E. The following drugs retain non-formulary status or be designated non-formulary on the Uniform Formulary:

| | | | |
|----------------|-------------------|------------|-------------|
| ADOXA | CYCLOGYL | ESGIC | METHYLIN ER |
| ALLEGRA | CYCLOSPORINE | ESGIC-PLUS | MIMYX |
| ALOCRIL | DARVOCET A500 | FML | MONONESSA |
| AMICAR | DARVOCET-N 100 | FML FORTE | NATAFORT |
| ANTABUSE | DARVOCET-N 50 | FML S.O.P. | NORCO |
| ARMOUR THYROID | DARVON | FRAGMIN | OCUFEN |
| AVAGE | DARVON-N | GENGRAF | OCUFLOX |
| AZASAN | DENAVIR | GLUCAGEN | OGEN |
| AZELEX | DILANTIN | GRANULEX | OPTASE |
| BANZEL | DILTZAC ER | HYCET | PACERONE |
| BETAGAN | DORAL | INDERAL LA | PERANEX HC |

| | | | |
|-------------------|-------------------------|-----------------------|-----------------|
| BIAXIN XL | DUET STUARTNATAL | KERAFOAM | PERPHENAZINE |
| BLEPHAMIDE | E.E.S. 200 | LAMICTAL ODT | PHRENILIN FORTE |
| BLEPHAMIDE SOP | E.E.S. 400 | LAMICTAL ODT (BLUE) | POLY-PRED |
| BRAVELLE | ELDOPAQUE FORTE | LAMICTAL ODT (GREEN) | POLYTRIM |
| BREVOXYL-4 | ELDOQUIN FORTE | LAMICTAL ODT (ORANGE) | PRED MILD |
| BREVOXYL-8 | ELESTAT | LAMICTAL XR | PRED-G |
| CAFCIT | ELIMITE | LINDANE | PRIMSOL |
| CAPITAL W-CODEINE | EMLA | LO-OVRAL-28 | PROCTOCORT |
| CARDENE SR | EPIFOAM ERGOLOID | LORCET 10-650 | PROCTOFOAM- HC |
| CITRANATAL 90 DH | MESYLATES | LORCET PLUS | PROGLYCEM |
| CITRANATAL DH | ERYPED 200 | LORTAB | REPRONEX |
| CITRANATAL RX | ERYPED 400 | MAGNACET | RIMSO-50 |
| CLARIFOAM EF | ERY-TAB ERYTHROCIN | MAVIK | ROCALTROL |
| CLINDESSE | STEARATE ERYTHROMYCI | MAXIDONE | ROSAC |
| CORZIDE | N | MEBARAL | VIVACTIL |
| SALAGEN | TRINESSA | ULTRASE MT 20 | XENADERM |
| SALKERA | TUSSICAPS | VICODIN ES | ZARONTIN |
| STIMATE | ULTRASE | VOCIPROFEN | UROKIT-K |
| SYNTHROID | ULTRASE MT 12 | VIMPAT | |
| THEO-24 | ULTRASE MT 18 | VIOKASE | |

- F. The implementation date for pre-authorization will not be prior to 1 April 2010 and not later than 180 days after the minutes of this meeting are signed by the Director, TMA.
- G. Formulary status of a drug recommended to move from Tier 2 to Tier 3 will stay in Tier 2 if a Price Agreement is received prior to 1 February 2010.
- H. The transition period at the MTF POS for drugs recommended to move from Tier 2 to Tier 3 as if there will still on Tier 2 for purposes of MTF availability until 1 January 2011.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that the branded drugs with generic equivalents will follow the standard TRICARE rules for brand-generic prior-authorization criteria.

- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that the implementation date for the medical necessity criteria for the branded drugs will not be prior to 1 April 2010 and not later than 180 days after the minutes of this meeting are signed.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that Aricept, Aricept ODT, Dilantin (Pediatric), Epipen, Epipen Jr., Fareston, Hexalen, Menopur, Mesnex, Qaliquin, Targretin, and Vancocin HC be retained on formulary status.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the recommendation to move the before mentioned medications from formulary to non-formulary status on the UF.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the implementation date of not being prior to April 2010 and not later than 180 days after the minutes being signed.
- The Panel voted 10 Concur, 0 Non-Concur, 0 Absent regarding the formulary status of a drug recommended to move from Tier 2 to Tier 3 staying in Tier 2 if a pricing agreement is received prior to 1 February 2010.

Director, TMA:

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



Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary

January 14, 2010

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
- Santiago Chavez, Association of Military Surgeons of the United States, representing the Military Coalition
- Barbara Cohoon, National Military Families Association, 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, Mt. Sinai School of Medicine
- Marissa Schlaifer, Medical Professional, Academy of Managed Care Pharmacy

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 9:40 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 November 5 and 6, 2009 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 classes:
 1. Phosphodiesterase Type 5 Inhibitors (PDE-5 inhibitors) for Pulmonary Arterial Hypertension
 2. Designated Newly-Approved Drugs:
 - Multiple Sclerosis-Disease Modulating Agents (MS-DMDs) – Extavia (interferon beta 1b injection)

- Anti-depressant-1 Agents (AD-1s) – Aplenzin (bupropion hydrobromide extended release tablets)
- Anti-depressant-1 Agents (AD-1s) – Savella (milnacipran tablets)
- Overactive Bladder Drugs (OABs) – Gelnique (oxybutynin topical gel)
- Narcotic Analgesics – Nucynta (tapentadol tablets)
- Narcotic Analgesics – Ryzolt (tramadol extended release tablets)
- Renin Angiotensin Antihypertensive Agents (RAAs) – Exforge HCT (valsartan/amlodipene/hydrochlorothiazide tablets)

3. Status of Wellbutrin XL (bupropion hydrochloride extended release tablets) on the Uniform Formulary

- Formulary Status of drugs not in compliance with 2008 NDAA Section 703
- Information Presentation: FY 2009 Formulary Performance and 2010 Prospectus

Opening Remarks

Lt Col Bacon 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 deems necessary and appropriate.

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 are:

- 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, Lt Col Bacon 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 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 Ms. Embry'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 then introduced the individual members of the Panel, noting there are three new members present for the first time (Ira. Salom, Katherine O'Neill and Santiago Chavez) and asked each to briefly highlight their background. LtCol Bacon also noted 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

BAP Chair, Deborah Fryar, thanked those present for coming, expressed the Panel's appreciation for the work done in preparation for today's meeting and thanked the individual Panel members for their continuing commitment to the BAP process. Before beginning the presentations, Ms. Fryar asked for clarification of the difference, if any, between "newly-approved" and "newly-launched" drugs. LTC Spridgen replied that the term "newly-approved" refers to a drug's status with the Federal Food and Drug Administration (FDA);

drugs recently receiving FDA approval are said to be “newly-approved.” The term “newly-launched” refers to a drug’s status on the market. FDA-approved drugs may not be marketed immediately. When they are put on the market by the manufacturer, they are termed “newly launched.”

Without further discussion, Ms. Fryar then turned the meeting over to LTC Spridgen, who is the PEC Director, to introduce the drug class review presentations.

DRUG CLASS REVIEW PRESENTATIONS

[PEC Script]

(LTC Spridgen): I’m LTC Stacia Spridgen, the PEC Director. Joining me today from the PEC are Dr. Teresa Anekwe, who is one of the clinical pharmacists on staff, and Dave Meade, a Clinical Pharmacist, retired Air Force Lieutenant Colonel, and Director of Clinical Operations at the DoD Pharmacoeconomic Center. LTC Hannah, a member of the P&T Committee, 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).

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 based upon its collective professional judgment when considering the analyses from both the relative clinical and relative cost-effectiveness evaluations of one Uniform Formulary drug class – the Phosphodiesterase Type-5 Inhibitors for Pulmonary Arterial Hypertension (PAH); seven newly approved drugs, Extavia injection, Aplenzin, Savella, Gelnique, Nucynta, Ryzolt, and Exforge HCT, and one non-formulary to UF change.
- 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 12. 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.

Before we begin, I'd like to update the information on page 12 of the background information under Section A: Uniform Formulary recommendation for Savella. It should read, "...the P&T Committee voted to recommend milnacipran tablets (Savella) be designated *non-formulary* on the UF.

Dr. Anekwe will now start with the relative clinical effectiveness evaluations for the drugs reviewed by the DoD P&T Committee.

UNIFORM FORMULARY CLASS REVIEWS

Phosphodiesterase Type-5 (PDE-5) INHIBITORS FOR PULMONARY ARTERIAL HYPERTENSION (PAH)

Relative Clinical Effectiveness

BAP Script (*Dr. Anekwe*):

The P&T Committee evaluated the clinical effectiveness of the Phosphodiesterase Type-5 inhibitors, which I will refer to as PDE-5s, for the treatment of pulmonary arterial hypertension (PAH). Sildenafil (Revatio) was previously reviewed for UF placement in August 2005. Tadalafil (Adcirca) is the second PDE-5 inhibitor FDA-approved for PAH, and was recently launched in August 2009.

Figure 1 on page 2 of the handout shows that for all three points of service, Revatio has the higher utilization of the two agents.

Sildenafil and tadalafil are FDA-approved for treating erectile dysfunction (ED), under the trade names of Viagra and Cialis, respectively. Information regarding the efficacy, safety, and clinical outcomes of the PDE-5 inhibitors in the management of PAH was considered. The clinical review included, but was not limited to, the requirements stated in the UF Rule, 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion — The P&T Committee recommended the following clinical effectiveness conclusions regarding PDE-5 inhibitors for PAH:

1. With regard to efficacy, the following conclusions were made:

a) Sildenafil (Revatio) and tadalafil (Adcirca) are FDA-approved to improve exercise ability in patients with PAH. Revatio has an additional indication specifically to delay clinical worsening in patients with PAH when used in combination with background intravenous epoprostenol (Flolan).

b) There are no head-to-head trials comparing the two PDE-5 inhibitors for PAH. Indirect comparisons of clinical trials using approved dosing regimens of Revatio and Adcirca show similar improvements in 6-minute walking distance (6MWD).

c) Revatio and Adcirca delay the time to clinical worsening of disease, which is broadly defined as a composite of death, transplantation, hospitalization for PAH, initiation of new therapy, or worsening functional class.

(1) A clinically significant delay in the time to clinical worsening with Revatio was shown in one trial that used doses four times higher than the FDA-approved dose, and used adjunctive IV Flolan treatment in all the patients.

(2) Adcirca was shown to delay the time to clinical worsening of PAH in one trial that used FDA-approved dosing and used adjunctive bosentan (Tracleer) therapy in 55% of the patients.

d) There is insufficient evidence to conclude that there are clinically relevant differences in clinical effectiveness of PDE-5 inhibitors for PAH.

2. With regards to safety and tolerability, the P&T Committee agreed that there is insufficient evidence to conclude there are clinically relevant differences in safety between PDE-5s for PAH. The product labeling for the two drugs is similar with regard to contraindications, precautions, and warnings, and reflects the safety section found in the package inserts for the ED products Viagra and Cialis. The doses of Revatio and Adcirca used for PAH treatment are associated with an increased incidence of adverse events than the doses for the treatment of ED. Headache is the most frequently reported adverse event with Revatio and Adcirca.
3. With regards to other factors, generic availability of sildenafil (trade names Viagra and Revatio) is expected in 2012, compared to 2020 for tadalafil (trade names, Cialis and Adcirca). Additionally, the P&T Committee recognized the convenience to the patient with the once daily dosing required with Adcirca, in contrast to the 3-times daily dosing needed with Revatio. Revatio and Adcirca require Prior Authorization when used for PAH. The full PA criteria for the PDE-5 inhibitors can be found in the August 2009 DoD P&T Committee meeting minutes.

COMMITTEE ACTION: The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) to accept the clinical effectiveness conclusion as stated.

Dr. Meade will now give the cost-effectiveness review.

PDE-5 INHIBITORS for PAH — Relative Cost-Effectiveness

BAP Script (Dr. Meade):

1. Results from the cost minimization analysis (CMA) of PDE-5 inhibitors for PAH agents revealed that sildenafil (Revatio) is the most cost effective PDE-5 inhibitor for PAH agent based on an analysis of the cost per day of treatment. Cost per day of therapy was calculated using average daily consumption rates for sildenafil (Revatio) and tadalafil (Adcirca).
2. Budget impact analysis (BIA) was used to evaluate the potential impact of scenarios with selected PDE-5 inhibitor agents designated formulary or non-formulary on the UF. Results

from the BIA of PDE-5 inhibitors for PAH revealed that placing sildenafil citrate (Revatio) on the UF was the most cost effective scenario overall.

The results of the BIA showed that tadalafil (Adcirca) is more costly than sildenafil (Revatio) in all scenarios evaluated.

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

PDE-5 INHIBITORS for PAH — Uniform Formulary Recommendation

BAP Script (*Dr. 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, voted (14 for, 0 opposed, 1 abstained, 1 absent):

- a) Sildenafil (Revatio 20 mg) remain classified as formulary on the UF.
- b) Tadalafil (Adcirca 20 mg) be designated as non-formulary under the UF, based on cost effectiveness.

PDE-5 INHIBITORS — NF JUSTIFICATION

BAP Script (*Dr. Meade*):

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

1. There are no direct comparative trials between the two PDE-5s for the treatment of PAH. Indirect comparisons of clinical trials show no major differences in efficacy.
2. Adcirca was not cost-effective relative to Revatio which is already included on the UF.

PDE-5 INHIBITORS — Uniform Formulary Implementation Plan

BAP Script (*Dr. Meade*):

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent)
1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

LTC Hannah will now give the physician perspective for the PDE-5s for PAH.

UNIFORM FORMULARY CLASS REVIEWS — Phosphodiesterase Type-5

(PDE 5) INHIBITORS FOR PAH — Physician Perspective:

LTC Hannah, a member of the P&T Committee provided the BAP with a physician’s perspective on these recommendations. He noted that Revatio has been on the market since 2005 and is already on the UF. Adcirca was launched in 2009. The Committee’s recommendations were based on the relative cost-effectiveness of Revatio and the fact that physicians have had more clinical experience with it than with Adcirca. Additionally, Revatio, along with Viagra, is expected to go generic in 2012.

BAP Questions — Phosphodiesterase Type-5 (PDE 5) Inhibitors for PAH

The Chair opened the meeting for questions and discussion of the P&T Committee’s review of the drug class. The Panel members asked no questions of the presenters.

BAP Discussion and Vote on Formulary Recommendations — Phosphodiesterase Type-5 (PDE 5) Inhibitors for PAH

Ms. Fryar read the P&T Committee’s formulary recommendations for the Phosphodiesterase Type-5 (PDE 5) Inhibitors for PAH drug class.

In view of the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations of Phosphodiesterase Type-5 inhibitors for pulmonary arterial hypertension, and other relevant factors, the P&T Committee voted to recommend Sildenafil (Revatio) remain classified as formulary on the UF and Tadalafil (Adcirca) be designated as non-formulary under the UF, based on cost effectiveness.

There was no further Panel discussion of the recommendation.

The BAP vote on the formulary recommendations for the Phosphodiesterase Type-5 (PDE 5) Inhibitors for PAH drug class was:

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0.

BAP Discussion and Vote on Uniform Formulary Implementation Plan Recommendations — Phosphodiesterase Type-5 (PDE 5) Inhibitors for PAH

The Chair next read the P&T Committee’s implementation plan recommendations for this drug class.

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

There was no BAP discussion of the implementation plan recommendation.

The Panel vote on the implementation plan recommendations for the Phosphodiesterase Type-5 (PDE 5) Inhibitors for PAH drug class was:

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0.

The Chair next asked the presenters to continue with the briefings.

REVIEWS OF NEWLY APPROVED DRUGS

1. Disease-Modulating Drugs for Multiple Sclerosis — Interferon Beta-1b Injection (Extavia)

Relative Clinical Effectiveness —

(BAP Script) Dr. Anekwe

Interferon beta-1b injection (Extavia) is an immunomodulator classified as a disease modulating drug for MS. These agents, shown in Table 2 on page 3 of your handout, were last reviewed for Uniform Formulary (UF) placement in August 2005. Please note that no products are currently designated non-formulary in this class.

Figure 2 on page 3 of the handout shows the utilization of the disease modulating agents for MS. As you can see, as of September 2009, there has been no utilization of Extavia at all points of service.

Extavia is a new branded version of interferon beta-1b, and is the same product as that found under the proprietary name Betaseron. The two manufacturers have agreed to this arrangement. FDA approval for Extavia was based on the same registration trials as the approval for Betaseron, but a separate Biologic License Agreement (BLA) was filed by the manufacturer of Extavia. Availability of generic formulations of biologic agents, including the disease modulators for MS, is unknown at this time. Extavia is supplied with a larger needle size and packaged with a 30-day supply as opposed to 28-day supply with Betaseron. The FDA-approved indications for Extavia are the same as Betaseron.

The interferon beta-1b clinical evaluation included, but was not limited to, the requirements stated in the UF rule, 32 CFR 199.21(e)(1). There are no head-to-head trials comparing Extavia to Betaseron and there is no conclusive data to support superiority of one drug over the other. After reviewing the clinical literature, interferon beta-1b (Extavia) does not have compelling clinical advantages over existing disease modulating drugs for MS on the UF.

COMMITTEE ACTION: The P&T Committee voted 15 for, 0 opposed, 0 abstained, 1 absent) to accept the clinical effectiveness conclusion as stated.

(Dr. Meade) Extavia - Relative Cost-Effectiveness

The P&T Committee evaluated the costs of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the other currently available disease modulating

drugs for MS. 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) was used to evaluate the relative cost-effectiveness of interferon beta-1b (Extavia). Results from the CMA showed the projected weighted average cost per day for interferon beta-1b (Extavia) is higher than the other formulary disease modulating drugs for MS, including interferon beta-1a (Avonex), interferon beta-1a (Rebif), interferon beta-1b (Betaseron), and glatiramer acetate (Copaxone).

COMMITTEE ACTION: The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstained, 1 absent) interferon beta-1b (Extavia) was not cost effective relative to the other UF agents in the disease modulating drugs for MS drug class.

(Dr. Meade): Extavia — Uniform Formulary 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, 0 abstained, 1 absent) interferon beta-1b injection (Extavia) be designated non-formulary on the UF.

Extavia — NF JUSTIFICATION

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

1. There are no direct comparative trials between Extavia and Betaseron, and no evidence to support any differences in clinical efficacy, or the superiority of one agent over the other.
2. Extavia was not cost-effective relative to other UF agents in the disease modulating drugs MS drug class.

Extavia — Uniform Formulary Implementation Plan

(Dr. Meade): The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at Military Treatment Facilities (MTFs) no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

(Dr. Meade):

LTC Hannah will now give the physician perspective for Extavia.

Multiple Sclerosis - Disease-Modulating Drugs (MS-DMDs) — Interferon Beta-1b Injection (Extavia) Physician Perspective

(LTC Hannah):

LTC Hannah informed the Panel that Exatavia comes off the same manufacturing line as

beta-interferon and is a newly-branded version of a drug that has been on the UF since 2005. The P&T Committee determined that Extavia, introduced in 2009, is the same product already on the formulary only at a higher cost. The only difference is the packaging and the name.

BAP Questions

Ms. Legette asked if there were any special instructions regarding the “medical necessity” requirements for this drug, especially concerning patient stabilization before they go on the drug. The answer provided was that the normal procedures should be used.

Mr. Hutchings noted that there were no users of this drug anywhere in the system as of September and asked if there had been any additions since. The answer provided was that there are now seven users. Mr. Hutchings asked if these users could be notified by telephone instead of by letter. Ms. Legette noted that the process used is to put all of the drugs into one letter.

BAP Discussion and Vote — Interferon Beta-1b Injection (Extavia) Formulary Recommendation

Without further discussion, Ms. Fryar read the P&T Committee’s UF recommendation for Extavia.

In view of the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations of the Multiple Sclerosis-Disease Modulating Drugs, and other relevant factors, the P&T Committee voted to recommend interferon beta-1b injection (Extavia) be designated non-formulary on the UF.

The BAP voted as follows:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

BAP Discussion and Vote — Interferon Beta-1b Injection (Extavia) Implementation Plan Recommendation

The Chair next read the P&T Committee’s implementation plan recommendation for Extavia.

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at Military Treatment Facilities (MTFs) no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Without discussion, the Panel voted on the recommendation:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

2. Bupropion Hydrobromide Extended Release (Bupropion HBr ER) Tablets (Aplenzin)

(BAP Script)

Relative Clinical Effectiveness — Dr. Anekwe

Bupropion HBr (Aplenzin) is a norepinephrine and dopamine reuptake inhibitor (NDRI) approved for the treatment of major depressive disorder (MDD) in adults. The antidepressants in the AD-1 drug class, shown in your handout in Table 3 on page 4, were last reviewed for UF placement in November 2005. The class is comprised of the selective serotonin reuptake inhibitors (SSRIs), NDRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), and the serotonin antagonist/reuptake inhibitors.

Figure 4 on page 5 of the handout shows the utilization of the NDRIs and the decline in utilization of branded Wellbutrin XL as generics become available.

Aplenzin was approved under section 505(b)(2) of the Federal Food, Drug, and Cosmetic (FDC) Act after demonstrating bioequivalence to bupropion hydrochloride extended release tablets (Wellbutrin XL). The other NDRIs on the UF are bupropion HCl immediate release (Wellbutrin IR, generics) and bupropion HCl sustained release (Wellbutrin SR, generics). Aplenzin tablets are dosed daily, whereas the IR and SR formulations of Wellbutrin are dosed three times and two times daily, respectively. Inclusion of the HBr salt in Aplenzin, rather than the HCl salt included in Wellbutrin products, allows the maximum bupropion dose to be contained in one tablet.

There are no direct comparative clinical trials between bupropion HBr ER tablets and the other NDRIs, and no trials are available that evaluate outcomes. The clinical trials used to obtain FDA approval were pharmacokinetic studies demonstrating bioequivalence to bupropion HCl ER (Wellbutrin XL). The safety profile of bupropion HBr is based on data collected for Wellbutrin SR (bupropion hydrochloride sustained release), thus it is identical to other bupropion products.

Relative Clinical Effectiveness Conclusion: P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) that bupropion HBr ER tablets (Aplenzin) do not have a significant, clinically meaningful therapeutic advantage in terms of effectiveness, safety, and clinical outcomes compared to other NDRIs currently included on the UF.

COMMITTEE ACTION: The P&T Committee voted to accept the clinical effectiveness conclusion as stated.

(Dr. Meade): Aplenzin — Relative Cost-Effectiveness

The P&T Committee evaluated the cost of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the other NDRIs in the AD-1 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) was used to evaluate the relative cost-effectiveness of bupropion HBr ER tablets (Aplenzin) relative to other UF NDRI. Results from the CMA showed the projected weighted average cost per day for bupropion HBr ER (Aplenzin) is higher than the bupropion HCl formulations (Wellbutrin IR, SR, and XL). The CMA also revealed the projected weighted average cost per day for bupropion HBr ER tablets (Aplenzin) is higher than the formulary NDRI, bupropion HCl 12-hour formulation (Wellbutrin SR) and the non-formulary 24-hour formulation (Wellbutrin XL).

Relative Cost-Effectiveness Conclusion —The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 1 abstained, 0 absent) that bupropion HBr ER tablets (Aplenzin) are not cost effective relative to other AD-1 NDRI included on the UF.

COMMITTEE ACTION: The P&T Committee voted to accept the cost effectiveness conclusion stated above.

(Dr. Meade): Aplenzin — Uniform Formulary Recommendation

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the AD-1s, and other relevant factors, the P&T Committee voted (14 for, 0 opposed, 2 abstained, 0 absent) to recommend bupropion HBr ER tablets (Aplenzin) be designated as non-formulary under the UF, based on cost effectiveness.

Aplenzin — NF JUSTIFICATION

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

1. There is insufficient evidence to support any differences in clinical efficacy, or safety between Aplenzin and other bupropion agents currently on the UF.
2. Aplenzin was not cost-effective relative to other NDRI in the AD-1 drug class included on the UF.

(Dr. Meade): Aplenzin — Uniform Formulary Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

(Dr. Meade): LTC Hannah will now give the physician perspective for Aplenzin.

Bupropion Hydrobromide Extended Release (Bupropion HBr ER) Tablets (Aplenzin) Physician Perspective

(LTC Hannah):

LTC Hannah noted that there are already equivalent bupropion agents on the formulary and used the same clinical trials as Wellbutrin XL. Aplenzin uses a different salt (hydrobromide instead of hydrochloride). LTC Hannah said there was no clinical data to show that the agent is more effective clinically and it is also not cost-effective. Moreover, generic formulations of Wellbutrin are becoming available.

BAP Questions

Ms. Fryar asked when generic formulations of Wellbutrin XL will be available. The answer provided was this summer (2010). Ms. Fryar also noted that the Panel would consider, as a later agenda item, the status of Wellbutrin XL on the Formulary once generic equivalents become available and asked whether there would be a generic equivalent of Aplenzin on the formulary. Dr. Meade answered that the generic would be on the formulary and would replace the branded drugs now there if they are cost-effective.

BAP Discussion and Vote — Bupropion Hydrobromide Extended Release (Bupropion HBr ER) Tablets (Aplenzin) Formulary Recommendation

The Chair read the P&T Committee's formulary recommendation for Aplenzin.

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the Antidepressant-1s drug class, and other relevant factors, the P&T Committee voted to recommend bupropion hydrobromide extended release tablets (Aplenzin) be designated as non-formulary under the UF, based on cost effectiveness.

There was no further Panel discussion of this recommendation, and the BAP voted as follows:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

BAP Discussion and Vote — Bupropion Hydrobromide Extended Release (Bupropion HBr ER) Tablets (Aplenzin) Implementation Plan Recommendation

Ms. Fryar next read the implementation plan recommendations of the P&T Committee.

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Without further discussion, the BAP voted:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

3. Antidepressant-1s (AD-1s) — Milnacipran Tablets (Savella) (BAP Script)

Relative Clinical Effectiveness — Savella (Dr. Anekwe)

Milnacipran (Savella) is an SNRI approved for the treatment of fibromyalgia in adults. The agents in the AD-1 drug class were last reviewed for UF placement in November 2005. The other SNRIs on the Uniform Formulary are venlafaxine immediate-release tablets (Effexor, generics), venlafaxine extended release capsules (Effexor XR), and venlafaxine extended-release tablets (no brand name). The UF also includes other drugs medically accepted to treat fibromyalgia, including several selective serotonin reuptake inhibitors (SSRIs), the tricyclic antidepressant (TCA) amitriptyline (Elavil, generics) and cyclobenzaprine (Flexeril, generics).

Figure 3 on page 5 of the handout shows utilization at all points of service for the SNRI on the UF, and other agents approved for fibromyalgia.

Savella is approved for depression outside of the US, but the manufacturer will not seek FDA approval for depression.

In clinical trials, Savella significantly improved a composite of fibromyalgia symptoms when compared to placebo. There are no direct comparative clinical trials between Savella and the other medications that are FDA-approved or used off-label for the management of fibromyalgia. Meta-analyses have shown that the antidepressants (SSRIs and TCAs) and Flexeril are efficacious in treating fibromyalgia.

Other Factors — The Pharmacy Outcomes Research Team (PORT) reported results of an analysis comparing the frequency of ICD-9 diagnosis codes indicative of fibromyalgia or related conditions among patients receiving SNRIs (Cymbalta or Effexor), GABA analogs (Lyrica or gabapentin), or the SSRI citalopram (Celexa).

Based on the results of the PORT analysis, the Committee agreed that it was unlikely that fibromyalgia represents the most common use for any of the studied medications. Considering Savella's regulatory approval and its use for depression outside the U.S., as well as the multiple uses for the other study agents with a fibromyalgia indication, the Committee did not feel that the analysis supported the need for a fibromyalgia drug class. The Committee also recognized that TCAs (particularly amitriptyline) and Flexeril, have a substantial body of evidence supporting their use as first-line agents for fibromyalgia.

Relative Clinical Effectiveness Conclusion — The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) that despite its FDA-approved status, milnacipran is one of many available treatments for fibromyalgia. Milnacipran (Savella) does not have a significant, clinically meaningful therapeutic advantage in terms of effectiveness, safety, and clinical outcomes compared to other SNRIs and medically-accepted drugs used for fibromyalgia currently included on the UF.

COMMITTEE ACTION: The P&T Committee voted to accept the clinical effectiveness conclusion as stated.

Relative Cost-Effectiveness — Savella (Dr. Meade)

The P&T Committee evaluated the cost of milnacipran (Savella) in relation to the efficacy, safety, tolerability, and clinical outcomes of the other SNRIs in the AD-1 class, as well as other medically-accepted treatments for fibromyalgia. 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) was used to evaluate the relative cost-effectiveness of milnacipran (Savella) relative to other UF SNRIs and medically-accepted treatments for fibromyalgia. Results from the CMA showed the projected weighted average cost per day for milnacipran (Savella) is higher than the UF alternatives commonly used to treat fibromyalgia, including the tricyclic antidepressant amitriptyline (Elavil, generics) and cyclobenzaprine (Flexeril, generics).

Relative Cost-Effectiveness Conclusion — The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 1 abstained, 0 absent) that milnacipran (Savella) is not cost effective relative to other medically-accepted drugs for the management of fibromyalgia included on the UF

COMMITTEE ACTION: The P&T Committee voted to accept the cost effectiveness conclusion stated above.

Uniform Formulary Recommendation — Savella

(Dr. Meade) Taking into consideration the conclusions from the relative clinical effectiveness, 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, 0 absent) that milnacipran (Savella) be designated non-formulary on the UF.

NF JUSTIFICATION — Savella

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

1. In the absence of direct comparative trials, there is insufficient evidence to suggest the superiority of Savella with respect to clinical efficacy, or safety over other agents approved or medically-accepted for fibromyalgia.
2. Savella was not cost-effective relative to other medically-accepted drugs for the management of fibromyalgia included on the UF.

Uniform Formulary Implementation Plan — Savella

(Dr. Meade) The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) 1) an effective date of the first Wednesday one week after the minutes are signed,

following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

(Dr. Meade): LTC Hannah will now give the physician perspective for Savella.

Physician Perspective – Savella

(LTC Hannah):

LTC Hannah presented the physician's perspective.

He said the Committee recognized that other drugs already on the UF are widely used to treat fibromyalgia. He noted that Savella is approved for depression outside the U.S. but the manufacturer is not seeking approval for depression in the U.S.. Lacking either a clinical or a cost-effectiveness advantage, the non-formulary recommendation was not controversial.

BAP Questions

Dr. Schlaifer asked about head-to-head comparisons with other drugs on the formulary, whether we know why the manufacturers has not sought FDA approval for depression treatment and when the drug came out. The answers provided were that head-to-head comparisons were not available; the manufacturer has not sought approval because it is not planning to market the drug for depression and the drug was released in 2009.

BAP Discussion and Vote — Antidepressant-1s (AD-1s) — Milnacipran Tablets (Savella) Uniform Formulary Recommendation

The Chair read the P&T Committee's UF recommendation for milnaciprin tablets (Savella).

In view of the conclusions from the relative clinical effectiveness, relative cost-effectiveness determinations of the Antidepressant-1s drug class, and other relevant factors, the P&T Committee voted to recommend that milnacipran (Savella) be designated non-formulary on the UF.

There was no further discussion of this agent. The BAP vote was:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

BAP Discussion and Vote — Antidepressant-1s (AD-1s) — Milnacipran Tablets (Savella) Implementation Plan Recommendation

Ms. Fryar next read the implementation plan recommendations for Savella.

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Without further discussion, the BAP voted as follows:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

4. Overactive Bladder Drugs (OABs) — Oxybutynin Topical Gel (Gelnique)

(BAP Script)

Relative Clinical Effectiveness — Gelnique

(Dr. Anekwe): Oxybutynin chloride 10% topical gel (Gelnique) is an antimuscarinic agent classified as an overactive bladder (OAB) drug. It is the second topical oxybutynin product to reach the market, following the transdermal patch (Oxytrol). Like the other OAB drugs, Gelnique is FDA-approved for the treatment of OAB with symptoms of urge urinary incontinence, urgency, and frequency. Figures 5 and 6 on pages 6 and 7 of the handout show that Detrol LA is the most utilized OAB drug in the class. There has been some utilization of Gelnique, slightly more than that of Oxytrol in September 2009.

Gelnique is a clear and colorless gel available in a 1 gram packet that contains 100 mg oxybutynin chloride, which is estimated to deliver approximately 4 mg of oxybutynin chloride per day. The OAB drug class was previously reviewed for UF placement in August 2008 and February 2006. Other oxybutynin products are included on the UF (oxybutynin immediate release (IR) and sustained release (SR) tablets [Ditropan, Ditropan SR, generics] and the Oxytrol patch).

There are no comparative clinical trials between Gelnique and the other OAB drugs, and no published trials evaluating outcomes other than changes in signs and symptoms of OAB. The clinical trials used to obtain FDA approval reported Gelnique was effective at reducing the number of incontinence episodes per day, number of urinary frequency episodes per day, and increasing the urinary volume per void in patients with OAB, comparable to the other OAB agents. The safety profile of Gelnique appears to be comparable to other OAB agents.

Relative Clinical Effectiveness Conclusion — The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) that oxybutynin 10% gel (Gelnique) did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcome over other OAB agents included on the UF.

COMMITTEE ACTION: The P&T Committee voted to accept the clinical effectiveness conclusion stated above.

Relative Cost Effectiveness — Gelnique

(Dr. Meade)

The P&T Committee evaluated the cost of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the anticholinergic agents in the overactive bladder (OAB) class.

CMA was used to evaluate the relative cost-effectiveness of oxybutynin 10% gel (Gelnique) relative to other UF anticholinergic OAB agents. Results from the CMA showed the projected weighted average cost per day for oxybutynin 10% gel (Gelnique) is higher than the other formulary OAB anticholinergic agents, including extended-release oral agents (oxybutynin ER [Ditropan XL] and tolterodine ER [Detrol LA]), and the UF transdermal patch formulation (Oxytrol).

Relative Cost-Effectiveness Conclusion — The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstained, 1 absent) that oxybutynin 10% gel (Gelnique) is not cost effective relative to the other UF anticholinergic agents in the OAB class

COMMITTEE ACTION: The P&T Committee voted to accept the cost effectiveness conclusion stated above.

Uniform Formulary Recommendation — Gelnique

(Dr. 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, 0 abstained, 1 absent) oxybutynin 10% gel (Gelnique) be designated non-formulary on the UF.

NF JUSTIFICATION — Gelnique

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

1. There is insufficient evidence to support any differences in clinical efficacy, or safety between Gelnique and other OAB agents currently on the UF.
2. Gelnique was not cost-effective relative to other agents in the OAB drug class included on the UF.

Uniform Formulary Implementation Plan — Gelnique

(Dr. Meade): The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

(Dr. Meade): LTC Hannah will now give the physician perspective for Gelnique.

Physician Perspective — Gelnique

(LTC Hannah):

LTC Hannah provided the Panel with a physician's perspective on the P&T Committee recommendations for Gelnique. He noted that the agent represents a new delivery mechanism for an existing drug. However, DoD already has several formulations of oxybutinin, the active ingredient of Gelnique, on the UF including tablets and topical patches. Generic formulations of oxytrol are anticipated for late 2010. The efficacy and safety of Gelnique are comparable to the other agents available and Gelnique was not cost-effective so it was designated non-formulary.

BAP Discussion and Vote — Overactive Bladder Drugs (OABs) — Oxybutynin Topical Gel (Gelnique) Uniform Formulary Recommendation

Ms. Fryar read the P&T Committee's UF recommendation for Gelnique.

In view of the conclusions from the relative clinical effectiveness, relative cost-effectiveness determinations of the Overactive Bladder Drugs, and other relevant factors, the P&T Committee voted to recommend that Gelnique be designated non-formulary on the UF, based on cost-effectiveness.

There was no further discussion. The Panel voted:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

BAP Discussion and Vote — Overactive Bladder Drugs (OABs) — Oxybutynin Topical Gel (Gelnique) Implementation Plan Recommendation

The Chair read the implementation plan recommendations for Gelnique.

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

Without further discussion, the BAP voted as follows:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

5. Narcotic Analgesics — Tapentadol Tablets (Nucynta) (BAP Script)

Relative Clinical Effectiveness — Nucynta

(Dr. Anekwe): Tapentadol (Nucynta) is a synthetic opioid analgesic. It is FDA-approved for the relief of moderate to severe acute pain in adults. Nucynta is a Schedule II controlled substance and is classified as a single component, high potency agent in the narcotic analgesic drug class. Please see Table 5 on page 8 of the handout for the agents in the class. The narcotic analgesics were last reviewed for UF in February 2007.

Figure 7 on page 9 of the handout shows the utilization of Nucynta in reference to the other high potency narcotic analgesics with over 1,000 prescriptions filled in September 2009. Nucynta's exact mechanism of action is unknown, but analgesia is thought to be conferred by mu-agonist activity and inhibition of norepinephrine reuptake. It has no active metabolites and requires multiple daily dosing since it is an immediate release product.

The clinical trials used to obtain FDA approval reported that Nucynta was superior to placebo, and non-inferior at specific doses to immediate release oxycodone in relieving acute pain. There are no published direct comparative trials between Nucynta and other narcotic analgesics. The safety profile of Nucynta reflects that of other narcotic analgesics on the UF, with the exception of a lower incidence of constipation observed in clinical trials compared to immediate-release oxycodone.

Relative Clinical Effectiveness Conclusion — The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) that although Nucynta may cause less constipation compared to oxycodone, this was an irrelevant benefit given its current indication for short-term therapy in the treatment of acute pain. There is insufficient evidence to suggest a clinically meaningful therapeutic advantage with Nucynta in terms of efficacy and safety, compared to the other narcotic analgesics already on the UF

COMMITTEE ACTION: The P&T Committee voted to accept the clinical effectiveness conclusion as previously stated.

Relative Cost Effectiveness — Nucynta

(Dr. Meade): The P&T Committee evaluated the cost of Nucynta in relation to the efficacy, safety, tolerability, and clinical outcomes of the other immediate release, single component high potency agents in the narcotic analgesic drug 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) was used to evaluate the relative cost-effectiveness of tapentadol (Nucynta) relative to other UF scheduled and non-scheduled agents in the narcotic analgesic class. Results from the CMA showed the projected weighted average cost per day for tapentadol (Nucynta) is higher than the other formulary immediate release, single component high potency agent in the narcotic analgesic drug class,

including morphine sulfate IR oral, oxycodone hydrochloride IR, and tramadol hydrochloride IR formulations.

Relative Cost-Effectiveness Conclusion — The P&T Committee, based upon its collective professional judgment, voted (16 for, 0 opposed, 0 abstained, 0 absent) that tapentadol (Nucynta) is not cost effective relative to the other immediate release, single component high potency agents in the narcotic analgesic drug class

COMMITTEE ACTION: The P&T Committee voted to accept the cost effectiveness conclusion stated above.

Uniform Formulary Recommendation — Nucynta

(Dr. 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, 0 absent) tapentadol (Nucynta) be designated non-formulary on the UF. This recommendation was based on the clinical effectiveness conclusion and the determination that morphine sulfate (MS-IR/generic; MS-Contin/generic) remains the most cost-effective narcotic analgesic on the UF compared to tapentadol (Nucynta).

NF JUSTIFICATION — Nucynta

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

1. There is insufficient evidence to support any compelling differences in clinical efficacy between Nucynta and other narcotic analgesics currently on the UF. The finding of less constipation compared to oxycodone has questionable value given the current indication.
2. Nucynta was not cost-effective relative to other single component, high potency narcotic analgesics included on the UF.

Uniform Formulary Implementation Plan — Nucynta

(Dr. Meade): The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

(Dr. Meade):

LTC Hannah will now give the physician perspective for Nucynta.

Physician Perspective — Tapentadol Tablets (Nucynta)

(LTC Hannah):

LTC Hannah briefed the BAP on the physician's view of the P&T Committee recommendations. He noted that the drug is only approved for acute pain and is taken every four-to-six hours instead of once daily. There are no studies evaluating Nucynta against other narcotic analgesics. The Committee recognized that the "less constipation" issue is important and discussed it, but felt that constipation was more of an issue for patients with chronic pain than for those with acute pain. He noted that an extended release version is due out in 2010. Nucynta was not found to be cost-effective.

BAP Questions — Nucynta

The Panel had no questions about this recommendation.

BAP Discussion and Vote — Narcotic Analgesics — Tapentadol Tablets (Nucynta) Uniform Formulary Recommendation

Ms. Fryar read the P&T Committee's UF recommendations for Nucynta.

In view of the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations of the Narcotic Analgesics and other relevant factors, the P&T Committee voted to recommend Nucynta be designated as non-formulary under the UF, based on cost-effectiveness.

Without further discussion, the BAP voted as follows:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

BAP Discussion and Vote — Narcotic Analgesics — Tapentadol Tablets (Nucynta) Implementation Plan Recommendation

The Chair then read the implementation plan recommendation for Nucynta:

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

There was no further discussion of the implementation plan and the Panel voted:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

6. Narcotic Analgesics — Tramadol Extended Release Tablets (Ryzolt) (BAP Script)

Relative Clinical Effectiveness — Ryzolt

(Dr. Anekwe): Tramadol extended-release (ER), (Ryzolt) is a centrally acting analgesic, and is classified as a single component, low-potency agent in the narcotic analgesic drug class; it is not a controlled drug. Ryzolt has the same active ingredient as Ultram IR and Ultram ER, but with a different delivery mechanism, and was approved under FDA's section 505(b)(2).

Figure 8 on page 10 of the handout shows that Ultram ER is more utilized at all points of service.

Ryzolt exhibits immediate-release and extended-release properties, due to its dual-matrix delivery system.

Tramadol ER is indicated for the management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time. The mechanism for analgesic efficacy is postulated to be a combination of mu-agonist activity and weak SNRI activity. The clinical evaluation for Ryzolt included, but was not limited to the requirements stated in the UF rule, 32 CFR 199.21(e)(1).

In three out of four pivotal trials, Ryzolt was unable to demonstrate superiority over a comparator. The study on which approval was based showed questionable efficacy over placebo. No direct comparative trials have been conducted between Ryzolt and other tramadol products available in the US or other narcotic analgesics. The safety profile of Ryzolt reflects that of other tramadol products on the UF.

Relative Clinical Effectiveness Conclusion — The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) that although Ryzolt offered a novel delivery mechanism, there was insufficient evidence to suggest a clinically meaningful therapeutic advantage in terms of efficacy and safety, compared to the other tramadol products available on the UF

COMMITTEE ACTION: The P&T Committee voted to accept the clinical effectiveness conclusion as stated.

Relative Cost Effectiveness — Ryzolt

(Dr. Meade): The P&T Committee evaluated the cost of the tramadol ER (Ryzolt) in relation to the efficacy, safety, tolerability, and clinical outcomes of the other extended release, single component low-potency agents in the narcotic analgesic drug 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) was used to evaluate the relative cost-effectiveness of tramadol ER (Ryzolt) relative to the other UF chemically identical chronic pain agents. Results from the CMA showed the projected weighted average cost per day for tramadol ER (Ryzolt) is higher than the non-formulary low-potency single analgesic agent, tramadol extended-release (Ultram ER) and significantly higher than the formulary product tramadol immediate-release (Ultram/generics)

Relative Cost-Effectiveness Conclusion — The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstained, 1 absent) that tramadol ER (Ryzolt) is not cost effective relative to tramadol extended-release (Ultram

ER).

COMMITTEE ACTION: The P&T Committee voted to accept the cost effectiveness conclusion stated above.

Uniform Formulary Recommendation — Ryzolt

(Dr. 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, 0 abstained, 1 absent) tramadol ER tablets (Ryzolt) be designated non-formulary on the UF. This recommendation was based on the clinical effectiveness conclusion and the determination that Ultram (tramadol IR) remains the most cost effective low-potency single narcotic agent on the UF compared to Ryzolt (tramadol ER).

NF JUSTIFICATION — Ryzolt

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

1. There is insufficient evidence to support any compelling differences in clinical efficacy, or safety between Ryzolt and other tramadol products currently on the UF.
2. Ryzolt was not cost-effective relative to Ultram IR, which is currently on the UF, and Ultram ER which is non-formulary.

Uniform Formulary Implementation Plan — Ryzolt

(Dr. Meade): The P&T Committee recommended (15 for, 0 opposed, 0 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 TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

(Dr. Meade): LTC Hannah will now give the physician perspective for Ryzolt.

Physician Perspective — Narcotic Analgesics — Tramadol Extended Release Tablets (Ryzolt)

(LTC Hannah):

LTC Hannah provided the BAP with the physician's perspective on this recommendation. He noted that there are already a number of products on the formulary that use tramadol as the active ingredient. Significant clinical differences between them and Ryzolt could

not be demonstrated. In addition, Ryzolt was found not to be cost-effective compared with drugs already on the UF.

BAP Questions

The Panel had no questions of the presenters regarding this recommendation.

BAP Discussion and Vote — Narcotic Analgesics — Teramadol Extended Release Tablets (Ryzolt) Uniform Formulary Recommendation

Ms. Fryar read the P&T Committee's formulary recommendation.

In view of the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations of the Narcotic Analgesics and other relevant factors, the P&T Committee voted to recommend Ryzolt be designated as non-formulary under the UF, based on cost-effectiveness.

Without further discussion, the BAP voted as follows:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

BAP Discussion and Vote — Narcotic Analgesics — Tramadol Extended Release Tablets (Ryzolt) Implementation Plan Recommendation

The Chair read the implementation plan recommendation for Nucynta:

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 60-day implementation period in the TPHARM, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval by the Director, TMA.

There was no further discussion of the implementation plan and the Panel voted:

Concur: 10; Non-Concur: 0; Abstain: 0; Absent: 0.

7. Narcotic Analgesics — Renin Angiotensin Aldosterone Antihypertensive Agents (RAAs) — Valsartan/Amlodipine/Hydrochlorothiazide (HCTZ) Tablets (Exforge HCT)

(BAP Script)

Relative Clinical Effectiveness — Exforge HCT

(Dr. Anekwe): Exforge HCT is a fixed-dose combination product containing three drugs: the Angiotensin Receptor Blocker (ARB) valsartan (Diovan), the calcium channel

blocker amlodipine (Norvasc, generics), and the diuretic hydrochlorothiazide (HCTZ, generics). It is the first three-drug combination product approved for hypertension. Exforge HCT is solely indicated for treating hypertension. Valsartan (Diovan) and the combination product valsartan/amlodipine (Exforge) are currently designated as non-formulary on the UF; amlodipine (Norvasc, generics) and HCTZ are on the UF (BCF products). Exforge HCT is included in the renin-angiotensin antihypertensive agents (RAAs) UF drug class, which is comprised of several sub-classes (ARBs, angiotensin converting enzyme (ACE) inhibitors, direct renin inhibitors and their combinations with CCBs or HCTZ).

Figure 9 on page 12 of the handout shows the utilization of the RAAs agents at all points of service with the combination of lisinopril-HCTZ being the most utilized.

Treatment with Exforge HCT has been shown in one randomized trial to produce additive BP lowering and superior BP control compared to combinations of the individual components administered as pairs.

The adverse event profile of Exforge HCT is similar to that of the individual ARB, calcium channel blocker, and diuretic components. In the clinical trial, the incidence of dizziness, which was 7%, was higher among patients taking the three-drug combination than with any of two-drug combinations, resulting in a 0.7% study drop-out rate, which is less than that seen in a typical ACE inhibitor trial. Hypokalemia and peripheral edema occurred less frequently with Exforge HCT than what is reported when two drugs combinations are administered.

Studies specifically evaluating patient compliance (adherence and persistence) using Exforge HCT have not been conducted. Nevertheless, there is significant evidence that adherence (short-term compliance) and persistence (long-term compliance) are improved by 15% when reducing from three tablets to two, and improve 10% when reducing from two tablets to one. No study has been conducted addressing reduction of three tablets to one.

Relative Clinical Effectiveness Conclusion — The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) that, while Exforge HCT does not have a significant, clinically meaningful therapeutic advantage in terms of safety or efficacy over other antihypertensive combinations/agents included on the UF, the benefits it offers in terms of improved compliance, via decreased tablet burden and simplified medication regimen, are clinically significant.

COMMITTEE ACTION: The P&T Committee voted to accept the clinical effectiveness conclusion as stated.

Relative Cost Effectiveness — Exforge HCT

(Dr. Meade): The P&T Committee evaluated the cost of Exforge HCT in relation to the efficacy, safety, tolerability, and clinical outcomes of the antihypertensive agents in the RAAs UF drug class as single ingredient agents and combination formulations. 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) was used to evaluate the relative cost-effectiveness of Exforge HCT relative to other UF RAAs. Results from the CMA showed the projected weighted average cost per day for amlodipine/valsartan/HCTZ (Exforge HCT) is higher than multi-tablet combinations of the other formulary RAAs, including amlodipine tablets with lisinopril/HCTZ (Prinzide, generics), telmisartan/HCTZ (Micardis HCT), aliskiren/HCTZ (Tekturna HCT) and losartan/HCTZ (Hyzaar).

Relative Cost-Effectiveness Conclusion — The P&T Committee voted (14 for, 0 opposed, 1 abstained, 1 absent) that amlodipine/valsartan/HCTZ (Exforge HCT) is cost effective relative to the other single ingredient or combination agents in the RAAs drug class. After extensive discussion, the P&T Committee determined that the minimal extra daily cost for the amlodipine/valsartan/HCTZ (Exforge HCT) single tablet formulation was offset by the added patient convenience, and may clinically improve patient compliance.

COMMITTEE ACTION: The P&T Committee voted to accept the cost effectiveness conclusion stated above.

Uniform Formulary Recommendation — Exforge HCT

(Dr. 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, voted (4 for, 11 opposed, 0 abstained, 1 absent) to recommend that valsartan/amlodipine/HCTZ (Exforge HCT) be designated as non-formulary on the UF, thus Exforge HCT will retain uniform formulary status.

Uniform Formulary Implementation Plan – Exforge HCT

Does not apply

(Dr. Meade): LTC Hannah will now give the physician perspective for Exforge HCT.

Physician Perspective — Exforge HCT

(LTC Hannah):

LTC Hannah presented the physician's perspective on the P&T Committee recommendations for Exforge HCT. He noted that this was an unusual case because the Committee had voted against non-formulary placement. Noting that this drug is the first on the market to contain a three-drug combination, LTC Hannah said the Committee discussed its placement extensively. Although Diovan and Amlodipine are not on the UF, the Exforge product was judged to have improved compliance and persistence factors which offset the higher daily cost of the agent stemming from reducing the daily dosage from three tablets to one. He noted that the Committee would be reviewing all of the drugs in this class later this year.

BAP Questions – Exforge HCT

Mr. Hutchings asked how many people would actually need this drug as a “triple,” that is, how many people are actually taking all three of its components. The answer given was that there is no information on that.

BAP Discussion and Vote — Renin Angiotensin Aldosterone Antihypertensive Agents (RAAs) Valsartan/Amlodipine/Hydrochlorothiazide (HCTZ) Tablets (Exforge HCT) — Uniform Formulary Recommendation

Continuing from the questioning, Mr. Hutchings commented that he sees an inconsistency that needs to be addressed, which is that patients who want Valsartan (Diovan) will wind up adding two non-formulary drugs to their prescription just so they can get the benefit of the lower co-pay from a formulary drug. He said he sees no reason why this drug should be on the formulary.

A more extensive discussion ensued during which several Panel members expressed agreement with the view that putting Exforge HCT on the UF would mean giving some people unnecessary drugs just to get the lower co-pay cost and felt that was not good practice. Some physicians apparently feel that all combination drugs are controversial.

LTC Hannah responded that The Committee’s feeling was that putting Exforge HCT on the formulary would simplify the medication for people who were already on two drugs and needing a third.

Ms. Fryar noted her understanding that this drug class would be reviewed again in its entirety in August and asked whether that was correct and if that was part of the reason why Exforge was kept on the UF now. Dr. Meade acknowledged that the class would be re-reviewed in August, but said he didn’t know now – before the analysis had been done – whether or not other drugs would be added to the UF at that time.

Mr. Hutchings expressed the view that most patients with hypertension are already taking a lot of different medications, so that the effect would be more like reducing the daily number of meds from seven to five, not from three to one. His view is that wouldn’t be much help. He indicated his intent to non-concur with this recommendation.

Other Panel members expressed concern about the side effects of taking unnecessary medications and about the need to consider the younger population as hypertension is not limited only to older people.

Following the discussion, the Chair read the P&T Committee’s formulary recommendation for the record.

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the Renin Angiotensin Antihypertensive Agents drug class, and other relevant factors, the P&T Committee voted to recommend that Exforge

HCT remain classified as formulary under the UF.

The BAP voted as follows:

Concur: 4; Non-concur: 6; Abstain: 0; Absent: 0

BAP Comment

The BAP comment regarding this action was that increased compliance may not occur, but that the possibility exists that some patients will be forced to take extra and unneeded medication simply to obtain the agents they do need at formulary co-pay cost. Finances are also a motivator in regard to compliance.

BAP Discussion and Vote — Renin Angiotensin Aldosterone Antihypertensive Agents (RAAs) Valsartan/Amlodipine/Hydrochlorothiazide (HCTZ) Tablets (Exforge HCT) — Implementation Plan

Because the P&T Committee recommended formulary placement for this agent, it made no implementation plan recommendations. However, LtCol Bacon, the DFO, suggested that the Panel might want to consider recommend an implementation timeframe in the comments its forwards to the Director, TMA, for consideration.

After a very brief discussion, the Panel agreed that a 60-day implementation period seemed adequate. A vote on the 60-day implementation period was taken with the following result:

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

RE-EVALUATION OF WELLBUTRIN XL's UNIFORM FORMULARY STATUS

(BAP Script)

Status of Bupropion HCl ER Tablets (Wellbutrin XL) on the UF

(Dr. Meade): Wellbutrin XL Clinical and Cost Effectiveness:

On an ongoing basis, the DoD PEC monitors changes in the clinical information, current costs, and utilization trends to determine whether the UF status of agents designated as non-formulary needs to be readdressed. The P&T Committee reevaluated the UF status of bupropion ER (Wellbutrin XL, generics) in light of recent price reductions in the generic 150 mg and 300 mg formulations across all three points of service.

Clinical Effectiveness Conclusion — The AD-1 agents were evaluated for UF status at the November 2005 meeting. At that meeting, the P&T Committee concluded bupropion appears similar in efficacy to SSRIs; its major advantage is a lower incidence of sexual adverse effects than the other AD-1 agents. The major disadvantages are the risk of seizures at high doses and its tendency to produce activation/agitation. The putative advantage of the once-daily ER formulation (Wellbutrin XL) is increased compliance,

although clinical trial data assessing compliance is not available.

Cost Effectiveness Conclusion — The P&T Committee agreed that the generic bupropion ER (Wellbutrin XL) formulations were now cost effective at all three points of service.

(Dr. Meade): Wellbutrin XL – Uniform Formulary 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, voted (15 for, 0 opposed, 1 abstained, and 0 absent) that bupropion ER (Wellbutrin XL, generic) be immediately reclassified as generic on the UF. Wellbutrin XL was included on the “list of non-formulary drugs for re-evaluation of UF status” presented to the Beneficiary Advisory Panel in January 2008 and approved by the Director, TMA on 13 February 2008. No further approval is needed.

(Dr. Meade): LTC Hannah will now give the physician perspective for Wellbutrin XL.

**Physician Perspective — Wellbutrin XL Re-Evaluation
(LTC Hannah):**

LTC Hannah, providing the physician’s perspective on this recommendation, informed the Panel that the recommendation was non-controversial. The introduction of generic formulations has resulted in price reductions.

BAP Questions

Members of the BAP had no questions regarding this recommendation.

BAP Discussion and Vote — Wellbutrin XL Formulary Recommendation

Ms. Fryar read the P&T Committee’s formulary 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, voted (15 for, 0 opposed, 1 abstained, and 0 absent) that bupropion ER (Wellbutrin XL, generic) be immediately reclassified as generic on the UF. Wellbutrin XL was included on the “list of non-formulary drugs for re-evaluation of UF status” presented to the Beneficiary Advisory Panel in January 2008 and approved by the Director, TMA on 13 February 2008. No further approval is needed.

The BAP voted as follows:

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

One Panel member asked when the change would take effect. The answer given was: immediately. We are unable to determine the response.

IMPLEMENTATION OF FEDERAL CEILING PRICE REGULATION

(BAP Script)

(LTC Spridgen):

The committee reviewed medical necessity criteria for drugs that were not included on a Department of Defense Retail Refund Pricing Agreement at the August 2009 meeting, and also reviewed drugs that were not included on a DoD Retail Refund Pricing Agreement at the November 2009 meeting. These drugs are not compliant with FY2008 National Defense Authorization Act, Section 703. The law stipulates that if a drug is not compliant with Section 703, these drugs will be designated non-formulary under the Uniform Formulary and will require a pre-authorization prior to use in the retail point of service (POS) and medical necessity in Military Treatment Facilities. These non-formulary drugs will remain available in the mail order POS without pre-authorization. Pre-authorization was determined at the November 2009 DoD P&T Committee meeting. Drugs with and without pricing agreements were systematically classified based along therapeutic and pharmacologic lines. The classification system was based on the American Hospital Formulary System Classification and First Data Bank classification.

The DoD P&T Committee recommended the following:

- A. The following branded drugs with generic equivalents follow the standard TRICARE rules for brand-generic prior-authorization criteria.

| | | |
|------------|----------|-----------------------|
| Aclovate | Altace | Carnitor, Carnitor SF |
| Cutivate | Cytosan | Depakene |
| Kaon-CL | Mobic | Omnicef |
| Persantine | Pletal | Septra; Septra DS |
| Silvadene | Tapazole | Temovate |
| Viroptic | Zonegran | |

- B. The implementation date for the medical necessity criteria for the branded drugs will not be prior to 1 April 2010 and not later than 180 days after the minutes of this meeting are signed.
- C. The transition period at the MTF POS for the medical necessity criteria for the branded drugs as ending no later than 1 January 2011.
- D. The following drugs retain formulary status on the Uniform Formulary.

ARICEPT
ARICEPT ODT
DILANTIN
EPIPEN
EPIPEN JR
FARESTON
HEXALEN

MENOPUR
 MESNEX
 QUALAQUIN
 TARGRETIN
 VANCOCIN HC

E. The following drugs retain non-formulary status or be designated non-formulary on the Uniform Formulary:

| | | | |
|-------------------|-------------------------|-----------------------|-----------------|
| ADOXA | CYCLOGYL | ESGIC | METHYLIN ER |
| ALLEGRA | CYCLOSPORINE | ESGIC-PLUS | MIMYX |
| ALOCRIIL | DARVOCET A500 | FML | MONONESSA |
| AMICAR | DARVOCET-N 100 | FML FORTE | NATAFORT |
| ANTABUSE | DARVOCET-N 50 | FML S.O.P. | NORCO |
| ARMOUR THYROID | DARVON | FRAGMIN | OCUFEN |
| AVAGE | DARVON-N | GENGRAF | OCUFLOX |
| AZASAN | DENAVIR | GLUCAGEN | OGEN |
| AZELEX | DILANTIN | GRANULEX | OPTASE |
| BANZEL | DILTZAC ER | HYCET | PACERONE |
| BETAGAN | DORAL DUET | INDERAL LA | PERANEX HC |
| BIAXIN XL | STUARTNATAL | KERAFOAM | PERPHENAZINE |
| BLEPHAMIDE | E.E.S. 200 | LAMICTAL ODT | PHRENILIN FORTE |
| BLEPHAMIDE SOP | E.E.S. 400 ELDOPAQUE | LAMICTAL ODT (BLUE) | POLY-PRED |
| BRAVELLE | FORTE ELDOQUIN | LAMICTAL ODT (GREEN) | POLYTRIM |
| BREVOXYL-4 | FORTE | LAMICTAL ODT (ORANGE) | PRED MILD |
| BREVOXYL-8 | ELESTAT | LAMICTAL XR | PRED-G |
| CAFCIT | ELIMITE | LINDANE | PRIMSOL |
| CAPITAL W-CODEINE | EMLA | LO-OVRAL-28 | PROCTOCORT |
| CARDENE SR | EPIFOAM ERGOLOID | LORCET 10-650 | PROCTOFOAM- HC |
| CITRANATAL 90 DH | MESYLATES | LORCET PLUS | PROGLYCEM |
| CITRANATAL DH | ERYPED 200 | LORTAB | REPRONEX |
| CITRANATAL RX | ERYPED 400 | MAGNACET | RIMSO-50 |
| CLARIFOAM EF | ERY-TAB ERYTHROCIN | MAVIK | ROCALTROL |
| CLINDESSE | STEARATE | MAXIDONE | ROSAC |

| | | | |
|-----------|---------------|---------------|----------|
| CORZIDE | ERYTHROMYCIN | MEBARAL | VIVACTIL |
| SALAGEN | TRINESSA | ULTRASE MT 20 | XENADERM |
| SALKERA | TUSSICAPS | VICODIN ES | ZARONTIN |
| STIMATE | ULTRASE | VOCIPROFEN | UROCIT-K |
| SYNTHROID | ULTRASE MT 12 | VIMPAT | |
| THEO-24 | ULTRASE MT 18 | VIOKASE | |

- F. The implementation date for pre-authorization will not be prior to 1 April 2010 and not later than 180 days after the minutes of this meeting are signed by the Director, TMA.
- G. Formulary status of a drug recommended to move from Tier 2 to Tier 3 will stay in Tier 2 if a Price Agreement is received prior to 1 February 2010.
- H. The transition period at the MTF POS for drugs recommended to move from Tier 2 to Tier 3 as if there will still on Tier 2 for purposes of MTF availability until 1 January 2011.

ITEMS FOR INFORMATION — SECTION 703

BAP Discussion

One BAP Member asked about other drugs in the same classes that were not included on this list or on the list of drugs previously considered by the Panel. Dr. Meade explained that there are a lot of drugs to be considered and that the P&T Committee is reviewing them in batches.

Panel Vote on Committee Recommendations

Without further discussion, the Chair read the P&T Committee recommendations on these drugs and had the Panel vote on them one item at a time. The results were as follows:

A. Branded drugs with generic equivalents will follow the standard TRICARE rules for brand-generic prior-authorization criteria.

| | | |
|------------|----------|-----------------------|
| Aclovate | Altace | Carnitor, Carnitor SF |
| Cutivate | Cytosan | Depakene |
| Kaon-CL | Mobic | Omnicef |
| Persantine | Pletal | Sepra; Septra DS |
| Silvadene | Tapazole | Temovate |
| Viroptic | Zonegran | |

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0

B. The implementation date for the medical necessity criteria for the branded drugs will not be prior to 1 April 2010 and not later than 180 days after the minutes of this meeting are signed.

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0

C. Not applicable.

D. Drugs retaining formulary status.

A panel member asked for clarification about which Dilantin this was, the adult or pediatric Dilantin. The answer given was that it was the pediatric Dilantin.

Aricept
Aricept ODT
Dilantin (Pediatric)
Epipen
Epipen Jr.
Fareston
Hexalen
Menopur
Mesnex
Qualaquin
Targretin
Vancocin HC

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0

E. Designated as Non-Formulary Under the UF

A panel member asked for clarification about which Dilantin this was, the adult or pediatric Dilantin. The answer given was that it was the Adult Dilantin. Also clarification was sought for Erythromycin, the answer given was the Adult Brand.

| | | | |
|-----------------------|--|--------------------------|-----------------|
| ADOXA | CYCLOGYL | ESGIC | METHYLIN ER |
| ALLEGRA | CYCLOSPORINE | ESGIC-PLUS | MIMYX |
| ALOCRIIL | DARVOCET A500 | FML | MONONESSA |
| AMICAR | DARVOCET-N 100 | FML FORTE | NATAFORT |
| ANTABUSE | DARVOCET-N 50 | FML S.O.P. | NORCO |
| ARMOUR THYROID | DARVON | FRAGMIN | OCUFEN |
| AVAGE | DARVON-N | GENGRAF | OCUFLOX |
| AZASAN | DENAVIR | GLUCAGEN | OGEN |
| AZELEX | DILANTIN (Adult) | GRANULEX | OPTASE |
| BANZEL | DILTZAC ER | HYCET | PACERONE |
| BETAGAN | DORAL | INDERAL LA | PERANEX HC |
| BIAXIN XL | DUET STUARTNATAL | KERAFOAM | PERPHENAZINE |
| BLEPHAMIDE | E.E.S. 200 | LAMICTAL ODT | PHRENILIN FORTE |
| BLEPHAMIDE SOP | E.E.S. 400 | LAMICTAL ODT (BLUE) | POLY-PRED |
| BRAVELLE | ELDOPAQUE FORTE | LAMICTAL ODT (GREEN) | POLYTRIM |
| BREVOXYL-4 | ELDOQUIN FORTE | LAMICTAL ODT (ORANGE) | PRED MILD |
| BREVOXYL-8 | ELESTAT | LAMICTAL XR | PRED-G |
| CAF CIT | ELIMITE | LINDANE | PRIMSOL |
| CAPITAL W- CODEINE | EMLA | LO-OVRAL-28 | PROCTOCORT |
| CARDENE SR | EPIFOAM | LORCET 10-650 | PROCTOFOAM- HC |
| CITRANATAL 90 DH | ERGOLOID | LORCET PLUS | PROGLYCEM |
| CITRANATAL DH | MESYLATES | LORTAB | REPRONEX |
| CITRANATAL RX | ERYPED 200 | MAGNACET | RIMSO-50 |
| CLARIFOAM EF | ERYPED 400 | MAVIK | ROCALTROL |
| CLINDESSE | ERY-TAB | MAXIDONE | ROSAC |
| CORZIDE | ERYTHROCIN | MEBARAL | VIVACTIL |
| SALAGEN | STEARATE | ULTRASE MT 20 | XENADERM |
| SALKERA | ERYTHROMYCIN (Adult Brand) | VICODIN ES | ZARONTIN |
| STIMATE | TRINESSA | VOCIPROFEN | UROCIT-K |
| SYNTHROID | TUSSICAPS | VIMPAT | |
| THEO-24 | ULTRASE | VIOKASE | |
| | ULTRASE MT 12 | | |
| | ULTRASE MT 18 | | |

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0

BAP Questions

A Panel member asked about erythromycin and why it was designated non-formulary. Dr. Meade explained that it was only the tablet brand formulation.

One Panel member asked about “Item F.” in the presentation: the implementation date for pre-authorization will not be prior to 1 April 2010 and not later than 180 days after the minutes of this meeting are signed by the Director, TMA. Dr. Meade explained that pre-authorization is not available through the network. Patients would have to go to mail order or MTF to get it.

Another asked about the reason why some drugs not in compliance with Section 703 are being allowed to remain on the formulary. Dr. Meade answered that these are drugs that the system really can’t do without.

F. The implementation date will not be prior to 1 January 2010 and not later than 180 days after the minutes of this meeting are signed.

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0

A Panel member raised the point that the presentation called for an implementation date not prior to 1 April, as opposed to 1 January. After a brief discussion with the staff, a motion was made to change the start date above to “1 April 2010” instead of “1 January 2010” as follows:

The implementation date will not be prior to 1 April 2010 and not later than 180 days after the minutes of this meeting are signed.

The Panel voted:

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0

Item G. Formulary status of a drug recommended to move from Tier 2 to Tier 3 in these lists will stay on Tier 2 if Pricing Agreement is received prior to 1 February 2010.

Concur: 10; Non-concur: 0; Abstain: 0; Absent: 0

Item H. Not applicable.

**INFORMATION ITEM:
FY 2009 FORMULARY PERFORMANCE**

Dr. Meade provided the BAP with a slide presentation covering the highlights of what had been done in FY 2009, the fiscal impact of those actions and a tentative outlook of the P&T Committee's agenda for the upcoming year (Dr. Meade's slides are attached).

Slide 1: Nov 08-Nov 09

Dr. Meade noted at the outset that the Committee usually reviews its progress for the Panel in January. This year Section 703 took a lot of time. But he will summarize what they did, concentrating on the decisions that had the greatest impact. After that, he will project what they will be working on into the next year.

Overall, he indicated that during fiscal year 2009 the Committee reviewed 40 drugs in six major classes affecting 706,921 beneficiaries. Before the Committee reviews, DoD was spending \$343,700,000 on the reviewed drugs. As a result of Committee actions, the estimated first-year cost avoidance will be \$108,820,554 (a combination of savings plus money DoD gets back on rebates).

Slide 2: Nov 08-Nov 09

Dr. Meade said the Committee also looked at drugs in previously-reviewed class, including 16 miscellaneous actions, such as BCF and ECF cleanup, PA reviews, safety reviews and Section 703 reviews. He said the Panel doesn't see the "cleanup" actions but they help to clarify things for people in the field and make the formulary available on electronic PDAs so they can be downloaded. MTFs should have a downloadable formulary for the providers.

The cost avoidance numbers do not yet reflect savings from Section 703. They are working on getting these numbers. Additionally, the collection of rebate monies hadn't really started yet.

Slides 3-6: Asthma Inhalers — Steroid/LABA Combo

As shown on the first bar graph (slide 4), two combo drugs have been available: Advair and Symbicort, with Advair Diskus being the number one drug used. Usage of Symbicort has grown from zero to about 10,000 over the past two years while Advair

Diskus usage has declined somewhat. Expenditures (shown on the second bar graph – slide 5) are now in the \$12-\$14 million range, with Symbicort expenditures increasing while Advair Diskus expenditures decreased from a high of about \$15 million to about \$12 million. By point of service (slide 6), expenditures have grown in retail from about \$5 million a month to about \$8 million a month; decreased in MTF from around \$5 million a month to about \$4 million a month and remained approximately level in mail order. Rebates from companies are expected to further reduce MTF expenditures by another \$2-\$3 million a month, with a similar result expected for the retail POS. These results will be shown in future graphs.

Slides 7-11: Short-Acting Beta Agonists

There are three UF drugs in the SABA class: Proair HFA, Proventil HFA, and Ventolin HFA. The first slide in this series (slide 7) shows the quantity of SABAs dispensed by POS by month from January 2007 through November 2009. Over this period of time, Ventolin has become the number one drug used, increasing dramatically from less than 100,000 GMs to about one million GMs a month. Use of Proventil, the leading agent in 2007, grew during the period but began to decline in February 2009 and is now back to its 2007 levels. Proair HFA use has increased since July 2008 and is now higher than Proventil. The graph shows the effect on Proventil of the formulary decision made in late 2008. The next slide (slide 8) shows Ventolin growth by point of service with the biggest increase coming from MTFs, followed by retail. There has been almost no growth in the mail order POS. Retail sales are going through a decline so the figures shown are somewhat artificially depressed.

In the mail order POS (slide 9), Proventil remain the number one seller at about 80,000 GMs per month, about what it was two years ago. Ventolin and Proair sales have increased during the period and are almost equal. Beginning in September 2009, Ventolin sales surpassed Proair sales in the mail order POS. Dr. Meade says these results make sense because they normally don't see the results of decisions reflected as fast or as much in mail order as at other points of service.

In retail (slide 10), Proair is the most used drug and sales have continued to climb, although there was a dip in mid-2009 as a result of the formulary decision. Ventolin has jumped even more dramatically, however, and its usage quadruples in calendar 2009. Dr. Meade attributed the continued growth of Proair to the fact that Proair has heavily marketed their product with the big chains. The result is that they have a choice of which drug to use.

In the MTFs (slide 11), the results of the formulary decision are shown clearly: Ventolin use has grown from about 100,000 GMs per month to almost 800,000 GMs per month. Proventil still has quite a bit of use, but is only about one-third of what it was before the decision. Proair use, never very high, has dropped even more.

Inhaled Corticosteroids: Slides 12-13

The next slide (slide 12) shows monthly usage for the 8 drugs in the inhaled corticosteroids class across all points of service between January 31 2007 and November 30 2009, although three agents in this drug class are not being manufactured anymore. The leading drug in this category, Flovent HFA, has increased from 120,000 gms per month to over 160,000 gms per month since the May 08 formulary decision. All of the other drugs, but especially Flovent (no longer manufactured) and Azmacort (made non-formulary), show decreased usage across all points of service. By point of service (slide 13), retail network expenditures for this drug class grew from a little over \$1 million to more than \$1.5 million and MTF expenditures grew from about \$1 million to about \$1.25 million. Mail order expenditures remained relatively steady at less than \$500,000. The drop in MTF expenditures at the start of 2009 reflects the expiration of the BPA for Flovent.

Long-Acting Beta Agonists (LABAs): Slide 14

Dr. Meade introduced the agents in this drug class by noting that they have turned out to be more detrimental than helpful. The leading agent in terms of quantity dispensed (Serevent Diskus) has dropped about a third in the past two years (from 300,000 GMs per month to less than 200,000 GMs per month). The second leading agent, Foradil, has also seen a decline in usage. Dr. Meade noted that these agents are also used to treat chronic pulmonary disease and have not been detrimental for that.

P&T Action for the Near Future (Slides 15-20)

Dr. Meade next discussed items on the P&T Committee's agenda for the upcoming year. In February 2010 (slide 16), the Committee will review basal insulins, IV clotting factors and new drugs in already reviewed drug classes. Basal insulins are being reviewed because the contract (BPA) expired in December and DoD is operating on a temporary contract through the VA. DoD is trying to coordinate its contracting but there has been a delay in the outcome. IV clotting factor drugs are also being taken up in February. The Committee was originally going to do ARBs but DoD lost its contract for Mycardis and the price went up significantly, which is important because that is the number one used drug in the ARB class. There are also a lot of other things going on with the ARB drug class and it needed to be delayed, so the IV clotting factors class was selected to replace it. In this class, several products lack Section 703 pricing agreements and DoD is trying to get all manufacturers to comply with the pricing requirements. There will also be reviews of five new drugs in already reviewed classes.

In May 2010 (slide 17), the Committee will take up BPH alpha blockers, Anti-lipidemic 1 (LIP1) drugs and more new drugs in already reviewed classes. Although the BAP has considered Committee recommendations in the BPH (benign prostatic hyperplasia) class multiple times, another review is necessary because Flomax generics will become available and because electronic pre-authorization along with generics can now replace step therapy for this class. Additionally, the Center's subject matter expert (SME) is retiring, so this will probably be the last review of this class for awhile. Since the Committee's last review of the LIP1 drug class four years ago, a lot of information has

come out raising issues with Vytorin and Zetia. In addition, Lipitor will be going generic. Again, the Committee wants to conduct a review before the SME retires. Lastly, about four new drugs in already-reviewed classes will be taken up in May.

In August 2010 (slide 18), the Committee will review the ARBs drug class again, the ophthalmology 1s (antihistamine.NSAIDs) drug class and additional new drugs in already reviewed classes. The ARBs will be reviewed, as previously noted, because of a terminated BPA for telmisartan (Mycardis), because a generic formulation of losartan will probably be available and because Joint National Committee (JNC8) recommendations should be available. The ophthalmology 1s are a growing drug class and need to be evaluated. Additionally, three subject matter expert positions will be vacated over the coming months and new staff will be hired and need to be trained. This class will be used to help in that process. The Committee will also probably be doing reviews of about four new drugs in previously reviewed classes in August.

In November 2010 (Slide 19), the Committee will evaluate diabetes drugs along with new drugs in previously reviewed classes. In the diabetes class, four different classes will be reviewed: oral sulfonylureas, thiazolidinedione (TZD) agents (a re-review), dipeptidyl peptidase - 4 (DPP-4) agents, and Glucagon-like peptides-1 (GLP-1) agents. New agents are available in the latter two classes.

A very tentative projection for February 2011 (slide 20) has the Committee considering irritable bowel syndrome (IBS) agents, because of new drugs and increased competition, and pancreatic enzymes, because FSDA actions have redefined the drug class. As previously, new drugs in already reviewed classes will be considered.

“Spanner in the works” (Slide 21)

The last slide, entitled “spanner in the works” details some of the “wild cards” that might come up to take the Committee’s attention during the next years. That list includes: smoking cessation drugs (to comply with new requirements); proton pump inhibitors (PPIs) already reviewed but there may be issues with the safety of preferred agents; narcotic analgesics, where new drugs have been problem prone; targeted immunomodulatory biologics (TIB) agents, where new drugs are being released and the Committee wants to evaluate them after a period of use to establish a history for safety; multiple sclerosis (MS) drugs, a class with new biologics coming out along with oral agents.

CLOSING REMARKS

LtCol Bacon closed the session by thanking the Panel members and the audience for coming and made several announcements. One is that at the next meeting, in March, the Panel will be asked to elect a new Chair for the coming year. This election has been delayed because of the delay in filling vacancies on the Panel, but he expects the Panel to have its full compliment of eleven

members by the next meeting. He also announced a tentative schedule of meeting dates for the rest of the year: 25 March, 24 June and 23 September. All meetings are planned for the Naval Heritage Center venue in Washington, D.C.

The DFO adjourned the meeting at 12:30 P.M.

Brief Listing of Acronyms Used in This Summary

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

- ACE — Angiotensin Converting Enzyme (a drug class)
- AD-1 — Antidepressant-1 (a drug class)
- ADHD — Attention Deficit Hyperactivity Disorder
- AE — Adverse event
- APR — Automated Profile Review
- ARB — Angiotensin Receptor Blocker (a drug class)
- BAP — Uniform Formulary Beneficiary Advisory Panel (the “Panel” referred to above)
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- BPA — Blanket Purchase Agreement
- BPH — Benign prostatic hyperplasia
- CCB — Calcium channel blockers (a drug class)
- CEA — Cost-effectiveness analysis
- C.F.R — Code of Federal Regulations
- CMA — Cost-Minimization Analysis
- CR — Controlled Release (a drug formulation)
- DEA — U.S. Drug Enforcement Administration
- DFO — Designated Federal Officer
- DoD — Department of Defense
- ECF — Extended Core Formulary
- ED — Erectile dysfunction
- 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
- HBr — Hydrobromide
- HCl — Hydrochloride
- HCTZ — Hydrochlorothiazide
- IIEF — International Index of Erectile Function
- IR — Immediate Release (a drug formulation)
- IV — Intravenous
- LIP1 — Antilipidemics (a drug class)

- MHS — Military Health System
- MN — Medical Necessity
- MSLT — Mean sleep latency testing
- MTF — Military Treatment Facility
- NDAA — National Defense Authorization Act
- NF — Non-formulary
- NIH — National Institutes of Health
- NNH — Number Needed to Harm
- NNT — Number Needed to Treat
- OAB — Overtactive bladder drugs (a drug class)
- OTC — Over the counter
- PA — Prior Authorization
- PAH — Pulmonary arterial hypertension
- P&T Committee — DOD Pharmacy and Therapeutics Committee
- PDE-5 — Phosphodiesterase Type 5 Inhibitors (a drug class)
- PDTS — Pharmacy Data Transaction Service
- PEC — DOD Pharmacoeconomic Center
- PORT — Pharmacy Outcomes Research Team
- POS — Point of Service
- PsA — Psoriatic arthritis
- RA — Rheumatoid arthritis
- RAAs — Renin-angiotensin antihypertensive agents (a drug class)
- RCTs — Randomized Control Trials
- SR — Sustained release (a drug formulation)
- SQ — Subcutaneously
- SNRI — Serotonin-norepinephrine reuptake inhibitor (a drug class)
- SSRIs — Selective serotonin reuptake inhibitors (a drug class)
- TBI — Traumatic brain injury
- TIB — Targeted Immunomodulatory Biologics (a drug class)
- TCA — Tricyclic antidepressant
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TPHARM — TRICARE Pharmacy Program
- 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
- VERT — Venlafaxine Extended Release Tablets (a drug)