28 April 2010

Executive Summary

UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL COMMENTS
25 March 2010

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy & Therapeutics (P&T) Committee January 2010 meeting.

1. **Basal Insulins 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 (15 for, 0 opposed, 1 abstained, 0 absent) to recommend the following:

a) Insulin glargine vials (Lantus), insulin glargine pen devices (Lantus SoloStar) and insulin detemir vials (Levemir) remain classified as formulary on the UF.

b) Insulin detemir pen devices (Levemir FlexPen) be designated as non-formulary on the UF.

The P&T Committee recommended (15 for, 0 opposed, 1 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 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 11 Concur, 0 Non-Concur, 0 Absent regarding the recommendations for formulary and non-formulary agents.
- The Panel voted 11 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. **ANTIHEMOPHILIC AGENTS – Factor VIII and Factor IX concentrates:** 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 (13 for, 0 opposed, 2 abstained, 1 absent):

a) The factor VIII products Koate DVI, Kogenate FS, Refacto, and Xyntha, and the factor IX products Alphanine SD and BeneFIX remain classified as formulary on the UF.

b) The factor VIII products Advate, Hemofil M, Helixate FS, Monoclate P, and Recombinate, and the factor IX product MonoNine be designated as non-formulary under the UF.

c) All factor VIII and factor IX products recommended for inclusion on the UF had existing Uniform Formulary Voluntary Agreement for Retail Refunds (UF VARR) submissions at or below the Federal Ceiling Price (FCP), or a required Mandatory Agreement for Retail Refund. None of the products recommended to be designated NF on the UF had the required pricing agreement.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent)
1) an effective date of the first Wednesday one week after the minutes are signed, following a 180-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at MTFs no later than a 180-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 11 Concur, 0 Non-Concur, 0 Absent regarding the recommendation for formulary and non-formulary agents.
- The Panel voted 11 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 180 days.

Director, TMA:

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

3. **ANTIHEMOPHILIC AGENTS – Factor VIII/von Willebrand Factor Complexes, Human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products:** 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 (11 for, 1 opposed, 3 abstained, 1 absent):

a) The factor VIII/vWF product Alphanate, the human PCC product Profilinine SD, and the inhibitor bypassing product NovoSeven RT remain classified as formulary on the UF.

b) The factor VIII/vWF product Humate-P, the human PCC product Bebulin VH, and the inhibitor bypassing product Feiba VH be designated as non-formulary under the UF.

c) All factor VIII/vWF, the human PCCs, and inhibitor bypassing product recommended for inclusion on the UF were covered by UF VARR submissions at or below the Federal Ceiling Price or a required Mandatory Agreement for Retail Refund. None of the products recommended to be designated NF on the UF had the required pricing agreement.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 180-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at MTFs no later than a 180-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 11 Concur, 0 Non-Concur, 0 Absent regarding the recommendation for formulary and non-formulary agents.
- The Panel voted 11 Concur, 0 Non-Concur, 0 Absent regarding the recommended implementation period of 180 days.

Director, TMA:

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

4. **Narcotic analgesics—Morphine Sulfate Extended Release (ER)/Naltrexone Capsules (Embeda):** 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 (11 for, 3 opposed, 1 abstained, 0 absent) morphine sulfate ER/naltrexone capsules (Embeda) be designated formulary on the UF.

The implementation plan is not applicable since it will be designated formulary on the UF.

Summary of Panel Vote/Comments:

- The Panel voted 8 Concur, 3 Non-Concur, 0 Absent regarding the recommendation that morphine sulfate extended release (ER)/naltrexone capsules (Embeda) be designated formulary on the UF.
- The non-concurring votes were based on the lack of evidence that the product would have the deterrent effect claimed by the manufacturer.

Director, TMA:

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

5. Attention Deficit/Hyperactivity Disorder (ADHD) — Guanfacine Extended Release (ER) tablets (Intuniv): 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 (11 for, 3 opposed, 1 abstained, 1 absent) guanfacine ER tablets (Intuniv) be designated formulary on the UF.

The implementation plan is not applicable since it will be designated formulary on the UF.

Summary of Panel Vote/Comments:

- The Panel voted 10 Concur, 1 Non-Concur, 0 Absent regarding the recommendation that guanfacine extended release (ER) tablets (Intuniv) be designated formulary on the UF.
- The non-concurring Panel member commented that his vote was because the two studies available are insufficient to ensure confidence.

Director, TMA:

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

6. Newer Sedative Hypnotics—Zolpidem Sublingual Tablets (Edluar): 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 (15 for, 0 opposed, 0 abstained, 1 absent) that zolpidem SL tablets (Edluar) be designated NF on the UF.

The P&T Committee recommended (14 for, 0 opposed, 1 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 11 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that Zolpidem sublingual tablets (Edluar) be designated non-formulary on the UF.
- The Panel voted 11 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. **Renin Angiotensin Antihypertensive Agents (RAAs)—Telmisartan/Amlodipine Tablets (Twynsta):** 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) telmisartan/amlodipine (Twynsta) be designated NF on the UF.

The P&T Committee recommended (15 for, 0 opposed, 1 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 11 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that telmisartan/amlodipine (Twynsta) be designated non-formulary on the UF.
- The Panel voted 11 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.

8. **Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Valsartan Tablets (Valturna):** 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, 0 opposed, 2 abstained, 0 absent) aliskiren/valsartan (Valturna) be designated NF on the UF.

The P&T Committee recommended (15 for, 0 opposed, 1 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 11 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that aliskiren/valsartin (Valturna) should be designated non-formulary on the UF.
- The Panel voted 11 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.

9. **Implementation of Federal Ceiling Price Regulation:**

A. ***Committee Action – Drugs retaining UF status:***

The P&T Committee recommended by consensus the drugs listed below, retain formulary status on the UF.

TARCEVA
TARGRETIN

B. ***Committee Action – Drugs retaining or designated NF:***

The P&T Committee recommended by consensus the drugs listed below retain NF status or be designated NF on the UF.

FLUOROPLEX
PANRETIN
SUBOXONE
SUBUTEX
TAZORAC

C. ***Committee Action – Implementation date for PA***

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

D. ***Committee Action – Transition date at the MTF POS:***

The P&T Committee recommended by consensus a transition period at the MTF POS as ending no later than January 1, 2011.

Summary of Panel Vote/Comments:

- The Panel voted 11 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that Tarceva and Targretin be retained as formulary on the UF.

- The Panel voted 11 Concur, 0 Non-Concur, 0 Absent regarding the recommendation that Fluoroplex, Panretin, Suboxone, Subutex and Tazorac be designated to non-formulary status on the UF.
- The Panel voted 11 Concur, 0 Non-Concur, 0 Absent regarding the implementation date of not being prior to 1 July 2010 and not later than 180 days after the minutes being signed.
- The Panel voted 11 Concur, 0 Non-Concur, 0 Absent recommended by consensus a transition period at the MTF POS as ending no later than January 1, 2011.

Director, TMA:

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

Charles L. Ri-
5 May 2010

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
March 25, 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 Family Association, representing the Military Coalition
- John Crum, Medical Professional, Humana Military Healthcare Services, Inc.
- Brian Casull, Medical Professional, TriWest Healthcare Alliance.
- 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 9:50 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 February 17 and 18, 2010 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. Basal Insulins
    2. Antihemophilic Factors
        - Factor VIII and Factor IX concentrates
        - Factor VIII/vonWillebrand factor complexes, human prothrombin concentrate complexes, inhibitor bypassing products

3. Designated Newly-Approved Drugs:
    - Narcotic Analgesics – Embeda (morphine extended release / naltrexone capsules)
    - Attention Deficit / Hyperactivity Disorder Drugs – Intuniv (guanfacine extended release tablets)
    - Newer Sedative Hypnotics – Edluar (zolpidem sublingual tablets)
    - Renin Angiotensin Antihypertensive Agents (RAAs) – Twynsta (telmisartan / amlodipine tablets)
    - Renin Angiotensin Antihypertensive Agents (RAAs) – Valturna (aliskiren/valsartan tablets)

- Formulary Status of drugs not in compliance with 2008 NDAA Section 703

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 the Director's decisions will be available on the TRICARE website in approximately four to 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 introduced the individual Panel members, including one new member present for the first time: Dr. Brian Casull, a medical professional from TriWest Healthcare. He said the Panel currently has eleven members and should eventually have fourteen members.

LtCol Bacon also noted housekeeping considerations pertaining to this meeting.

Private Citizen Comments

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

Chairperson's Opening Remarks

The Panel Chairperson, Ms. Fryar, briefly thanked everyone in attendance for coming and asked that the PEC proceed with its presentation of drug class reviews.

DRUG CLASS REVIEW PRESENTATIONS

[PEC Script]

(Dave Meade): I'm Dave Meade, the Director of Clinical Operations at the DoD Pharmacoeconomic Center Director. Joining me today from the PEC is CPT Brian Haney, our army physician. Col Lounsbery, a member of the P&T Committee, will provide the physician perspective and comment on the recommendations made by the Committee. Also present is Dr. James Ellzy, the P&T Committee Chair, and the TMA Counsel, who also sits on 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 Regulations (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 two Uniform Formulary drug classes – the Basal Insulins and the Antihemophilic Factors, and five newly approved drugs, Embeda, Intuniv, Edluar, Twynsta and Valturna.
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. There are tables and utilization figures for all the drug classes. We'll be using trade names as much as possible, so you can refer to your handout throughout the presentation.

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

I. UNIFORM FORMULARY CLASS REVIEWS — BASAL INSULINS

(CPT Haney) PEC Script

A. Basal Insulins — Relative Clinical Effectiveness

Please turn to page 2 of the handout for the table of drugs in the basal insulin class. The P&T Committee evaluated the clinical effectiveness of the long-acting basal insulin analogues (e.g., basal insulins) for the treatment of diabetes mellitus (DM). Insulin detemir (Levemir) and insulin glargine (Lantus) were FDA approved on June 16, 2005, and April 30, 2000, respectively. Insulin detemir and insulin glargine are available in both vials and pre-filled pen devices (Lantus SoloStar and Levemir FlexPen). Insulin glargine vials are currently on the BCF. Information regarding the safety, effectiveness, and clinical outcomes of the long-acting basal insulin analogues was considered. NPH, an intermediate-acting basal insulin was not included in the review; it remains a BCF drug. The clinical review included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1). MHS expenditures for the long-acting basal insulin analogues exceeded $4M per month at the retail, mail order, and MTF POS from January 2008 to December 2009.

Figure 1 on page 2 of the handout shows that for all three points of service, the Lantus vials have the highest utilization of the basal insulin.

Relative Clinical Effectiveness Conclusion —The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions regarding the basal insulin drug class:

1. With regard to efficacy, the following conclusions were made:
    a) In pivotal trials, both Levemir and Lantus produced similar reductions in glycosylated hemoglobin A1c (HbA1c) when compared to NPH insulin, in subjects with type-1 or type-2 DM.
    b) In head-to-head studies, there was a statistically significant difference in the reduction in fasting plasma glucose (FPG) values between Levemir and Lantus in subjects with type-1 DM; larger reductions in FPG were seen with Lantus. This difference was not observed in subjects with type-2 DM. The clinical significance of this finding is unknown.
    c) In head-to-head studies, the total Levemir dose required to achieve goal HbA1C levels (<7%) was larger than the dose of Lantus used to achieve goal HbA1C levels in subjects with type-1 DM. Levemir was dosed twice-daily more often than once-daily in subjects with type-2 DM. The clinical significance of these findings is unknown.
2. With regard to safety and tolerability, the following conclusions were made:
    a) Existing evidence does not support clinically relevant differences concerning hypoglycemia or weight gain between Levemir and Lantus. In subjects with type-2 DM, once-daily dosing of Levemir produced less weight gain (absolute difference 1.4 kg) when compared to twice-daily dosing of Levemir. In subjects with type-2 DM, Lantus was more likely to cause weight gain when compared to once daily Levemir (absolute difference 1.6 kg). There was no significant difference in weight gain when twice daily Levemir was compared to once daily Lantus (absolute difference 0.2 kg).

b) There is insufficient evidence to determine if there are clinically relevant differences between Levemir and Lantus with respect to cancer risk. Observational studies raised concerns of an association between the use of Lantus and cancer incidence. These studies had inconsistent findings and many study design flaws. FDA is uncertain of this association.

3. With regard to other factors

   a) There are no clinically relevant differences between the pen devices for insulin glargine (Lantus SoloStar) and insulin detemir (Levemir FlexPen) in terms of refrigeration requirements and expiration date after opening.

   b) Patient preference studies report that patients overall prefer using insulin pen devices compared to insulin vials. Although one study reported patients preferred the insulin glargine pen device (Lantus SoloStar) compared to the insulin detemir pen device (Levemir FlexPen); other studies have shown no patient preferences among various pen devices.

   c) A request for input from MTF providers revealed that the majority of responders ranked Lantus as their first preference for a basal insulin, followed by Levemir as the second choice, primarily due to perceived differences in efficacy and availability on the local formulary. The majority of responders stated that availability of one basal insulin on the local formulary was adequate to meet their prescribing needs

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

B. Basal Insulins — Relative Cost-Effectiveness

(Dave Meade) PEC Script

Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

a) Cost minimization analysis (CMA) results of the basal insulin agents revealed that glargine vials (Lantus) and pen devices (Lantus SoloStar) were the most cost-effective basal insulin products based on cost per ml of treatment. Cost per ml of treatment was calculated using average quarterly consumption rates for glargine vials (Lantus) and pen devices (Lantus SoloStar) and detemir vials (Levemir) and pen devices (Levemir FlexPen).

b) The potential impact of scenarios with selected basal insulin agents designated formulary or non-formulary on the UF was evaluated using budget impact analysis (BIA). Scenarios evaluating the impact of designating basal insulins on the BCF were also considered. Results from the BIA for the basal insulins revealed that placing glargine vials (Lantus) and pen devices (Lantus SoloStar) on the BCF and UF, with detemir vials (Levemir) on the UF, and designating detemir pen devices (Levemir FlexPen) NF was the most cost-effective scenario overall.

c) BIA results showed that detemir vials (Levemir) and detemir pen devices (Levemir FlexPen) were more costly than glargine vials (Lantus) and glargine pen

devices (Lantus SoloStar) in all scenarios that do not require automated prior authorization. Glargine vials (Lantus) and glargine pen devices (Lantus SoloStar) were more costly than detemir vials (Levemir) and detemir pen devices (Levemir FlexPen) in one scenario involving an automated prior authorization. However, The P&T Committee decided that an automated prior authorization was not clinically appropriate for the basal insulin class.

C. Basal Insulins — Uniform Formulary Recommendation

(Dave Meade) PEC Script

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, 0 absent) to recommend the following:

a) Insulin glargine vials (Lantus), insulin glargine pen devices (Lantus SoloStar) and insulin detemir vials (Levemir) remain classified as formulary on the UF.

b) Insulin detemir pen devices (Levemir FlexPen) be designated as non-formulary on the UF.

D. Basal Insulins — Uniform Formulary Implementation Plan

(Dave Meade) PEC Script

The P&T Committee recommended (15 for, 0 opposed, 1 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 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.

Col Lounsbery will now provide the physician perspective.

E. Basal Insulins — Physician Perspective

(Col Lounsbery)

Col Lounsberry informed the Panel that this was not a very difficult process. Two of the products were recommended for inclusion on the UF and the Levemir pen was made non-formulary because it had no advantages over the other pen and was more expensive. Additionally, the Committee was concerned about using step therapy with a prior authorization lest a patient get turned away at the pharmacy and wind up not using the products on the formulary.

F. Basal Insulins — BAP Questions and Discussion

Ms. Fryar opened the floor to Panel questions and discussion of the recommendations for this drug class.

Dr. Casull asked why Detemir was left on the formulary if is not as effective, causes more weight gain and is less cost-effective. Col Lounsberry replied that patients who use it once a day would have less weight gain.

Dr. Crum, referring to the handout at page 2, item 2.a, asked whether Lantus was more likely to cause weight gain. CPT Haney's reply was that is incorrect. There was no significant difference in weight gain between Levemir twice a day and Lantus once a day. The only difference was with Levemir once a day.

G. Basal Insulins — BAP Vote on UF Recommendations

The Panel Chair next read the P&T Committee's Uniform Formulary recommendations for the basal insulins drug class.

In view of the conclusions from the relative clinical effectiveness and relative cost effectiveness determinations of the basal insulins, the P&T Committee voted to recommend insulin glargine vials (Lantus), insulin glargine pen devices (Lantus SoloStar) and insulin detemir vials (Levemir) remain classified as formulary on the UF, and insulin detemir pen devices (Levemir FlexPen) be designated as non-formulary under the UF based on cost effectiveness.

Without further discussion the Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0

H. Basal Insulins — BAP Vote on Implementation Plan Recommendations

The Chair read the P&T Committee's implementation plan recommendations for the basal insulins 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 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.

Ms. Fryar noted that there were over 11,000 beneficiaries who would be affected by the

recommendations of this drug class and asked whether TMA was confident that the 60 day period would allow for ample notification. Ms. LeGette replied that her organization, Express Scripts, Inc., has been getting the letters out approximately 30 days in advance of the actual change, so 60 days should be fine.

The Panel vote on the implementation plan was:

Concur: 11 Non-concur: 0 Abstain: 0

II. UNIFORM FORMULARY CLASS REVIEWS — ANTIHEMOPHILIC AGENTS – Factor VIII and Factor IX concentrates

(CPT Haney) PEC Script

A. Antihemophilic Agents – Factor VIII and Factor IX concentrates — Relative Clinical Effectiveness

Please turn to Table 2 on page 3 of the handout for the table of drugs in Antihemophilic agents drug class. The P&T Committee evaluated the clinical effectiveness of the antihemophilic agents. The class was divided into the factor VIII and factor IX concentrates; and the factor VIII/von Willebrand (vWF) factor complexes; human prothrombin concentrate complexes; and inhibitor bypassing products. The antihemophilic agents have not previously been reviewed for UF placement; they are an extended core formulary (ECF) drug class.

Purified factor VIII drugs are used to treat hemophilia A and are manufactured from two sources: plasma-derived (human) and recombinant. The human factor VIII products include Hemofil M, Koate DVI, and Monoclate P. The recombinant factor VIII products include Advate, Helixate FS, Kogenate FS, Recombinate, Refacto, and Xyntha. Although Refacto is still available for use, it was no longer manufactured at the time of this review, and therefore, not considered for ECF status.

Purified factor IX drugs used to treat hemophilia B are likewise derived from two sources: human and recombinant. The human factor IX concentrates include AlphaNine SD and MonoNine. There is only one recombinant factor IX product: BeneFIX. Only uses that pertain to the outpatient pharmacy benefit were considered for all these drugs.

Utilization of the factors is given on Table 4 in page 4 of the handout. Military Health System (MHS) expenditures for the all antihemophilic agents (factor VIII, factor IX, factor VIII/vWF complexes, prothrombin complex concentrates (PCCs), and inhibitor bypassing products) exceeded $39M from December 2008 to November 2009 predominantly at the retail point of service (POS). There are approximately 190 unique utilizers in the MHS. There were no MHS utilizers of Monoclate P or AlphaNine SD during this time period.

Relative Clinical Effectiveness Conclusion — The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions

regarding purified factor VIII and IX concentrates:

1. With regard to efficacy, the following conclusions were made:
   a) There are no head-to-head comparative trials evaluating the factor VIII or factor IX products. Efficacy studies were limited to open-label clinical trials.
   b) Many products obtained FDA approval based on pharmacokinetic demonstration of bioequivalence to previously approved (e.g., earlier generation) products following improvements in production and viral depletion or inactivation methods.
   c) There is no evidence to conclude that there are clinically relevant differences in efficacy between the respective factor VIII and factor IX concentrates.
2. With regard to safety and tolerability, the P&T Committee agreed that, although the overall risk is small, there is a lower risk of viral transmission with recombinant products than with plasma-derived products. There is insufficient evidence to conclude there are clinically relevant differences in safety between the recombinant factor VIII products.
3. With regard to other factors, the following conclusions were made:
   a) National professional group guidelines and national hemophilia patient advocacy groups caution against switching between products once a patient is stabilized, due to potentially detrimental outcomes, including development of immunogenicity.
   b) There are differences among the factor VIII and factor IX products with regard to viral deactivation/depletion methods, storage and refrigeration requirements, vial sizes available, reconstitution and administration kits, patient support programs, and stabilizers/cell culture media used in recombinant products

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

B. Antihemophilic Agents – Factor VIII and Factor IX concentrates — Relative Cost-Effectiveness

(Dave Meade) PEC Script

Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

a) CMA results for the antihemophilic factor VIII agents revealed that Xyntha was the most cost-effective recombinant factor VIII product based on cost per unit of treatment. Cost per unit of treatment was calculated using the average drug price per unit rates for Xyntha and the following antihemophilic factor VIII products: Advate, Helixate FS, Hemofil M, Koate DVI, Kogenate FS, Recombinate, and Refacto. The cost of Monoclate P could not be evaluated due to no MHS utilization.

b) CMA results for the antihemophilic factor IX agents revealed that BeneFIX was the most cost-effective antihemophilic recombinant factor IX product based on the cost per unit of treatment. Cost per unit of treatment was calculated using

average drug price per unit rates for the recombinant factor IX products AlphaNine SD and MonoNine.

C. Antihemophilic Agents – Factor VIII and Factor IX concentrates — Uniform Formulary Recommendation

(Dave Meade) PEC Script

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 (13 for, 0 opposed, 2 abstained, 1 absent):

a) The factor VIII products Koate DVI, Kogenate FS, Refacto, and Xyntha, and the factor IX products Alphanine SD and BeneFIX remain classified as formulary on the UF.

b) The factor VIII products Advate, Hemofil M, Helixate FS, Monoclate P, and Recombinate, and the factor IX product MonoNine be designated as non-formulary under the UF.

c) All factor VIII and factor IX products recommended for inclusion on the UF had existing Uniform Formulary Voluntary Agreement for Retail Refunds (UF VARR) submissions at or below the Federal Ceiling Price (FCP), or a required Mandatory Agreement for Retail Refund. None of the products recommended to be designated NF on the UF had the required pricing agreement.

D. Antihemophilic Agents – Factor VIII and Factor IX concentrates — Uniform Formulary Implementation Plan

(Dave Meade) PEC Script

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 180-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at MTFs no later than a 180-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.

Col Lounsbery will now provide the physician perspective.

E. Antihemophilic Agents – Factor VIII and Factor IX concentrates Physician Perspective

(Col Lounsbery)

Col Lounsberry noted that the physicians on the P&T Committee were very appreciative of CPT Haney's efforts on this topic since most of them don't see these patients. Both Factor VIII and Factor IX concentrates all have the same product in them, so there aren't many significant clinical differences other than things like whether they can be kept out of the refrigerator. She stressed that making some of the agents non-formulary doesn't mean they will be unavailable. The MHS doesn't want people to switch because of the potential for immunogenicity. Overall, the Committee thinks there will be a good choice available with sufficient variety for people who come on to these medications, but people who are already on one won't have to switch.

F. Antihemophilic Agents - Factor VIII and Factor IX Concentrates — BAP Questions and Discussion

Dr. Schlaifer asked for an explanation of the notification process to be used in this class, noting that patients would normally get a letter notifying them that a drug will no longer be on the formulary and advising them how to handle it. But it seems as though maybe a different approach will be needed for this class because MHS wants the patients to stay on the drug and not switch. Dr. Meade replied that in this case they will be able to identify everybody involved in the formulary decision and make appropriate notification.

Dr. Cohoon asked for and received verification that the patients affected by the non-formulary decisions will be protected and not forced to move to a different medication. She asked what the protocol will be. Dr. Ellzy answered that the medical necessity criteria specify formulary exemptions if the patient would, or are likely to have problems switching to a formulary drug. In this case, they already know that would be the case.

Dr. Cohoon also asked about the implementation time period, noting that one document provided to the Panel specifies 60 days and another specifies 180 days. The answer provided was that the recommendation is for 180 days; the 60-day period was a misprint.

Dr. Casull asked about the number of patients using these medications and how much weight was given to the number in the decision-making process given the very significant potential for harm. Col Lounsberry answered that the number of patients was never very large, but after deciding that none of them would have to switch, the number affected was even further reduced. Dr. Casull asked whether the total number of beneficiaries affected is 980 and Dr. Meade replied that the number is 190. Dr. Casull noted that 142 of those are using the drug that is being made non-formulary and expressed concern. Col Lounsberry reiterated that these recommendations will apply only to new entrants into the system.

Mr. Hutchings asked whether the $9 co-pay would automatically be granted to current users of the agents being moved to non-formulary. He also asked if those patients automatically being "grandfathered" would need to be sent a letter telling them that their drug was being moved to non-formulary but that they will not be affected. Dr. Meade answered that will not be necessary and that patients will automatically get the formulary

co-pay.

Ms. Legette noted that the medical necessity designation is a process that has to be gone through and that it isn't automatic. She asked if the standard UF medical necessity process would be followed for the mail order and retail pharmacies. She asked whether, for people who have started on a drug and stabilized, that would be considered an approval. Dr. Meade replied that the system will try to make it all happen behind the scenes so the patient doesn't even know. Alternatively, they can have the physician fill out the form and just turn it in. Ms. Legette commented that it shouldn't be a problem since there are so few beneficiaries and a 180-day implementation period is being recommended.

Dr. Casull asked why Alphanine will be on formulary and not removed because it has no users. The answer provided was because the other drug in that sub-class was being made non-formulary. The Committee wants to have at least on agent available in the sub-class.

G. Antihemophilic Agents – Factor VIII and Factor IX Concentrates — BAP Vote on UF Recommendations

Ms. Fryar read the P&T Committee's recommendations regarding agents in this drug class:

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted:

a) The factor VIII products Koate DVI, Kogenate FS, Refacto, and Xyntha, and the factor IX products Alphanine SD and BeneFIX remain classified as formulary on the UF.

b) The factor VIII products Advate, Hemofil M, Helixate FS, Monoclate P, and Recombinate, and the factor IX product MonoNine be designated as non-formulary under the UF.

Without further discussion the Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0

H. Antihemophilic Agents – Factor VIII and Factor IX Concentrates — BAP Vote on Implementation Plan Recommendations

Before proceeding with the vote on the implementation plan, the Chair noted a correction to the handout materials, indicating that the recommendation is for a 180-day implementation period, not a 60-day implementation period. She then read the P&T Committee's recommendation.

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 180-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.

Without further discussion, the BAP voted:

Concur: 11 Non-concur: 0 Abstain: 0

III. UNIFORM FORMULARY CLASS REVIEWS — ANTIHEMOPHILIC AGENTS – Factor VIII/von Willebrand Factor Complexes, Human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products

(CPT Haney) PEC Script

A. Antihemophilic Agents – Factor VIII/von Willebrand Factor Complexes, Human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products — Relative Clinical Effectiveness

Please turn to Table 3 on page 3 of the handout for the table of the remaining drugs in Antihemophilic agents drug class. The P&T Committee evaluated the clinical effectiveness of the remainder of the antihemophilic drug class, comprised of the human factor VIII/vWF complexes, the human PCCs, and the inhibitor bypassing products.

Humate-P and Alphanate are the two human factor VIII products containing a measured amount of vWF that are used to treat certain types of von Willebrand disease and to replace factor VIII in patients with hemophilia A. Human PCCs were formerly the treatment of choice for hemophilia B before highly purified products became available and now are used to treat factor II and factor X deficiency. The PCCs include Bebulin VH and Profilnine SD. The inhibitor bypassing products include one recombinant activated factor VII, NovoSeven RT, and one human activated prothrombin complex concentrate, Feiba VH. These two products are indicated for use in patients with hemophilia A or hemophilia B who have developed inhibitors, and are used to treat bleeding episodes, or to prevent bleeding episodes during surgical interventions. NovoSeven also has additional indications that Feiba does not have.

Utilization of the factors is given on Table 4 on page 4 of the handout. There were no MHS utilizers of Humate-P or Profilnine from December 2008 to November 2009. Only uses that pertain to the outpatient drug benefit were considered.

Relative Clinical Effectiveness Conclusion — The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) the following clinical effectiveness conclusions:

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

a) There is no evidence to conclude that there are clinically relevant differences in efficacy between NovoSeven RT and Feiba VH in the outpatient treatment of bleeding episodes in hemophilia patients who have inhibitors.

b) There is no evidence to conclude that there are clinically relevant differences in efficacy between Bebulin VH and Profilnine SD in the outpatient treatment of factor II or factor X deficiency.

c) There is no evidence to conclude that there are clinically relevant differences in efficacy between Humate-P and Alphanate in the outpatient treatment of von Willebrand disease or hemophilia A.

2. With regard to safety and tolerability, the P&T Committee agreed that:

a) Although the risk is small, there is a lower risk of viral transmission with a recombinant product (NovoSeven RT) than with a plasma-derived product (Feiba VH). Feiba VH may also cause an anamnestic response in patients with inhibitors who are classified as high responders to therapy, and can cause anaphylaxis or nephrotic syndrome in hemophilia B patients who have developed inhibitors. Both products carry a very low risk of thrombotic complications. Feiba VH has a warning advising extreme caution when using in patients with hepatic impairment.

b) Bebulin VH contains heparin and may not be appropriate to use in patients with a history of type II heparin induced thrombocytopenia (HIT); otherwise, there is no evidence that there are clinically relevant differences in safety between Bebulin VH and Profilnine SD.

c) Alphanate contains heparin and may not be appropriate to use in patients with a history of type II HIT; otherwise, there is no evidence that there are clinically relevant differences in safety between Humate-P and Alphanate.

3. With regard to other factors:

a) Feiba VH has a longer half-life than Novoseven RT and may be more appropriate when considering prophylactic treatment in a hemophilia patient who has developed inhibitors.

b) National professional group guidelines and national hemophilia patient advocacy groups caution against switching between products once a patient is stabilized, due to potentially detrimental outcomes, including development of immunogenicity.

c) There are differences among the factor VIII/vWF concentrates, the human PCCs, and the inhibitor bypassing products with regard to viral deactivation/depletion methods, storage and refrigeration requirements, vial sizes available, reconstitution and administration kits, and patient support programs.

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

B. Antihemophilic Agents – Factor VIII/von Willebrand Factor Complexes, human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products — Relative Cost-Effectiveness

(Dave Meade) PEC Script

Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (13 for, 0 opposed, 2 abstained, 1 absent) the following:

a) CMA results for the Factor VIII/vWF antihemophilic subgroup revealed that Alphanate was the most cost-effective factor complex for this subclass based on cost per patient per year of treatment. Cost per patient per year of treatment was calculated using yearly consumption rates for Alphanate and Humate-P.

b) CMA results for the PCCs antihemophilic subgroup revealed that Profilnine SD was the most cost-effective factor complex for this subclass based on cost per patient per year of treatment. Cost per patient per year of treatment was calculated using yearly consumption rates for Bebulin VH and Profilnine SD.

c) CMA results for the inhibitor bypassing products antihemophilic subgroup revealed that NovoSeven RT was the most cost-effective factor complex based on a cost per patient per year of treatment. Cost per patient per year of treatment was calculated using yearly consumption rates for NovoSeven RT and Feiba VH.

C. Antihemophilic Agents – Factor VIII/von Willebrand Factor Complexes, Human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products — Uniform Formulary Recommendation

(Dave Meade) PEC Script

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 (11 for, 1 opposed, 3 abstained, 1 absent):

a) The factor VIII/vWF product Alphanate, the human PCC product Profilinine SD, and the inhibitor bypassing product NovoSeven RT remain classified as formulary on the UF.

b) The factor VIII/vWF product Humate-P, the human PCC product Bebulin VH, and the inhibitor bypassing product Feiba VH be designated as non-formulary under the UF.

c) All factor VIII/vWF, the human PCCs, and inhibitor bypassing product recommended for inclusion on the UF were covered by UF VARR submissions at or below the Federal Ceiling Price or a required Mandatory Agreement for Retail Refund. None of the products recommended to be designated NF on the UF had the required pricing agreement.

D. Antihemophilic Agents – Factor VIII/von Willebrand Factor Complexes, human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products — Uniform Formulary Implementation Plan

(Dave Meade) PEC Script

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday one week after the minutes are signed, following a 180-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at MTFs no later than a 180-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.

Col Lounsbery will now provide the physician perspective

E. Antihemophilic Agents – Factor VIII/von Willebrand Factor Complexes, Human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products — Physician Perspective

(Col Lounsbery)

Col Lounsberry indicated that from a physician's standpoint there is nothing different to say about this sub-class from the previous sub-class. Again the key factor was the immunogenicity and not making people switch.

F. Antihemophilic Agents — Factor VIII/von Willebrand Factor Complexes, Human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products — BAP Questions and Discussion

With the floor open for Panel questions and discussion, Dr. Schlaifer noted that there was one vote opposed and asked if this set of recommendations was more controversial than the previous sub-class and whether there was any discussion of the reason for the no vote. Col Lounsberry replied that no reasons for the no vote were given nor were any provided for the votes to abstain. She said that sometimes happens.

There was also a brief discussion during which the vote tally reported in the pre-meeting handout was corrected to show the actual vote : 11 for, 1 opposed, 3 abstained, 1 absent.

Dr. Casull asked whether there was any Committee discussion of the pharmacodynamics of people already on heparin and whether there might be any augmentation of effects from the two products that contain heparin. CPT Haney answered that the amount of heparin is very small and was considered irrelevant.

Dr. Cohoon verified that the implementation plan for MTF would be 180 days and that the system would get the word out to the affected beneficiaries about the potential for adverse events involved in switching medications.

G. Antihemophilic Agents — Factor VIII/von Willebrand Factor Complexes, Human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products — BAP Vote on UF Recommendations

Ms. Fryar read the P&T Committee's UF recommendations for this drug sub-class:

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted:

a) The factor VIII/vWF product Alphanate, the human PCC product Profilinine SD, and the inhibitor bypassing product NovoSeven RT remain classified as formulary on the UF.

b) The factor VIII/vWF product Humate-P, the human PCC product Bebulin VH, and the inhibitor bypassing product Feiba VH be designated as non-formulary under the UF.

The Panel vote on the formulary recommendation was:

Concur: 11 Non-concur: 0 Abstain: 0

H. Antihemophilic Agents — Factor VIII/von Willebrand Factor Complexes, Human Prothrombin Concentrate Complexes, and Inhibitor Bypassing Products — BAP Vote on Implementation Plan Recommendation

The Chair next read the P&T Committee's implementation plan recommendations, again noting that the recommendation should read "180 days":

The P&T Committee recommended 1) an effective date of the first Wednesday one week after the minutes are signed, following a 180-day implementation period in the TRICARE Pharmacy Benefits Program (TPHARM), and at MTFs no later than a 180-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: 11 Non-concur: 0 Abstain: 0

IV. NEWLY APPROVED DRUGS — NARCOTIC ANALGESICS—Morphine Sulfate Extended Release (ER)/Naltrexone Capsules (Embeda)

(CPT Haney) PEC Script

A. Embeda— Relative Clinical Effectiveness

Please turn to table 5 on pages 5 and 6 of the handout. Embeda is the first abuse-

deterrent formulation of morphine to reach the market. Each capsule contains round pellets of morphine ER that surround a naltrexone core. Morphine sulfate ER/naltrexone is a Schedule II controlled substance and is classified as a high-potency single analgesic agent in the narcotic analgesic drug class, which was last reviewed in February 2007. Embeda is indicated for the treatment of moderate to severe pain in adults when continuous, around-the-clock analgesia is required for an extended period of time.

Utilization of the narcotic analgesics is shown in Figure 2 on page 6 of the handout. Oxycontin and the fentanyl patch have the highest utilization.

Morphine is a pure opioid agonist selective for the mu receptor, while naltrexone is a mu antagonist that reverses the effects of the mu agonists. When the capsules are taken whole as directed, the morphine provides analgesia, with no clinical effects from the naltrexone. Attempts to tamper with the pellets either by crushing or dissolving will cause a rapid release and absorption of the naltrexone, antagonizing the effects of the morphine released.

The unpublished trial used to gain FDA approval reported that Embeda was superior to placebo in relieving pain in patients with osteoarthritis. A study in recreational opioid users reported reduced drug liking for crushed Embeda capsules and whole Embeda capsules, when compared to immediate release morphine solution. The clinical significance of reduction in drug liking is unknown. The product labeling states, "There is no evidence that the naltrexone in Embeda reduces the abuse liability of Embeda." There are no other abuse deterrent opioids on the market yet, though several are currently in development.

The safety profile for Embeda reflects that of other morphine ER products and narcotic analgesics on the Uniform Formulary (UF). Crushing, chewing or dissolving pellets can cause fatal release of morphine or precipitate withdrawal in opioid-tolerant individuals.

The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) there was a potential benefit, that Embeda reduces drug liking when crushed compared to other high potency narcotics. However, the abuse deterrence of Embeda has not been proven.

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

B. Embeda— Relative Cost-Effectiveness

(Dave Meade) PEC Script

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 narcotic analgesics. 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 the agent. Results from the CMA showed the projected weighted average cost per day for Embeda is higher than the other formulary narcotic analgesics, including transdermal fentanyl, morphine sulfate ER (Avinza and MS Contin), oxycodone (OxyContin), and oxymorphone (Opana ER). However, the projected weighted average cost per day for

Embeda was lower than the UF agent morphine sulfate (Kadian).

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (16 for, 0 opposed, 0 abstained, 0 absent) morphine sulfate ER/Naltrexone HCl (Embeda) was cost effective relative to the other UF agents in the narcotic analgesics drug class.

C. Embeda — Uniform Formulary Recommendation
(Dave Meade) PEC Script

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 (11 for, 3 opposed, 1 abstained, 0 absent) morphine sulfate ER/naltrexone capsules (Embeda) be designated formulary on the UF.

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D Embeda — Uniform Formulary Implementation Plan – Not applicable
(Dave Meade) PEC Script

The implementation plan is not applicable.

Col Lounsbery will now provide the physician perspective

E. Embeda — Physician Perspective

(Col Lounsbery)

Col Lounsberry noted that this drug was the first narcotic analgesic that might have an abuse deterrent effect. The Committee considered the possibility that it would work that way. She noted that it was at least as clinically effective as the other products in this class already on formulary, might have the added benefit of deterring abuse and was also less costly than one of the extended release formulations of morphine on the UF.

F. Embeda — BAP Questions and Discussion

Ms. Fryar asked about the cost figures on page 14, specifically whether Embeda is lower or higher than the UF agent (Kadian). The answer given was that it is lower than Kadian.

Dr. Casull commented that it might be premature to put the drug on the UF based on its claimed abuse deterrent effect, but gave the Committee kudos for taking into consideration the need for such an agent in view of the drug abuse epidemic that exists. He pointed out, however, that the main problem is not with prescription drugs, but with street drugs. He noted that the package insert says the product shouldn't be used for a

deterrent since that effect hasn't been proven.

Dr. Crum agreed with Dr. Casull's comment that there is no scientific evidence that the drug acts as an abuse deterrent. He views the claim as a marketing strategy intended to distinguish this product from the others on the market.

Mr. Hutchings asked whether the Committee seriously considered making this drug non-formulary because of the lack of evidence that it reduces the potential for abuse. CPT Haney said there were some concerns raised but overall the Committee wanted the drug on the UF.

Mr. Chavez asked about the anticipated level of need for this drug. Col Lounsbery said she had no way of estimating the number of presecriptions DoD would have for this drug, but stated that the issue is significant for DoD and has high visibility. It has even put together a task force and update its opiate use guidelines, as has VA. She knows there is a need for the drug even though she can't quantify it.

Dr. Cohoon asked about the comments of the VA pharmacist who sits on the Committee. Dr. Meade, noting that the subject is outside the BAP process, said that the PEC has been working with the VA.

G. Embeda — BAP Vote on UF Recommendation

The Chair then read the P&T Committee's formulary recommendation for Embeda :

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 morphine sulfate ER/naltrexone capsules (Embeda) be designated formulary on the UF.

The BAP vote on this recommendation was:

Concur: 8 Non-concur: 3 Abstain: 0

The Panel also asked to include a comment to the effect that the non-concurring votes were based on the lack of evidence that the product would have the deterrent effect claimed by the manufacturer.

V. NEWLY APPROVED DRUGS — Attention Deficit/Hyperactivity Disorder (ADHD) — Guanfacine Extended Release (ER) tablets (Intuniv)

(CPT Haney) PEC Script

A. Intuniv — Relative Clinical Effectiveness

Please turn to table 6 on page 7 of the handout. Intuniv is indicated for the treatment of ADHD in children and adolescents aged 6 to 17 years. Intuniv is included in the ADHD/Narcolepsy drug class, which was reviewed in November 2006.

Utilization of the entire ADHD drug class is shown in Figures 3 and 4 on page 8 of the handout. Figure 3 shows both the stimulants and non-stimulants, while Figure 4 shows only the non-stimulants.

Guanfacine immediate release (IR) (Tenex, generics) is FDA-approved for treating hypertension, but is well accepted for off-label use in ADHD. Intuniv is dosed once daily for ADHD and is approved as monotherapy. Guanfacine IR is usually dosed twice daily for ADHD. Guanfacine is an alpha-2A agonist, and is not a scheduled substance, unlike the stimulants (methylphenidate and amphetamine). Clonidine is a non-selective alpha-2A agonist used off-label for ADHD. Clonidine is available in tablets and transdermal formulations. Intuniv has a longer half-life than clonidine and causes less sedative and hypotensive effects.

Atomoxetine (Strattera), another nonstimulant, is FDA-approved as monotherapy for children with ADHD and has a different mechanism of action (norepinephrine reuptake inhibitor) than guanfacine. It is also approved for ADHD in adults. Atomoxetine has more established efficacy data than Intuniv, but safety concerns include suicidal ideation and hepatotoxicity.

There are no direct comparative trials with Intuniv and other ADHD nonstimulants (guanfacine IR or atomoxetine). In two 8-week studies, Intuniv was superior to placebo in reducing symptoms associated with ADHD. Its efficacy in adolescents and the optimal dose for heavier adolescents remain to be determined. The duration of action of Intuniv ranged between 8 to 12 hours and was dose-dependent. Longer-term trials are necessary to delineate its place in therapy.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) that guanfacine ER (Intuniv) has a different mechanism of action and adverse effect profile than atomoxetine (Strattera). The P&T Committee acknowledged that Intuniv offers the convenience of once-daily dosing and a defined dosing regimen compared to guanfacine IR and clonidine, but there is insufficient data to suggest whether there are additional clinical advantages compared to the other UF nonstimulants.

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

B. Intuniv — Relative Cost-Effectiveness

(Dave Meade) PEC Script

The P&T Committee evaluated the cost of guanfacine ER (Intuniv) in relation to the efficacy, safety, tolerability, and clinical outcomes of the ADHD agents in the ADHD/Narcolepsy UF 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).

CMA was used to evaluate the relative cost-effectiveness of Intuniv relative to other UF ADHD agents. Results from the CMA showed the projected weighted average cost per day for Intuniv is higher than other formulary ADHD agents except clonidine patch.

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstained, 1 absent) that guanfacine ER (Intuniv) is comparable in cost to branded stimulant and nonstimulant products in the ADHD/Narcolepsy drug class. In comparison to generics in this class, the P&T Committee determined that the higher daily cost for Intuniv was offset by its FDA-approved dosing regimen and once-daily administration.

C. Intuniv — Uniform Formulary Recommendation *(Dave Meade) PEC Script*

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 (11 for, 3 opposed, 1 abstained, 1 absent) guanfacine ER tablets (Intuniv) be designated formulary on the UF.

D. Intuniv — Uniform Formulary Implementation Plan – Not applicable *(Dave Meade)*

The implementation plan is not applicable on this drug.

Col Lounsbery will now provide the physician perspective

E. Intuniv - Physician Perspective

(Col Lounsbery)

Col Lounsbery informed the Panel that Committee had a discussion about an old drug finding a new use. It wasn't sure about the dosing in older kids and noted that a lot of times with ADHD drugs a second dose had to be added later in the day. But the Committee felt that it would be good to have this drug as an option to its main competitor, Strattera, because of Strattera's side effects. That was the main factor in the Committee's recommendation.

F. Intuniv — BAP Questions and Discussion

Ms. Fryar asked why three P&T Committee members had been opposed to this recommendation. Dr. Meade replied that physicians are very familiar with this drug in its immediate release form as it has been around a long time. The concern was with the less frequent dosing requirements of this formulation. There was also some concern about the cost, but its cost is offset by the once-a-day dosing.

Dr. Salom asked about the basis for the claims regarding reduced dosing and noted that the evidence was weak (only two eight-week studies).

G. Intuniv — BAP Vote on UF Recommendation

Ms. Fryar read the P&T Committee's recommendation for the attention deficit / hyperactivity disorder (ADHD) agent Intuniv:

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 guanfacine ER tablets (Intuniv) be designated formulary on the UF.

Without further discussion, the BAP voted as follows:

Concur: 10 Non-concur: 1 Abstain: 0

The non-concurring Panel member commented that his vote was because the two studies available are insufficient to ensure confidence.

VI. NEWLY APPROVED DRUGS Newer Sedative Hypnotics—Zolpidem Sublingual Tablets (Edluar)

(CPT Haney) PEC Script

A. Edluar — Relative Clinical Effectiveness

Please turn to table 8 on page 11 of the handout. Zolpidem sublingual (SL) tablets (Edluar) is a newer sedative hypnotic approved for the short-term treatment of insomnia characterized by difficulties in sleep initiation. The newer sedative hypnotics were last reviewed in February 2007. Generic zolpidem immediate release (IR) oral tablets are currently included on the BCF.

Expenditures of the class are shown in Figure 7 on page 11. Lunesta and Ambien CR have the highest expenditures. However, for utilization (not shown in the figure), the generic zolpidem (Ambien) tablets have the highest utilization.

Zolpidem SL tablets were approved under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act by demonstrating bioequivalence to Ambien tablets. The SL tablets disintegrate when placed under the tongue and are not swallowed. The pharmacokinetic profiles of zolpidem SL, zolpidem IR (Ambien), and zolpidem sustained release (Ambien CR) tablets are similar with regard to bioavailability, time to reach maximal concentration, half-life, protein binding, and elimination. There are no direct

comparative trials evaluating the final commercially-marketed formulation of Edluar with zolpidem IR tablets or newer sedative hypnotics. Two small studies comparing an early zolpidem SL formulation with Ambien IR reported sleep onset measures were 6 to 7 minutes faster with the SL product than Ambien; however, the clinical relevance of this difference is unknown The safety profile of zolpidem SL reflects that of other zolpidem formulations (e.g., Ambien IR and Ambien CR).

Relative Clinical Effectiveness Conclusion—The P&T Committee voted (16 for, 0 against, 0 abstained, 0 absent) that although zolpidem SL tablets (Edluar) offer an alternative sedative hypnotic formulation for patients with swallowing difficulties, there is insufficient data to conclude Edluar offers improved efficacy, safety, or tolerability in the treatment of insomnia compared to zolpidem IR tablets.

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

B. Edluar — Relative Cost-Effectiveness

(Dave Meade)PEC Script

The P&T Committee evaluated the costs of zolpidem SL tablets (Edluar) in relation to the efficacy, safety, tolerability, and clinical outcomes of the other newer sedative hypnotics. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of zolpidem SL tablets (Edluar). Results from the CMA showed the projected weighted average cost per day for Edluar is higher than the UF newer sedative hypnotics, zolpidem IR (Ambien), and non-formulary (NF) newer sedative hypnotics, ramelteon (Rozerem) and zaleplon (Sonata).

C. Edluar — Uniform Formulary Recommendation

(Dave Meade) PEC Script

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 (15 for, 0 opposed, 0 abstained, 1 absent) that zolpidem SL tablets (Edluar) be designated NF on the UF.

D. Edluar— Uniform Formulary Implementation Plan

(Dave Meade) PEC Script

The P&T Committee recommended (14 for, 0 opposed, 1 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.

Col Lounsbery will now provide the physician perspective

E. Edluar — Physician Perspective

(Col Lounsbery)

Col Lounsbery said this was an easy decision for the Committee: the drug costs more and has no clinical advantages over the drugs already on the formulary.

F. Edluar — BAP Questions and Discussion

Dr. Salom commented that the only advantage he can see is that some people were able to get to sleep faster. Even so, he concurs with the recommendation.

Dr. Cohoon asked about beneficiaries already using this product because of swallowing difficulties. Col Lounsbery replied they would be able to get a medical necessity exemption if required.

Dr. Casull commented that the proven differences between all the drugs in this class against placebo are kind of small. He said that makes it a moot point.

G. Edluar — BAP Vote on UF Recommendation

The Chair read the P&T Committee's UF recommendation for Zolpidem SL tablets (Edluar):

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 that zolpidem SL tablets (Edluar) be designated NF on the UF.

The Bap voted:

Concur: 11 Non-concur: 0 Abstain: 0

H. Edluar — BAP Vote on Implementation Plan Recommendation

Ms. Fryar then read the implementation plan recommendation for Edluar:

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.

The BAP vote on the implementation plan was :

Concur: 11 Non-concur: 0 Abstain: 0

VII. NEWLY APPROVED DRUGS — Renin Angiotensin Antihypertensive Agents (RAAs)—Telmisartan/Amlodipine Tablets (Twynsta)

(CPT Haney) PEC Script

A. Twynsta — Relative Clinical Effectiveness

Please turn to table 7 on page 9 of the handout. Twynsta is a fixed-dose combination product containing telmisartan (Micardis) and amlodipine (Norvasc, generics). It is the third two-drug combination product containing an angiotensin receptor blocker (ARB; Micardis) and dihydropyridine calcium channel blocker (DHP CCB; amlodipine) to reach the market. Azor (olmesartan [Benicar]/amlodipine) and Exforge (valsartan [Diovan]/amlodipine) were previously marketed. Telmisartan/amlodipine is solely indicated for treating hypertension; it can be substituted for the individual titrated components or used as initial therapy in patients likely to require two or more drugs to control blood pressure (BP). Current national guidelines for treating hypertension recommend when more than one drug is needed for BP control, one of the components should comprise a diuretic.

Utilization of the CCB/ARB combinations is shown in Figure 5 on page 10 of the handout.

Telmisartan is currently designated as formulary on the UF; amlodipine is designated as BCF. Twynsta is included in the renin-angiotensin antihypertensive agents (RAAs) drug class, which is comprised of several subclasses (ARBs, angiotensin-converting enzyme (ACE) inhibitors, direct renin inhibitors and their combinations with CCBs or diuretics). The RAAs class will be re-evaluated at an upcoming meeting.

Treatment with various combinations of telmisartan/amlodipine was shown in one randomized trial to significantly reduce BP compared to baseline and placebo. There are no trials evaluating clinical outcomes of mortality or morbidity with Twynsta, although outcomes trials are available with the individual components.

The adverse reaction profile of Twynsta reflects that of the individual components. Although no studies are available specifically addressing the potential for increased compliance with Twynsta over the individual components administered together, other studies have shown an increase in persistence with fixed-dose antihypertensive combination products.

The clinical evaluation for Twynsta included, but was not limited to the requirements

stated in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) telmisartan/amlodipine (Twynsta) did not have a significant, clinically meaningful, therapeutic advantage in terms of safety, effectiveness, or clinical outcome over other antihypertensive drugs included on the UF.

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

B. Twynsta — Relative Cost Effectiveness

(Dave Meade) PEC Script

The P&T Committee evaluated the cost of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the combination antihypertensive agents in this class as well as the individual components, telmisartan and amlodipine. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of telmisartan/amlodipine (Twynsta) relative to other UF agents in this class. Results from the CMA showed the projected weighted average cost per day for telmisartan/amlodipine (Twynsta) is higher than the other formulary combination antihypertensive agents, including triple-therapy oral agent amlodipine/valsartan/hydrochlorothiazide (Exforge HCT) and the individual components amlodipine and telmisartan (Micardis).

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (15 for, 1 opposed, 0 abstained, 0 absent) telmisartan/amlodipine (Twynsta) is not cost effective relative to the other combination antihypertensive agents in this class. The P&T Committee evaluated the cost of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the other combination antihypertensive agents in this class. Please note that in the background information, the phrase "anticholinergic agents in the overactive bladder (OAB) class" is incorrect and replaced by my previous sentence.

C. Twynsta — Uniform Formulary Recommendation

(Dave Meade) PEC Script

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) telmisartan/amlodipine (Twynsta) be designated NF on the UF.

D. Twynsta — Uniform Formulary Implementation Plan

(Dave Meade) PEC Script

The P&T Committee recommended (15 for, 0 opposed, 1 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.

Col Lounsbery will now provide the physician perspective.

E. Twynsta — Physician Perspective

(Col Lounsbery)

Col Lounsbery told the Panel that the Committee focused on the lack of a diuretic in this drug as a key factor in the decision. She said most combination antihypertensive agents include a diuretic, but this one does not. Additionally, the drug carries a higher cost. She said the Committee will be reviewing the entire class later this year and is also expecting new guidelines on hypertension agents.

F. Twynsta — BAP Questions and Discussion

Ms. Fryar asked when this drug was released. She said the graph looks like the date was in October. CPT Haney said he did not have that information readily available.

G. Twynsta — BAP Vote on UF Recommendation

Ms. Fryar read the P&T Committee's UF recommendation for the rennin angiotensin antihypertensive (RAA) agent, telmisartan/amlodipide tablets (Twynsta):

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 telmisartan/amlodipine (Twynsta) be designated NF on the UF.

The Panel voted as follows :

Concur: 11 Non-concur: 0 Abstain: 0

H. BAP Vote — Twynsta Implementation Plan Recommendation

The chair next read the implementation plan recommendation for Twynsta:

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: 11 Non-concur: 0 Abstain: 0

VIII. NEWLY APPROVED DRUGS — Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Valsartan Tablets (Valturna)

(CPT Haney) PEC Script

A. Valturna — Relative Clinical Effectiveness

Please turn back to table 7 on page 9 of the handout. Valturna is a fixed-dose combination product containing the ARB valsartan (Diovan) and aliskiren (Tekturna), a direct renin inhibitor. Tekturna is also available in a fixed-dose combination tablet containing the diuretic hydrochlorothiazide (HCTZ); both Tekturna and Tekturna HCT are designated as formulary on the UF. Valsartan (Diovan) is designated NF. Valturna is included in the renin-angiotensin antihypertensive agents (RAAs) drug class, which will be re-evaluated at an upcoming meeting.

Utilization of Valturna is shown on Figure 6 on page 10 of the handout, along with Tekturna and some of the other RAAS.

Valturna is indicated for treating hypertension. Valsartan has other indications based on clinical trials showing positive clinical outcomes; outcomes trials with aliskiren are currently underway. Current national guidelines for treating hypertension have not yet addressed the place in therapy for direct renin inhibitors, although updated guidelines are anticipated later this year.

Treatment with Valturna was shown in one randomized trial to significantly reduce BP compared to and placebo or administering the components individually. However, the BP reduction seen with Valturna in this study was not as large as that seen in other studies evaluating fixed-dose antihypertensive combination products. The adverse reaction profile of Valturna reflects that of the individual components.

The clinical evaluation for Valturna included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) that although aliskiren/valsartan (Valturna) has a unique mechanism of action due to the direct renin inhibitor component and offers the potential

for increased persistence, it did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over other antihypertensive drugs included on the UF.

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

B. Valturna — Relative Cost Effectiveness

(Dave Meade) PEC Script

The P&T Committee evaluated the cost of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the combination antihypertensive agents in this class as well as the individual components, aliskiren and valsartan. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of aliskiren/valsartan (Valturna) compared to other UF agents. Results from the CMA showed the projected weighted average cost per day for Valturna is higher than the other formulary combination antihypertensive agents, including triple-therapy oral agent amlodipine/valsartan/hydrochlorothiazide (Exforge HCT) and the individual components, aliskiren (Tekturna) and valsartan (Diovan).

Relative Cost-Effectiveness Conclusion—The P&T Committee voted (16 for, 0 opposed, 0 abstained, 0 absent) that aliskiren/valsartan (Valturna) is not cost effective relative to the other combination antihypertensive agents in this class.

C. Valturna — Uniform Formulary Recommendation

(Dave Meade) PEC Script

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, 0 opposed, 2 abstained, 0 absent) aliskiren/valsartan (Valturna) be designated NF on the UF.

D. Valturna — Uniform Formulary Implementation Plan

(Dave Meade) PEC Script

The P&T Committee recommended (15 for, 0 opposed, 1 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.

Col Lounsbery will now provide the physician perspective

E. Valturna — Physician Perspective

(Col Lounsbery)

Col Lounsbery told the Panel that the Committee agreed this drug had no clinical advantages over the drugs already on formulary and it costs more. She noted that the Committee was aware that the drug has a unique mechanism of action and could offer improved persistence, but its place in therapy hasn't been established yet.

F. Valturna — BAP Questions and Discussion

Dr. Crum asked about the reason for FDA's approval of this drug. CPT Haney replied he didn't know the specific reason.

Dr. Casull commented that, as a new Panel member, he is impressed with the process and thinks that a thorough job was done, even in those cases where he disagrees with the recommendation.

G. Valturna — BAP Vote on UF Recommendation

The Chair read the P&T Committee's UF recommendation for the antihypertensive agent aliskiren/valsartan tablets (Valturna):

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 aliskiren/valsartan (Valturna) be designated NF on the UF.

Without further discussion or comment, the Panel voted:

Concur: 11 Non-concur: 0 Abstain: 0

H. Valturna — BAP Vote on Implementation Plan Recommendation

Ms. Fryar read the Valturna implementation plan:

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.

The Panel again voted:

Concur: 11 Non-concur: 0 Abstain: 0

IX. IMPLEMENTATION OF FEDERAL CEILING PRICE REGULATION – NATIONAL DEFENSE AUTHORIZATION ACT, SECTION 703 — INCLUSION OF TRICARE RETAIL PHARMACY PROGRAM IN FEDERAL PROCUREMENT OF PHARMACEUTICALS UPDATE

(Dave Meade) PEC Script

The P&T Committee reviewed drugs that were not included on a DoD Retail Refund Pricing Agreement; these drugs are not compliant with Fiscal Year 2008 National Defense Authorization Act, Section 703. The law stipulates that if a drug is not compliant with Section 703, these drugs will be designated NF on the UF and will require pre-authorization prior to use in the retail POS and medical necessity in MTFs. These NF drugs will remain available in the mail order POS without pre-authorization. Pre-authorization criteria will be determined at a future DoD P&T Committee meeting. Drugs with and without pricing agreements were systematically classified according to therapeutic and pharmacologic lines. The classification system was based on the American Hospital Formulary System Classification and First Data Bank classification. See Appendix C for the full list of affected medications.

A. *COMMITTEE ACTION — DRUGS RETAINING UF STATUS*:

The P&T Committee recommended by consensus the drugs listed below, retain formulary status on the UF.

TARCEVA
TARGRETIN

B. *COMMITTEE ACTION — DRUGS RETAINING OR DESIGNATED NF:*

The P&T Committee recommended by consensus the drugs listed below retain NF status or be designated NF on the UF.

FLUOROPLEX
PANRETIN
SUBOXONE
SUBUTEX
TAZORAC

C. *COMMITTEE ACTION — IMPLEMENTATION DATE FOR PA:*

The P&T Committee recommended by consensus the implementation date will not be prior to July 1, 2010, and not later than 180 days after the minutes of this meeting are signed.

D. *COMMITTEE ACTION — TRANSITION DATE AT THE MTF POS:*

The P&T Committee recommended by consensus a transition period at the MTF POS as ending no later than January 1, 2011.

E. Section 703 — BAP Questions and Discussion

The Panel had no questions or comments regarding these recommendations.

F. BAP Vote on Section 703 Recommendations

The Chair read, and the Panel voted on, each group of recommendations separately as follows:

- The P&T Committee recommended by consensus the drugs listed below, retain formulary status on the UF.

  TARCEVA
  TARGRETIN

BAP vote:

Concur: 11 Non-concur: 0 Abstain: 0

- The P&T Committee recommended by consensus the drugs listed below retain NF status or be designated NF on the UF.

  FLUOROPLEX
  PANRETIN
  SUBOXONE
  SUBUTEX
  TAZORAC

BAP vote:

Concur: 11 Non-concur: 0 Abstain: 0

- The P&T Committee recommended by consensus the implementation date will not be prior to July 1, 2010, and not later than 180 days after the minutes of this meeting are signed.

BAP vote:

Concur: 11 Non-concur: 0 Abstain: 0

- The P&T Committee recommended by consensus a transition period at the MTF POS as ending no later than January 1, 2011.

BAP vote:

Concur: 11 Non-concur: 0 Abstain: 0

Closing Remarks

The Panel Chair, Ms. Fryar, thanked the Panel members for their attendance and thanked the presenters for a fine job. She also tanked Lt Col Bacon for all of his efforts in support of the Panel as this will be his last BAP meeting.

In closing, Ms. Fryar said she believes many improvements have been made in the process since the Panel started its work but also believes still more work is needed to improve both the quality and quantity of the feedback the Panel receives from beneficiaries.

The DFO, Lt Col Bacon, announced that Ms. Fryar had been re-elected as the Chair of the Panel for the coming year and that the next meeting has been scheduled for 24 June at the Naval Heritage Center in Washington, DC. He thanked the TMA and PEC staffs for the support he has received while in this position and expressed his appreciation for all the hard work that went into preparing for each meeting. He thanked the Panel members for serving on the BAP in a volunteer capacity and for devoting their time and attention to its business. He also thanked the industry reps and others who have shown an interest in the work of the Panel and who come to the meetings.

The DFO then adjourned the meeting at 11:45 A.M..

Brief Listing of Acronyms Used in This Summary

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

- ACE — Angiotensin Converting Enzyme (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
- BP — Blood pressure
- BPA — Blanket Purchase Agreement
- 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
- DHP — Dihydropyridine
- DoD — Department of Defense
- DM — Diabetes mellitus
- ECF — Extended Core Formulary
- ER — Extended Release (a drug formulation)
- ESI — Express-Scripts, Inc.
- FACA — Federal Advisory Committee Act
- FCP — Federal Ceiling Price
- FDA — U.S. Food and Drug Administration
- FPG — Fasting plasma glucose
- HbA 1c — Glycosylated hemoglobin A1C
- HCTZ — Hydrochlorothiozide
- IR —- Immediate Release (a drug formulation)
- IV — Intravenous
- LIP1 — Antilipidemics (a drug class)
- MHS — Military Health System

- MN — Medical Necessity
- 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 — Overractive bladder drugs (a drug class)
- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DOD Pharmacy and Therapeutics Committee
- PCCs — Prothrombin complex concentrates
- PDTS — Pharmacy Data Transaction Service
- PEC — DOD Pharmacoeconomic Center
- PORT — Pharmacy Outcomes Research Team
- POS — Point of Service
- RAAs — Renin-angiotensin antihypertensive agents (a drug class)
- RCTs — Randomized Control Trials
- SR — Sustained release (a drug formulation)
- SQ — Subcutaneously
- 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
- vWF — vonWillebrand factor