

Executive Summary

Uniform Formulary Beneficiary Advisory Panel Comments 27 September 2012

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy and Therapeutics (P&T) Committee August 2012 Meeting.

UF CLASS REVIEWS—ANDROGENS ANABOLIC STEROIDS—TRANSDERMAL AND BUCCAL TESTOSTERONE REPLACEMENT THERAPIES (TRT)

1. TESTOSTERONE REPLACEMENT THERAPY

a. UNIFORM FORMULARY RECOMMENDATIONS

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

- testosterone transdermal 2% gel pump (Fortesta) be designated step-preferred and formulary on the UF;
- testosterone transdermal patch (Androderm), testosterone transdermal gel tubes (Testim), and testosterone buccal tablets (Striant) be designated non-preferred and formulary on the UF; and
- testosterone transdermal 1% gel pump and gel packets (Androgel 1%), testosterone transdermal 1.62% gel pump (Androgel 1.62%), and testosterone transdermal solution (Axiron) be designated non-preferred and NF on the UF.
- This recommendation includes step therapy, which requires a trial of testosterone transdermal 2% gel pump (Fortesta) prior to using other transdermal and buccal TRTs.

Summary of Panel Vote/Comments:

The Chair opened the floor for Panel questions about this drug class. Dr. Sampsel noted that grandfathering was not included in the recommendation and asked whether any special provision would be made for beneficiaries who will have to switch. Dr. Meade replied that notification letters to individual beneficiaries will go out about 30 days before the change is to take place. Dr. Sampsel asked whether the 30-day period would be enough to allow for getting a new prescription. Dr. Meade said he believes it will be; Ms. Le Gette agreed they should be okay. She also asked about the three opposing votes. Dr.

Meade said there was no explanation given.

Dr. Khurana asked whether there was any recommendation as to monitoring patients who are switched over. Dr. Selvester said they would follow the recommendations of the applicable professional society, which usually recommends 30 days but sometimes 90 days immediately following the switch, then every six months to a year after that. Dr. Khurana asked whether the increased monitoring was taken into account in calculating the cost considerations. Dr. Meade replied that it was.

Dr. Cohoon commented that the beneficiaries would face increased copay costs for the 90-day period and then also be charged a copay for going in to see their provider to get new lab tests. So there will be an impact on the beneficiaries.

Ms. Fryar asked how many patients would be affected by the decision. Dr. Selvester said the number is 23,000. Dr. Meade stated that is a very workable number, not large by DoD standards.

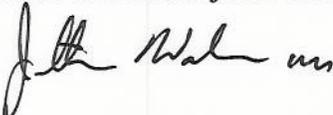
Dr. Khurana asked about dosage differences between the various products and their impact on the recommendations and the copay. Dr. Meade answered.

The Panel had no further questions.

• **Without further discussion, the Panel votes on the UF recommendation were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA: 

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

b. PRIOR AUTHORIZATION CRITERIA RECOMMENDATION

The P&T Committee recommended that the following manual PA criteria should apply to all current and new users of the testosterone replacement therapies. Coverage would be approved if the patient met any of the following criteria:

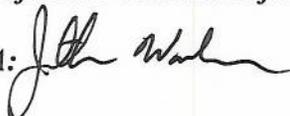
- a) Manual PA criteria for all transdermal and buccal testosterone replacement products:
 - Patient is male and has a diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism.
 - Patient is a female and receiving testosterone for the following uses:
 - Treatment of hypoactive sexual desire in menopausal women (whether natural or surgical); or

- Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone).
 - Note that coverage of transdermal or buccal testosterone replacement therapies is not approved for osteoporosis or urinary incontinence.
 - Note that coverage for use in women will be by appeal only.
 - Note that use in adolescents under the age of 17 is not approved and will be by appeal only.
- b) In addition to the above criteria, the following PA criteria would apply specifically to transdermal gel tubes (Testim), transdermal patch (Androderm), buccal tablets (Striant), transdermal 1% gel pump and gel packets (AndroGel 1%), transdermal 1.62% gel pump (AndroGel 1.62%), and transdermal solution (Axiron):
- The patient requires a testosterone replacement therapy that has a low risk of skin-to-skin transfer between family members (for Striant and Androderm only).
 - The patient has tried transdermal 2% gel pump (Fortesta) for a minimum of 90 days AND failed to achieve total testosterone levels above 400ng/dL (lab must be drawn 2 hours after Fortesta application) AND denied improvement in symptoms.
 - The patient has a contraindication or relative contraindication to Fortesta (e.g., hypersensitivity to a component [including alcohol]; concomitant disulfiram use) that does not apply to Testim, Androderm, Striant, AndroGel 1%, AndroGel 1.62%, or Axiron.
 - The patient has experienced a clinically significant skin reaction to Fortesta that is not expected to occur with Testim, Androderm, Striant, AndroGel 1%, AndroGel 1.62%, or Axiron.

● **Without further discussion, the Panel votes on the PA Criteria were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA: 

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

c. IMPLEMENTATION PLAN RECOMMENDATIONS

The P&T Committee recommended 1) an effective date of the first Wednesday after a 90-day implementation period in all POS and 2) TMA send a letter to beneficiaries affected by this UF decision.

Summary of Panel Vote/Comments:

Dr. Salom commented that he believes it is appropriate to have a 90-day implementation period for these recommendations.

- **Without further discussion, the Panel votes on the Implementation Plan were.**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA: 

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

**UF CLASS REVIEWS—ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS
DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS**

1. ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS

a. UNIFORM FORMULARY RECOMMENDATIONS

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based on its collective professional judgment, recommended enoxaparin, dalteparin (Fragmin), and fondaparinux remain designated as formulary on the UF.

Summary of Panel Vote/Comments:

The Chair opened the floor for questions of the presenters. The Panel had no questions on the recommendations for this class.

- **Without further discussion, the Panel votes on the UF Recommendations were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA: 

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

No implementation plan was needed for this set of recommendations.

DESIGNATED NEWLY APPROVED DRUGS

1. TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)

a. UNIFORM FORMULARY RECOMMENDATION

The P&T Committee based on its collective professional judgment, recommended abatacept SC (Orencia SC) be designated non-formulary (NF) due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

Summary of Panel Vote/Comments:

Dr. Sampsel asked if the current form of Orencia (IV) is covered under the medical benefit. Dr. Meade answered that it is. Dr. Sampsel then asked if any of the patients already taking Orencia IV would be candidates for conversion to the subcutaneous form, which is self-administered. Dr. Meade answered that the Committee looked at that but there was no good data available because IV use is covered under the medical benefit, not the pharmacy benefit.

Dr. Khurana asked how many beneficiaries are currently using the drug. Dr. Meade said 542 patients. Dr. Khurana noted that 351 of these are retail users and asked whether that would affect the cost analysis. Dr. Meade replied that this is one of the factors taken into account when doing the cost analysis.

• Without further discussion, the Panel votes on the UF recommendations were:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA: 

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

b. IMPLEMENTATION PLAN RECOMMENDATION

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

- **Without further discussion, the Panel votes on the Implementation Plan were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA:

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

2. GLAUCOMA DRUGS: PROSTABLANDIN ANALOG DRUG CLASS - TAFLUPROST (ZIOPTAN)

a. UNIFORM FORMULARY RECOMMENDATIONS

The P&T Committee, based on its collective professional judgment, recommended tafluprost (Zioptan) be designated NF because it has no compelling clinical advantages over the other ophthalmic prostaglandin analogues and is not cost-effective compared to latanoprost (Xalatan), the most utilized drug in the Military Health System (MHS).

Summary of Panel Vote/Comments:

The members of the BAP asked no questions of the presenters regarding this recommendation.

- **Without further discussion, the Panel votes on the UF Recommendations were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA:

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

b. IMPLEMENTATION PLAN RECOMMENDATIONS

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

Summary of Panel Vote/Comments:

The members of the BAP asked no questions of the presenters regarding this recommendation.

- **Without further discussion, the Panel votes on the Implementation Plan were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA:

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

**3. ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) -
IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)**

a. UNIFORM FORMULARY RECOMMENDATIONS

The P&T Committee, in its collective professional judgment, recommended ibuprofen/famotidine (Duexis) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

Summary of Panel Vote/Comments:

The members of the BAP asked no questions of the presenters regarding this recommendation.

- **Without further discussion, the Panel votes on the UF recommendations were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA:

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

b. IMPLEMENTATION PLAN RECOMMENDATIONS

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

Summary of Panel Vote/Comments:

The members of the BAP asked no questions of the presenters regarding this recommendation.

• **Without further discussion, the Panel votes on the Implementation Plan were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA: 

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

4. ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) - KETEROLAC NASAL SPRAY (SPRIX)

a. UNIFORM FORMULARY RECOMMENDATIONS

The P&T Committee, based on its collective professional judgment, recommended ketorolac nasal spray (Sprix) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

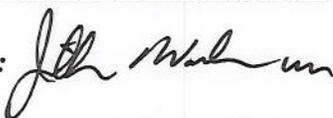
Summary of Panel Vote/Comments:

Ms. Le Gette and Dr. Cohoon offered comments on the implementation plan, noting that the great majority of current users are from the retail POS. It was also noted that beneficiaries who need to use an alternative form of dosing would still be able to obtain this drug.

• **Without further discussion, the Panel votes on the UF recommendation were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA: 

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

b. IMPLEMENTATION PLAN RECOMMENDATIONS

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

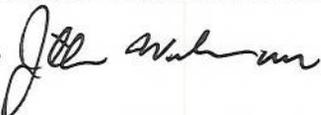
Summary of Panel Vote/Comments:

The members of the BAP asked no questions of the presenters regarding this recommendation.

• **Without further discussion, the Panel votes on the Implementation Plan were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA: 

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

5. NON-INSULIN DIABETES DRUGS: DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS-SITAGLIPTIN/METFORMIN EXTENDED RELEASE (JANUMET XR) AND LINAGLIPTIN/METFORMIN (JENTADUETO)

a. UNIFORM FORMULARY RECOMMENDATIONS

The P&T Committee, based on its collective professional judgment, recommended the following:

- sitagliptin/metformin ER (Janumet XR) be designated step-preferred and formulary on the UF; and
- linagliptin/metformin (Jentadueto) be designated non-preferred and formulary on the UF.
- This recommendation includes step therapy, which requires a trial of sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/simvastatin (Juvistat), or sitagliptin/metformin ER (Janumet XR) (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors also requires a trial of metformin or sulfonylurea for new patients.

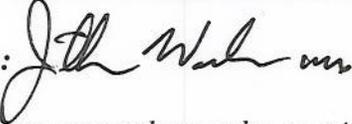
Summary of Panel Vote/Comments:

Ms. Fryar asked about the wording of the PA criteria, inquiring whether the metformin criteria will be (a) or (b) or (c). LCDR Selvester replied that the patient will have to use either metformin or a sulfonylurea first before they can be moved on to the other agent. Ms. Fryar clarified her question regarding whether the word “or” should be included in the manual PA criteria between paragraphs (2) and (3) of criterion “b” to be consistent with previous practice. Dr. Meade replied that the correct wording includes “or”.

- Without further discussion, the Panel votes on the UF recommendation were:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA: 

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

b. PRIOR AUTHORIZATION CRITERIA

The P&T Committee recommended the following PA criteria should apply to the DPP-4 inhibitors subclass. Coverage would be approved if the patient met any of the following criteria

a) Automated PA criteria:

- (1) The patient has filled a prescription for metformin or a sulfonylurea at any MHS pharmacy POS [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.
- (2) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, Juvisync, Janumet XR, Tradjenta, Jentadueto, Onglyza, or Kombiglyze XR) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

b) Manual PA criteria, if automated criteria are not met:

The fixed-dose combination product Janumet XR or Jentadueto is approved (e.g., a trial of sulfonylurea is not required if):

- (1) The patient has had an inadequate response to metformin or sulfonylurea.
- (2) The patient has experienced the following adverse event while receiving a sulfonylurea: hypoglycemia requiring medical treatment. **[or]**
- (3) The patient has a contraindication to a sulfonylurea.

c) In addition to the above criteria regarding metformin and sulfonylurea, the following PA criteria would apply specifically to linagliptin/metformin (Jentadueto):

- (1) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with linagliptin-containing products.
- (2) The patient has had an inadequate response to a sitagliptin-containing product.

(3) The patient has a contraindication to sitagliptin.

Summary of Panel Vote/Comments:

The members of the BAP asked no questions of the presenters regarding this recommendation.

• **Without further discussion, the Panel votes on the PA Criteria were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA: 

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

c. IMPLEMENTATION PLAN RECOMMENDATIONS

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

Summary of Panel Vote/Comments:

The members of the BAP asked no questions of the presenters regarding this recommendation.

• **Without further discussion, the Panel votes on the UF recommendation were:**

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel:

Director, TMA: 

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

BENEFICIARY PUBLIC COMMENTS AND LETTERS

Abbott Verbal Public Presentation to the BAP

(Mr. Michael J. Roggi):

Abbott understands that the P&T Committee did a thorough clinical review of all of the Testosterone Replacement agents and in their recommendations stated, “there appear to be no clinically relevant differences in efficacy between products.” However, after the recommendations were put forth, the FDA issued a class label change for Testosterone Replacement Therapy products that makes this finding now factually inaccurate. In the past two weeks, the FDA required a label change on AndroGel that will be a class change for all topical testosterone therapies. The label change could impact the DoD’s current recommendation to switch and not maintain controlled patients on their topical testosterone therapy.

Abbott’s current package insert states that AndroGel is not interchangeable with other topical testosterone products. To add emphasis to this point, effective September 12, 2012, a new Limitation of Use was added by the FDA to the Highlights and Section 1 (INDICATIONS and USAGE) of the Full prescribing Information for AndroGel. The new Limitation of Use states the following important information.

- Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure.

The Limitation of Use label change by the FDA is being added to all topical testosterone product labels. Since the Testosterone Replacement Therapy products have different application sites, doses, strengths, and instructions for use, the clinical results may vary by product as well as per patient and, therefore, should not be viewed as interchangeable.

For those patients whose hypogonadism is currently controlled on a Testosterone Replacement Therapy product, there could be considerable additional incremental costs associated with switching these patients to a new agent. When switching patients on Testosterone Replacement Therapy, considerations have to be given to multiple lab tests to measure the patient’s testosterone level. This is due to patients on Testosterone Replacement Therapy being required to be titrated to ensure appropriate treatment and that their testosterone levels be maintained in the therapeutic range. These costs are amplified in a therapeutic area such as Testosterone Replacement Therapy where there is a significant market leader such as AndroGel which has over 70 percent share and almost 23,000 TRICARE beneficiaries currently on therapy who would be disrupted and also have to pay a higher copay to remain on their therapy.

Based on now being aware of this new FDA information and requirement, Abbott would not support, and we also believe the BAP would not support, any recommendation to switch currently controlled beneficiaries and would allow them to remain on therapy.

Abbott would also like to comment on the condition sets around step therapy. Based on history with the P&T Committee and past bids that Abbott has been part of with the bid language, the P&T Committee has historically weighed in favor of the beneficiary and maintained patients on product indicated therapy. With very few if any exceptions, commercial plans state up front if there will be grandfathering of current patients. By not actually soliciting for a separate condition set that states controlled patients would also be

subject to step therapy, it is assumed that the most likely P&T Committee course of action, based on past decisions, would be to grandfather current patients on therapy. By not specifying a separate condition set to step current patients, we feel the bid process is unfair for any class where there is a significant market leader. If the Panel recommendation were to rebid the class and specify a separate condition set for stepping current patients, they would receive more aggressive bids and most likely cause less disruption for beneficiaries.

In light of now knowing the new FDA label requirement along with probable financial and therapeutic impact not only on the DoD and most importantly the beneficiary, Abbott believes the Beneficiary Advisory Panel should reconsider the current recommendation.

Abbott Letter Submitted as part of the Public Record: *See Attachment*

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary September 27, 2012 Washington, D.C.

Panel Members Present:

- Deborah Fryar, National Military Family Association, Chairperson
- Kathryn Buchta, Health Net Federal Services
- Barbara Cohoon, National Military Family Association
- John Crum, Humana Military Healthcare Services, Inc.
- Amit Khurana, TriWest Healthcare Alliance
- Lisa Le Gette, Express-Scripts, Inc.
- Ira Salom, Indian Health Service
- Elizabeth Sampsel, Academy of Managed Care Pharmacy
- Robert Duane Tackitt, Association of the Military Service of the United States

Members Not Present:

- Katherine O'Neill-Tracy, Military Officers Association of America

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. CDR Joseph Lawrence, the Designated Federal Officer (DFO), called the proceedings to order at 9:00 A.M. CDR Lawrence indicated the Panel has been convened to review and comment on the therapeutic drug class recommendations resulting from the August 15 and 16, 2012 Department of Defense (DoD) Pharmacy and Therapeutic (P&T) Committee meeting held in San Antonio, TX.

CDR Lawrence announced that Ms. Deborah Fryar had been re-elected as the BAP Chair for the coming year.

Agenda

The agenda for this meeting of the Panel is:

- Welcome and opening remarks
- Public citizen comments
- Review and Panel discussion of P&T Committee recommendations for the following therapeutic drug classes:
 - *Drug Class Reviews:*
 - Androgens Anabolic Steroids—Transdermal and Buccal Testosterone Replacement Therapies (TRT)

- Anticoagulants—Heparin and Related Products Dipeptidyl Peptidase-4 (DPP-4) Inhibitors
- *Designated Newly Approved Drugs:*
 - Targeted Immunomodulatory Biologics (TIBS)—Abatacept subcutaneous injection (Orencia SC)
 - Glaucoma Drugs: Prostaglandin Analogs—Tafluprost ophthalmic solution (Zioptan)
 - Oral Non-steroidal Anti-inflammatory Drugs (NSAIDS)—Ibuprofen/famotidine tablets (Duexis)
 - Oral NSAIDS—Ketorolac Nasal Spray (Sprix)
 - Non-Insulin Diabetes Drugs: Dipeptidyl Peptidase-4 (DPP-4) Inhibitors—Sitagliptin/metformin extended release (Janumet XR) and linagliptin/metformin (Jentadueto)

Opening Remarks

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

In addition, 10 U.S.C. section 1074g subsection c also requires the Secretary to establish a UF Beneficiary Advisory Panel (BAP) to review and comment on the development of the UF. The Panel includes members that represent non-governmental organizations and associations that represent the views and interests of a large number of eligible covered beneficiaries. Comments of the Panel must be considered by the Director, TRICARE Management Activity (TMA) before establishing the UF or implementing changes to the UF. The Panel’s meetings are conducted in accordance with the Federal Advisory Committee Act (FACA).

The duties of the Uniform Formulary Beneficiary Advisory Panel include:

- To review and comment on the recommendations of the P&T Committee concerning the establishment of the UF and subsequent recommended changes. Comments to the Director, TMA, regarding recommended formulary status, pre-authorizations, and the effective dates for changing drugs from “formulary” to “non-formulary” status must be reviewed by the Director, TMA 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, CDR Lawrence 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 11 hours conducting its reviews of the drug class recommendations presented today. Since this meeting is considerably shorter, the Panel will not receive the same extensive information that is presented to the P&T Committee members. However, the BAP will receive an abbreviated version of each presentation and its discussion. The materials provided to the Panel are available on the TRICARE website.

Detailed minutes of this meeting are being prepared. The BAP minutes, the DoD P&T Committee meeting minutes and the Director's decisions will be available on the TRICARE website in approximately four to six weeks.

The DFO next provided the ground rules for conducting the meeting:

- All discussions take place in the open public forum. There is to be no committee discussion outside the room, during breaks or at lunch.
- Audience participation is limited to private citizens who signed up to address the Panel.
- Members of the Pharmacoeconomic Center (PEC) and the P&T Committee are available to answer questions related to the BAP's deliberations. Should a misstatement be made, these individuals may interrupt to ensure the minutes accurately reflect relevant facts, regulations or policy.

CDR Lawrence then introduced the individual Panel members (see list above) and noted housekeeping considerations.

Private Citizen Comments

The DFO opened the meeting for private citizen comments, indicating that one individual had asked to be heard.

Mr. Mike Roggi, National Program Manager of Abbott's Pharmaceutical Products Division, addressed the Panel regarding the P&T Committee's recommendations on Testosterone Replacement Therapy, summarizing a letter sent to the DFO earlier.

Abbott Verbal Public Presentation to the BAP

(Mr. Michael J. Roggi):

Abbott understands that the P&T Committee did a thorough clinical review of all of the Testosterone Replacement agents and in their recommendations stated, "there appear to be no

clinically relevant differences in efficacy between products.” However, after the recommendations were put forth, the FDA issued a class label change for Testosterone Replacement Therapy products that makes this finding now factually inaccurate. In the past two weeks, the FDA required a label change on AndroGel that will be a class change for all topical testosterone therapies. The label change could impact the DoD’s current recommendation to switch and not maintain controlled patients on their topical testosterone therapy.

Abbott’s current package insert states that AndroGel is not interchangeable with other topical testosterone products. To add emphasis to this point, effective September 12, 2012, a new Limitation of Use was added by the FDA to the Highlights and Section 1 (INDICATIONS and USAGE) of the Full prescribing Information for AndroGel. The new Limitation of Use states the following important information.

- Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure.

The Limitation of Use label change by the FDA is being added to all topical testosterone product labels. Since the Testosterone Replacement Therapy products have different application sites, doses, strengths, and instructions for use, the clinical results may vary by product as well as per patient and, therefore, should not be viewed as interchangeable.

For those patients whose hypogonadism is currently controlled on a Testosterone Replacement Therapy product, there could be considerable additional incremental costs associated with switching these patients to a new agent. When switching patients on Testosterone Replacement Therapy, considerations have to be given to multiple lab tests to measure the patient’s testosterone level. This is due to patients on Testosterone Replacement Therapy being required to be titrated to ensure appropriate treatment and that their testosterone levels be maintained in the therapeutic range. These costs are amplified in a therapeutic area such as Testosterone Replacement Therapy where there is a significant market leader such as AndroGel which has over 70 percent share and almost 23,000 TRICARE beneficiaries currently on therapy who would be disrupted and also have to pay a higher copay to remain on their therapy.

Based on now being aware of this new FDA information and requirement, Abbott would not support, and we also believe the BAP would not support, any recommendation to switch currently controlled beneficiaries and would allow them to remain on therapy.

Abbott would also like to comment on the condition sets around step therapy. Based on history with the P&T Committee and past bids that Abbott has been part of with the bid language, the P&T Committee has historically weighed in favor of the beneficiary and maintained patients on product indicated therapy. With very few if any exceptions, commercial plans state up front if there will be grandfathering of current patients. By not actually soliciting for a separate condition set that states controlled patients would also be subject to step therapy, it is assumed that the most likely P&T Committee course of action, based on past decisions, would be to continue to grandfather current patients on therapy. By not specifying a separate condition set to step current patients, we feel the bid process is unfair for any class where there is a significant market leader. If the Panel recommendation were to rebid the class and specify a separate

condition set for stepping current patients, they would receive more aggressive bids and most likely cause less disruption for beneficiaries.

In light of now knowing the new FDA label requirement along with probable financial and therapeutic impact not only on the DoD and most importantly the beneficiary, Abbott believes the Beneficiary Advisory Panel should reconsider the current recommendation.

The DFO indicated that the full Abbott letter summarized above is available and has been submitted as part of the public record of the meeting per the request of the Chairperson. The September 26, 2012 letter from Jeffrey N. Haas, Divisional Vice President to CDR Joseph Lawrence, BAP/DFO is included as Attachment 2 to these minutes.

Chairperson's Opening Remarks

The DFO next turned the meeting over to the Panel Chair, Ms. Deborah Fryar, who asked Dr. Meade of the Pharmacoeconomic Center (PEC) to begin the drug class presentations.

DRUG CLASS REVIEW PRESENTATIONS

(PEC Script)

I'm Dave Meade, Director of Clinical Operations at the Pharmacoeconomic Center. Joining me today from the PEC is LCDR Bob Selvester, the PEC Navy medical consultant. Also joining us today is Col Doreen Lounsbery, one of the DoD P&T Committee members who will provide the physician perspective and comment on the recommendations made by the P&T Committee. Dr John Kugler, the chairman of the P&T Committee and a retired Army Colonel and physician, is also here.

The DoD Pharmacoeconomic Center (PEC) supports the DoD P&T Committee by conducting the relative (relative meaning in comparison to the other agents defined in the same class) clinical-effectiveness analyses and relative cost-effectiveness analyses of drug classes under review and consideration by the DoD P&T Committee for the Uniform Formulary (UF).

We are here to present an overview of the analyses presented to the DoD P&T Committee. 32 Code of Federal Regulation (C.F.R.) establishes procedures for inclusion of pharmaceutical agents on the Uniform Formulary based upon both relative clinical effectiveness and relative cost effectiveness.

The goal of this presentation is not to provide you with the same in-depth analyses presented to the DoD P&T Committee but a summary of the processes and analyses presented to the DoD P&T Committee. These include:

- 1) A brief overview of the relative clinical-effectiveness analyses considered by the DoD P&T Committee. All reviews include but are not limited to, sources of information listed in 32 CFR 199.21(e)(1).

- 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.
 - A. The DoD P&T Committee's Uniform Formulary recommendation is based upon its collective professional judgment when considering the analyses from both the relative clinical and relative cost-effectiveness evaluations. The Committee reviewed two Uniform Formulary drug class – androgens and anabolic steroids and heparin and related products. Six newly approved drugs that were reviewed were abatacept (Orencia SC), tafluprost ophthalmic solution (Zioptan), ibuprofen/famotidine tablet (Duexis), ketorolac nasal spray (Sprix), sitagliptan/metformin ER tablets (Janumet XR) and linagliptin/metformin tablets (Jentadueto)
- 3) The DoD P&T Committee's recommendation as to the effective date of the agents being changed from formulary tier to the non-formulary tier of the Uniform Formulary. Based on 32 C.F.R. 199.21, such change will not be longer than 180 days from the final decision date but may be less.

We've given you a handout which includes the Uniform Formulary recommendations for all the drugs discussed today; these are found on pages 2 through 9. There are tables and utilization figures for all the drug classes. We'll be using trade names as much as possible, so you can refer to your handout throughout the presentation.

I. UF CLASS REVIEWS—ANDROGENS ANABOLIC STEROIDS—TRANSDERMAL AND BUCCAL TESTOSTERONE REPLACEMENT THERAPIES (TRT)

(PEC Script)

TESTOSTERONE REPLACEMENT THERAPY— RELATIVE CLINICAL EFFECTIVENESS

(LCDR Selvester)

Background: This is the first review of the testosterone replacement therapies. Additionally, consistent growth in Military Health System (MHS) expenditures and utilization has occurred over several years and is expected to continue with increasing patient demand. The testosterone replacement therapy agents account for approximately \$66 million in expenditures and 248,000 30-day equivalent prescriptions annually in the MHS.

Drugs for testosterone replacement therapy are listed in Table 1 on page 2. Products are available in transdermal (gel, solutions, and patches) and buccal (placed in the cheek) products. All of the products are schedule CIII control products. The products are approved for replacement therapy in men with conditions associated with deficiencies or absence of endogenous (self-made) testosterone.

Relative Clinical Effectiveness— The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) the following clinical effectiveness conclusions:

- Although high-quality comparative data is lacking, there appear to be no clinically relevant differences in efficacy between products.
- Transdermal and buccal testosterone replacement products effectively raise testosterone levels in hypogonadal men to the normal range when used in accordance with product labeling.
- Skin-to-skin transfer of transdermal testosterone to women and children should be minimized due to risk of virilization or premature onset of puberty. Testosterone buccal tablets (Striant) carry the lowest risk while the topically applied products carry the highest risk.
- Transdermal and buccal testosterone replacement therapies have a low overall incidence of systemic adverse events, which are not considered to differ clinically across products.
- The most frequent adverse events are dermal application site reactions for the transdermal products and oral application site reactions for buccal tablets; most are mild or transient in nature.

TESTOSTERONE REPLACEMENT THERAPY — RELATIVE COST EFFECTIVENESS

(Dr. Meade)

Relative Cost-Effectiveness Conclusion— Cost minimization analyses (CMAs), and cost-effectiveness analyses (CEAs) and budget impact analyses (BIA) were used to evaluate the relative cost-effectiveness of the testosterone replacement agents. Based on the results of the cost analyses and other cost considerations, the P&T Committee (17 for, 0 against, 0 abstained, 0 absent) the following:

2% gel pump (Fortesta) was the least costly agent, followed by transdermal solution (Axiron), transdermal patch (Androderm), transdermal 1.62% gel pump (Androgel 1.62%), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal gel tubes (Testim), and testosterone buccal tablets (Striant).

BIA results showed the scenario where transdermal 2% gel (Fortesta) is step-preferred on the UF, all other TRTs are designated non-preferred on the UF or NF, and step therapy is applied to all current and new users of TRTs, was determined to be the most cost-effective scenario.

TESTOSTERONE REPLACEMENT THERAPY— UF RECOMMENDATIONS

(Dr. Meade)

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (14 for, 1 opposed, 2 abstained, 0 absent):

- testosterone transdermal 2% gel pump (Fortesta) be designated step-preferred and formulary on the UF;

- testosterone transdermal patch (Androderm), testosterone transdermal gel tubes (Testim), and testosterone buccal tablets (Striant) be designated non-preferred and formulary on the UF; and
- testosterone transdermal 1% gel pump and gel packets (Androgel 1%), testosterone transdermal 1.62% gel pump (Androgel 1.62%), and testosterone transdermal solution (Axiron) be designated non-preferred and NF on the UF.
- This recommendation includes step therapy, which requires a trial of testosterone transdermal 2% gel pump (Fortesta) prior to using other transdermal and buccal TRTs.

TESTOSTERONE REPLACEMENT THERAPY— PA CRITERIA

(Dr. Meade)

The P&T Committee recommended (12 for, 0 opposed, 1 abstained, 4 absent) that the following manual PA criteria should apply to all current and new users of the testosterone replacement therapies. Coverage would be approved if the patient met any of the following criteria:

a) Manual PA criteria for all transdermal and buccal testosterone replacement products:

- Patient is male and has a diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism.
- Patient is a female and receiving testosterone for the following uses:
 - Treatment of hypoactive sexual desire in menopausal women (whether natural or surgical); or
 - Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone).
 - Note that coverage of transdermal or buccal testosterone replacement therapies is not approved for osteoporosis or urinary incontinence.
 - Note that coverage for use in women will be by appeal only.
- Note that use in adolescents under the age of 17 is not approved and will be by appeal only.

b) In addition to the above criteria, the following PA criteria would apply specifically to transdermal gel tubes (Testim), transdermal patch (Androderm), buccal tablets (Striant), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), and transdermal solution (Axiron):

- The patient requires a testosterone replacement therapy that has a low risk of skin-to-skin transfer between family members (for Striant and Androderm only).
- The patient has tried transdermal 2% gel pump (Fortesta) for a minimum of 90 days AND failed to achieve total testosterone levels above 400ng/dL (lab must be drawn 2 hours after Fortesta application) AND denied improvement in symptoms.

- The patient has a contraindication or relative contraindication to Fortesta (e.g., hypersensitivity to a component [including alcohol]; concomitant disulfiram use) that does not apply to Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.
- The patient has experienced a clinically significant skin reaction to Fortesta that is not expected to occur with Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

TESTOSTERONE REPLACEMENT THERAPY— PROGRAM IMPLEMENTATION PLAN

(Dr. Meade)

The P&T Committee recommended —(16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

TESTOSTERONE REPLACEMENT THERAPY — COMMITTEE PHYSICIAN’S PERSPECTIVE

Dr. Lounsbery provided the Panel with the Committee physician’s perspective on the recommendations in this drug class. The Committee reviewed this class because of the importance of the impact of its increase in utilization over the past year and because one of the products has a large advertising campaign. All of the drugs contain testosterone and they raise testosterone levels in hypogonadal men but there is insufficient evidence that these drugs improve libido or sexual performance in men or reverse the aging process or obesity. The testosterone products are scheduled to reduce risk of aversion and inappropriate use. The Committee didn’t find any difference in efficacy that were relevant to their decision. As has been discussed, the buccal tablet and the patch have lower risk for transfer to the skin of a family member or another individual. The majority of members agreed that Fortesta should be the preferred product and that all patients should undergo Prior Authorization. There was a little concern expressed about switching but there was no major discussion. The Committee also agreed to put the buccal tablets and the caps (Testim) on the UF. The Committee agreed that a PA would be required for all cases and that the PA would require lab testing. Because of this and the number of beneficiaries, the Committee recommended a longer implementation period.

TESTOSTERONE REPLACEMENT THERAPY — PANEL QUESTIONS AND COMMENTS

The Chair opened the floor for Panel questions about this drug class. Dr. Sampsel noted that grandfathering was not included in the recommendation and asked whether any special provision would be made for beneficiaries who will have to switch. Dr. Meade replied that notification letters to individual beneficiaries will go out about 30 days before the change is to take place. Dr. Sampsel asked whether the 30-day period would be enough to allow for getting a new

prescription. Dr. Meade said he believes it will be; Ms. Le Gette agreed they should be okay. She also asked about the three opposing votes. Dr. Meade said there was no explanation given.

Dr. Khurana asked whether there was any recommendation as to monitoring patients who are switched over. Dr. Selvester said they would follow the recommendations of the applicable professional society, which usually recommends 30 days but sometimes 90 days immediately following the switch, then every six months to a year after that. Dr. Khurana asked whether the increased monitoring was taken into account in calculating the cost considerations. Dr. Meade replied that it was.

Dr. Cohoon commented that the beneficiaries would face increased copay costs for the 90-day period and then also be charged a copay for going in to see their provider to get new lab tests. So there will be an impact on the beneficiaries.

Ms. Fryar asked how many patients would be affected by the decision. Dr. Selvester said the number is 23,000. Dr. Meade stated that is a very workable number, not large by DoD standards.

Dr. Khurana asked about dosage differences between the various products and their impact on the recommendations and the copay. Dr. Meade answered.

The Panel had no further questions.

TESTOSTERONE REPLACEMENT THERAPY— PANEL VOTE ON UF RECOMMENDATIONS

The Chair read the UF recommendations for the androgens anabolic steroids, transdermal and buccal testosterone replacement therapy (TRT) agents.

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:

- testosterone transdermal 2% gel pump (Fortesta) be designated step-preferred and formulary on the UF;
- testosterone transdermal patch (Androderm), testosterone transdermal gel tubes (Testim), and testosterone buccal tablets (Striant) be designated non-preferred and formulary on the UF; and
- testosterone transdermal 1% gel pump and gel packets (Androgel 1%), testosterone transdermal 1.62% gel pump (Androgel 1.62%), and testosterone transdermal solution (Axiron) be designated non-preferred and NF on the UF.
- This recommendation includes step therapy, which requires a trial of testosterone transdermal 2% gel pump (Fortesta) prior to using other transdermal and buccal TRTs.

The Panel then voted as follows:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

TESTOSTERONE REPLACEMENT THERAPY— PANEL VOTE ON PA CRITERIA RECOMMENDATIONS

With no further questions, Ms. Fryar read the recommended PA criteria.

The P&T Committee recommended that the following manual PA criteria should apply to all current and new users of the testosterone replacement therapies. Coverage would be approved if the patient met any of the following criteria:

- a) Manual PA criteria for all transdermal and buccal testosterone replacement products:
 - Patient is male and has a diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism.
 - Patient is a female and receiving testosterone for the following uses:
 - Treatment of hypoactive sexual desire in menopausal women (whether natural or surgical); or
 - Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone).
 - Note that coverage of transdermal or buccal testosterone replacement therapies is not approved for osteoporosis or urinary incontinence.
 - Note that coverage for use in women will be by appeal only.
 - Note that use in adolescents under the age of 17 is not approved and will be by appeal only.

- b) In addition to the above criteria, the following PA criteria would apply specifically to transdermal gel tubes (Testim), transdermal patch (Androderm), buccal tablets (Striant), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), and transdermal solution (Axiron):
 - The patient requires a testosterone replacement therapy that has a low risk of skin-to-skin transfer between family members (for Striant and Androderm only).
 - The patient has tried transdermal 2% gel pump (Fortesta) for a minimum of 90 days AND failed to achieve total testosterone levels above 400ng/dL (lab must be drawn 2 hours after Fortesta application) AND denied improvement in symptoms.
 - The patient has a contraindication or relative contraindication to Fortesta (e.g., hypersensitivity to a component [including alcohol]; concomitant disulfiram use) that does not apply to Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.
 - The patient has experienced a clinically significant skin reaction to Fortesta that is not expected to occur with Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

The Panel vote on the PA criteria was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

TESTOSTERONE REPLACEMENT THERAPY— PANEL VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

Dr. Salom commented that he believes it is appropriate to have a 90-day implementation period for these recommendations.

The Chair next read the Committee's implementation recommendations for the TRT class.

The P&T Committee recommended 1) an effective date of the first Wednesday after a 90-day implementation period in all POS and 2) TMA send a letter to beneficiaries affected by this UF decision.

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

II. UF CLASS REVIEWS—ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS

(PEC Script)

ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS —RELATIVE CLINICAL EFFECTIVENESS

(LCDR Selvester)

Background Relative Clinical Effectiveness— The P&T Committee evaluated the relative clinical effectiveness of the heparin and related products used for various clotting disorders. The individual drug members of the class are listed in Table 2 on page 3 of the Handout. Generic formulations of Lovenox and Arixtra are available and considered therapeutically equivalent to their respective branded products.

This is the first time the class has been reviewed.

Figure 2 of the handout on page 3 shows the utilization of the agents. Lovenox and generic products have the highest usage.

Moving on to the P&T conclusions:

The P&T Committee agreed (15 for, 0 opposed, 0 abstained, 2 absent) on the following clinical effectiveness conclusions:

- Enoxaparin (Lovenox, generic) has the widest clinical utility of the subclass, due to its long history of use and largest number of FDA-approved indications.

- Fondaparinux (Arixtra, generic) has fewer FDA-approved indications than enoxaparin. It has a therapeutic niche for patients with a history of heparin-induced thrombocytopenia (HIT) - a blood disorder characterized by low platelets that puts patients at risk for bleeding.
- The major limitation with dalteparin (Fragmin) is the lack of an FDA-approved indication for treating deep venous thrombosis (clots in the leg) and pulmonary embolism (blood clots to the lung). The package insert also cautions against use in patients with a history of HIT.

ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS—RELATIVE COST EFFECTIVENESS

(Dr. Meade):

Relative Cost-Effectiveness: Pharmacoeconomic analyses were performed for the heparin and related products, including cost minimization analysis (CMA) and budget impact analyses (BIA). A sensitivity analysis was performed to evaluate the impact of movement between generic drugs.

Refer to Table 2 on page 3 for the drugs in this class.

Relative Cost-Effectiveness Conclusion— The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that generic enoxaparin was the most cost-effective agent based on a weighted average cost per unit across all three POS, followed by branded dalteparin (Fragmin), and generic fondaparinux. Budget impact analysis (BIA) results showed that scenarios where one or more agent was made non-formulary showed no more cost avoidance than the scenario with all agents on the uniform formulary.

ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS—UF RECOMMENDATIONS

(Dr. Meade):

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based on its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 1 absent) enoxaparin, dalteparin (Fragmin), and fondaparinux remain designated as formulary on the UF.

ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS —UF IMPLEMENTATION PLAN

Not applicable as no products are being made NF.

ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS —COMMITTEE PHYSICIAN’S PERSPECTIVE

(Dr. Lounsbery):

Dr. Lounsbery said not a lot of extra comment is needed as all three products will remain on formulary. She noted that while retail and mail order points of service will switch patients to generics the MTFs will stock some branded products only because it is more cost effective to so.

ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS —PANEL QUESTIONS AND COMMENTS

The Chair opened the floor for questions of the presenters. The Panel had no questions on the recommendations for this class.

ANTICOAGULANTS—HEPARIN AND RELATED PRODUCTS —PANEL VOTE ON UF RECOMMENDATIONS

Ms. Fryar read the P&T Committee's UF recommendations for the anticoagulants: Heparin and related products Dipeptidyl Peptidase-4 (DPP-4) inhibitors.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based on its collective professional judgment, recommended enoxaparin, dalteparin (Fragmin), and fondaparinux remain designated as formulary on the UF.

The Panel vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

No implementation plan was needed for this set of recommendations.

III. DESIGNATED NEWLY APPROVED DRUGS

(PEC Script)

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs)—ABATACEPT SUBCUTANEOUS INJECTION (ORENCIA SC)

(LCDR Selvester):

A. TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—RELATIVE CLINICAL EFFECTIVENESS

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of a newly approved Oencia SC. Oencia has been available only as an IV infusion until this product came onto the market. The drugs in the Targeted Immunomodulatory Biologics Class are listed in Table 3 on page 4 of your handout. Oencia inhibits activation of T cells, part of the immune system, as its mechanism for action. Enbrel and Humira inhibit tumor

necrosis factor alpha.

Figure 3 on page 4 of your handout shows Humira is a most used agent followed by Enbrel. Humira and Enbrel are approved by the FDA for several indications, while Orenzia is only approved for rheumatoid arthritis.

This class was previously reviewed in 2007, and two new drugs were reviewed in 2009 (Cimzia and Simponi). Prior authorizations are required for all the drugs in this class based on FDA indications and available clinical evidence.

Relative Clinical Effectiveness Conclusion—The P&T Committee (17 for, 0 opposed, 0 abstained, 0 absent) that although abatacept SC (Orenzia SC) provides an alternative to the tumor necrosis factor (TNF) alpha inhibitors used for treatment of rheumatoid arthritis and offers patient convenience over the abatacept intravenous formulation, there is currently insufficient data to conclude that Orenzia SC offers improved efficacy, safety, or tolerability compared to the TNF alpha inhibitors in the TIBs class.

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—RELATIVE COST EFFECTIVENESS

(Dr. Meade):

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—Cost minimization analysis (CMA) was performed. The weighted average cost per day at all three points of service (POS) was evaluated for Orenzia in relation to other drugs in the Targeted Immunomodulatory Biologics Drug Class. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that abatacept SC (Orenzia SC) was not cost-effective when compared to other TIBs included on the Uniform Formulary (UF).

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—UF RECOMMENDATION

(Dr. Meade):

The P&T Committee based on its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 0 absent) abatacept SC (Orenzia SC) be designated non-formulary (NF) due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—PA CRITERIA

(Dr. Meade):

The PA for Orenzia was previously reviewed at the Jan 2012 BAP meeting

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—IMPLEMENTATION PLAN

(Dr. Meade):

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—COMMITTEE’S PHYSICIAN’S PERSPECTIVE

(Dr. Lounsbery):

Dr. Lounsbery said again there are very few comments about this recommendation. She noted that the drug is available for those who may need it at the lower copay through medical necessity. Other drugs already on the UF have more approved indications than Orencia SC.

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—PANEL QUESTIONS AND COMMENTS

Ms. Fryar opened the floor to questions from the Panel.

Dr. Sampsel asked if the current form of Orencia (IV) is covered under the medical benefit. Dr. Meade answered that it is. Dr. Sampsel then asked if any of the patients already taking Orencia IV would be candidates for conversion to the subcutaneous form, which is self-administered. Dr. Meade answered that the Committee looked at that but there was no good data available because IV use is covered under the medical benefit, not the pharmacy benefit.

Dr. Khurana asked how many beneficiaries are currently using the drug. Dr. Meade said 542 patients. Dr. Khurana noted that 351 of these are retail users and asked whether that would affect the cost analysis. Dr. Meade replied that this is one of the factors taken into account when doing the cost analysis.

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—PANEL VOTE ON UF RECOMMENDATION

Ms. Fryar read the P&T Committee’s UF recommendation for the newly-approved Orencia SC.

The P&T Committee based on its collective professional judgment, recommended abatacept SC (Orencia SC) be designated non-formulary (NF) due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs) DRUG CLASS — ABATACEPT (ORENCIA SC)—PANEL VOTE ON IMPLEMENTATION PLAN RECOMMENDATION

The Chair then read the implementation plan recommendation.

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

Without comment, the Panel vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

B. GLAUCOMA DRUGS: PROSTAGLANDIN ANALOG DRUG CLASS—TAFLUPROST (ZIOPTAN)

(PEC Script)

TAFLUPROST (ZIOPTAN)—RELATIVE CLINICAL EFFECTIVENESS (LCDR Selvester):

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of a newly approved glaucoma drug, Zioptan. Zioptan is the fourth prostaglandin ophthalmic agent on the market. Drugs in the prostaglandin agent Class are listed in Table 4 on page 5 of your handout.

Figure 4 on page 5 of your handout shows Xalatan and its generics are the most used agent followed by Lumigan

This class was previously reviewed in February 2007

Prostaglandins reduce intraocular pressure by increasing the outflow of intraocular fluid. Like all other products in this class, Zioptan is dosed once daily. It contains no preservative and supplied in single dose containers. Zioptan lowers intraocular pressure similar to other agents but was not shown to be non-inferior to Xalatan. Even though Zioptan doesn't contain a preservative, this hasn't translated into a decreased adverse event profile.

Tafluprost (Zioptan)- Relative Clinical Effectiveness- Relative Clinical Effectiveness Conclusion— The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 0 absent) that tafluprost (Zioptan) offers no compelling clinical advantages over the other ophthalmic prostaglandins available on the UF.

TAFLUPROST (ZIOPTAN)—RELATIVE COST EFFECTIVENESS

(Dr. Meade):

Cost minimization analysis (CMA) was performed. The weighted average cost per day at all three points of service (POS) was evaluated for Zioptan in relation to other drugs in the prostaglandin eye drops drug class. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that tafluprost (Zioptan) was not cost-effective when compared to the other

ophthalmic prostaglandins currently included on the UF.

TAFLUPROST (ZIOPTAN)—UF RECOMMENDATION

(Dr. Meade):

The P&T Committee, based on its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 0 absent) tafluprost (Zioptan) be designated NF because it has no compelling clinical advantages over the other ophthalmic prostaglandin analogues and is not cost-effective compared to latanoprost (Xalatan), the most utilized drug in the Military Health System (MHS).

TAFLUPROST (ZIOPTAN)—IMPLEMENTATION PLAN

(Dr. Meade):

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

TAFLUPROST (ZIOPTAN)—COMMITTEE PHYSICIAN'S PERSPECTIVE

(Dr. Lounsbery):

Dr. Lounsbery noted that this is the first new drug in this class since the class was reviewed in 2007. The Committee felt that there was no clinical advantage offered by this drug and there would be no new benefit from adding it to the formulary.

TAFLUPROST (ZIOPTAN)—PANEL QUESTIONS AND COMMENTS

The members of the BAP asked no questions of the presenters regarding this recommendation.

TAFLUPROST (ZIOPTAN)—PANEL VOTE ON UF RECOMMENDATIONS

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

The P&T Committee, based on its collective professional judgment, recommended tafluprost (Zioptan) be designated NF because it has no compelling clinical advantages over the other ophthalmic prostaglandin analogues and is not cost-effective compared to latanoprost (Xalatan), the most utilized drug in the Military Health System (MHS).

The BAP voted as follows:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

TAFLUPROST (ZIOPTAN)—PANEL VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

Ms. Fryar read the implementation plan recommendations.

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

The Panel then voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

**C. ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)—
IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)**

LCDR Selvester noted that the next two drugs are members of the previously-reviewed non-steroidal anti-inflammatory drugs class—NSAIDs.

(PEC Script)

**IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)—RELATIVE CLINICAL
EFFECTIVENESS**

(LCDR Selvester):

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of a newly approved product, Duexis, which is a combination product containing NSAID and an H2 blocker. The drugs in the class are listed in Table 5 on page 6 of your handout. Duexis is the third combination of an NSAID and a G.I. protect.

Figure 5 on page 7 of your handout shows ibuprofen is the most used agent followed by Celebrex.

This class was previously reviewed in August 2011.

Duexis is in the GI-protective subclass of the NSAIDs, which also includes esomeprazole/naproxen (Vimovo) and diclofenac/misoprostol (Arthrotec). The COX-2 inhibitor celecoxib (Celebrex) is also considered gastro-protective. Duexis requires three times a day dosing versus twice a day dosing for Vimovo. This is based on the famotidine dose of 26.2 mg per tablet. Duexis was approved by 505(b)(2) filing with FDA, where the safety of the product approved based on the safety profile of the component agents. There are no head-to-head trials of Duexis versus the other G.I. protective agents.

Duexis Relative Clinical Effectiveness- Relative Clinical Effectiveness Conclusion— The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) ibuprofen/famotidine (Duexis) offers no distinct clinical advantages to the combination NSAID/gastroprotective agents already on the UF.

IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)—RELATIVE COST EFFECTIVENESS

(Dr. Meade):

Cost minimization analysis (CMA) was performed. The weighted average cost per day at all three points of service (POS) was evaluated for Duexis relative to other drugs in the NSAID class - the G.I. protectant subclass. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that ibuprofen/famotidine (Duexis) was not cost-effective when compared to other oral NSAIDs agents included on the UF; it was also more costly than the individual

components, ibuprofen and famotidine.

IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)—UF RECOMMENDATIONS

(Dr. Meade):

The P&T Committee, in its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 0 absent) ibuprofen/famotidine (Duexis) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)—IMPLEMENTATION PLAN

(Dr. Meade):

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)—COMMITTEE PHYSICIAN'S PERSPECTIVE

(Dr. Lounsbery):

Dr. Lounsbery noted that this drug has to be taken three times a day, unlike other drugs already on the UF, and the Committee saw no clinical advantage to putting it on the UF. It is also more costly.

IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)—PANEL QUESTIONS AND COMMENTS

The Chair opened the floor to questions from the BAP. The Panel had no questions regarding this recommendation.

IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)—PANEL VOTE ON UF RECOMMENDATIONS

The Chair read the UF recommendation:

The P&T Committee, in its collective professional judgment, recommended ibuprofen/famotidine (Duexis) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

Ms. Fryar called for the BAP vote on the UF recommendation for Duexis. The vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

IBUPROFEN/FAMOTIDINE TABLETS (DUEXIS)—PANEL VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

Ms. Fryar read the implementation plan recommendations:

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

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

C. ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)—KETEROLAC NASAL SPRAY (SPRIX)

(PEC Script)

KETEROLAC NASAL SPRAY (SPRIX)—RELATIVE CLINICAL EFFECTIVENESS

(LCDR Selvester):

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of a newly approved Sprix nasal spray. Sprix is an intranasal formulation of ketorolac, which is also available in oral tablets and IV and IM injections. It is a first intranasal NSAID on the market. The drugs in the class, once again, are listed in Table 5 on page 6 of your handout.

Figure 5 on page 7 of your handout shows ibuprofen are the most used agent followed by Celebrex.

Sprix is indicated for short-term, up to five days, management of moderate to severe pain. The 5-day limited duration of use is similar to the IM/IV and oral ketorolac formulations.

Each Sprix bottle contains 8 sprays, enough for one day. Patients should be instructed to discard the bottle after one day, as there is no preservative. It offers an alternative route of drug administration for patients with moderate to severe pain unable to tolerate NSAIDs by oral or injected routes. There is no direct comparative data with Sprix and other analgesics

Ketorolac Nasal Spray (Sprix)- Relative Clinical Effectiveness- Relative Clinical Effectiveness Conclusion— The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) there is no evidence to suggest ketorolac nasal spray (Sprix) has a compelling clinical advantage over the other oral NSAIDs already on the UF.

KETEROLAC NASAL SPRAY (SPRIX)—RELATIVE COST EFFECTIVENESS

(Dr. Meade):

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that ketorolac nasal spray (Sprix) was more costly, based on an average weighted cost per day of therapy at all three points of service (POS), than the other oral NSAIDs and low-potency narcotic analgesics currently on UF.

KETEROLAC NASAL SPRAY (SPRIX)—UF RECOMMENDATION

(Dr. Meade):

The P&T Committee, based on its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 0 absent) ketorolac nasal spray (Sprix) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

KETEROLAC NASAL SPRAY (SPRIX)—IMPLEMENTATION PLAN RECOMMENDATION

(Dr. Meade):

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

KETEROLAC NASAL SPRAY (SPRIX)—COMMITTEE PHYSICIAN’S PERSPECTIVE

(Dr. Lounsbery):

Dr. Lounsbery noted that there were limitations on the use of this drug: each bottle contains 8 sprays (enough for one day) and it must then be discarded and the drug can only be used for five days. She said the Committee wasn’t sure of its place in therapy, but the drug offered no clear clinical advantages and was not cost-effective.

KETEROLAC NASAL SPRAY (SPRIX)—PANEL QUESTIONS AND COMMENTS

Ms. Le Gette and Dr. Cohoon offered comments on the implementation plan, noting that the great majority of current users are from the retail POS. It was also noted that beneficiaries who need to use an alternative form of dosing would still be able to obtain this drug.

KETEROLAC NASAL SPRAY (SPRIX)—PANEL VOTE ON UF RECOMMENDATIONS

Ms. Fryar read the UF recommendations for this agent.

The P&T Committee, based on its collective professional judgment, recommended ketorolac nasal spray (Sprix) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

The Panel vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

KETEROLAC NASAL SPRAY (SPRIX)—PANEL VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

The Chair read the implementation plan for Sprix.

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

decision.

The Panel concurred by a vote of:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

D. NON-INSULIN DIABETES DRUGS: DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS—SITAGLIPTIN/METFORMIN EXTENDED RELEASE (JANUMET XR) AND LINAGLIPTIN/METFORMIN (JENTADUETO)

(PEC Script)

JANUMET XR AND JENTADUETO—RELATIVE CLINICAL EFFECTIVENESS

(LCDR Selvester):

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of two newly approved diabetic agents Janumet XR and Jentadueto. Janumet XR is a combination of two anti-diabetic agents sitagliptin and metformin extended-release. Jentadueto is a combination of linagliptin and metformin immediate release. The drugs in the class are listed in Table 6 on page 8 of your handout. Figure 6 on page 8 of your handout shows Janumet products are the most used agents in the MHS.

This class was previously reviewed in Nov 2010 and Feb 2012.

- Janumet XR and Jentadueto are indicated as adjunct to diet and exercise to improve glycemic control in patients with type II diabetes mellitus.
- Janumet XR is dosed as either one or two tablets once daily, and Jentadueto is given as one tablet twice daily.
- Janumet XR provides a once daily fixed-dose combination, but supplemental metformin tablets are required to reach the maximum recommended metformin dose.
- A meta-analysis comparing sitagliptin/metformin to linagliptin/ metformin showed that the linagliptin combination was non-inferior to the sitagliptin combination in lowering A1c, a lab test used to measure diabetes control.
- Janumet XR and Jentadueto, like all DPP-4 inhibitors, are considered lipid neutral.
- When added to metformin, sitagliptin and linagliptin have shown a decrease in weight ranging from 0.4-1.4kg.
- Due to metformin and the risk of lactic acidosis, a blood balance disorder, both Janumet XR and Jentadueto require renal dose adjustments for patients with kidney problems, and should be avoided in patients with liver failure.
- In general, the incidence of hypoglycemia, low blood sugar, with DPP-4 inhibitors is not significantly different than placebo.
- Although safety and tolerability have not been studied with Janumet XR or Jentadueto, DPP-4 inhibitors are generally well-tolerated, with the most common side effects being upper respiratory in nature, while metformin shows mostly GI-related side effects.

Janumet XR and Jentadueto - Relative Clinical Effectiveness- Relative Clinical

Effectiveness Conclusion— The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) there is no evidence to suggest either sitagliptin/metformin ER (Janumet XR) or

linagliptin/metformin (Jentadueto) have a compelling clinical advantage over the other DPP-4 inhibitor/metformin fixed-dose combinations included on the UF.

JANUMET XR AND JENTADUETO—RELATIVE COST EFFECTIVENESS

(Dr. Meade):

A cost minimization analysis and budget impact analysis were performed. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that Janumet XR and Jentadueto were cost-effective when compared to other DPP-4 inhibitors included on the UF.

JANUMET XR AND JENTADUETO—UF RECOMMENDATIONS

(Dr. Meade):

The P&T Committee, based on its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following:

- sitagliptin/metformin ER (Janumet XR) be designated step-preferred and formulary on the UF; and
- linagliptin/metformin (Jentadueto) be designated non-step-preferred and formulary on the UF.
- This recommendation includes step therapy, which requires a trial of sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/simvastatin (Juvisync), or sitagliptin/metformin ER (Janumet XR) (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors also requires a trial of metformin or sulfonylurea for new patients.

JANUMET XR AND JENTADUETO—PRIOR AUTHORIZATION (PA) CRITERIA

(Dr. Meade):

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to the DPP-4 inhibitors subclass. Coverage would be approved if the patient met any of the following criteria

a) Automated PA criteria:

- (1) The patient has filled a prescription for metformin or a sulfonylurea at any MHS pharmacy POS [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.
- (2) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, Juvisync, Janumet XR, Tradjenta, Jentadueto, Onglyza, or Kombiglyze XR) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

b) Manual PA criteria, if automated criteria are not met:

The fixed-dose combination product Janumet XR or Jentadueto is approved (e.g., a trial of sulfonylurea is not required if):

- (1) The patient has had an inadequate response to metformin or sulfonylurea.
 - (2) The patient has experienced the following adverse event while receiving a sulfonylurea: hypoglycemia requiring medical treatment.
 - (3) The patient has a contraindication to a sulfonylurea.
- c) In addition to the above criteria regarding metformin and sulfonylurea, the following PA criteria would apply specifically to linagliptin/metformin metformin (Jentadueto):
- (1) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with linagliptin-containing products.
 - (2) The patient has had an inadequate response to a sitagliptin-containing product.
 - (3) The patient has a contraindication to sitagliptin.

JANUMET XR AND JENTADUETO—UF IMPLEMENTATION PLAN

(Dr. Meade):

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

JANUMET XR AND JENTADUETO—COMMITTEE PHYSICIAN’S PERSPECTIVE

(Dr. Lounsbery):

Dr. Lounsbery noted that what the Committee did was add two new DPP-4 combinations on the formulary. Sitagliptin and some combos are already step-preferred on the formulary and the linagliptin is formulary but not preferred. The Committee action extends the combinations in the same category. The sitagliptin/metformin will be step-preferred; the linagliptin combo stays on the UF but not preferred.

JANUMET XR AND JENTADUETO—PANEL QUESTIONS AND COMMENTS

Ms. Fryar asked about the wording of the PA criteria, inquiring whether the metformin criteria will be (a) or (b) or (c). LCDR Selvester replied that the patient will have to use either metformin or a

sulfonylurea first before they can be moved on to the other agent. Ms. Fryar clarified her question regarding whether the word “or” should be included in the manual PA criteria between paragraphs (2) and (3) of criterion “b” to be consistent with previous practice. Dr. Meade replied that the correct wording includes “or”.

JANUMET XR AND JENTADUETO—PANEL VOTE ON UF RECOMMENDATIONS

Ms. Fryar read the P&T Committee’s UF recommendations for the DPP-4 inhibitors Janumet XR and Jentaduetto.

The P&T Committee, based on its collective professional judgment, recommended the following:

- sitagliptin/metformin ER (Janumet XR) be designated step-preferred and formulary on the UF; and
- linagliptin/metformin (Jentaduetto) be designated non-preferred and formulary on the UF.
- This recommendation includes step therapy, which requires a trial of sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/simvastatin (Juvisync), or sitagliptin/metformin ER (Janumet XR) (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors also requires a trial of metformin or sulfonylurea for new patients.

The BAP voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

JANUMET XR AND JENTADUETO—PANEL VOTE ON PA CRITERIA

The Chair next read the PA criteria recommendations.

The P&T Committee recommended the following PA criteria should apply to the DPP-4 inhibitors subclass. Coverage would be approved if the patient met any of the following criteria

a) Automated PA criteria:

- (1) The patient has filled a prescription for metformin or a sulfonylurea at any MHS pharmacy POS [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.
- (2) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, Juvisync, Janumet XR, Tradjenta, Jentaduetto, Onglyza, or Kombiglyze XR) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

b) Manual PA criteria, if automated criteria are not met:

The fixed-dose combination product Janumet XR or Jentadueto is approved (e.g., a trial of sulfonylurea is not required if):

- (1) The patient has had an inadequate response to metformin or sulfonylurea.
- (2) The patient has experienced the following adverse event while receiving a sulfonylurea: hypoglycemia requiring medical treatment.
[or]
- (3) The patient has a contraindication to a sulfonylurea.

c) In addition to the above criteria regarding metformin and sulfonylurea, the following PA criteria would apply specifically to linagliptin/metformin metformin (Jentadueto):

- (1) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with linagliptin-containing products.
- (2) The patient has had an inadequate response to a sitagliptin-containing product.
- (3) The patient has a contraindication to sitagliptin.

The Panel voted as follows:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

JANUMET XR AND JENTADUETO—PANEL VOTE ON UF IMPLEMENTATION PLAN

Ms. Fryar read the UF implementation plan recommendations.

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

The Panel voted was:

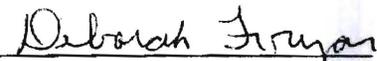
Concur: 9 Non-concur: 0 Abstain: 0 Absent: 1

Closing Statement

Ms. Fryar closed by thanking each of the Panel members for the time they put in to this meeting and thanked the briefers —Dr. Meade, Dr. Selvester and Dr. Lounsbery.

She indicated that the next tentative scheduled public meeting of the Panel is January 9, 2013 and confirmed that the date falls on a Wednesday instead of the usual Thursday.

CDR Lawrence, the DFO, closed the meeting at 10:25 A.M.



Ms. Deborah Fryar
Chairperson

Brief Listing of Acronyms Used in This Summary

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

- AE — Adverse event
- APR — Automated Profile Review
- BAP — Uniform Formulary Beneficiary Advisory Panel (the “Panel” referred to above)
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- CEA — Cost-effectiveness analysis
- CFR — Code of Federal Regulations
- CMA — Cost-Minimization Analysis
- CPG — Clinical Practice Guideline
- CR — Controlled Release (a drug formulation)
- DFO — Designated Federal Officer
- DoD — Department of Defense
- DPP-4—Dipeptidyl Peptidase-4 inhibitors (A drug class)
- ECF — Extended Core Formulary
- ER — Extended Release (a drug formulation)
- ESI — Express-Scripts, Inc.
- FACA — Federal Advisory Committee Act
- FDA — U.S. Food and Drug Administration
- GI—Gastro-intestinal
- HIT—Heparin-induced thrombocytopenia
- IR — Immediate Release (a drug formulation)
- MHS — Military Health System
- MN — Medical Necessity
- MTF — Military Treatment Facility
- NF — Non-formulary
- NIH — National Institutes of Health
- NSAID—Non-Steroidal Anti-Inflammatory Drug (a drug class)
- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DoD Pharmacy and Therapeutics Committee
- PDTS — Pharmacy Data Transaction Service
- PEC — DoD Pharmacoeconomic Center
- PORT — Pharmacy Outcomes Research Team

- POS — Point of Service
- RCTs — Randomized Control Trials
- SR — Sustained release (a drug formulation)
- SU—Sulfonylurea
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TPHARM — TRICARE Pharmacy Program
- TRRx — TRICARE Retail Pharmacy Program
- TRT—Testosterone Replacement Therapy
- UF — DoD Uniform Formulary
- USC — United States Code
- VA — U.S. Department of Veterans Affairs

Abbott Public Comment Letter

September 26, 2012

CDR Joseph Lawrence
Beneficiary Advisory Panel
Designated Federal Officer (DFO)
2450 Stanley Road, Suite 208
Fort Sam Houston, TX 78234-6102

Dear CDR Lawrence:

Based on the e-mail notice sent on September 20, 2012 that provided a link to the Sept 27th BAP meeting agenda and handouts that summarized the Pharmacy and Therapeutics Committee's recommendations on the topical testosterone therapy calls, Abbott would like to provide the following to be included in comments for the BAP to consider when making their recommendation. Typically, written comments would be provided five days prior to the BAP meeting but the date of the notice and subsequent meeting did not permit sufficient time to meet this requirement. However, some important factors have changed or may not have been fully vetted by the P&T.

1. P&T Comments

A. Relative Clinical Effectiveness Conclusion Concerning the TRT Agents

In Section II(a)(1) the P&T concluded that [A]lthough high-quality comparative data is lacking, there appear to be no clinically relevant differences in efficacy between products. This is factually inaccurate based on recent FDA requirements. In the past 2 weeks, the FDA required a label change on AndroGel that will be a class change for all topical testosterone therapies. The label change could impact the DoD's current recommendation to switch and not maintain controlled patients on their topical testosterone therapy.

Abbott's current package insert states that **AndroGel is not interchangeable** with other topical testosterone products. To add emphasis to this point, effective September 12, 2012, a new Limitation of Use was added to the Highlights and Section I (INDICATIONS and USAGE) of the Full Prescribing Information for AndroGel 1% and 1.62% which includes the following important information:

- **Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure**

We understand the DoD Pharmacoeconomic Center has done a thorough clinical review of all the products, however since the FDA issued this class label after those recommendations, we thought it was highly pertinent to consider before any final recommendations are made. The Limitation of Use label change by the FDA is being added to all topical testosterone product labels. Since these products have different application sites, doses, strengths and instructions for use, the clinical results may vary by product and per patient and should not be viewed as interchangeable. Patients would most likely require additional physician visits and additional laboratory blood tests to start therapy on a different agent and titrate to the appropriate dose of the new drug. This would increase overall healthcare expenditures for the DoD and be both disruptive and inconvenient for patients. Abbott would not suggest switching patients' testosterone therapy and empirically estimating the appropriate dose. Based on the FDA class label change, Abbott would not support any recommendation to switch controlled patients off current therapy for the DoD's topical testosterone review.

B. TRT's—Relative Cost-Effectiveness Analysis

In Section II(B) the P&T addressed the pharmacoeconomic analysis performed for the topical and buccal testosterone class, including cost minimization analysis (CMA) and budget impact analysis (BIA) as well as cost scenarios related to step therapy. Certain realities and costs to the DoD for current users of TRTs appear not to have been considered. For those patients whose Hypogonadism is currently controlled on TRT therapy, there are considerable incremental costs associated with switching these patients to a new TRT agent. These costs are amplified in a therapeutic area such as

TRTs where there is a **significant** market leader (over 70% of current DoD TRT patients use AndroGel). The P&T recommendation mandates that patients using AndroGel must to change from the current and effective treatment based on the proposed step therapy. When switching patients on TRTs, there are not only drug cost considerations but also multiple lab tests to measure the patients' testosterone levels. This is due to the fact that patients on TRTs are required to be titrated to ensure appropriate treatment and that their testosterone levels are maintained in the therapeutic ranges. It is not merely changing the drug but managing this change and the impact on the patient where a currently controlled patient must switch therapies and then must be titrated (requiring additional lab tests and blood draws) and may be forced to experience symptoms once again while going through this step therapy process. We believe this is not "cost-effective" for the DoD or the "most clinically and cost effective option for the Military Health Systems" especially in light of the possible impact on currently controlled patients.

Furthermore, Abbott would also like to comment on the DoD's condition sets around step therapy / PA process and as it applies to new or both new and current patients. Based on history with the DoD and all past bids that Abbott has been part of with this bid language, the DoD has always weighed in favor of the beneficiary and grandfathered /; maintained current controlled patients on therapy. By not actually soliciting for a separate condition set that states controlled patients would also be subject to the step therapy, it is assumed that the most likely DoD course of action based on past decisions, would be to continue to grandfather current patients on therapy. In fact, by not giving the option to bid on a separate condition set to step current controlled patients, Abbott feels that the DoD may not be getting the best bids by putting the market share leading product at a disadvantage to other products in the bid. This is especially true in this class where there is a market leader with over 70% share. The non market leaders have nothing to lose and can bid aggressively not knowing if current patients will be grandfathered or not because most patients have elected not to use their products. The market leader, not having a separate option to bid for stepping current patients and knowing the history of how DoD makes decisions, is at a disadvantage and therefore may not bid aggressively. However, if the DoD provided a separate option to bid for stepping current patients,

September 26, 2012

then the market leading product would know the risk and bid more aggressively. In the end, this is better for the DoD as they get a more aggressive price point, and they do not have to disrupt the majority of their patient population that is receiving effective therapy by keeping the market leading drug available to current patients.

We feel that if DoD is going to move to being more aggressive in formulary management over what has been the norm in the past and start making recommendations to switch controlled patients as in the current topical testosterone therapy P&T recommendation, then it is an unfair bid process to the market leading drug manufacturer to not offer a condition set up front to provide a bid on stepping current and new patients. We believe that in the end, this option will also provide a better outcome to DoD by receiving more aggressive pricing by everyone and the potential to maintain controlled patients in a class where there is a significant market leader.

C. TRTs – UF Recommendation

Further exacerbating the therapeutic issue for currently controlled patients is the fact that the P&T has recommended the AndroGel (currently used by over 70% of the DoD patients to manage their Hypogonadism) is designated non-preferred and NF on the UF (see Section II(C)(3)) thereby increasing costs to the patients who may want to choose to stay on AndroGel which is effectively treating their Hypogonadism.

II. Conclusion

For all of the above-referenced reasons Abbott believes the P&T and BAP should reconsider the current recommendations in light of the potential financial and therapeutic impact to not only the DoD but especially the patients.

Best regards,

/S/

Jeffrey N. Haas
Divisional Vice President, Managed Health Care
Proprietary Pharmaceuticals, U.S.