

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary

January 9, 2013

Washington, D.C.

Panel Members Present:

- Deborah Fryar, National Military Family Association, Chairperson
- Kathryn Buchta, Health Net Federal Services
- John Crum, Humana Military Healthcare Services, Inc.
- Steven Hein, Medical Association of the Uniformed Services
- Amit Khurana, TriWest Healthcare Alliance
- Lisa Le Gette, Express-Scripts, Inc.
- Katherine O'Neill-Tracy, Military Officers Association of America
- 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:

- Barbara Cohoon, National Military Family Association

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 November 14, 2012 Department of Defense (DoD) Pharmacy and Therapeutic (P&T) Committee meeting held in San Antonio, TX.

Agenda

The agenda for this meeting of the Panel is:

- Welcome and opening remarks
- Public citizen comments
- Review and Panel discussion of P&T Committee recommendations for the following therapeutic drug classes:
 - *Drug Class Reviews:*
 - Non-Insulin Diabetes Drugs—Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)
 - Overactive Bladder Drugs (OABs)
 - Gastrointestinal-2 Oral Antibiotic Drugs (GI-2)

- Hepatitis C Drugs
- *Designated Newly Approved Drugs:*
 - High Potency Narcotic Analgesics—Oxycodone immediate release (Oxecta)
- *Re-evaluation of Non-formulary Agents—Status of escitalopram (Lexapro) and pantoprazole (Protonix) on the Uniform Formulary*
- *Utilization Management Issues*
 - Prior Authorization Criteria
 - Drug Phosphodiesterase-5 (PDE-5) Inhibitors
 - Topical Testosterone Replacement Therapy (TRT)—Use in women
 - Injectable Gonadotropins
 - Targeted Immunomodulatory Biologics—Adalimumab (Humira)
 - Prostate Cancer Drugs—Enzalutamide (Xtandi) and Abiraterone (Zytiga)

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 9 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. There were none.

Chairperson's Opening Remarks

The DFO next turned the meeting over to the Panel Chair, Ms. Deborah Fryar. Ms. Fryar welcomed the attendees and reminded the Panel that the process calls for the BAP to vote to concur or non-concur on the recommendations presented. If it so desires, the Panel can also make comments that will be incorporated into the record. Ms. Fryar then 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 ("PEC" for short). Joining me today from the PEC are Lieutenant Colonel Chris Conrad, the Deputy Director of the PEC and Lieutenant Commander Bob Selvester, the Navy Physician Consultant. Also joining us today is Doctor and retired Army Colonel John Kugler, the Chairman of the P & T Committee, who will provide the physician perspective and comment on the recommendations made by the P & T Committee. Joining us from the Tricare Management Activity is Captain Nita Sood, Chief of Staff of the Pharmacy Operations Directorate.

The DoD Pharmacoeconomic Center 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 the 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 P & T Committee. 32 Code of Federal Regulations (CFR) 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 the 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 four Uniform Formulary Drug Classes (or sub-classes) – the Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs) sub-class of the Non-Insulin Diabetes Drug Class; the Overactive Bladder Agents (OABs) Drug Class; the Gastrointestinal-2 Oral Antibiotics (GI-2) Drug Class; and the Hepatitis C Drug Class. Additionally, one newly approved drug was reviewed – Oxecta (Oxycodone IR). Two previously reviewed Non-Formulary agents were also re-evaluated – Lexapro (escitalopram) and Protonix (pantoprazole).

- 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 CFR 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 5. There are tables and utilization figures for each of 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/SUBCLASS REVIEWS— Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)

Relative Clinical Effectiveness

(PEC Script)

(LCDR Selvester)

Background: The GLP1RA drugs are injectable products typically used in addition to older oral agents in the treatment of Type II Diabetes Mellitus or high blood sugar (though they also carry FDA indication for single drug therapy). The GLP1RAs are a subclass of the Non-Insulin Diabetes Drug Class, which is comprised of Byetta (exenatide twice daily injection), Victoza (liraglutide once daily injection), and Bydureon (exenatide once weekly injection). Bydureon is the newest entrant to the class.

Drugs in the GLP-1RA sub-class are listed in Table 1 on page 2. The GLP1RA class was previously reviewed for UF placement in November 2010. Figure 1 of the handout on page 2 shows the utilization of the agents.

Step therapy implemented in April 2011 requires that new GLP1RA users try metformin or a sulfonylurea first, and that new GLP1RA users try Byetta before TRICARE® will cover the other agents in this drug subclass.

The Pharmacy Outcomes Research Team (PORT) provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Metformin is the most cost-effective agent and remains the first line treatment in all patients with type 2 diabetes mellitus, unless contraindications exist, due to positive outcomes data from the United Kingdom Prospective Diabetes Study.

- Byetta, Victoza, and Bydureon all decrease hemoglobin A1c (the most widely used blood test used to monitor diabetes) ~ 1%-2% from baseline when used as monotherapy or in combination with other oral agents.
- When compared head-to-head, overall there are no clinically relevant differences between the three GLP1RAs with regard to effect on glycemic (blood sugar) control.
- Bydureon offers additional patient convenience given its once weekly dosing regimen and does not require titration compared to Byetta, but is not available in a pre-filled syringe.
- There are no studies evaluating adherence with the three GLP1RAs.

Pharmacy Outcomes Research Team report: The PORT analysis illustrated the following trends:

- A majority of patients with diabetes are using metformin and/or a sulfonylurea.
- There was a stronger tendency toward migration to Bydureon from patients previously taking Byetta than Victoza.
- Among those patients receiving rejections at the pharmacy, the ultimate “No Fill Rate” was quite low.

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs) Relative Cost Effectiveness

(Dr. Meade)

Relative Cost-Effectiveness Conclusion—Pharmacoeconomic analyses were performed for the GLP1RA subclass, including cost minimization analysis (CMA) and budget impact analysis (BIA). For the BIAs, several of the model’s key assumptions were varied, with corresponding sensitivity analyses conducted. Methods used for CMA and BIAs were based on current step therapy requiring a trial of metformin or a sulfonylurea prior to a patient receiving a GLP1RA.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Byetta was the most cost-effective GLP1RA, based on the weighted average cost per day of treatment across all three points of service (POS), followed by Bydureon and Victoza. Results from the cost minimization and budget impact analyses showed scenarios where Byetta, Bydureon and Victoza are all designated UF presented a cost avoidance projection comparable to the current UF scenario where all GLP1RAs are UF. Data was not available to assess the potential pharmacoeconomic impact of longer-acting GLP1RA formulations on medication adherence and health-related outcomes in this cost-effectiveness evaluation.

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)—UF Recommendation

(Dr. Meade)

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

- Designating Byetta, Victoza, and Bydureon as formulary on the UF;

- Removing the current requirement for a trial of Byetta prior to the other GLP1RAs. As a result, there would no longer be a preferred GLP1RA product.

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)—Prior Authorization (PA) Criteria

(Dr. Meade)

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining the current PA requiring a trial of metformin or a sulfonylurea prior to the use of Byetta, Victoza, or Bydureon in new users. A trial of metformin or a sulfonylurea would not be required for patients with an adverse event, contraindication to, or inadequate response with metformin or sulfonylurea. Automated PA criteria (step-therapy) and manual PA criteria remain the same as recommended at the November 2010 P&T Committee meeting, and implemented in April 2011.

Automated PA criteria: The patient has received a prescription for metformin or sulfonylurea (SU) at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria: If automated criteria are not met: Byetta, Bydureon, or Victoza is approved (e.g., trial of metformin or SU is NOT required) if:

- 1) The patient has a confirmed diagnosis of Type 2 Diabetes Mellitus **AND**
- 2) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis. **OR**
- 3) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment. **OR**
- 4) The patient has a contraindication to both metformin and a SU. **OR**
- 5) The patient has had an inadequate response to metformin and a SU.

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)—UF and PA Implementation Plan

(Dr. Meade)

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 30-day implementation period in all POS.

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)—Committee Physician's Perspective

Dr. Kugler provided the Panel with the Committee physician's perspective on the recommendations in this drug class. He began by noting that when the sub-class was reviewed in November 2010 the Committee recommended step therapy, i.e., a trial of metformin or sulfonylurea. The Committee agreed that all three drugs in this sub-class should be made UF and that the requirement for a step-therapy trial of Byetta as a preferred agent should be removed.

He said there are no formal studies of any of the three products, although evaluation studies are underway. The Committee also agreed that the requirement for a trial of metformin or a sulfonylurea should be continued and that one subclass should be discontinued. There are several new products in the pipeline now being evaluated.

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)—Panel Questions and Comments

The BAP members had no questions of the presenters in this drug class.

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)—Panel Vote on UF Recommendation

The Chairperson, Ms. Fryar, read the P&T Committee's UF recommendations for this drug class.

The P&T Committee recommended the following:

- 1) Designating Byetta, Victoza, and Bydureon as formulary on the UF;
- 2) Removing the current requirement for a trial of Byetta prior to the other GLP1RAs. As a result, there would no longer be a preferred GLP1RA product.

Without further discussion, the Panel voted as follows:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)—Panel Vote on PA Criteria

Ms. Fryar read the Committee's recommended PA criteria.

The P&T Committee recommended maintaining the current PA requiring a trial of metformin or a sulfonylurea prior to the use of Byetta, Victoza, or Bydureon in new users. A trial of metformin or a sulfonylurea would not be required for patients with an adverse event, contraindication to, or inadequate response with metformin or sulfonylurea. Automated PA criteria (step-therapy) and manual PA criteria remain the same as recommended at the November 2010 P&T Committee meeting, and implemented in April 2011.

Automated PA criteria: The patient has received a prescription for metformin or sulfonylurea (SU) at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, **AND**

Manual PA criteria: If automated criteria are not met: Byetta, Bydureon, or Victoza is approved (e.g., trial of metformin or SU is NOT required) if:

- 1) The patient has a confirmed diagnosis of Type 2 Diabetes Mellitus **AND**
- 2) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis. **OR**
- 3) The patient has experienced the following adverse event while receiving a SU: hypoglycemia

requiring medical treatment. **OR**

4) The patient has a contraindication to both metformin and a SU. **OR**

5) The patient has had an inadequate response to metformin and a SU.

The BAP vote on the PA criteria was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RAs)—Panel Vote on Implementation Plan

The Chair read the implementation plan.

The P&T Committee recommended an effective date of the first Wednesday after a 30-day implementation period in all POS.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

II. UF CLASS REVIEWS—Overactive Bladder Agents (OABs)

(PEC Script)

Overactive Bladder Agents (OABs)—Relative Clinical Effectiveness

(LCDR Selvester)

Background: The OAB agents are used to reduce (but infrequently eliminate) the number of episodes of urge incontinence. The baseline number of episodes of incontinence was 1.8-5 episodes per day. Only 6-10% of patients achieve a reduction to zero of urge incontinence episodes while taking the active drug. The Overactive Bladder (OAB) Drug Class is comprised of Enablex (darifenacin), Toviaz (fesoterodine), oxybutynin IR (Ditropan, generics), oxybutynin extended release (ER) (Ditropan XL, generics), Oxytrol (oxybutynin transdermal delivery system (TDS)), Gelnique (oxybutynin 10% gel), Vesicare (solifenacin), tolterodine IR (Detrol, generics), Detrol LA (tolterodine ER), trospium IR (Sanctura, generics), and trospium ER (Sanctura XR, generics). Generic formulations of Detrol IR, Sanctura IR and Sanctura XR recently entered the market. Drugs in the OAB Drug Class are listed in Table 2 on page 3.

The OAB drug class has been previously reviewed for UF placement in August 2008, and May and November 2009. Figure 2 of the handout on page 3 shows the utilization of the agents.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Review of the clinical literature for efficacy, safety, and tolerability data since the last P&T Committee UF decision in 2008 did not add substantial new information.
- The OAB agents are statistically superior to placebo, but the placebo response rates are high for the class, ranging from 30% to 50%.
- There is insufficient evidence to suggest whether one OAB drug is superior to another. Small studies of low quality evidence reported Toviaz was statistically superior to tolterodine, and Vesicare was statistically superior to tolterodine, but the clinical effect is small, relating to a reduction in urge incontinence episodes of approximately one episode/day.
- No OAB agent has a superior safety profile. Oxytrol causes less dry mouth than tolterodine ER, but has higher withdrawal rates. There is scant safety data for Gelnique formulation, but the effects are likely to be similar to Oxytrol with regards to dry mouth.
- Overall, adverse drug effects are lower with the ER formulations than IR formulations. The newer agents do not have significantly lower incidence of dry mouth or constipation than the older OAB drugs.
- Persistence rates within the Military Health System (MHS) remain low at 12% for all the OAB drugs. As needed use of the OAB drugs is 26% in the MHS.
- There are no studies evaluating clinical outcomes, such as reduced fall risk or delayed nursing home placement with the OAB drugs.

Overactive Bladder Agents (OABs)—Relative Cost Effectiveness

(Dr. Meade):

Analyses were performed for the OABs, including CMA and BIA. For the BIAs, several of the model's key assumptions were varied, with corresponding sensitivity analyses conducted. The P&T Committee concluded (17 for, 0 against, 0 abstained, 0 absent) that for preferred formulary placement status, oxybutynin immediate release (IR) (Ditropan, generics) was the least costly agent based on the weighted average cost per day of treatment across all three POS, followed by oxybutynin extended release (ER) (Ditropan XL, generics), Detrol LA, Vesicare, Gelnique, Toviaz, Oxytrol, trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), Enablex, and tolterodine IR (Detrol, generics).

Budget impact analysis (BIA) results were presented to the P&T Committee and indicated that step therapy scenarios were more cost-effective compared to the current baseline (non step therapy). Results from the cost minimization analysis (CMA) and BIA showed that among available formulary options examined, the scenario where oxybutynin IR, oxybutynin ER, and Detrol LA were designated as step-preferred, with step therapy applied to ALL current and new users of non-preferred OAB products, was most cost-effective. This is referred to as “no grandfathering” of patients.

Overactive Bladder Agents (OABs)—UF Recommendation

(Dr. Meade):

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

- UF and step-preferred (e.g., “in front of the step”): Detrol LA, oxybutynin IR (Ditropan, generics), and oxybutynin ER (Ditropan XL, generics). Automated prior authorization (step therapy) would require that all patients try Detrol LA, oxybutynin IR, or oxybutynin ER before TRICARE will cover the other agents in this drug class.
- UF and non step-preferred (e.g., “behind the step”): trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), tolterodine IR (Detrol, generics) and Vesicare.
 - o When the generics to Sanctura, Sanctura XR, and Detrol become cost-effective relative to the step-preferred agents, the generics will become step-preferred without further action by the P&T Committee, Beneficiary Advisory Panel, or Director, TMA. A generic agent is cost-effective relative to step-preferred agents when the generic agent’s total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the step-preferred agent.
- NF and non step-preferred: Enablex, Toviaz, Oxytrol, and Gelnique.
- Step therapy would apply to all users (current and new) of the OAB drugs.

Overactive Bladder Agents (OABs)—PA Criteria

(Dr. Meade)

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) PA criteria for all current and new users of the OAB drugs, requiring a trial of Detrol LA, oxybutynin IR, or oxybutynin ER prior to the use of the other OAB drugs.

Automated PA Criteria: The patient has received a prescription for Detrol LA, oxybutynin IR or oxybutynin ER at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, **AND**

Manual PA criteria: If automated criteria are not met (e.g., a trial of Detrol LA, oxybutynin IR, or oxybutynin ER is not required) if:

- 1) The patient has experienced any of the following issues while receiving Detrol LA, oxybutynin IR, or oxybutynin ER, which is not expected to occur with Detrol IR, Sanctura, Sanctura XR, Vesicare, Enablex, Toviaz, Oxytrol, or Gelnique 10%:
 - a. inadequate response; **OR**
 - b. intolerable adverse effects (e.g., the patient requires Sanctura due to intolerable dry mouth with Detrol LA); **OR,**

- c. contraindication, **AND**
- 2) Coverage is only approved for the following FDA-approved indications:
- a. The patient has a confirmed diagnosis of OAB with symptoms of urge incontinence, urgency, and urinary frequency (for all 11 OAB drugs).
 - b. The patient is older than 6 years with symptoms of detrusor overactivity associated with a neurological condition (e.g., spina bifida), for oxybutynin ER.

Other uses, including stress incontinence, will not be approved.

Overactive Bladder Agents (OABs)—UF and PA Implementation Plan (Dr. Meade)

P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 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.

Addendum to UF Recommendation—After the meeting it was determined that bids could not be accepted by the contracting officer if a “no grandfather” scenario was recommended. On the advice of counsel, The P&T Committee was presented with the new pharmacoeconomic analysis and asked to provide their recommendation via electronic vote.

OABs—Addendum to UF Recommendation

The P&T Committee recommended (9 for, 5 opposed, 0 abstained, 3 absent) to approve the current scenario, which maintains the UF recommendation, step therapy requirements for all new and current users of OAB drugs, and PA criteria.

Overactive Bladder Agents (OABs)—Committee Physician’s Perspective

Dr. Kugler then briefed the BAP on the Committee physician’s perspective regarding this drug class. He noted that this is the third time that the Committee has reviewed the OAB drugs. Several products are now generic and Detrol LA is expected to go generic in 2014. Additionally, several new drugs were recently launched. The persistence rate of the drugs was evaluated and new clinical studies were considered. Persistence rates are low within DoD, with the mail order pharmacy having the highest persistence rates. The safety profiles of the agents in this class were also evaluated. At the meeting the Committee was unanimous in recommending step therapy for this class, requiring all patients to try Detrol LA, oxybutynin IR, or oxybutynin ER before using the other agents and that current users would not be grandfathered. After the meeting, the Committee was notified that contract considerations would require grandfathering of current users. An electronic vote was held and the Committee again voted that step therapy requirements should apply to all users.

Overactive Bladder Agents (OABs)—Panel Questions and Comments

Dr. Sampsel noted that DoD has a 180-day “look back” period built into the system and asked what the trial period would be for patients who wish to switch agents. Dr. Meade answered that the PA criteria take into account failures during the trial period and also noted that the turnover rate in this drug class is very high with people switching drugs all the time.

Dr. Khurana asked whether there would be notification of those patients already using the drugs about the new step therapy requirements. Dr. Meade said there would be and that was the reason for the 90-day implementation period. She also asked about the process for taking into account when drugs like Detrol and other non-formulary agents go generic. Dr. Meade answered that the PEC regularly evaluates what’s going on with these drugs and when they go generic they are evaluated and when they meet the “weighted average cost per day” threshold they are automatically moved from NF to UF status and the co-pay is reduced to zero.

Ms. Le Gette asked about the 90-day implementation period and whether that would be adequate, especially for Enablex and Oxytrol. Dr. Meade said that it would, especially because of the turnover rate.

Overactive Bladder Agents (OABs)—Panel Vote on UF Recommendations

The Chair indicated the BAP would take four votes on this drug class, voting first on the P&T Committee’s original recommendations and then on the addendum.

She then read the Committee’s original UF recommendation.

The P&T Committee recommended the following:

- 1) UF and step-preferred (e.g., “in front of the step”): Detrol LA, oxybutynin IR (Ditropan, generics), and oxybutynin ER (Ditropan XL, generics). Automated prior authorization (step therapy) would require that all patients try Detrol LA, oxybutynin IR, or oxybutynin ER before TRICARE will cover the other agents in this drug class.
- 2) UF and non step-preferred (e.g., “behind the step”): trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), tolterodine IR (Detrol, generics) and Vesicare.
 - o When the generics to Sanctura, Sanctura XR, and Detrol become cost-effective relative to the step-preferred agents, the generics will become step-preferred without further action by the P&T Committee, Beneficiary Advisory Panel, or Director, TMA. A generic agent is cost-effective relative to step-preferred agents when the generic agent’s total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the step-preferred agent.
- 3) NF and non step-preferred: Enablex, Toviaz, Oxytrol, and Gelnique.
- 4) Step therapy would apply to all users (current and new) of the OAB drugs.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Dr. Buchta noted an apparent typo in the first paragraph in the handout material. The staff agreed that there was a typo and indicated that it had been corrected in the final materials. The wording of the recommendation given above is correct. Dr. Buchta voted to concur.

Overactive Bladder Agents (OABs)—Panel Vote on PA Criteria

Ms. Fryar then read the P&T Committee's PA criteria recommendations.

The P&T Committee recommended PA criteria for all current and new users of the OAB drugs, requiring a trial of Detrol LA, oxybutynin IR, or oxybutynin ER prior to the use of the other OAB drugs.

Automated PA Criteria: The patient has received a prescription for Detrol LA, oxybutynin IR or oxybutynin ER at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, **AND**

Manual PA criteria: If automated criteria are not met (e.g., a trial of Detrol LA, oxybutynin IR, or oxybutynin ER is not required) if:

- 1) The patient has experienced any of the following issues while receiving Detrol LA, oxybutynin IR, or oxybutynin ER, which is not expected to occur with Detrol IR, Sanctura, Sanctura XR, Vesicare, Enablex, Toviaz, Oxytrol, or Gelnique 10%:
 - a. inadequate response; **OR**
 - b. intolerable adverse effects (e.g., the patient requires Sanctura due to intolerable dry mouth with Detrol LA); **OR**,
 - c. contraindication. **AND**
- 2) Coverage is only approved for the following FDA-approved indications:
 - a. The patient has a confirmed diagnosis of OAB with symptoms of urge incontinence, urgency, and urinary frequency (for all 11 OAB drugs).
 - b. The patient is older than 6 years with symptoms of detrusor overactivity associated with a neurological condition (e.g., spina bifida), for oxybutynin ER.

Other uses, including stress incontinence, will not be approved.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Overactive Bladder Agents (OABs)—Panel Vote on UF and PA Implementation Plan

Ms. Fryar read the Committee’s recommendation.

The P&T Committee recommended 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 BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Overactive Bladder Agents (OABs)—Panel Vote on Addendum

The Chair read the addendum to the previous P&T Committee UF recommendation.

Addendum to UF Recommendation—After the meeting it was determined that bids could not be accepted by the contracting officer if a “no grandfather” scenario was recommended. On the advice of counsel, The P&T Committee was presented with the new pharmacoeconomic analysis and asked to provide their recommendation via electronic vote.

The P&T Committee recommended to approve the current scenario, which maintains the UF recommendation, step therapy requirements for all new and current users of OAB drugs, and PA criteria.

Ms. Fryar asked for a clarification of the considerations that led to the second Committee vote. Dr. Meade answered that a post-meeting bid review determined that there were problems with the wording of the bid solicitations. The PEC re-did the cost-effectiveness calculations and presented them to the Committee along with alternative decisions. By an electronic vote, the Committee again approved the original recommendations.

Ms. Fryar indicated that she would vote to non-concur with the recommendation because of the large number of dissenting Committee votes (five) on the second pass. The number of dissenting Committee vote indicates that there was concern among P&T committee members.

The BAP vote was:

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

Comment: The Chair voted to non-concur for the reason noted.

III. UF CLASS REVIEWS— Gastrointestinal-2 Oral Antibiotics (GI-2)

(PEC Script)

Gastrointestinal-2 Oral Antibiotics (GI-2)—Relative Clinical Effectiveness

(LCDR Selvester)

Background: The GI-2 oral antibiotics are used for many FDA-labeled and unlabeled indications, often with relatively little high-quality clinical data supporting their use. The common thread is a local site of action in the GI tract, frequently with little systemic absorption. The Gastrointestinal-2 Oral Antibiotics (GI-2) Drug Class includes metronidazole (Flagyl, generics), vancomycin (Vancocin, generics), Xifaxan (rifaximin), Dificid (fidaxomicin), Alinia (nitazoxanide) and neomycin (Neo-Fradin, generics). This review focused on clinical effectiveness with regard to hepatic encephalopathy (which is altered brain function as a result of metabolic abnormalities that occur in patients with liver failure), Clostridium difficile infection (a diarrheal illness associated with recent antibiotic use), travelers' diarrhea, and non FDA-approved (off-label) uses.

Drugs in the GI-2 Drug Class are listed in Table 3 on page 4. The class has not been previously reviewed for UF placement. Figure 3 of the handout on page 4 shows the utilization of the agents.

The PORT provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- For hepatic encephalopathy (HE), Xifaxan is superior to lactulose in improving symptoms. While Xifaxan is approved for monotherapy, it is commonly used in combination with lactulose, and is better tolerated than lactulose.
- For Clostridium difficile infection (CDI):
 - Metronidazole is equally effective as vancomycin in treating mild to moderate CDI, but for severe CDI vancomycin results in higher clinical cure rates.
 - Dificid and vancomycin provide similar clinical cure rates for CDI; however, Dificid decreases recurrence and increases global cure rates to a greater extent than vancomycin.
 - Comparative efficacy for Alinia and Xifaxan for CDI cannot be assessed, given the small numbers of trials.
- For travelers' diarrhea (TD), practice guidelines and a systematic review recommend fluoroquinolones (e.g., levofloxacin, ciprofloxacin) as first line treatment. Xifaxan is FDA-approved for TD but is limited to TD caused by noninvasive strains of Escherichia coli.
- Xifaxan is not FDA-approved for irritable bowel syndrome, and there is insufficient evidence to support its use for that indication. Other non-supportable uses of Xifaxan include inflammatory bowel diseases (like Crohn's and Ulcerative Colitis), chronic abdominal pain, hepatitis, diabetes, rosacea, and many other non FDA-approved indications.

Pharmacy Outcomes Research Team report: The PORT analysis illustrated the following trends:

- Within the MHS, there is little utilization of Difucid, of which about 10% appears to be outside of the MHS's supportable uses.
- Use of Xifaxan within the MHS appears to be largely for indications outside of the MHS's supportable uses and for durations inconsistent with those supportable uses.

Gastrointestinal-2 Oral Antibiotics (GI-2)—Relative Cost Effectiveness

(Dr. Meade)

Pharmacoeconomic analyses, including CMA, were performed for the GI-2 Drug Class. Cost analyses were based on the disease states discussed in the clinical section. Cost analyses were based on the disease states discussed in the clinical section. Comparative costs for agents from other drug classes were considered (e.g., lactulose, fluoroquinolones), due to the conclusions from the clinical effectiveness review.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following: for hepatic encephalopathy, lactulose was the least costly agent, followed by lactulose in combination with neomycin, and then Xifaxan. For CDI, metronidazole was the least costly agent, followed by vancomycin, with Difucid as the most costly agent. For travelers' diarrhea, ciprofloxacin was the least costly agent followed by Xifaxan and Alinia.

Gastrointestinal-2 Oral Antibiotics (GI-2)—UF Recommendation

(Dr. Meade)

The P&T Committee recommended (14 for, 2 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the MHS.

- On the UF: metronidazole, vancomycin, neomycin, Xifaxan, Alinia, and Difucid

Gastrointestinal-2 Oral Antibiotics (GI-2)—PA Criteria

(Dr. Meade)

The P&T Committee recommended (15 for, 1 opposed, 1 abstained, 0 absent) PA criteria for Xifaxan 200 mg for travelers' diarrhea, and recommended (14 for, 2 opposed, 1 abstained, 0 absent) PA criteria for Xifaxan 550 mg for hepatic encephalopathy. Other uses of Xifaxan are not covered, including *C. difficile* infection, irritable bowel syndrome, inflammatory bowel diseases, chronic abdominal pain, hepatitis, diabetes, and rosacea.

Xifaxan 200 mg PA criteria: New users of Xifaxan 200 mg for travelers' diarrhea are required to undergo the PA process.

Automated PA Criteria: The patient has received a prescription for a fluoroquinolone at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 60 days, **AND**

Manual PA Criteria:

- 1) 200 mg tablets are approved for the following:
 - a. Documented use in travelers' diarrhea caused by noninvasive strains of *Escherichia coli* **AND**
 - b. Patient is between 12 and 18 years of age **OR**
 - c. Documented trial of a fluoroquinolone for patients > 18 years of age in last 60 days **OR**
 - d. Documented contraindication or allergy to fluoroquinolone antibiotics **OR**
 - e. Returning from area with high fluoroquinolone resistance **OR**
 - f. 200 mg tablets are being used to treat hepatic encephalopathy

- 2) 200 mg tablets are not approved for the following
 - a. Diarrhea complicated by fever or bloody stool
 - b. Treatment of dysentery
 - c. Diarrhea associated with use of antibiotics
 - d. Diarrhea caused by bacteria other than *E. coli*
 - e. *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved use

Xifaxan 550 mg PA criteria for hepatic encephalopathy: New users of Xifaxan 550 mg for hepatic encephalopathy are required to undergo the PA process. Prior authorization will expire after 365 days.

Manual PA Criteria:

- 1) 550 mg tablets are approved for the following:
 - a. Documented use in hepatic encephalopathy
- 2) 550 mg tablets are not approved for the following:
 - b. Travelers' diarrhea, *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved uses.

Gastrointestinal-2 Oral Antibiotics (GI-2)—UF and PA Implementation Plan

(Dr. Meade)

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS.

Gastrointestinal-2 Oral Antibiotics (GI-2)—Committee Physician’s Perspective

Dr. Kugler began by stating that this drug class had not been reviewed previously. The Committee looked at it in connection with drugs in other classes because of the various uses of these drugs. The Committee recommended that all six drugs be included on the UF. The Committee recognized that for travel diarrhea fluoroquinolone antibiotics are the preferred treatment and that Xifaxan 550 mg tablets are not a cost-effective treatment. The 550 mg tablets are also not approved for any uses not approved by the FDA, such as irritable bowel syndrome.

Gastrointestinal-2 Oral Antibiotics (GI-2)—Panel Questions and Comments

The Chair opened the floor for questions from the Panel and asked whether Difucid was now available both at MTFs and by mail order. Dr. Meade answered that it was not at the time the decision was made because a waiver was required but he understands that the waiver has now been obtained and is available at all points of service. Dr. Salom noted that a correction was needed on page 13 of the handout regarding the order in which the PA criteria are listed. Dr. Selvester agreed and indicated that the correction has already been made. Dr. Khurana asked for a clarification of the numbers shown on Table 3 found on page 4 of the handout. Dr. Meade replied that the graph is correct; there is very low or no usage for three of the agents in this class.

Gastrointestinal-2 Oral Antibiotics (GI-2)—Panel Vote on UF Recommendation

Ms. Fryar read the Committee’s UF recommendation.

The P&T Committee recommended the following scenario for the UF, which is the most clinically and cost-effective option for the MHS.

- Metronidazole, vancomycin, neomycin, Xifaxan, Alinia, and Difucid be maintained on the UF.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Gastrointestinal-2 Oral Antibiotics (GI-2)—Panel Vote on PA Criteria

The Chair read the recommended PA criteria.

The P&T Committee recommended PA criteria for Xifaxan 200 mg for travelers’ diarrhea, and recommended (14 for, 2 opposed, 1 abstained, 0 absent) PA criteria for Xifaxan 550 mg for hepatic encephalopathy. Other uses of Xifaxan are not covered, including *C. difficile* infection, irritable bowel syndrome, inflammatory bowel diseases, chronic abdominal pain, hepatitis, diabetes, and rosacea.

Xifaxan 200 mg PA criteria: New users of Xifaxan 200 mg for travelers’ diarrhea are required to undergo the PA process.

Automated PA Criteria: The patient has received a prescription for a fluoroquinolone at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 60 days, **AND**

Manual PA Criteria:

- 1) 200 mg tablets are approved for the following:
 - a. Documented use in travelers' diarrhea caused by noninvasive strains of *Escherichia coli* **AND**
 - b. Patient is between 12 and 18 years of age **OR**
 - c. Documented trial of a fluoroquinolone for patients > 18 years of age in last 60 days **OR**
 - d. Documented contraindication or allergy to fluoroquinolone antibiotics **OR**
 - e. Returning from area with high fluoroquinolone resistance **OR**
 - f. 200 mg tablets are being used to treat hepatic encephalopathy

- 2) 200 mg tablets are not approved for the following
 - a. Diarrhea complicated by fever or bloody stool
 - b. Treatment of dysentery
 - c. Diarrhea associated with use of antibiotics
 - d. Diarrhea caused by bacteria other than *E. coli*
 - e. *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved use

Xifaxan 550 mg PA criteria for hepatic encephalopathy: New users of Xifaxan 550 mg for hepatic encephalopathy are required to undergo the PA process. Prior authorization will expire after 365 days.

Manual PA Criteria

- 1) 550 mg tablets are approved for the following:
 - Documented use in hepatic encephalopathy
- 2) 550 mg tablets are not approved for the following:
 - Travelers' diarrhea, *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved uses.

Without further discussion, the BAP voted as follows:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Gastrointestinal-2 Oral Antibiotics (GI-2)—Panel Vote on UF and PA Implementation Plan

Ms. Fryar read the Committee's implementation plan recommendation.

The P&T Committee recommended an effective date of the first Wednesday after a 90-day implementation period in all POS.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

IV. UF CLASS REVIEWS— Hepatitis C Drug Class

(PEC Script)

Hepatitis C Drug Class—Relative Clinical Effectiveness

(LCDR Selvester)

Background: With the introduction of two new highly efficacious Direct Acting Antiviral drugs—boceprevir and telaprevir—in 2011, and the resultant updates in national clinical practice guidelines on the treatment of Hepatitis C, triple therapy (a DAA, ribavirin, and pegylated-interferon) supplanted traditional dual therapy (ribavirin and pegylated-interferon) as the standard of care. The main outcome is Sustained Viral Response, or SVR, which essentially means the virus is eradicated in the patient. The Hepatitis C Drug Class includes the direct acting antiviral agents (DAAs) Victrelis (boceprevir) and Incivek (telaprevir); the interferon products Pegasys (PEG-interferon alfa-2a), PEG-Intron (PEG-interferon alfa-2b), and Infergen (interferon alfacon-1); and, various ribavirin products, including generics. Intron A (Interferon alfa-2b) is no longer used for treating hepatitis C virus infection and will not be discussed further.

Drugs in the Hepatitis C Drug Class are listed in Table 4 on page 5. This drug class has not been previously reviewed for UF placement. Figures 4-6 of the handout on pages 5-6 show the utilization of these agents.

The PORT provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Triple therapy with a direct acting antiviral agent (boceprevir or telaprevir), PEG-interferon, and ribavirin increases sustained viral response (SVR) rates to a greater extent than dual therapy with PEG-interferon and ribavirin (PR).
- There is insufficient evidence to conclude whether Victrelis or Incivek is superior to the other, due to the lack of direct comparative trials. Incivek offers patient convenience due to its shorter treatment course than Victrelis (12 weeks versus 44 weeks), but this has not resulted in higher SVR rates.
- There is insufficient evidence to prefer Pegasys over PEG-Intron, but there do not appear to be clinically relevant differences in efficacy.
- Response-guided therapy for clinically appropriate patient populations maintains high levels

of efficacy while shortening drug exposure times and treatment course duration.

- Compared with PR dual therapy, Victrelis triple therapy increases the risk for anemia (a decrease in hemoglobin concentration) and Incivek triple therapy increases the risk for anemia and rash.

Pharmacy Outcomes Research Team report: The PORT analysis illustrated the following trends:

- Within the MHS, utilization patterns for the Hepatitis C agents are similar between MTF and civilian providers.
- There has been a rapid shift from dual-therapy to triple-therapy since publication of the new national guidelines.
- Small numbers of patients/providers have utilized the Direct-Acting Antivirals outside of guideline-recommended parameters.

Hepatitis C Drugs—Relative Cost Effectiveness

(Dr. Meade)

CMA was performed to compare each regimen for hepatitis C treatment (ribavirin, PEG-interferons, and DAAs). A cost-effectiveness analysis (CEA) was also performed comparing triple therapy (DAAs, PEG-interferon, and ribavirin) with dual therapy (PEG-interferon alfa and ribavirin). Additionally, a BIA was performed to compare competing formulary scenarios.

CMA results for the evaluated agents showed most dosage forms of ribavirin were generic and cost-effective. However, Ribapak was deemed not cost-effective compared with other ribavirin dosage forms. Both PEG-interferon alfa products (Pegasys and PEG-Intron) had comparable costs. Interferon alfacon-1 (Infergen) was identified as not cost-effective when compared with the PEG-interferon agents. CMA results for the DAAs showed response-guided therapy could be less costly with boceprevir than with telaprevir, based on current dosing recommendations. However, when each agent was taken over its full treatment duration, telaprevir was less costly than boceprevir.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that the most cost-effective scenario placed ribavirin (generics), Pegasys, Intron A, PEG-Intron, Victrelis, and Incivek as formulary on the UF, and ribavirin (Ribapak) and Infergen as NF on the UF.

Hepatitis C Drugs—UF Recommendation

(Dr. Meade)

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

- UF status for Victrelis, Incivek, Pegasys, PEG-Intron, Intron A, and ribavirin (except for the Ribapak formulation); and,
- NF status for Infergen and the ribavirin Ribapak formulation, due to the lack of compelling clinical advantages and cost disadvantages when compared to the UF products.

Hepatitis C Drugs—PA Criteria

(Dr. Meade)

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for Victrelis and Incivek. New users of Victrelis and Incivek are required to undergo the PA process. Prior authorization will expire after 12 weeks for Incivek and 44 weeks for Victrelis.

Manual PA Criteria:

- 1) Age \geq 18 **AND**
- 2) Has laboratory evidence of chronic hepatitis C—a quantified viral load (above undetectable) **AND**
- 3) Has laboratory evidence of genotype-1 hepatitis C infection **AND**
- 4) Is not co-infected with the human immunodeficiency virus (HIV) or Hepatitis B virus **AND**
- 5) Boceprevir or telaprevir will be co-administered with both a PEG-interferon alfa-2a or PEG-interferon alfa-2b product **AND** ribavirin, **AND**
- 6) The patient has not previously used Victrelis and Incivek. **AND**
- 7) For Victrelis, the patient will begin with a 4-week lead-in of both a PEG-Interferon alfa-2a or PEG-interferon alfa-2b product and ribavirin.

Hepatitis C Drugs—UF and PA Implementation Plan

(Dr. Meade)

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 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.

Hepatitis C Drugs—Committee Physician’s Perspective

Dr. Kugler began by stating this drug class has not previously been reviewed. The two new DAA drugs, Victrelis and Incivek, have improved the efficacy of hepatitis C treatment. One advantage of Incevik over Victrelis is that it takes a shorter time to get beneficial results. The risk of a potentially adverse reaction using these agents in triple therapy was discussed and factored in to the recommendations. The PA criteria require new users of Incevik and Victrelis to undergo the PA process, however there is no data on switching from one drug to another and no data on what to do if one course of treatment fails, so the terms of the PS are limited. There was no controversy over making Infergen and the ribavirin Ribapak NF as the other agents were more cost-effective. Dr. Kugler also noted there are several new products in the pipeline in this drug class and the Committee will re-review the class when they come out.

Hepatitis C Drugs—Panel Questions and Comments

Dr. Crum commented that it appears to him that the antiviral drugs are appropriate for triple therapy and he doesn't see how the Prior Authorization requirements add value to the administration of this drug class. Dr. Selvester answered that the PA requirements will help to ease a potential administrative problem stemming from the number of different drugs now being used to treat hepatitis C patients, help to ensure appropriate therapy and help to hold down costs.

Hepatitis C Drugs—Panel Vote on UF Recommendations

Ms. Fryar read the P&T Committee's UF recommendations for the hepatitis C drug class.

The P&T Committee recommended the following:

- UF status for Victrelis, Incivek, Pegasys, PEG-Intron, Intron A, and ribavirin (except for the Ribapak formulation); and,
- NF status for Infergen and the ribavirin Ribapak formulation, due to the lack of compelling clinical advantages and cost disadvantages when compared to the UF products.

Without further discussion, the BAP voted:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Hepatitis C Drugs—Panel Vote on PA Criteria

The Chair then read the recommended PA criteria for this drug class:

The P&T Committee recommended PA criteria for Victrelis and Incivek. New users of Victrelis and Incivek are required to undergo the PA process. Prior authorization will expire after 12 weeks for Incivek and 44 weeks for Victrelis.

Manual PA Criteria:

- 1) Age \geq 18 **AND**
- 2) Has laboratory evidence of chronic hepatitis C—a quantified viral load (above undetectable) **AND**
- 3) Has laboratory evidence of genotype-1 hepatitis C infection **AND**
- 4) Is not co-infected with the human immunodeficiency virus (HIV) or Hepatitis B virus **AND**
- 5) Boceprevir or telaprevir will be co-administered with both a PEG-interferon alfa-2a or PEG-interferon alfa-2b product **AND** ribavirin, **AND**
- 6) The patient has not previously used Victrelis and Incivek. **AND**
- 7) For Victrelis, the patient will begin with a 4-week lead-in of both a PEG-Interferon alfa-2a or PEG-interferon alfa-2b product and ribavirin.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Hepatitis C Drugs—Panel Vote on Implementation Plan

The Chair read the recommended implementation plan:

The P&T Committee recommended 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 BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

V. RECENTLY APPROVED U.S. FDA AGENTS

The Chair then called for the presentations on agents recently-approved by the FDA.

(PEC Script)

High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—Relative Clinical Effectiveness Conclusion

Background: Oxecta is a formulation of oxycodone IR that is tamper resistant but not tamper proof. FDA approval was based on demonstrated bioequivalence to the Roxycodone proprietary formulation of oxycodone IR. One small “drug liking” study showed a reduced “liking” for Oxecta versus Roxycodone, but the widespread clinical applicability of these results is unknown.

The P & T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Oxecta is the first abuse deterrent IR oxycodone formulation marketed. There is no evidence to suggest Oxecta has a compelling clinical advantage over the other high potency narcotic analgesics included on the UF.

High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—Relative Cost- Effectiveness Analysis and Conclusion

(Dr. Meade)

A pharmacoeconomic analysis was performed. The weighted average cost per tablet at all three points of service (POS) was evaluated for Oxecta in relation to the other drugs in the high potency narcotic subclass.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Oxecta was not

cost-effective when compared to other high potency narcotic analgesics included on the UF.

High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—UF Recommendation

(Dr. Meade)

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) Oxecta be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—UF 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.

High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—Committee Physician’s Perspective

Dr. Kugler said there was no controversy over the agent being recommended for NF placement. He also noted that there are several new narcotic analgesics products currently in the pipeline.

High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—Panel Questions and Comments

Dr. Sampsel asked whether current users would be grandfathered and whether they would be notified. Dr. Meade answered that at the time of the P&T Committee meeting there were no users of this drug in the MHS and even now there may be only a very few. They will be notified.

High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—Panel Vote on UF Recommendation

Ms. Fryar read the UF recommendation for Oxecta.

The P&T Committee recommended Oxecta be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—Panel Vote on UF Implementation Plan

Ms. Fryar read the UF implementation plan :

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 BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

VI. RE-EVALUATION OF NF AGENTS

(PEC Script)

(Dr. Meade)

On an ongoing basis, the DoD Pharmacoeconomic Center monitors changes in the clinical information, current costs, and utilization trends to determine whether the UF status of agents designated as NF needs to be readdressed. The P&T Committee's process for the re-evaluation of NF agents established at the May 2007 meeting was approved by the Director, TMA on June 24, 2007, and is outlined in Appendix A on page 36.

The P&T Committee reevaluated the UF status of escitalopram (Lexapro, generics) and pantoprazole (Protonix, generics) in light of recent price reductions in the generic formulations across all three POS.

Escitalopram—UF Recommendation and Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) reclassification of escitalopram (Lexapro, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

Pantoprazole—UF Recommendation and Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) reclassification of pantoprazole (Protonix, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

Re-evaluation of NF Agents—Committee Physician's Perspective

Dr. Kugler informed the Panel that these recommendations were non-controversial.

Re-evaluation of NF Agents—Panel Questions and Comments

The BAP members had no questions or comments on these recommendations.

Re-evaluation of NF Agents—Panel Vote on Escitalopram

The Chair read the recommendation.

The P&T Committee recommended reclassification of escitalopram (Lexapro, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Re-evaluation of NF Agents—Panel Vote on Pantoprazole

Ms. Fryar read the Committee’s recommendation.

The P&T Committee recommended reclassification of pantoprazole (Protonix, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

VII. UTILIZATION MANAGEMENT

(PEC Script)

(Dr. Meade)

Prior Authorizations

Phosphodiesterase-5 (PDE-5) Inhibitors—

The PA criteria for the PDE-5 Inhibitor Drug Class was reviewed. Prior authorization allows use of a PDE-5 inhibitor following prostatectomy for preservation/restoration of erectile function for one year. There is no published evidence suggesting benefit if the PDE-5 inhibitor is initiated beyond one year after surgery. Recommendations were to clarify the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed.

The additional recommendations were:

- For Cialis: that existing criteria that apply to patients with benign prostatic hyperplasia (BPH) also apply to patients with BPH and erectile dysfunction (ED); and,
- For sildenafil used for primary pulmonary hypertension (PPH): that the sildenafil dosage formulation specifically state 20 mg tablets to discourage use of sildenafil 20 mg tablets for ED.

Phosphodiesterase-5 (PDE-5) Inhibitors—Committee Physician’s Perspective

Dr. Kugler said these recommendations were non-controversial.

Phosphodiesterase-5 (PDE-5) Inhibitors—Panel Questions and Comments

The Panel had no questions on the PDE-5 inhibitor PA recommendations.

Phosphodiesterase-5 (PDE-5) Inhibitors—Panel Vote on PA Criteria

Ms. Fryar read the recommended PA criteria.

The P&T Committee recommended PA criteria for the PDE-5 inhibitors (1) clarifying the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed; (2) for Cialis, that the existing criteria also apply to patients with BPH and ED; and (3) for sildenafil for PPH, that the sildenafil dosage formulation will specifically state 20 mg tablets.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Utilization Management—Testosterone Replacement Therapy (TRT)—PA Criteria

(PEC Script)

(Dr. Meade)

PA criteria for the TRT Drug Class were developed at the August 2012 meeting and signed by the Director, TMA on November 8, 2012. The P&T Committee reviewed the PA criteria for use of TRT in women, which was based on level A evidence from the American College of Obstetrics and Gynecology, as outlined in a 2011 Clinical Bulletin. The Clinical Bulletin specifically mentions that there is little evidence to support long-term TRT use (longer than 6 months) in women.

TRT USE IN WOMEN PA CRITERIA—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the PA criteria for use of TRT in women to limit use to six months.

TRT Use in Women PA Criteria—Committee Physician’s Perspective

Dr. Kugler said this recommendation was not controversial.

TRT Use in Women PA Criteria—Panel Questions and Comments

Dr. Salom asked about the reason for the one abstaining vote on the P&T Committee since there was nothing controversial about the recommendation. Dr. Meade answered that one member of the P&T Committee represents the Veterans Administration and that he votes only on clinical effectiveness and cost considerations.

TRT Use in Women PA Criteria—Panel Vote

The Chair read the Committee’s recommendation.

The Committee recommended revising the PA criteria for use of TRT in women to limit use to six months.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Utilization Management—Injectable Gonadotropins—PA Criteria

(PEC Script)

(Dr. Meade)

PA criteria currently apply to the injectable gonadotropins (fertility agents). Injectable gonadotropins are not covered under the TRICARE pharmacy benefit if they are being used in conjunction with a noncoital reproductive technology. In 2010, the Assistant Secretary of Defense for Health Affairs (ASD(HA)) authorized in vitro fertilization services for the benefit of severely or seriously ill/injured active duty service members. Implementation guidance for these services was developed in an April 2012 ASD(HA) policy.

INJECTABLE GONADOTROPINS PA CRITERIA—The P&T Committee recommended (15 for, 0 opposed, 2 abstained, 0 absent) revising the PA criteria for the injectable gonadotropins (fertility agents), to allow for use in conjunction with a noncoital reproductive technology, as outlined in the ASD(HA) April 2012 “Policy for Assisted Reproductive Services for the Benefit of Seriously or Severely Ill/Injured (Category II or III) Active Duty Service Members.” A Signed Authorization Memorandum from TMA must be included with the prescription.

Injectable Gonadotropins—Committee Physician’s Perspective

Dr. Kugler said there was no controversy regarding this recommendation.

Injectable Gonadotropins—Panel Questions and Comments

Ms. Fryar asked what the process would be for validating the eligibility of potential beneficiaries. Dr. Meade indicated that the requests would go through Dr. Kugler’s Office; Dr. Kugler confirmed that process.

Injectable Gonadotropins—Panel Vote on PA Criteria

Ms. Fryar read the Committee’s PA criteria recommendations.

The P&T Committee recommended revising the PA criteria for the injectable gonadotropins (fertility agents), to allow for use in conjunction with a noncoital reproductive technology, as outlined in the

ASD(HA) April 2012 “Policy for Assisted Reproductive Services for the Benefit of Seriously or Severely Ill/Injured (Category II or III) Active Duty Service Members.” A Signed Authorization Memorandum from TMA must be included with the prescription.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Utilization Management—Adalimumab (Humira)—PA Criteria

(PEC Script)

(Dr. Meade)

The FDA recently approved a new indication for Humira, the designated ECF agent in the targeted immunomodulatory biologics (TIBs) Drug Class. Humira is now indicated for the treatment of moderately to severely active ulcerative colitis following inadequate response to immunosuppressants such as corticosteroids, azathioprine, and 6-mercaptopurine.

ADALIMUMAB (HUMIRA) PA CRITERIA—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the existing PA criteria for Humira to incorporate the new indication for ulcerative colitis, consistent with the FDA-approved product labeling.

Adalimumab (Humira)—Committee Physician’s Comments

Dr. Kugler said this recommendation was non-controversial also.

Adalimumab (Humira)—Panel Comments and Questions

The BAP members had no questions or comments regarding this recommendation.

Adalimumab (Humira)—Panel Vote on PA Criteria

Ms. Fryar read the recommended PA criteria.

The P&T Committee recommended revising the existing PA criteria for Humira to incorporate the new indication for ulcerative colitis, consistent with the FDA-approved product labeling.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

Utilization Management—Enzalutamide (Xtandi) and Abiratone (Zytiga)

(PEC Script)

(Dr. Meade)

Two new drugs for metastatic castration-resistant prostate cancer were recently approved. Xtandi and Zytiga are costly agents with specific FDA-indications, requiring use of prior docetaxel-containing regimens.

ENZALUTAMIDE (XTANDI) AND ABIRATONE (ZYTIGA) PA CRITERIA—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for enzalutamide (Xtandi), and abiratone (Zytiga), consistent with the FDA-approved product labeling.

Enzalutamide (Xtandi) and Abiratone (Zytiga)—Committee Physician’s Perspective

Dr. Kugler had no comments to add regarding this recommendation.

Enzalutamide (Xtandi) and Abiratone (Zytiga)—Panel Questions and Comments

There were no questions or comments on this recommendation.

Enzalutamide (Xtandi) and Abiratone (Zytiga)—Panel Vote on PA Criteria

The Chair read the PA criteria recommended.

The P&T Committee recommended PA criteria for enzalutamide (Xtandi), and abiratone (Zytiga), consistent with the FDA-approved product labeling.

- 1) Xtandi PA Criteria: Coverage approved for treatment of patients:
 - a. With a documented diagnosis of metastatic castration-resistant prostate cancer, **AND**
 - b. Previous treatment with docetaxel.

- 2) Zytiga PA Criteria: Coverage approved for treatment of patients:
 - a. With a documented diagnosis of metastatic castration-resistant prostate cancer, **AND**
 - b. Prior chemotherapy with docetaxel, **AND**
 - c. Patient is receiving concomitant therapy with prednisone.

The BAP vote was:

Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

UTILIZATION MANAGEMENT—SECTION 703 REVIEWS

(PEC Script)

(Dr. Meade)

Section 703—The P&T Committee reviewed Kaon (branded potassium gluconate) and Pamine (branded methscopolamine) to determine Medical Necessity and pre-authorization criteria. These two products were identified as not fulfilling refund requirements required in section 703 of the 2008 National Defense Authorization Act (the drug manufacturers have not signed an agreement). These drugs were designated NF on the UF at previous P&T Committee meetings.

Section 703—Panel Comments and Questions

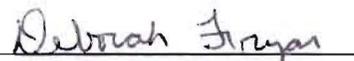
The Chair noted that there was no recommendation for action on this item. Dr. Meade explained that this a “for information” item and no Panel action is needed. Both products were previously made non formulary and voted on by the BAP. The Committee action means that the physician must now state why these drugs cannot be obtained through the Mail Order Pharmacy in order to qualify for a refund.

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. Kugler.

She indicated that the next tentative scheduled public meeting of the Panel is Thursday, March 28, 2013.

CDR Lawrence, the DFO, closed the meeting at 10:45 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
- ASD(HA)—Assistant Secretary of Defense for Health Affairs
- BAP — Uniform Formulary Beneficiary Advisory Panel (the “Panel” referred to above)
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- CDI—Clostridium difficile infection
- CEA — Cost-effectiveness analysis
- CFR — Code of Federal Regulations
- CMA — Cost-Minimization Analysis
- CPG — Clinical Practice Guideline
- CR — Controlled Release (a drug formulation)
- DAA—Direct Acting Antiviral drugs
- DFO — Designated Federal Officer
- DoD — Department of Defense
- 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-2—Gastrointestinal Oral Antibiotics (a drug class)
- GLP1RAs—Glucagon-Like Peptide-1 Receptor Agonists (a drug subclass)
- HE—Hepatic encephalopathy
- 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)
- OAB—Overactive Bladder Drugs (a drug class)
- OTC — Over the counter
- PA — Prior Authorization

- P&T Committee — DoD Pharmacy and Therapeutics Committee
- PDE-5—Phosphodiesterase-5 Inhibitors (a drug class)
- PDTS — Pharmacy Data Transaction Service
- PEC — DoD Pharmacoeconomic Center
- PORT — Pharmacy Outcomes Research Team
- POS — Point of Service
- PR—Peg-Interferon and ribavirin dual therapy
- RCTs — Randomized Control Trials
- SR — Sustained release (a drug formulation)
- SU—Sulfonylurea
- SVR—Sustained viral response
- TD—Travelers' diarrhea
- 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

Criteria for Re-evaluation of Nonformulary Drugs for Uniform Formulary Status

The P&T Committee's process for the re-evaluation of nonformulary (NF) agents established at the May 2007 meeting was approved by the Director, TMA on June 24, 2007, according to the criteria below:

- 1) The NF agent becomes generically available and a) The generic product is "A-rated" as therapeutically equivalent to the brand name product according to the FDA's classification system.
b) The generic market supply is stable and sufficient to meet the DoD Military Health System supply demands.

- 2) The NF agent is cost-effective relative to similar agents on the Uniform Formulary (UF). A NF agent becomes cost-effective when: a) The NF agent's total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the UF class to which they were compared.
b) The NF agent's total weighted average cost based on an alternate measure used during the previous review is less than or equal to that for the UF class to which they were compared. For example, antibiotics may be compared on the cost per course of therapy used to treat a particular condition.