EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel (BAP) Comments
27 June 2013

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy and Therapeutics Committee May 2013 Meeting.

1. UF CLASS REVIEWS – ANTI-GOUT DRUGS:

A. ANTI-GOUT DRUGS – UF RECOMMENDATIONS: The P&T Committee recommended (12 for, 4 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the Military Health System (MHS):

- allopurinol be designated UF and step-preferred (e.g., "in front of the step");
- febuxostat (Uloric) be designated NF and non step-preferred (e.g., "behind the step"); and
- colchicine (Colcrys), probenecid, and the fixed dose combination of colchicine/probenecid be designated formulary on the UF and exempt from step therapy.
- This recommendation includes step therapy, which requires a trial of allopurinol prior to using febuxostat (Uloric) in all current and new users of febuxostat.

***Summary of Physician's Perspective*:**

Dr. Kugler provided the BAP with the physician's perspective on the P&T Committee's recommendations. Dr. Kugler noted that Uloric is being recommended for NF placement and non-step preferred. There will be no grandfathering, which means that all exiting Uloric patients as well as new users will need to try allopurinol first. The recommendation includes notification of current Uloric users as well as notification of retail pharmacies. Colcrys is recommended for UF designation and is exempt from step therapy as it is used for acute gout. However it is high cost because it is administered with prednisone.

***Summary of Panel Vote/Comments*:**

Dr. Salom asked how many patients will be affected by making Uloric NF and placing it behind the step. The answer provided was about 10,000. Dr. Salom then asked how many patients are expected to switch from Uloric. Dr. Meade answered that it would be less than 10,000 but there is no definite number as yet.

Dr. Khurana noted that the manual PA criterion (a)(1) requires at least 300 mg per day of allopurinol in an adequate trial of that drug. She asked if there is a duration associated with that trial. Dr. Meade answered that the duration is left up to the

physician.

- Without further discussion, the Panel voted on the UF Recommendations as follows:

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA: 

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

B. ANTI-GOUT DRUGS — PA CRITERIA RECOMMENDATIONS: After extensive discussion, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for all current and new users of febuxostat (Uloric), requiring a trial of allopurinol prior to use of febuxostat. Coverage will be approved if the patient meets any of the following criteria:

1. Automated PA Criteria: The patient has received a prescription for allopurinol at any MHS pharmacy point service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order)] during the previous 180 days, AND

2. Manual PA Criteria: If automated criteria are not met, febuxostat (Uloric) is approved (e.g., a trial of allopurinol is not required) if:

   a) The patient has experienced any of the following issues with at least one of the following with allopurinol, which is not expected to occur with febuxostat (Uloric):

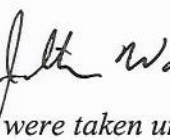
      (1) The patient has had an inadequate response to allopurinol (failure to achieve serum uric acid levels < 6 mg/day) after an adequate trial (at least 300 mg per day of allopurinol)

      (2) The patient has had intolerable adverse effects (e.g., hypersensitivity) to allopurinol

      (3) The patient has a contraindication to allopurinol (e.g., renal impairment)

- Without further discussion, the Panel voted on the PA Criteria as follows:

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA: 

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

C. ANTI-GOUT DRUGS— IMPLEMENTATION PLAN RECOMMENTATIONS: 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 points of service (POS); 2) TMA send a letter to beneficiaries affected by the UF and PA decisions. Additional recommendations made by the P&T Committee were to provide messaging to retail pharmacies to designate that PA and step therapy is required, with a trial of allopurinol prior to febuxostat (Uloric) and that the Anti-Gout Drug Class be added to the Rapid Response Program for the Retail Network and Mail Order Pharmacy.

- Without further discussion, the Panel voted on the Implementation Plan as follows:

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA: *These comments were taken under consideration prior to my final decision.*

II. UF CLASS/SUBCLASS REVIEWS— CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) AGENTS – PULMONARY II DRUGS

A. PULMONARY II DRUGS— UF RECOMMENDATIONS: The P&T Committee recommended (12 for, 1 opposed, 2 abstained, 2 absent) aclidinium inhaler (Tudorza), tiotropium inhaler (Spiriva), ipratropium nebulized solution (Atrovent; generic), ipratropium/albuterol nebulized solution (DuoNeb; generic), ipratropium HFA MDI (Atrovent HFA), ipratropium/albuterol soft mist inhaler (Combivent Respimat), and roflumilast (Daliresp) remain designated UF. Ipratropium/albuterol MDI (Combivent) will remain designated UF, pending discontinuation in December 2013.

Summary of Physician's Perspective:

Dr. Kugler informed the Panel that the Pulmonary I Drug Class will be reviewed at the November meeting of the P&T Committee. He noted that no drugs in the Pulmonary II Class are recommended for NF placement. He also said that there are several new COPD drugs in the pipeline now that are close to FDA approval.

Summary of Panel Vote/Comments:

Dr. Khurana asked whether existing Combivent users will automatically be given the new Combivent when the CFC inhaler is phased out in December. Dr. Meade answered that it depends on which pharmacy the beneficiary is using. Dr. Salom suggested that it might be a good idea to let those people affected by the switch know that the change is coming. He recommended that users be notified.

- Without further discussion, the Panel voted on the UF recommendations as follows:

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Additional Panel Comments/Questions:

Later in the meeting the question was asked whether the Panel needs to formally vote on the recommendation to make notification on the discontinuation of Combivent. The answer given by the Alternate DFO was that no formal BAP action is required beyond including the comment that the Panel agreed to recommend that notification should be given.

Additional Note from the Alternate DFO:

The transition from Combivent will be handled by individual pharmacies in the normal course of business. The pharmacist should contact the physician to facilitate the change.

Director, TMA: *These comments were taken under consideration prior to my final decision.*

III. RECENTLY – APPROVED USFDA AGENTS:

A. NON-INSULIN DIABETES DRUGS: SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITORS – CANAGLIFLOZIN (INVOKANA)

1) **Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) — UF Recommendations:** The P&T Committee recommended (13 for, 1 opposed, 1 abstained, 2 absent) canagliflozin (Invokana) be designated NF due to the lack of compelling clinical advantages, safety concerns, lack of long-term outcomes and adverse event data, and cost disadvantage compared to UF products.

Summary of Physician's Perspective:

Dr. Kugler noted that the P&T Committee discussed the agent's modest efficacy as well as safety concerns. He said there is limited data available regarding both its effectiveness and its safety so the Committee wanted to take a conservative approach to Invokana. The agent is also more costly than other agents in its class. He also noted that the PA criteria recommended are similar to those in place for other DPP-4 inhibitors. New users will be required to try metformin, a sulfonylurea or a DPP-4 inhibitor before Invokana.

Summary of Panel Vote/Comments:

Dr. Khurana asked whether the 30-day implementation period would be enough time. Dr. Meade said that there are very few users so far so the change can be made quickly.

Note: A pharmaceutical manufacturer representative asked to address the panel. The request was denied. Per DoDI 5105.04, Department of Defense Federal Advisory Committee Management Program, the public shall not participate in the Committee member's deliberations, unless otherwise authorized. The process to address the Panel is outlined in the Federal Register Notice which was published on 3 June 2013. Interested parties or groups may register prior to the meeting to address the Panel or submit written comments to be read into the minutes.

- Without further discussion, the Panel voted on the UF Recommendations:

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA: *These comments were taken under consideration prior to my final decision.*

2) NON-INSULIN DIABETES DRUGS: SGLT2 INHIBITORS CANAGLIFLOZIN (INVOKANA) — PA CRITERIA:

In the Non-Insulin Diabetes Drug Class, existing automated prior authorization (step therapy) requires a trial of metformin or a sulfonylurea, prior to the use of a DPP-4 inhibitor, a TZD, or a GLP1RA, based on positive efficacy and long-term outcomes data with metformin and the sulfonylureas.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) a trial of metformin, a sulfonylurea, or a DPP-4 inhibitor in all new and current users of SGLT2 inhibitors, canagliflozin (Invokana), due to the modest hemoglobin A1c lowering and safety concerns.

1. Automated PA criteria: The patient has filled a prescription for metformin, a sulfonylurea or a DPP4-inhibitor at any Military Health System (MHS) pharmacy point of service (POS) [military treatment facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.
2. Manual PA criteria, if automated criteria are not met: An SGLT2 inhibitor, canagliflozin (Invokana), is approved (e.g., trial of metformin or sulfonylurea or a DPP-4 inhibitor is NOT required) if:

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

   b) The patient has experienced any of the following adverse events on sulfonylurea: hypoglycemia requiring medical treatment.

c) The patient has had inadequate response to metformin or a sulfonylurea or a DPP-4 inhibitor.

d) The patient has a contraindication to metformin or a sulfonylurea or a DPP-4 inhibitor.

- Without further discussion, the Panel voted on the PA Criteria as follows:

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA: *These comments were taken under consideration prior to my final decision.*

3) **NON-INSULIN DIABETES DRUGS: SGLT2 INHIBITORS CANAGLIFLOZIN (INOKANA) — IMPLEMENTATION PLAN:** The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) 1) an effective date of the first Wednesday after a 30-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by the UF and PA decisions.

Without further discussion, the Panel voted on the Implementation Plan as follows:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA *These comments were taken under consideration prior to my final decision.*

IV. UTILIZATON MANAGEMENT ISSUES — PANTOPRAZOLE:

A. PROTON PUMP INHIBITORS (PPIs): PANTOPROZOLE CHANGE FROM NON-PREFERRED TO STEP-PREFERRED STATUS: The PPIs currently have PA criteria (step therapy) requiring a trial of omeprazole or esomeprazole (Nexium) prior to use of the other PPIs. Omeprazole and esomeprazole are BCF and step-preferred. In November 2012, the P&T Committee recommended reclassification of pantoprazole as formulary on the UF, due to availability of cost-effective generic formulations; pantoprazole remained non-preferred. The other PPIs, lansoprazole (Prevacid), rabeprazole (Aciphex), and omeprazole/sodium bicarbonate (Zegerid), are NF and non-preferred. The cost of generic pantoprazole tablets has continued to decline since November 2012. The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the PA criteria to designate pantoprazole as step-preferred (i.e., in front of the step) on the UF.

***Summary of Physician's Perspective*:**

Dr. Kugler informed the Panel that there was no controversy about making this change as the price of generic pantoprazole has continued to fall since last November's P&T Committee meeting.

***Summary of Panel Vote/Comments*:**

Dr. Salom asked whether this is one of the largest drug classes. Dr. Meade replied that it is.

- Without further discussion, the Panel voted on the revised PA Criteria as follows:

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA: *These comments were taken under consideration prior to my final decision.*

B. UTILIZATION MANAGEMENT ISSUES — VASCEPA:

1) ANTILIPIDEMIC-2: ICOSAPENT ETHYL(VASCEA)—PA CRITERIA: Icosapent ethyl (Vascepa) is the second prescription fish oil product marketed. Icosapent ethyl has the same FDA-approved labeling and dosing as omega-3-acid ethyl esters (Lovaza). Vascepa is not as effective as Lovaza at lowering triglycerides, but does not adversely affect LDL levels. PA criteria apply to Lovaza, limiting use to the FDA-approved indications, due to the large number of off-label, non-supportable uses. The P&T Committee recommended manual PA criteria for all current and new users of Vascepa, limiting use to the FDA-approved indication; the manual PA criteria for Vascepa will be the same as criteria for Lovaza.

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) manual PA criteria for all current and new users of Vascepa, limiting use to the FDA-approved indication.

New and current users of Vascepa are required to undergo the PA process.

1. Manual PA Criteria—Vascepa is approved if:

   a) Patients Receiving Statins:

      (1) Patients with triglyceride (TG) Levels > 500 mg/dL AND

      (2) Inadequate TG-lowering response to a therapeutic trial of niacin (1-g/day), unable to tolerate niacin/fibrate or who are not a candidate for niacin/fibrate therapy * †

   b) Patients NOT Receiving Statins:

      (1) Patients with TG Levels > 500 mg/dL AND

(2) Inadequate response to a therapeutic trial of monotherapy with both a fibrate and niacin (1-2 g/day), unable to tolerate a fibrate and niacin or who are not candidates for fibrates † and niacin therapy

c) Patients with TG <500 mg/dL or <500 mg/dL with an inadequate TG-lowering response to niacin or fibrates or who are unable to tolerate/are not candidates for niacin or fibrates

d) Coverage is not approved for the use of Vascepa for the treatment of other conditions, including: a*ttention deficit hyperactivity disorder*, Alzheimer's disease, bipolar disorder, Crohn's disease, cystic fibrosis, dementia, depression, inflammatory bowel disease, intermittent claudication, metabolic syndrome, osteoporosis, post-traumatic stress disorder, renal disease (IgA nephropathy), rheumatoid arthritis, schizophrenia, Type 2 diabetes mellitus, and ulcerative colitis.

* Not candidates for niacin: patients with a history of confirmed PUD (perforation, ulceration, or upper GIB), gouty attacks (presence of intra-articular uric acid crystals in the affected joint), and/or poorly controlled diabetes.

† Not candidates for fibrates: patients with hepatic or severe renal dysfunction, including primary biliary cirrhosis and preexisting gallbladder disease.

Summary of Physician's Perspective:

Dr. Kugler said the Committee had discussed the several off-label uses of Vascepa, noting that it has the same approved label and dosing as Lovaza, another prescription fish oil product. PA criteria have been applied to Lovaza due to the large number of unsupportable off-label uses. The Committee voted to limit use to FDA-approved indications and recommended the same PA criteria as used for Lovaza.

Summary of Panel Vote/Comments:

Dr. Salom asked how many patients are using this medication. The answer is 639.

- Without further discussion, the Panel voted on the PA Criteria as follows:

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA: *These comments were taken under consideration prior to my final decision.*

2) **ANTILIPIDEMIC-2: ICOSAPENT ETHYL (VASCEPT)—PA IMPLEMENTATION PLAN:** 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.

- Without further discussion, the Panel voted on the Implementation Plan as follows::

  Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Director, TMA:

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

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
June 27, 2013
Washington, D.C.

Panel Members Present:

- Ira Salom, Chairperson
- Kathryn Buchta
- Steven Hein
- Amit Khurana
- Lisa Le Gette
- Katherine O'Neill-Tracy

Members Not Present:

- John Crum
- Elizabeth Sampsel
- Robert Duane Tackitt

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. William Blanche, the Alternate Designated Federal Officer (DFO), called the proceedings to order at 9:00 A.M. Mr. Blanche indicated the Panel has been convened to review and comment on the therapeutic drug class recommendations resulting from the May 15, 2013 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:*
    - Anti-Gout Medications
    - Chronic Obstructive Pulmonary Disease Agents – Pulmonary II Drugs
  - *Designated Newly Approved Drugs:*
    - Non-Insulin Diabetes Drugs – Sodium Glucose Co-Transporter (SGLT2) Inhibitors – canagliflozin (Invokana)

- *Utilization Management Issues*
    - Prior Authorization Criteria
        - Proton Pump Inhibitors: Generic Pantoprazole – move to preferred therapy
        - Antilipidemics 2 – Prescription fish oil: Icosapent ethyl (Vascepa) – Prior Authorization

Opening Remarks

Mr. Blanche 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, Mr. Blanche 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 Alternate 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.

Mr. Blanche introduced the individual Panel members (see list above) and noted housekeeping considerations.

Private Citizen Comments

The Alternate DFO then opened the meeting for private citizen comments. Mr. Blanche stated that a letter had been received from Legacy and distributed to Panel members for their consideration. An observer at the meeting requested to comment, however the Alternate DFO informed him that FACA procedures require private citizens to register in advance in order to comment at the meeting. There were no other public comments.

Chairperson's Opening Remarks

The alternate DFO next turned the meeting over to Dr. Ira Salom who opened the meeting for the first drug class review presentation.

DRUG CLASS REVIEW PRESENTATIONS

(PEC Script)
(Dr. Meade)

I'm Dave Meade, Director of Clinical Operations at the Pharmacoeconomic Center ("PEC" for short). Joining me 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. Also joining us is LT Kendra Jenkins, a managed care pharmacy resident.

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 two Uniform Formulary Drug Classes (or sub-classes) gout agents and chronic obstructive pulmonary disease agents (Pulm 2) Additionally, one newly approved drug was reviewed – canagliflozin (Invokana)

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 CLASSREVIEWS— Anti-Gout Drugs

(PEC Script)
(Dr. Meade)

P&T Comments

A. Anti-Gout Drugs—Relative Clinical Effectiveness and Conclusion

The Anti-Gout Drug Class has not been previously reviewed for UF placement. Drugs in the class include allopurinol (Zyloprim, generic), probenecid, colchicine (Colcrys), colchicine/probenecid, and febuxostat (Uloric).

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

- Colchicine is a very old drug that is available in one branded formulation, (Colcrys), which has a patent extending to 2029.
- For an acute gout attack, clinical practice guidelines support colchicine as first line treatment, along with non-steroidal anti-inflammatory agents (NSAIDs) or prednisone. Treatment should be initiated within the first 24 hours of symptom onset.
- For chronic gout, urate-lowering therapy (ULT) with allopurinol or febuxostat is recommended as first line. Based on head-to-head trials, febuxostat (Uloric) 40 mg and allopurinol 300 mg were equally efficacious in lowering serum uric acid (sUA) to less than 6mg/dL in one study (CONFIRMS). Febuxostat 80 mg was superior to allopurinol 300 mg in lowering sUA to less than 6mg/dL in two studies (FACT and APEX).
- Higher doses of allopurinol (doses > 300mg), while commonly used and not well studied, may be required to decrease sUA in some patients.
- Use of colchicine for prophylaxis helps prevent gout flares during initiation of ULT. However, in published trials, gout flares increased when prophylaxis was discontinued. Guidelines recommend administering colchicine or NSAID prophylaxis for up to 6 months.
- Head-to-head studies show similar rates of adverse events with febuxostat and allopurinol.
- Febuxostat warnings from the U.S. Food and Drug Administration (FDA) include liver enzyme elevations. Liver function tests should be tested at initiation of therapy and monitored throughout treatment.
- Febuxostat warnings from the European Medicines Association (EMA) include the potential for increased cardiovascular (CV) events. According to the EMA, febuxostat should not be used in patients with ischemic heart disease or congestive heart failure, due to increased risk of CV events.

B. Anti-Gout Drugs—Relative Cost-Effectiveness Analysis and Conclusion

Pharmacoeconomic analyses were performed for the Anti-Gout Drug Class, including cost-minimization analysis (CMA) and budget impact analyses (BIAs). The class was subdivided into chronic drugs (allopurinol and febuxostat) and acute drugs (colchicine). 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 opposed, 0 abstained, 0 absent) generic allopurinol (Zyloprim) was the most cost-effective of the chronic drugs, followed by branded febuxostat (Uloric), based on the weighted average cost per day of treatment across all three POS. Branded colchicine (Colcrys) was the only acute agent examined in the analysis; a cost analysis was conducted. CMA and BIA results showed that among available formulary options examined, scenarios where allopurinol (Zyloprim) is the step-preferred agent, febuxostat (Uloric) is the NF non-preferred agent (with all current and new users required to try allopurinol first), and colchicine (Colcrys) is UF presented a maximum cost-avoidance projection.

C. Anti-Gout Drugs—UF Recommendation The P&T Committee recommended (12 for, 4 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the Military Health System (MHS):

- allopurinol be designated UF and step-preferred (e.g., "in front of the step");
- febuxostat (Uloric) be designated NF and non step-preferred (e.g., "behind the step"); and
- colchicine (Colcrys), probenecid, and the fixed dose combination of colchicine/probenecid be designated formulary on the UF and exempt from step therapy.
- This recommendation includes step therapy, which requires a trial of allopurinol prior to using febuxostat (Uloric) in all current and new users of febuxostat.

D. Anti-Gout Drugs—Prior Authorization (PA) Criteria

After extensive discussion, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for all current and new users of febuxostat (Uloric), requiring a trial of allopurinol prior to use of febuxostat. Coverage will be approved if the patient meets any of the following criteria:

1. Automated PA Criteria: The patient has received a prescription for allopurinol at any MHS pharmacy point service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order)] during the previous 180 days, AND

2. Manual PA Criteria: If automated criteria are not met, febuxostat (Uloric) is approved (e.g., a trial of allopurinol is not required) if:

    a) The patient has experienced any of the following issues with at least one of the following with allopurinol, which is not expected to occur with febuxostat (Uloric):

        (1) The patient has had an inadequate response to allopurinol (failure to achieve serum uric acid levels < 6 mg/day) after an adequate trial (at least 300 mg per day of allopurinol)

(2) The patient has had intolerable adverse effects (e.g., hypersensitivity) to allopurinol

(3) The patient has a contraindication to allopurinol (e.g., renal impairment)

E. Anti-Gout Drugs—UF and PA Implementation Plan

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 points of service (POS); 2) TMA send a letter to beneficiaries affected by the UF and PA decisions. Additional recommendations made by the P&T Committee were to provide messaging to retail pharmacies to designate that PA and step therapy is required, with a trial of allopurinol prior to febuxostat (Uloric) and that the Anti-Gout Drug Class be added to the Rapid Response Program for the Retail Network and Mail Order Pharmacy.

F. Anti-Gout Drugs— Physician's Perspective

Dr. Kugler provided the BAP with the physician's perspective on the P&T Committee's recommendations. Dr. Kugler noted that Uloric is being recommended for NF placement and non-step preferred. There will be no grandfathering, which means that all exiting Uloric patients as well as new users will need to try allopurinol first. The recommendation includes notification of current Uloric users as well as notification of retail pharmacies. Colcrys is recommended for UF designation and is exempt from step therapy as it is used for acute gout. However it is high cost because it is administered with prednisone.

G. Anti-Gout Drugs— Panel Questions and Comments

Dr. Salom asked how many patients will be affected by making Uloric NF and placing it behind the step. The answer provided was about 10,000. Dr. Salom then asked how many patients are expected to switch from Uloric. Dr. Meade answered that it would be less than 10,000 but there is no definite number as yet.

Dr. Khurana noted that the manual PA criterion (a)(1) requires at least 300 mg per day of allopurinol in an adequate trial of that drug. She asked if there is a duration associated with that trial. Dr. Meade answered that the duration is left up to the physician.

H. Anti-Gout Drugs— Panel Vote on UF Recommendations

The Chair then read the P&T Committee's UF recommendation to be voted on:

The P&T Committee recommended the following scenario for the UF, which is the most clinically and cost-effective option for the Military Health System (MHS):

- allopurinol be designated UF and step-preferred (e.g., "in front of the step");

- febuxostat (Uloric) be designated NF and non step-preferred (e.g., "behind the step"); and
- colchicine (Colcrys), probenecid, and the fixed dose combination of colchicine/probenecid be designated formulary on the UF and exempt from step therapy.
- This recommendation includes step therapy, which requires a trial of allopurinol prior to using febuxostat (Uloric) in all current and new users of febuxostat.

There was no further discussion by the Panel.

The BAP then voted:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

I. Anti-Gout Drugs— Panel Vote on PA Recommendations

Dr. Salom next read the PA recommendations for this drug class.

The P&T Committee recommended PA criteria for all current and new users of febuxostat (Uloric), requiring a trial of allopurinol prior to use of febuxostat. Coverage will be approved if the patient meets any of the following criteria:

1. Automated PA Criteria: The patient has received a prescription for allopurinol at any MHS pharmacy point service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order)] during the previous 180 days, AND

2. Manual PA Criteria: If automated criteria are not met, febuxostat (Uloric) is approved (e.g., a trial of allopurinol is not required) if:

    a) The patient has experienced any of the following issues with at least one of the following with allopurinol, which is not expected to occur with febuxostat (Uloric):

        (1) The patient has had an inadequate response to allopurinol (failure to achieve serum uric acid levels < 6 mg/day) after an adequate trial (at least 300 mg per day of allopurinol)

        (2) The patient has had intolerable adverse effects (e.g., hypersensitivity) to allopurinol

        (3) The patient has a contraindication to allopurinol (e.g., renal impairment)

Without further discussion, the Panel voted as follows:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

J. Anti-Gout Drugs— Panel Vote on Implementation Plan Recommendations

The Chair called for the vote on the anti-gout drug class implementation plan, on which there was no discussion.

The P & T Committee recommended 1) an effective date of the first Wednesday after a 90- day implementation period in all POS: 2) TMA send a letter to beneficiaries affected by the UF and PA decisions. Additional recommendations made by the P & T Committee were to provide messaging to retail pharmacies to designate that PA and step therapy is required, with a trial of allopurinol prior to febusostat (Uloric) and the Anti-Gout Drug Class be added to the Rapid Response Program for the Retail Network and Mail Order Pharmacies.

The BAP voted:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Dr. Salom then asked for the next review.

II. UF CLASS/SUBCLASS REVIEWS— Chronic Obstructive Pulmonary Disease (COPD) Agents — Pulmonary II Drugs

(PEC Script)
(Dr. Meade)

P&T Comments

A. Pulmonary II Drugs—Relative Clinical Effectiveness and Conclusion

The Pulmonary II Drug Class is comprised of two subclasses, the long-acting muscarinic agents (LAMAs), aclidinium inhaler (Tudorza) and tiotropium inhaler (Spiriva), and the chronic obstructive pulmonary disease (COPD) drugs [comprised of the short-acting muscarinic agents (SAMAs), short-acting beta agonist (SAMA/SABA) combinations and the phosphodiesterase type 4 (PDE-4) inhibitors].

Combivent metered dose inhaler (MDI) is one of the last available chlorofluorocarbon (CFC) MDIs on the market and will have supplies exhausted by December 2013. Its replacement is Combivent Respimat, a new CFC- and propellant-free formulation.

Drugs in the COPD drug class are listed on page 3.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following at the February 2013 meeting:

- With regard to the long-acting muscarinic agents (LAMAs), aclidinium (Tudorza) and tiotropium (Spiriva), and the short-acting muscarinic agent (SAMA), ipratropium (Atrovent HFA), the P&T Committee concluded the following:
- Aclidinium (Tudorza) is a dry powder inhaler (DPI) administered twice daily. The three clinical trials used to obtain FDA approval reported statistically significant improvement in lung function/spirometric (breathing test) endpoints [forced expiratory volume in 1 second (FEV1)] compared with placebo at 12 weeks. Two of the trials reported statistically significant reductions in chronic obstructive pulmonary disease (COPD) exacerbations versus placebo.
- In a small-dose ranging trial with 30 participants lasting for 15 days, there was no significant difference between aclidinium and tiotropium in terms of improvements in spirometric (breathing test) endpoints (FEV1).
- For aclidinium, the adverse event profile appears minimal, with primarily anticholinergic (drying) events reported. However, there is limited safety data with the approved 400 mcg dose. The FDA is requiring a prospective clinical trial to assess cardiovascular (CV) safety. Longer duration and larger comparative trials are needed to determine aclidinium's place in therapy.
- Tiotropium is administered once daily. Several trials have documented tiotropium is associated with clinically significant improvements in FEV1 and forced vital capacity (breathing tests) compared with placebo or ipratropium. Additional benefits include reductions in the risk for COPD exacerbations as well as reduced hospitalizations due to COPD exacerbations.
- Reports of a possible link between tiotropium and adverse CV events including death, stroke, and myocardial infarction (MI) were first raised in 2008, based on meta-analysis and retrospective analyses of health claims data. New data based on a large 4-year prospective trial (UPLIFT) and other analyses does not support an association with tiotropium and CV adverse events.
- The other common adverse effects of tiotropium are anticholinergic (dryng) in nature. There are reports of incorrect administration of the inhaler, with patients swallowing the capsule, instead of administering it via the HandiHaler device.
- Ipratropium has been marketed since 1995. Review of the clinical literature for efficacy did not add substantial new information. For safety, while there may be a possible signal between ipratropium use and CV adverse events, the data is limited due to study design (cohort studies), influence of underlying CV disease, and presence of underlying pulmonary cancers.
- With regard to the SAMA/LAMA combination products, Combivent Respimat demonstrated similar improvements in FEV1 as Combivent CFC MDI in the clinical trial used to obtain FDA approval. Some older patients or those with hand joint problems may require assistance for the initial assembly of the Combivent Respimat inhaler and cartridge. Combining bronchodilators may improve efficacy and decrease the risk of side effects, as compared to maximizing the dose of a single bronchodilator, and also provide a convenience to the patient. The safety profile of Combivent Respimat is similar to Combivent CFC MDI.

- Roflumilast (Daliresp) is the first oral phosphodiesterase type 4 inhibitor marketed in the United States, and is administered once daily. It has a narrow FDA indication, limited to reducing the incidence of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.
- Roflumilast should not be used to treat acute bronchospasm, as it has modest effects on FEV1, is not a bronchodilator, and instead has anti-inflammatory actions. Combining roflumilast with a long-acting bronchodilator [salmeterol (Serevent) or tiotropium] results in improvements in FEV1. The two trials used to obtain FDA approval reported roflumilast reduced COPD exacerbation rates by 15%–19% compared to placebo.
- For roflumilast, safety issues identified by the FDA included psychiatric events (including suicide), weight loss, GI upset and severe diarrhea, and nasal tumors. However, the FDA did not require additional prospective safety studies. A risk evaluation and mitigation strategy program was not required.

B. Pulmonary II Drugs—Relative Cost-Effectiveness Analysis and Conclusion

The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 2 absent) the following:

- CMA within the LAMA subclass showed that tiotropium (Spiriva) was more cost-effectivthan aclidinium (Tudorza). BIA results where Spiriva and Tudorza were designated UF resulted in the greatest cost-avoidance to the MHS.
- CMA was conducted within the COPD subclass, which includes the SAMAs, SABA/SAMA combination drugs, and PDE-4 inhibitors. The results showed ipratropium nebulized solution (Atrovent; generic) was the most cost-effective agent, followed by ipratropium/albuterol nebulized solution (DuoNeb; generic), ipratropium hydrofluoroalkane (HFA) MDI (Atrovent HFA), ipratropium/albuterol soft mist inhaler (Combivent Respimat), and roflumilast (Daliresp). Ipratropium/albuterol (Combivent) was not included in the cost-effectiveness analysis due to market discontinuation by December 2013. BIA projections for all scenarios were very similar.

C. Pulmonary II Drugs—UF Recommendation

The P&T Committee recommended (12 for, 1 opposed, 2 abstained, 2 absent) aclidinium inhaler (Tudorza), tiotropium inhaler (Spiriva), ipratropium nebulized solution (Atrovent; generic), ipratropium/albuterol nebulized solution (DuoNeb; generic), ipratropium HFA MDI (Atrovent HFA), ipratropium/albuterol soft mist inhaler (Combivent Respimat), and roflumilast (Daliresp) remain designated UF. Ipratropium/albuterol MDI (Combivent) will remain designated UF, pending discontinuation in December 2013.

D. Pulmonary II Drugs— Physician's Perspective

Dr. Kugler informed the Panel that the Pulmonary I Drug Class will be reviewed at the November meeting of the P&T Committee. He noted that no drugs in the Pulmonary II

Class are recommended for NF placement. He also said that there are several new COPD drugs in the pipeline now that are close to FDA approval.

E. Pulmonary II Drugs— Panel Questions and Comments

The Chair opened the floor for Panel questions and comments. Dr. Khurana asked whether existing Combivent users will automatically be given the new Combivent when the CFC inhaler is phased out in December. Dr. Meade answered that it depends on which pharmacy the beneficiary is using. Dr. Salom suggested that it might be a good idea to let those people affected by the switch know that the change is coming. He recommended that users be notified.

F. Pulmonary II Drugs— Panel Vote on UF Recommendation

Dr. Salom read the P&T Committee's UF recommendations for the Pulmonary II drugs.

The P&T Committee recommended aclidinium inhaler (Tudorza), tiotropium inhaler (Spiriva), ipratropium nebulized solution (Atrovent; generic), ipratropium/albuterol nebulized solution (DuoNeb; generic), ipratropium HFA MDI (Atrovent HFA), ipratropium/albuterol soft mist inhaler (Combivent Respimat), and roflumilast (Daliresp) remain designated UF. Ipratropium/albuterol MDI (Combivent) will remain designated UF, pending discontinuation in December 2013.

There was no discussion of the recommendation.

The BAP vote was:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Later in the meeting the question was asked whether the Panel needs to formally vote on the recommendation to make notification on the discontinuation of Combivent. The answer given by the Alternate DFO was that no formal BAP action is required beyond including the comment that the Panel agreed to recommend that notification should be given.

III. Recently-Approved USFDA Agents

(PEC Script)
(Dr. Meade)

A. Non-Insulin Diabetes Drugs: Sodium Glucose Co-Transporter 2 (SGLT2) Inhibitors— Canagliflozin (Invokana)

Relative Clinical Effectiveness Conclusion—Canagliflozin (Invokana) is a new diabetes drug with a novel mechanism of action and the first FDA-approved SGLT2 inhibitor. SGLT2 inhibitors are a new subclass of the Non-Insulin Diabetes Drug Class, which was

originally reviewed in November 2010. The Non-Insulin Diabetes Drug Class also includes the following subclasses: biguanides (metformin), sulfonylureas, thiazolidinedione (TZD), dipeptidyl-dipeptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 receptor agonists (GLP1RAs), pramlintide, dopamine agonists, meglitinides, and alpha glucosidase inhibitors.

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

- Efficacy of canagliflozin is limited to eight clinical trials, showing moderate decreases in hemoglobin A1c from baseline ranging from 0.63% (with insulin) to 1.11% (monotherapy in treatment-naïve patients).
- Canagliflozin has safety concerns of hypotension, impaired renal function, hyperkalemia, hypermagnesemia, hyperphosphatemia, (low blood potassium, magnesium and phosphate) increases in l*ow-density lipoprotein* (LDL) cholesterol and hemoglobin, hypoglycemia (low blood sugar), urinary tract infections in both men and women, and genital fungal infections.
- There is limited safety information available and no long-term outcomes trials have been completed to date with canagliflozin.
- Despite its unique mechanism of action to increase urinary glucose excretion, canagliflozin (Invokana) does not offer a clinically compelling advantage over the other non-insulin drugs included on the UF.

B. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) Relative Cost-Effectiveness Analysis and Conclusion

The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that canagliflozin (Invokana) is not cost-effective compared to other non-insulin diabetes drugs currently available on the UF. CMA showed canagliflozin is more costly than metformin, glyburide, pioglitazone (Actos, generic), sitagliptin (Januvia), and exenatide (Byetta), in terms of cost per day of therapy.

C. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) UF Recommendation

The P&T Committee recommended (13 for, 1 opposed, 1 abstained, 2 absent) canagliflozin (Invokana) be designated NF due to the lack of compelling clinical advantages, safety concerns, lack of long-term outcomes and adverse event data, and cost disadvantage compared to UF products.

D. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) PA Criteria

In the Non-Insulin Diabetes Drug Class, existing automated prior authorization (step therapy) requires a trial of metformin or a sulfonylurea**,** prior to the use of a DPP-4

inhibitor, a TZD, or a GLP1RA, based on positive efficacy and long-term outcomes data with metformin and the sulfonylureas.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) a trial of metformin, a sulfonylurea, or a DPP-4 inhibitor in all new and current users of SGLT2 inhibitors, canagliflozin (Invokana), due to the modest hemoglobin A1c lowering and safety concerns.

1. Automated PA criteria: The patient has filled a prescription for metformin, a sulfonylurea or a DPP4-inhibitor at any Military Health System (MHS) pharmacy point of service (POS) [military treatment facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.
2. Manual PA criteria, if automated criteria are not met: An SGLT2 inhibitor, canagliflozin (Invokana), is approved (e.g., trial of metformin or sulfonylurea or a DPP-4 inhibitor is NOT required) if:

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

    b) The patient has experienced any of the following adverse events on sulfonylurea: hypoglycemia requiring medical treatment.

    c) The patient has had inadequate response to metformin or a sulfonylurea or a DPP-4 inhibitor.

    d) The patient has a contraindication to metformin or a sulfonylurea or a DPP-4 inhibitor.

E. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) UF and PA Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) 1) an effective date of the first Wednesday after a 30-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by the UF and PA decisions.

F. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) — Committee Physician's Perspective

Dr. Kugler noted that the P&T Committee discussed the agent's modest efficacy as well as safety concerns. He said there is limited data available regarding both its effectiveness and its safety so the Committee wanted to take a conservative approach to Invokana. The agent is also more costly than other agents in its class. He also noted that the PA criteria recommended are similar to those in place for other DPP-4 inhibitors. New users will be required to try metformin, a sulfonylurea or a DPP-4 inhibitor before Invokana.

G. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) — Panel Questions and Comments

Dr. Khurana asked whether the 30-day implementation period would be enough time. Dr. Meade said that there are very few users so far so the change can be made quickly.

Note: A pharmaceutical manufacturer representative asked to address the panel. The request was denied. Per DoDI 5105.04, Department of Defense Federal Advisory Committee Management Program, the public shall not participate in the Committee member's deliberations, unless otherwise authorized. The process to address the Panel is outlined in the Federal Register Notice which was published on 3 June 2013. Interested parties or groups may register prior to the meeting to address the Panel or submit written comments to be read into the minutes.

H. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) — Panel Vote on UF Recommendation

Dr. Salom read the P&T Committee's recommendation for Invokana.

The P&T Committee recommended canagliflozin (Invokana) be designated NF due to the lack of compelling clinical advantages, safety concerns, lack of long-term outcomes and adverse event data, and cost disadvantage compared to UF products.

Without further discussion, the vote was:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

I. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) — Panel Vote on PA Criteria

The Chair then read the recommended PA criteria.

In the Non-Insulin Diabetes Drug Class, existing automated prior authorization (step therapy) requires a trial of metformin or a sulfonylurea**,** prior to the use of a DPP-4 inhibitor, a TZD, or a GLP1RA, based on positive efficacy and long-term outcomes data with metformin and the sulfonylureas.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 2 absent) a trial of metformin, a sulfonylurea, or a DPP-4 inhibitor in all new and current users of SGLT2 inhibitors, canagliflozin (Invokana), due to the modest hemoglobin A1c lowering and safety concerns.

1. Automated PA criteria: The patient has filled a prescription for metformin, a sulfonylurea or a DPP4-inhibitor at any Military Health System (MHS) pharmacy point of service (POS) [military treatment facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.
2. Manual PA criteria, if automated criteria are not met: An SGLT2 inhibitor, canagliflozin (Invokana), is approved (e.g., trial of metformin or sulfonylurea or a DPP-4 inhibitor is NOT required) if:

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

    b) The patient has experienced any of the following adverse events on sulfonylurea: hypoglycemia requiring medical treatment.

    c) The patient has had inadequate response to metformin or a sulfonylurea or a DPP-4 inhibitor.

    d) The patient has a contraindication to metformin or a sulfonylurea or a DPP-4 inhibitor.

Without further discussion, the BAP voted:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

J. Non-Insulin Diabetes Drugs: SGLT2 Inhibitors—Canagliflozin (Invokana) — Panel Vote on Implementation Plan

Dr. Salom put the implementation plan before the Panel.

The P&T Committee recommended 1) an effective date of the first Wednesday after a 30-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by the UF and PA decisions.

Again without further discussion, the BAP vote was:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

IV. Utilization Management Issues — Pantoprazole

(PEC Script)
(Dr. Meade)

A. Proton Pump Inhibitors (PPIs): Pantoprazole Change from Non-Preferred to Step-Preferred Status

The PPIs currently have PA criteria (step therapy) requiring a trial of omeprazole or

esomeprazole (Nexium) prior to use of the other PPIs. Omeprazole and esomeprazole are BCF and step-preferred. In November 2012, the P&T Committee recommended reclassification of pantoprazole as formulary on the UF, due to availability of cost-effective generic formulations; pantoprazole remained non-preferred. The other PPIs, lansoprazole (Prevacid), rabeprazole (Aciphex), and omeprazole/sodium bicarbonate (Zegerid), are NF and non-preferred. The cost of generic pantoprazole tablets has continued to decline since November 2012. The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the PA criteria to designate pantoprazole as step-preferred (i.e., in front of the step) on the UF.

B. Proton Pump Inhibitors (PPIs): Committee Physician's Perspective

Dr. Kugler informed the Panel that there was no controversy about making this change as the price of generic pantoprazole has continued to fall since last November's P&T Committee meeting.

C. Proton Pump Inhibitors (PPIs): Panel Questions and Comments

Dr. Salom asked whether this is one of the largest drug classes. Dr. Meade replied that it is.

D. Proton Pump Inhibitors (PPIs): Panel Vote on Revised PA Criteria Recommendation

The Chair read the recommendation.

The P&T Committee recommended revising the PA criteria to designate pantoprazole as step-preferred (i.e., in front of the step) on the UF.

The BAP vote was:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

V. Utilization Management Issues — Vascepa

(PEC Script)
(Dr. Meade)

A. Antilipidemics-2: Icosapent ethyl (Vascepa)—PA Criteria

Icosapent ethyl (Vascepa) is the second prescription fish oil product marketed. Icosapent ethyl has the same FDA-approved labeling and dosing as omega-3-acid ethyl esters (Lovaza). Vascepa is not as effective as Lovaza at lowering triglycerides, but does not adversely affect LDL levels. PA criteria apply to Lovaza, limiting use to the FDA-approved indications, due to the large number of off-label, non-supportable uses. The P&T Committee recommended manual PA criteria for all current and new users of Vascepa, limiting use to the FDA-approved indication; the manual PA criteria for Vascepa will be the same as criteria for Lovaza.

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) manual PA criteria for all current and new users of Vascepa, limiting use to the FDA-approved

indication.

New and current users of Vascepa are required to undergo the PA process.

1. Manual PA Criteria—Vascepa is approved if:

   a) Patients Receiving Statins:

      (1) Patients with triglyceride (TG) Levels > 500 mg/dL AND

      (2) Inadequate TG-lowering response to a therapeutic trial of niacin (1-g/day), unable to tolerate niacin/fibrate or who are not a candidate for niacin/fibrate therapy [*] [†]

   b) Patients NOT Receiving Statins:

      (1) Patients with TG Levels > 500 mg/dL AND

      (2) Inadequate response to a therapeutic trial of monotherapy with both a fibrate and niacin (1-2 g/day), unable to tolerate a fibrate and niacin or who are not candidates for fibrates [†] and niacin therapy

   c) Patients with TG <500 mg/dL or <500 mg/dL with an inadequate TG-lowering response to niacin or fibrates or who are unable to tolerate/are not candidates for niacin or fibrates

   d) Coverage is not approved for the use of Vascepa for the treatment of other conditions, including: a*ttention deficit hyperactivity disorder*, Alzheimer's disease, bipolar disorder, Crohn's disease, cystic fibrosis, dementia, depression, inflammatory bowel disease, intermittent claudication, metabolic syndrome, osteoporosis, post-traumatic stress disorder, renal disease (IgA nephropathy), rheumatoid arthritis, schizophrenia, Type 2 diabetes mellitus, and ulcerative colitis.

[*] Not candidates for niacin: patients with a history of confirmed PUD (perforation, ulceration, or upper GIB), gouty attacks (presence of intra-articular uric acid crystals in the affected joint), and/or poorly controlled diabetes.

[†] Not candidates for fibrates: patients with hepatic or severe renal dysfunction, including primary biliary cirrhosis and preexisting gallbladder disease.

B. Antilipidemics-2: Icosapent ethyl (Vascepa)—PA Implementation Plan

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.

C. Antilipidemics-2: Icosapent ethyl (Vascepa) — Committee Physician's Perspective

Dr. Kugler said the Committee had discussed the several off-label uses of Vascepa, noting that it has the same approved label and dosing as Lovaza, another prescription fish

oil product. PA criteria have been applied to Lovaza due to the large number of unsupportable off-label uses. The Committee voted to limit use to FDA-approved indications and recommended the same PA criteria as used for Lovaza.

D. Antilipidemics-2: Icosapent ethyl (Vascepa) — Panel Questions and Commenrts

Dr. Salom asked how many patients are using this medication. The answer is 639.

E. Antilipidemics-2: Icosapent ethyl (Vascepa) — Panel Vote on PA Criteria

The Chair read the P&T Committee's recommended PA criteria.

The P&T Committee recommended manual PA criteria for all current and new users of Vascepa, limiting use to the FDA-approved indication.

New and current users of Vascepa are required to undergo the PA process.

1. Manual PA Criteria—Vascepa is approved if:

   a) Patients Receiving Statins:

      (1) Patients with triglyceride (TG) Levels > 500 mg/dL AND

      (2) Inadequate TG-lowering response to a therapeutic trial of niacin (1-g/day), unable to tolerate niacin/fibrate or who are not a candidate for niacin/fibrate therapy * †

   b) Patients NOT Receiving Statins:

      (1) Patients with TG Levels > 500 mg/dL AND

      (2) Inadequate response to a therapeutic trial of monotherapy with both a fibrate and niacin (1-2 g/day), unable to tolerate a fibrate and niacin or who are not candidates for fibrates † and niacin therapy

   c) Patients with TG <500 mg/dL or <500 mg/dL with an inadequate TG-lowering response to niacin or fibrates or who are unable to tolerate/are not candidates for niacin or fibrates

   d) Coverage is not approved for the use of Vascepa for the treatment of other conditions, including: a*ttention deficit hyperactivity disorder,* Alzheimer's disease, bipolar disorder, Crohn's disease, cystic fibrosis, dementia, depression, inflammatory bowel disease, intermittent claudication, metabolic syndrome, osteoporosis, post-traumatic stress disorder, renal disease (IgA nephropathy), rheumatoid arthritis, schizophrenia, Type 2 diabetes mellitus, and ulcerative colitis.

There was no discussion. The BAP voted:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

F. Antilipidemics-2: Icosapent ethyl (Vascepa) — Panel Vote on Implementation Plan

Dr. Salom read the PA implementation plan.

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

The BAP vote was:

Concur: 6 Non-concur: 0 Abstain: 0 Absent: 3

Closing Statement

Dr. Salom thanked the presenters. The next meeting date is TBD.

Mr. Blanche, the Alternate DFO, thanked the Panel members and attendees and closed the meeting at 9:50 A.M.

Ira Salom MD

Dr. Ira Salom
Chair

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
- CEA — Cost-effectiveness analysis
- CFC — Chloroflurocarbon
- CFR — Code of Federal Regulations
- CMA — Cost-Minimization Analysis
- COPD — Chronic Obstructive Pulmonary Disease
- CPG — Clinical Practice Guideline
- CR — Controlled Release (a drug formulation)
- CV — Cardiovascular
- DFO — Designated Federal Officer
- DoD — Department of Defense
- DPP-4 — Dipeptidyl-dipeptidiase inhibitor (a drug subclass)
- ECF — Extended Core Formulary
- EMA — European Medicines Association
- ER — Extended Release (a drug formulation)
- ESI — Express-Scripts, Inc.
- FACA — Federal Advisory Committee Act
- FDA — U.S. Food and Drug Administration
- GLP1RAs — Glucagon-like peptide-1 receptor agonists (a drug subclass)
- IR — Immediate Release (a drug formulation)
- LAMAs — Long-acting muscularinic agents
- LDL — Low-density lipoprotein
- MDI — Metered Dose Inhaler
- 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
- PDE-4 — Phosphodiesterase type 4 (a drug class)
- 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
- SABAs — Short-acting beta agonists
- SAMAs — Short-acting muscularinic agents
- SGLT2 — Sodium Glucose Co-Transporter 2 (a drug subclass)
- SR — Sustained release (a drug formulation)
- sUA — Serum Uric Acid
- TG — Triglyceride
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TPHARM — TRICARE Pharmacy Program
- TRRx — TRICARE Retail Pharmacy Program
- TZD — Thiazolidedione
- UF — DoD Uniform Formulary
- ULT — Urate-Lowering Therapy
- USC — United States Code
- VA — U.S. Department of Veterans Affairs

Attachment 1
June 27, 2013 – BAP Meeting

LEGACY Public Comment Letter

June 18, 2013

CDR Joseph Lawrence
DFO
Uniform Formulary Beneficiary Advisory Panel
4130 Stanley Road, Suite 208, Building 1000
San Antonio, TX 78234-6012

Re: June 27th Meeting of the Uniform Formulary Beneficiary Advisory Panel

The American Legacy foundation (Legacy) is pleased to submit the following comments to the Uniform Formulary Beneficiary Advisory Panel regarding the meeting agenda item "Tobacco Cessation Agents".

Legacy is a national, independent, public health foundation created in 1998 out of the landmark Master Settlement Agreement ("MSA") between the tobacco industry, 46 state governments and five U.S. territories. Our mission is to build a world where young people reject tobacco and anyone can quit. Our program includes:

truth® - A national youth smoking prevention media campaign responsible for preventing approximately 450,000 youth from initiating smoking from 2000 – 2004.

EX® - An innovative smoking cessation public education campaign designed to help smokers "re-learn" life without cigarettes, available at www.becomeanex.org.

Research Initiatives - Examining the various causes and effects of tobacco use in the United States.

Outreach to Priority Populations – Priority Populations Initiatives and grants provide critical interventions using methods that are culturally competent and tailored for the specific needs of communities disproportionately affected by the toll of tobacco.

Current smoking rates among military personnel are 30.5%. Like civilian smokers, many smokers in the military report trying to quit. In 2008, about 16% of military personnel that were smokers in the past year had quit, and 48% had tried unsuccessfully to quit.[i] The use of tobacco compromises military readiness and the performance or our men and women in the armed forces. Studies have found that smoking is one of the best predictors of training failure, and it has also been shown to increase soldiers' chances of physical injury and hospitalization. Tobacco use not only costs the DoD in troops readiness and health, it also costs the DoD money. The Pentagon spends over $1.6

billion on tobacco-related medical care, increased hospitalization, and lost days of work[ii]

Legacy applauds the Department of Defense with the release of the final rule establishing a smoking cessation program under TRICARE. One of the provisions of the rule requires TRICARE to provide access to smoking cessation drugs, which were to be determined by the TRICARE Pharmacy and Therapeutics Committee based on clinical and cost effectiveness.

Legacy encourages making available to TRICARE beneficiaries all seven Food and Drug Administration (FDA)-approved tobacco cessation medications. The U.S. Public Health Service details the most current science on tobacco cessation treatment in the *Treating Tobacco Use and Dependence* Guideline. The most recent edition of the Guideline recommends seven medications, which are nicotine replacement therapies (gums, inhalers, lozenges, nasal sprays, and patches), bupropion, and varencicline. These medications, both alone and in certain combinations, have been shown to at least double a smoker's chance of quitting.[iii]

Medications are an important part of effective smoking cessation treatments. It is important that cessation benefits offered to smokers be comprehensive, meaning they include all treatments proven effective. The *Treatment Tobacco Use and Dependence* Guideline also recommends three types of counseling (individual, group and phone counseling) as evidence-based treatments to help tobacco users quit.[iv] We applaud DoD now providing counseling services for all TRICARE beneficiaries age 18 and older and providing cessation resources through a quitline and website, www.ucanquit2.org.[v]

We appreciate the opportunity to submit comments as the Uniform Formulary Beneficiary Advisory Panel moves forward with recommendations on tobacco cessation agents. We look forward to working with you on this important issue. Please contact Diane Canova, Vice President of Government Affairs at 202-454-5559 or deanova@legacyfor health.org if you have questions or need further information.

Sincerely,

David Dobbins
Chief Operating Officer

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[i] Bray RM, Pembetton MR, Hourani LL, Witt M, Olmstead, KLR, Brown JM, et al. 2008 Department of Defense Survey of Health Related Behaviors Among Active Duty Military Personnel. A Component of the Defense Lifestyle Asstssment Program (DLAP). RTI International: 2009.

[ii] Institute of Medicine. Combating Tobacco Use in Military and Veteran Populations, 2009; 3-4, 56.

[iii] Fiore MC, Jaén CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008 ("2008 Clinical Practice Guideline"). The Guideline is available here:

http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat2chapter.28163

[iv] Fiore MC, Jaén CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008 ("2008 Clinical Practice Guideline"). The Guideline is available here: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat2chapter.28163

[v] Department of Defense. TRICARE Smoking Cessation Program Fact Sheet. April 2013. Available at: http://www.tricare.mil/CoveredServices/SeeWhatsCovered/SmokingCessationServices.aspx