7 April 2011

Executive Summary

UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL COMMENTS
7 April 2011

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy & Therapeutics (P&T) Committee February 2011 meeting.

1. GASTRINTESTINAL-1s (GI-1s) CLASS REVIEW UF RECOMMENDATION.

Taking into consideration the conclusions from the relative clinical and cost effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following:

For the aminosalicylates, sulfasalazine, Colazal, Dipentum, Asacol, Asacol HD, Pentasa, Lialda, Apriso, Canasa, sulfite-free Rowasa, and mesalamine enema remain classified with formulary status on the UF.

For the GI steroids and Miscellaneous IBS agents, Entocort EC, hydrocortisone enema, hydrocortisone foam (Cortifoam) and Lotronex remain classified with formulary status on the UF. Zelnorm is only available from the FDA under a treatment investigational new drug application.

Summary of Panel Vote/Comments:

- Without further discussion/comment, the Panel voted on the GI-1 UF recommendation as follows: Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

No further comments from the Panel.

Director, TMA:

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

2. ANTILIPIDEMIC-2s (LIP-2s) DRUG CLASS REVIEW UF RECOMMENDATION.

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

1) For the Fibric Acid Derivatives:

Generic Lopid, Triglide, generic Lofibra, and Lipofen remain designated with formulary status on the UF. Antara, Tricor, Fibricor, and Trilipix will be designated with formulary status on the UF (16 for, 0 opposed, 0 abstained, 2 absent).

2) For the Omega-3 fatty acids:

Lovaza will be designated with formulary status on the UF (12 for, 4 opposed, 1 abstained, 1 absent) and subject to PA criteria that allows use in all current and new users, only for FDA-approved indications.

3) For Bile Acid Sequestrants:

Generic Questran, generic Questran Light, generic Colestid remain formulary on the UF; and, Welchol will remain designated with non-formulary status on the UF (14 for, 2 opposed, 1 abstained, 1 absent).

Summary of Panel Vote/Comments:

Dr. Cohoon asked about the two opposing votes regarding the bile acid sequestrants. Dr. Meade explained the votes. Dr. Cohoon also asked whether a 60-day implementation period would be enough as there is to be no grandfathering. Dr. Meade said it should be.

Ms. LeGette asked what people were using Lovaza for. Dr. Meade said for triglycerides, without trying other agents that would be more cost effective. One field request also indicated Lovaza is being used for behavioral health and cited articles. However, research showed that it was another supplement, not Lovaza, causing the changes.

- Without further discussion, the Panel voted on the LIP-2 UF recommendation as follows: Concur: 10 Non-concur: 0 Abstain: 0 Absent: 1

No further comments from the Panel

Director, TMA:

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

b. ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON FIBRIC ACID DERIVATIVES PA CRITERIA RECOMMENDATION. The P&T Committee recommended the following:

PA criteria should apply to the nonpreferred fibric acid derivatives, Antara, Triglide, Lipofen, Fibricor, Trilipix. Coverage would be approved if the patient met any of the following criteria:

1. Automated PA criteria:
    a) The patient has received a prescription for gemfibrozil, generic fenofibrate micronized/nonmicronized formulations (including Lofibra) or Tricor (at the MTFs, retial network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:
    a) The patient has a contraindication to the preferred fibric acid derivatives that is not expected to occur with the nonpreferred fibric acid derivatives.

Summary of Panel Vote/Comments:

- Without discussion or comment, the Panel voted on the Fibric Acid Derivatives PA criteria recommendation as follow:

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

No further comments from the Panel

Director, TMA:

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

ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON FIBRIC ACID DERIVATIVES PA IMPLEMENTATION PLAN. The P&T Committee recommended the following:

1) An effective date of the first Wednesday after a 60-day implementation period in all points of service; and 2) that TMA send a letter to beneficiaries affected by this UF decision.

Summary of Panel Vote/Comments:

- Without further discussion, the Panel voted on the Fibric Acid Derivatives PA implementation plan recommendations as follows:

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

No further comments from the Panel

Director, TMA:

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

d. ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON LOVAZA PA CRITERIA. The P&T Committee recommended the following:

PA criteria should apply to the prescription omega-3 fatty acid product, Lovaza. Lovaza would be approved only for the FDA-approved indications. All current and new users of Lovaza must meet one of the criteria outlined in section 4, subsection, F [of the Committee's recommendations] to pass through the PA process.

That subsection reads as follows:

a) Patients with TG > 500 mg/mL who are receiving statins AND have had an inadequate TG-lowering response to a therapeutic trial of niacin (1-2 g/day) or fibrates, are unable to tolerate niacin or fibrates, or are not candidates for niacin or fibrate therapy.

b) Patients with TG > 500 mg/mL who are not receiving statins AND who have had an inadequateTG-lowering response to a therapeutic trial of monotherapy with both a fibrate and niacin, are unable to tolerate niacin and fibrates, or are not candidates for niacin and fibrate therapy.

c) Coverage is not approved for Lovaza for use in non-FDA approved conditions, including the following: Attention Deficit Hyperactivity Disorder, Alzheimer's disease, bipolar disease, Crohn's disease, cystic fibrosis, dementia, depression, inflammatory bowel disease, intermittent claudication, metabolic syndrome, osteoporosis, post-traumatic stress disorder, renal disease (immunoglobulin A nephropathy), rheumatoid arthritis, schizophrenia, Type 2 diabetes mellitus, and ulcerative colitis.

Summary of Panel Vote/Comments:

- Without further discussion or comment, the Panel voted on the Lovaza PA criteria recommendation as follows:

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

No further comments from the Panel

Director, TMA:

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

ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON LOVAZA PA IMPLEMENTATION PLAN.

The P&T Committee recommended an effective date of the first Wednesday after a 60-day implementation period in all points of service; and that TMA send a letter to beneficiaries affected by this UF decision.

Summary of Panel Vote/Comments:

Ms. LeGette commented that it is important to get the letter out as soon as possible on this one. Ms. Fryar asked whether 60 days is a long enough implementation period. Mr. Hutchings said he has been struggling with this question and thinks that 90 days might be better because we are adding a requirement for patients to have to get to their doctor. Dr. Cohoon said she also prefers a longer implementation period. Dr. Schlaifer said that the longer the period is the more problems there will be because the problem is highly marketed so there will be more people using the meds. In addition, she would take into consideration the fact that there would be little or no harm to the patient from missing a dose. There should be no implications at all. She intends to vote to concur. Mr. Hutchings asked about who would get the PA forms, then said that as long as the only form required is a letter, the 60-days would be okay.

- Without further discussion, the Panel voted on the Lovaza PA implementation plan recommendation as follows:

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

No further comments from the Panel

Director, TMA:

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

3. PANCREATIC ENZYME PRODUCTS (PEPs) UF RECOMMENTATION.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended Creon, Pancreaze, and Zenpep be designated with formulary status on the UF. As a result of this action, no PEPs are designated NF.

Summary of Panel Vote/Comments:

- Without further discussion, he Panel voted on the PEPs UF recommendation as follows:

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

No further comments from the Panel.

Director, TMA:

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

4. NEW DRUGS IN ALREADY REVIEWED CLASSES.

a. RENIN ANGIOTENSIN ANTIHYPERTENSIVE AGENTS (RAAs)— ALISKIREN/AMLODIPINE TABLETS (TEKAMLO) UF RECOMMENDATION

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended Tekamlo be designated with NF status on the UF.

Summary of Panel Vote/Comments:

Mr. Hutchings noted that the decision in this case seems to be inconsistent with the Committee's previous review of this class and asked about the basis for it. Dr. Meade replied that the Uniform Formulary rule requires that when a new drug is considered, there has to be a showing of some advantage to the drug. The decision was consistent with that rule. If it were to be reviewed along with all of the drugs in this class instead of by itself, there might be a different outcome, but the class as a whole was reviewed just recently.

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

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

No further comments from the Panel.

Director, TMA:

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

RENIN ANGIOTENSIN ANTIHYPERTENSIVE AGENTS (RAAs)— ALISKIREN/AMLODIPINE TABLETS (TEKAMLO®) PA CRITERIA RECOMMENDATION. The P&T Committee recommended the following PA criteria should apply to aliskiren/amlodipine (Tekamlo):

1. Automated PA criteria:

   a) The patient has received a prescription for a step-preferred RAA — losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), or valsartan/amlodipine/HCTZ (Exforge HCT) — at any Military Health System (MHS) pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:

   a) The patient has tried one of the preferred RAAs and was unable to tolerate treatment due to adverse effects.

   b) The patient has tried one of the preferred RAAs and has had an inadequate response.

   c) The patient has a contraindication to the preferred RAAs, which is not expected to occur with the non-preferred RAAs (e.g., history of angioedema).

Summary of Panel Vote/Comments:

- Without comment or discussion, the Panel voted on the Tekamlo PA criteria as follows:

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

No further comment from the Committee.

Director, TMA:

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

RENIN ANGIOTENSIN ANTIHYPERTENSIVE AGENTS (RAAs)— Aliskiren/Amlodipine Tablets (Tekamlo) PA IMPLEMENTATION PLAN RECOMMENDATION.

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

Summary of Panel Vote/Comments:

- Without further comment of discussion, the Panel voted on the Tekamlo PA implementation plan recommendation as follows:

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

No further comments from the Panel.

***Director, TMA*:**

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

b. RENIN ANGIOTENSIN ANTIHYPERTENSIVE AGENTS (RAAs)—OLMESARTAN/AMLODIPINE/HCTZ TABLETS (TRIBENZOR) UF RECOMMENDATION. The P&T Committee recommended the following:

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended olmesartan/amlodipine/HCTZ (Tribenzor) be designated NF on the UF.

Summary of Panel Vote/Comments:

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

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

No further comments from the Panel.

***Director, TMA*:**

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

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) PA CRITERIA RECOMMENDATION. The P&T Committee recommended the following:

1. Automated PA criteria:

   a) The patient has received a prescription for a step-preferred RAA — losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), or valsartan/amlodipine/HCTZ (Exforge HCT) — at any Military Health System (MHS) pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:

   a) The patient has tried one of the preferred RAAs and was unable to tolerate treatment due to adverse effects.

   b) The patient has tried one of the preferred RAAs and has had an inadequate response.

   c) The patient has a contraindication to the preferred RAAs, which is not expected to occur with the non-preferred RAAs (e.g., history of angioedema).

Summary of Panel Vote/Comments:

- Without further discussion, the Panel voted on the Tribenzor PA criteria recommendation as follows:

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

No further comments from the Panel.

Director, TMA:

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

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) PA IMPLEMENTATION PLAN.

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

Summary of Panel Vote/Comments:

- The further discussion, the Panel voted on the Tribenzor PA implementation plan as follows:

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

No further comments from the Panel.

Director, TMA:

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

c. ANTIEMETICS—ONDANSETRON SOLUBLE FILM (ZUPLENZ) UF RECOMMENDATION.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended ondansetron oral soluble film (Zuplenz) be designated NF on the UF.

Summary of Panel Vote/Comments:

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

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

No further comments from the Panel.

***Director, TMA*:**

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

Antiemetics—Ondansetron Soluble Film (Zuplenz) IMPLEMENTATION PLAN. The P&T Committee recommended the following:

An effective date of the first Wednesday after a 60 days implementation period in all points of service, and that TMA send a letter to beneficiaries affected by this UF decision.

Summary of Panel Vote/Comments:

- Without further discussion, the Panel voted on the Zuplenz UF implementation plan recommendation as follows:

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

No further comments from the Panel.

***Director, TMA*:**

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

d. ALZHEIMER'S DRUGS—DONEPEZIL 23 MG TABLETS (ARICEPT 23 MG) UF RECOMMENDATION.

Ms. Fryar, read for the record, read a letter received from the Eisai Medical Director by the DFO concerning Aricept 23 MG before introducing the presentation of P&T Committee recommendations. Letter included with EXSUM

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LTC Stacia Spridgen
Director, DoD Pharmacoeconomic Center
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LTC Spridgen:

This letter is in response to the Department of Defense's recent evaluation of Aricept 23 mg and the decision to place Aricept 23 mg on Tier 3 – nonformulary for TRICARE.

After reviewing the Pharmacy & Therapeutic (P&T) committee comments available from the evaluation meeting, it is my desire to clarify for the P&T committee several points regarding the efficacy and safety of Aricept 23mg.

In the comments, it is noted that the P&T committee concluded that Aricept 23mg did not have a significant, clinically meaningful therapeutic advantage in terms of effectiveness or clinical outcomes over donepezil 10mg.

While the P&T comments correctly note that there was one clinical trial used to gain FDA approval, I think it is important to note that the trial was a large, multinational head-to-head study with over 1,400 patients.

In that clinical trial Aricept 23mg demonstrated statistically significant improvement in cognition, as measured by the Severe Impairment Battery, a validated measure of cognition in moderate to severe patients, as is noted in the P&T comments.

The comments go on to state that Aricept 23mg demonstrated "no benefit in improving global function." Now while it is accurate that Aricept 23mg did not demonstrate statistically significant difference versus Aricept 10mg when measured by the CIBIC+, it should be noted that the majority of patients in both treatment groups experienced no change to minimal worsening in global function.

The P&T comments also make a comparison of the efficacy of Aricept 23 mg to the efficacy of the combination of donepezil 10 mg and memantine. Although it is noted in the comments that the comparison is indirect, the study used to gain approval for Aricept 23mg was not designed to compare Aricept 23mg versus donepezil 10 mg and memantine. Thus, there is no clinical evidence available to support the conclusion that the efficacy of Aricept 23 mg appears similar to the combination of 10 mg of donepezil with memantine.

It is also noted in the P&T comments that "tolerability to the donepezil 23 mg formulation will be limited by the increased incidence of adverse events, particularly gastrointestinal (GI) effects, compared with donepezil 10 mg."

It is accurate that patients titrated to Aricept 23mg experienced a dose-related increase in adverse events versus those patients who remained stable on Aricept 10 mg for greater than three months. It should also be noted that the most common adverse events with ARICEPT 23 mg were often of mild to moderate intensity.

And while the incidence of nausea and vomiting was markedly greater in patients taking ARICEPT 23 mg, in most cases, these effects have been mild and transient, sometimes lasting 1 to 3 weeks, and have resolved during continued use of ARICEPT.

I would welcome the opportunity to discuss the information above with you further. Please feel free to contact me by phone (number redacted) or by e-mail (redacted), if you have any questions.

Sincerely,

Dr. Harry Ramos, MD
Medical Director, Aricept
Eisai, Inc.

The P&T Committee recommended the following:

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (13 for, 4 opposed, 1 abstained, 0 absent) donepezil 23 mg tablets (Aricept 23 mg) be designated NF on UF.

Summary of Panel Vote/Comments:

Ms. Fryar referenced the smaller doses available and asked what the normal dosage is. COL Lounsbery said the usual is 10 mg. Ms. Fryar asked if the smaller doses could be increased. COL Lounsbery said it could, but it usually doesn't get increased, and justifiably so.

Dr. Cohoon asked if Aricept 23 would be more cost effective. Dr. Meade replied it would be more costly.

- Without further discussion, the Panel voted on the Donepezil 23 mg UF recommendation as follows:

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

Mr. Chavez commented that his non-concurring vote was because he believes some patients would benefit from having this drug available on the UF.

Director, TMA:

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

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) IMPLEMENTATION PLAN. The P&T Committee recommended the following:

An effective date of the first Wednesday after a 60 days implementation period in all points of service, and that TMA send a letter to beneficiaries affected by this UF decision.

Summary of Panel Vote/Comments:

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

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

Ms. Fryar commented for the record that concern has been expressed about whom would actually receive the letter: the caretaker or the patient. The PEC Staff commented that they would not have information concerning caretakers, so the letter will have to be sent to the patient.

Director, TMA:

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

e. SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS UF RECOMMENDATION.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 2 absent):

1. Glucocard 01, Glucocard Vital, and Embrace test strips be designated with formulary status on the UF;

2. Nova Max be designated with NF status on the UF; and

3. Advocate Redi-code, Blood Sugar Diagnostic, EasyMax, EZ Smart Plus, Fifty50, Liberty, Microdot, Rightest GS100, Rightest GS300, Ultratrak Ultimate, Wavesense Jazz, and Wavesense Presto be designated with NF status on the UF because they do not meet the minimum technical standards required for inclusion on the UF or Federal Government contracting regulations.

Summary of Panel Vote/Comments:

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

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

Director, TMA:

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

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS IMPLEMENTATION PLAN.

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

Summary of Panel Vote/Comments:

- Without further discussion, the Panel vote on the SMBGs UF implementation plan was:

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

Director, TMA:

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

5. UTILIZATION MANAGEMENT —MODIFICATION OF QUININE (QUALAQUINE) PRIOR AUTHORIZATION CRITERIA.

To ensure the appropriate use of Qualaquin, consistent with the product labeling, the P&T Committee recommended implementing a quantity limit of 42 capsules per fill, one fill per prescription, with no refills, which will allow quinine (Qualaquin) use in patients who have a documented diagnosis of malaria.

Summary of Panel Vote/Comments:

- Without further discussion, the Panel vote on the Qualaquin PA criteria as follows:

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

Although the BAP concurs with the need for a modification, several members agree that the time period is too restrictive and recommends that consideration be given to allowing one prescription only with 365 days worth of refills.

Dr. Crum offered a comment to the PEC concerning physicians who are writing prescriptions for leg cramps and putting "malaria" on the PA. He said those practitioners should be investigated and reported for possible criminal action.

Director, TMA:

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

MODIFICATION OF QUININE PRIOR AUTHORIZATION IMPLEMENTATION PLAN. The P&T Committee recommended the following:

The quantity limits for Qualaquin become effective the first Wednesday after a 60-day implementation period in all points of service.

Summary of Panel Vote/Comments:

- Without further discussion, the Panel vote on the Qualaquine PA implementation plan was:

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

***Director, TMA*:**

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

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
March 24, 2011
Washington, D.C.

Panel Members Present:

- Deborah Fryar, National Military Family Association, representing The Military Coalition, Chairperson
- Kathryn Buchta, Medical Professional, Health Net Federal Services
- Barbara Cohoon, National Military Families Association, representing The Military Coalition
- Santiago Chavez, Association of Military Surgeons of the United States, representing The Military Coalition
- John Crum, Medical Professional, Humana Military Healthcare Services, Inc.
- Rance Hutchings, Medical Professional, Uniformed Services Family Health Plan
- Lisa Le Gette, Medical Professional, Express-Scripts, Inc.
- Katherine O'Neill-Tracy, Military Officers Association of America, representing The Military Coalition
- Ira Salom, Medical Professional, Clinical Associate Professor, Mt. Sinai School of Medicine
- Marissa Schlaifer, Medical Professional, Academy of Managed Care Pharmacy

Panel member Dr. Brian Casull, Medical Professional representing TriWest Healthcare Alliance was absent from the meeting.

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. LTC Stacia Spridgen, the Designated Federal Officer (DFO), called the proceedings to order at 9:00 A.M.

LTC Spridgen stated the Panel has been convened to review and comment on the recommendations of the Department of Defense (DoD) Pharmacy and Therapeutic (P&T) Committee meeting held February 16 and 17, 2011 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*
    - *Gastrointestinal-1 (GI-1s) Drugs*

        - *Aminosalicylates (ASAs)*
        - *GI Topical Steroids*
        - *Miscellaneous Agents (tegaserod, alosetron)*

    - *Antilipidemic-2 (LIP-2s) Drugs*
        - *Fibric Acids*
        - *Prescription Omega-3 Fatty Acids*
        - *Bile Acid Sequestrants*

    - *Pancreatic Enzyme Products (PEPs)*

- *Designated Newly Approved Drugs*
    - *Renin Angiotensin Hypertensive Agents (RAAs)*
        - *Tekamlo (aliskiren/amlodipine tablets)*
        - *Tribenzor (olmesartan/amlodipine/hydrochlorothiazide tablets)*
    - *Antiemetics*
    - *Alzheimer's Drugs—Aricept 23 mg (donepezil 23 mg tablets)*
    - *Self Monitoring Blood Glucose Systems (SMBGS) test strips*
        - *Glucocard 01*
        - *Glucocard Vital*
        - *Nova Max*
        - *Embrace*

- *Utilization Management—Prior Authorization:*
    - *Qualaquin (quinine sulfate) prior authorization—recommendation for quantity limits*

- *Items for Information —Darvon/Darvocet (propxyphene) withdrawal from the market*

Opening Remarks

LTC Spridgen began by indicating that Title 10 United States Code (U.S.C.) section 1074g subsection b requires the Secretary of Defense to establish a DoD Uniform Formulary (UF) of pharmaceutical agents, and establishes the P&T Committee to review the formulary on a periodic basis and make additional recommendations regarding the formulary as the Committee 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 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, LTC Spridgen said the role of the BAP is to comment on the UF recommendations made by the P&T Committee at their last meeting. While the Department appreciates that the BAP may be interested in the drug classes selected for review, drugs recommended for the basic core formulary (BCF) or specific pricing data, these topics do not fall under the purview of the BAP.

The P&T Committee met for approximately 20 hours 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.

After introducing the individual Panel members (see list above), LTC Spridgen then noted the housekeeping considerations pertaining to the meeting.

Private Citizen Comments

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

Chairperson's Opening Remarks

The Panel Chairperson, Ms. Deborah Fryar, welcomed and thanked those in attendance for coming. She especially thanked the Panel members for their advance preparation and noted that she is expecting an interesting meeting with a lot of discussion. She also reminded the Panel members that the BAP cannot make recommendations and when it votes it is voting on the recommendations brought forth by the P&T Committee. However, the Panel is free to comment and all of its comments are actually reviewed and taken into account before any action is final.

Ms. Fryar asked Dr. Meade to briefly review the definition of "medical necessity" (MN) as the BAP has several of these recommendations before it today.

Dr. Meade informed the Panel that TMA uses two management tools when a drug is made non-formulary: one is "prior authorization (PA)," which requires a beneficiary to use a preferred agent first. The other is "medical necessity," which requires a justification from a clinical physician for using a specific drug. With a medical necessity waiver, patients can obtain the specific drug at the formulary co-pay through the retail and mail order points of service as well as at MTFs, which normally would not carry the agent on their formulary.

The Chair then asked to begin the scheduled drug class review presentations.

DRUG CLASS REVIEW PRESENTATIONS

[PEC Script]

(Dave Meade): I'm Dave Meade, Director of Clinical Operations at the Pharmacoeconomic Center. Joining me today from the PEC are COL Cynthia Clagett, our Army physician consultant, and LCDR Marisol Martinez, one of the PEC clinical pharmacists. Also joining us today is COL Doreen Lounsbery, one of the DoD P&T Committee members who will provide the physician perspective and comment on the recommendations made by the Committee and LCDR Heather Helwig, our pharmacy resident from Bethesda. Dr. Kugler, the chairmen of the P&T Committee and a retired Army Colonel and physician, is also here.

The DoD Pharmacoeconomic Center (PEC) supports the DoD P&T Committee by conducting the relative (relative meaning in comparison to the other agents defined in the same class) clinical-effectiveness analyses and relative cost-effectiveness analyses of drug classes under review and consideration by the DoD P&T Committee for the Uniform Formulary (UF).
We are here to present an overview of the analyses presented to the DoD P&T Committee. 32 Code of Federal Regulation (C.F.R.) establishes procedures for inclusion of pharmaceutical agents on the Uniform Formulary based upon both relative clinical effectiveness and relative cost

effectiveness.

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

1) A brief overview of the relative clinical-effectiveness analyses considered by the DoD P&T Committee.
2) A brief general overview of the relative cost-effectiveness analyses. This overview will be general in nature since we are unable to disclose the actual costs used in the economic models. This overview will include the factors used to evaluate the costs of the agents in relation to the safety, effectiveness, and clinical outcomes.
3) The DoD P&T Committee's Uniform Formulary recommendation is based upon its collective professional judgment when considering the analyses from both the relative clinical and relative cost-effectiveness evaluations. The Committee reviewed three Uniform Formulary drug classes – the Gastrointestinal Agents-1 class, the Pancreatic Enzyme Product class, and the Antilipidemic Agents-2 class. The five newly approved drugs that were reviewed were Tekamlo, Tribenzor, Aricept 23 mg, Zuplenz, and Blood Glucose Monitoring Strips. Lastly, one prior authorization will also be discussed.
4) The DoD P&T Committee's recommendation as to the effective date of the agents being changed from formulary tier to the non-formulary tier of the Uniform Formulary. Based on 32 C.F.R. 199.21, such change will not be longer than 180 days from the final decision date but may be less.

We've given you a handout which includes the Uniform Formulary recommendations for all the drugs discussed today; these are found on pages 2 through 16. There are tables and utilization figures for all the drug classes. We'll be using trade names as much as possible, so you can refer to your handout throughout the presentation.

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

UNIFORM FORMULARY CLASS REVIEWS — GASTROINTESTINAL-1s DRUG CLASS

(PEC Script)
(COL Cynthia Clagett): We will now discuss our first UF drug class review, the Gastrointestinal Agents-1 class.

GASTROINTESTINAL-1s—RELATIVE CLINICAL EFFECTIVENESS

The P&T Committee evaluated the relative clinical effectiveness of the Gastrointestinal Agents-1 class which had not been reviewed previously. The GI-1 Drug Class expenditures exceed $60 million annually and is comprised of three subclasses: aminosalicylates, GI steroids, and miscellaneous agents for irritable bowel syndrome (IBS). In the MHS, Asacol is the highest

utilized oral aminosalicylate agent as you can see in Figure 1 on Page 2. In Figure 2 on Page 3, you can see that mesalamine is the highest utilized rectal aminosalicylate. Looking at the GI steroid agents in Figure 3 on Page 3, Entocort EC and hydrocortisone are the top 2 agents utilized in the MHS. The miscellaneous agents for IBS have restrictive distribution and limited utilization within the MHS.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following clinical effectiveness conclusions for the GI-1Drug Class:

For the 5-ASAs:

1. For the induction of remission in active ulcerative colitis, evidence from a systematic review by the Cochrane group found no clinically relevant differences in efficacy between sulfasalazine and the newer 5-ASA formulations.
2. For maintenance of remission in ulcerative colitis, another systematic review showed a therapeutic advantage of sulfasalazine over the 5-ASA formulations. This advantage was offset by an increase in adverse events observed with sulfasalazine.
3. Aminosalicylates are often used in clinical practice for induction of mild to moderate Crohn's disease, a Cochrane review showed minimal benefit over placebo and less effect compared to budesonide and conventional steroids.
4. In terms of safety, 5-ASAs are generally well tolerated. Olsalazine induces a secretory-type diarrhea, which largely limits its use. Otherwise, the safety profile is similar for the 5-ASA products.
5. Current guidelines recommend combination of oral and rectal therapy for treating mild to moderate distal ulcerative colitis since combination therapy is more effective than either therapy alone.

For the GI steroids:

1. For induction of remission in Crohn's disease, a systematic review found Entocort EC was more effective than placebo and mesalamine, but corticosteroids were more effective.
2. For the maintenance of remission in Crohn's disease, another systematic review found Entocort EC was no more effective than placebo after 6-12 months, and Entocort EC was no more effective than glucorticoids. Entocort EC was more effective at maintaining remission in Crohn's disease compared to mesalamine.
3. Entocort EC is not effective for maintenance of remission in ulcerative colitis, based on a systematic review comparing budesonide with placebo, oral mesalamine, and corticosteroids.

4. The rectally-administered topical steroids include the hydrocortisone enemas, Colocort, and Cortenema, and foam, Cortifoam, preparations, which are effective and safe for the treatment of distal ulcerative colitis.

For the Miscellaneous IBS agents:

1. Due to severe adverse effects, including death due to bowel obstruction, Lotronex is restricted to women with severe refractory diarrhea-predominant IBS under an FDA-mandated risk evaluation and mitigation strategy program.
2. Due to severe adverse cardiovascular effects, Zelnorm is available only for emergency use in cases of severe constipation-predominant IBS.

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

Dr. Meade will now discuss the GI-1 class cost effectiveness conclusion and Uniform Formulary recommendations.

GASTROINTESTINAL-1s—RELATIVE COST EFFECTIVENESS

(PEC Script)
(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of the GI-1 Drug Class. Cost-minimization analyses and budget impact analyses were performed.

For the aminosalicylates, budget impact analyses results showed that all investigated scenarios resulted in lower cost estimates compared to current MHS expenditures. Overall, cost analyses indicated that the placement of all agents on the UF was the most cost-effective scenario.

For the GI steroids and Miscellaneous IBS agents, cost analysis results and budget estimates indicated that the placement of all agents on the UF was the most cost-effective scenario.

Relative Cost-Effectiveness Conclusion— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee voted to accept the relative cost-effectiveness of the aminosalicylates (17 for, 0 opposed, 0 abstained, 1 absent) and GI Steroids and Miscellaneous IBS agents (17 for, 0 opposed, 0 abstained, 1 absent) in the GI-1 Drug Class.

GASTROINTESTINAL-1s—UF RECOMMENDATION
(PEC Script)

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

For the aminosalicylates, sulfasalazine, Colazal, Dipentum, Asacol, Asacol HD, Pentasa, Lialda, Apriso, Canasa, sulfite-free Rowasa, and mesalamine enema remain classified with formulary status on the UF (15 for, 1 opposed, 1 abstained, 1 absent).

For the GI steroids and Miscellaneous IBS agents, Entocort EC, hydrocortisone enema, hydrocortisone foam (Cortifoam) and Lotronex remain classified with formulary status on the UF (16 for, 0 opposed, 1 abstained, 1 absent). Zelnorm is only available from the FDA under a treatment investigational new drug application.

As a result of the above recommendations, there are no GI-1 agents designated with non-formulary status on the UF.

(Dave Meade) COL Lounsbery will now provide the physician perspective for the GI-1 class.

GASTROINTESTINAL-1s—COMMITTEE PHYSICIAN PERSPECTIVE

COL Lounsbery told the Panel that there isn't much to say about this drug class because all of the agents are on formulary – there was no clinical reason not to put them on there -- and it saves money to have them on.

GASTROINTESTINAL-1s—PANEL QUESTIONS AND DISCUSSION

Dr. Schlaifer asked for clarification regarding the agent tegaserod (Zelnorm). COL Lounsbery said FDA has a Risk Evaluations and Mitigation Strategy (REMS) in lace for this drug which absolutely limits its use to FDA-approved cases.

There was no further discussion of the recommendations in this class.

GASTROINTESTINAL-1s—BAP VOTE ON UF RECOMMENDATION

Ms. Fryar read the P&T Committee's UF recommendations for the gastrointestinal 1s drug class.

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

For the aminosalicylates, sulfasalazine, Colazal, Dipentum, Asacol, Asacol HD, Pentasa, Lialda, Apriso, Canasa, sulfite-free Rowasa, and mesalamine enema remain classified with formulary status on the UF.

For the GI steroids and Miscellaneous IBS agents, Entocort EC, hydrocortisone enema, hydrocortisone foam (Cortifoam) and Lotronex remain classified with formulary status on the UF. Zelnorm is only available from the FDA under a treatment investigational new drug application.

The Panel voted as follows:

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

No Panel comments were offered.

No implementation plan was required for this drug class as all agents are on the UF.

ANTILIPIDEMIC-2s (LIP-2s) DRUG CLASS REVIEW

(PEC Script)

(COL Cynthia Clagett): *We will now discuss our second UF drug class review, the Antilipidemic Agents 2 (Lip-2s).*

ANTILIPIDEMIC-2s (LIP-2s) —RELATIVE CLINICAL EFFECTIVENESS

(COL Cynthia Clagett) The P&T Committee evaluated the relative clinical effectiveness of the LIP-2 Drug Class, which was previously reviewed at the May 2007 P&T Committee meeting.

The LIP-2 Drug Class accounted for $111 million in MHS expenditures in FY 2010. This class is comprised of three subclasses: fibric acid derivatives, prescription omega-3 fatty acids, and bile acid sequestrants (BAS). For the omega-3 fatty acids (fish oil products), there are a number of nutritional supplement products available over-the-counter, but are not eligible for inclusion on the UF.

Relative Clinical Effectiveness Conclusion— The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following clinical effectiveness conclusions for the LIP-2s:

For the Fibric acid derivatives:

1. Both gemfibrozil and fenofibrate reduce triglycerides 20%–50% and raised HDL 10%–20%. There is insufficient evidence to conclude that gemfibrozil and fenofibrate differ in their ability to reduce TG and raise HDL.
2. In terms of clinical outcomes, there are no head-to-head trials comparing gemfibrozil with fenofibrate. In two trials (HHS and VA-HIT trials), Gemfibrozil was shown to reduce nonfatal heart attacks and coronary heart disease (CHD) death. Mixed results have been shown with fenofibrates. A reduction in nonfatal heart attack was seen with fenofibrates in the FIELD trial, but there was a nonsignificant increase in CHD death. In the ACCORD trial when fenofibrate was used in combination with a statin, there was a trend for a reduction in nonfatal heart attack, nonfatal stroke or death from cardiovascular (CV) causes in individuals with TG > 204 mg/dl and HDL < 34 mg/dl.
3. Despite differences in dosage strength, particle technology, or active ingredient, the fenofibrates are bioequivalent to the original Tricor 200 mg formulation approved in 1988. In terms of efficacy, these newer fenofibrate formulations do not offer a clinical advantage over the original Tricor fenofibrate formulation.
4. Trilipix is the only fenofibrate indicated for combination use with a statin, but other fenofibrate formulations are frequently given concurrently with a statin.
5. The ACCORD trial demonstrated the combination of a fenofibrate with a statin was well tolerated. Although pharmacokinetic and FDA spontaneous adverse event reporting data suggest that gemfibrozil is more likely to interact with statins

than fenofibrates, there is a lack of clinical evidence to support that the incidence of myopathy/rhabdomyolysis is lower with fenofibrates. Current guidelines from the American Heart Association and the American College of Cardiology conclude there is a risk with all fibric acid and statin combinations that is not limited to just gemfibrozil.

For the Omega-3 fatty acids:

1. Lovaza is the only prescription omega-3 fatty acid product approved by the FDA. It is indicated for use as an adjunct to diet in patients with very high triglyceride levels (>500 mg/dL).
2. Overall, Lovaza decreases triglycerides 20%–45%. Lovaza has also been associated with increases in LDL.
3. Lovaza's TG-lowering effects are slightly lower than those achieved with fibric acid derivatives or niacin. Lovaza is associated with similar increases in HDL compared to fibric acid derivatives and niacin. Niacin and gemfibrozil both have clinical trial evidence supporting long-term benefits on cardiovascular outcomes.
4. The Lovaza product marketed in the United States does not have outcomes studies showing beneficial effects of reducing death, MI, or stroke, and is not indicated to prevent CHD. The evidence of fish oil supplements or dietary fish consumption for reducing CHD risk is supportive but not conclusive.
5. There is insufficient evidence to support the use of Lovaza for non-CV conditions, including behavioral health/psychiatric conditions. The results of small clinical trials have been conflicting, and used formulations of fish oil different than that found in the Lovaza product.
6. Gastrointestinal disturbances and bad taste are the most commonly reported adverse effects of Lovaza.
7. Lovaza provides an alternative therapy in patients with elevated TGs who are not candidates for niacin or fibrates due to a history of adverse effects.

For the Bile Acid Sequestrants:

1. The bile acid sequestrants reduce LDL 15%–30%. This subclass has largely been replaced by the statins, which reduce LDL 18%–55%. There is insufficient evidence to conclude that bile acid sequestrants differ in their ability to lower LDL. Cholestyramine is the only bile acid sequestrant to show beneficial effects on cardiovascular outcomes.
2. Welchol has no major efficacy advantages compared to cholestyramine or colestipol.
3. Welchol is now FDA-approved for glycemic control in patients with Type 2 diabetes mellitus, when used as adjunctive therapy with other glucose-lowering drugs.

COMMITTEE ACTION: The P&T Committee voted to accept the clinical effectiveness

conclusion stated above.

Dr. Meade will now discuss the Lip-2 Class cost effectiveness conclusion and Uniform Formulary recommendations.

ANTILIPIDEMIC-2s (LIP-2s) —RELATIVE COST EFFECTIVENESS

(PEC Script)

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of LIP-2 Drug Class. Cost minimization analyses and budget impact analyses were performed based on findings that there were no clinically relevant differences in efficacy, safety, tolerability, and other factors among the LIP-2 subclasses.

For the Fibric acid derivatives, budget impact analyses results showed that all investigated scenarios resulted in lower cost estimates than current MHS expenditures. Overall, scenarios where Tricor, generic gemfibrozil, and generic fenofibrate were selected as step-preferred agents, while designating all other fibric acids as UF, were the most cost-effective scenarios. A sensitivity analysis was performed regarding the date of generic competition for Tricor and Trilipix. Sensitivity analysis results supported the above conclusion.

For Omega-3 fatty acids, budget impact analyses were used to assess the potential impact of cost scenarios where Lovaza was designated with formulary or NF status on the UF. Cost scenarios evaluating the impact of implementing prior authorization were also considered. Overall, scenarios where Lovaza was subject to a prior authorization, which would apply to all current and new users, were the most cost-effective. Results from a sensitivity analysis performed supported the above conclusion.

For the bile acid sequestrants, results from the cost minimization analyses performed showed that Welchol was less cost effective than generic bile acid sequestrants currently available on the UF.

Relative Cost-Effectiveness Conclusion— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee voted to accept the relative cost-effectiveness of the fibric acid derivatives (17 for, 0 opposed, 0 abstained, 1 absent), Lovaza (16 for, 0 opposed, 0 abstained, 2 absent), and bile acid sequestrants (17 for, 0 opposed, 0 abstained, 1 absent).

ANTILIPIDEMIC-2s (LIP-2s) —COMMITTEE ACTION

ANTILIPIDEMIC-2s (LIP-2s) —UF RECOMMENDATION

(PEC Script)

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

a) For the Fibric Acid Derivatives:

Generic Lopid, Triglide, generic Lofibra, and Lipofen remain designated with formulary status on the UF. Antara, Tricor, Fibricor, and Trilipix will be designated with formulary status on the UF (16 for, 0 opposed, 0 abstained, 2 absent).

There is a prior authorization for the fenofibrate acid derivatives that would require a trial of gemfibrozil, generic fenofibrate micronized/nonmicronized formulations, or Tricor (step-preferred drugs) for new patients (16 for, 0 opposed, 0 abstained, 2 absent).

b) For the Omega-3 fatty acids:

Lovaza will be designated with formulary status on the UF (12 for, 4 opposed, 1 abstained, 1 absent) and subject to PA criteria that allows use in all current and new users, only for FDA-approved indications.

c) For Bile Acid Sequestrants:
Generic Questran, generic Questran Light, generic Colestid remain formulary on the UF; and, Welchol will remain designated with non-formulary status on the UF (14 for, 2 opposed, 1 abstained, 1 absent).

ANTILIPIDEMIC-2s (LIP-2s) —FIBRIC ACID DERIVITIVES PA CRITERIA

(Dave Meade)

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 2 absent) the following PA criteria should apply to the nonpreferred fibric acid derivatives, Antara, Triglide, Lipofen, Fibricor, Trilipix. Coverage would be approved if the patient met any of the following criteria:

a) Automated PA criteria:

1. The patient has received a prescription for gemfibrozil, generic fenofibrate micronized/nonmicronized formulations (including Lofibra) or Tricor during the previous 180 days.

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

1. The patient has a contraindication to the preferred fibric acid derivatives that is not expected to occur with the nonpreferred fibric acid derivatives.

ANTILIPIDEMIC-2s (LIP-2s) —FIBRIC ACID DERIVITIVES PA IMPLEMENTATION PLAN

(Dave Meade)

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 2 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service; and that TMA send a

letter to beneficiaries affected by this UF decision.

ANTILIPIDEMIC-2s (LIP-2s) —LOVAZA PA CRITERIA

(Dave Meade)

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to the Lovaza. Lovaza would be approved only for the FDA-approved indications. All current and new users of Lovaza must meet one of the following criteria to pass through the PA process.

a) Patients with TG > 500 mg/mL who are receiving statins AND have had an inadequate TG-lowering response to a therapeutic trial of niacin (1-2 g/day) or fibrates, are unable to tolerate niacin or fibrates, or are not candidates for niacin or fibrate therapy.

b) Patients with TG > 500 mg/mL who are not receiving statins AND who have had an inadequateTG-lowering response to a therapeutic trial of monotherapy with both a fibrate and niacin, are unable to tolerate niacin and fibrates, or are not candidates for niacin and fibrate therapy.

c) Coverage is not approved for Lovaza for use in non-FDA approved conditions.

ANTILIPIDEMIC-2s (LIP-2s) —LOVAZA PA IMPLEMENTATION PERIOD

(Dave Meade)

The P&T Committee recommended (13 for, 3 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service; and that TMA send a letter to beneficiaries affected by this UF decision.

ANTILIPIDEMIC-2s (LIP-2s) —WELCHOL MN CRITERIA

(Dave Meade)

Based on the clinical evaluation of the bile acid sequestrants and the conditions for establishing MN for a NF medication, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) maintaining the current MN criteria for Welchol.

(Dave Meade) COL Lounsbery will now give the physician perspective for the LIP-2 agents.

ANTILIPIDEMIC-2s (LIP-2s) —PHYSICIAN'S PERSPECTIVE

COL Lounsbery again provided the BAP with the Committee Physician's perspective on this drug class, noting that the fibric acid derivitives were previously reviewed in 2007. At that time, several

agents were made non-formulary. However, further analyses showed that putting them all of the formulary with a step requirement would allow TMA to do better economically. The reason for the step is that although the products are different they all contain the same acid ingredient. Because there are so many formulations available, the best way to go is to put the ones that are more costly behind the step. As a result, right now the generic formulations along with Tricor, which will go off-patent sometime next year, are in front of the step. For the step therapy, gemfibrozil was chosen as a preferred drug because it was the only one to show positive data in depth in the Helsinki study and it's also cost effective. For the omega-3 fatty acids, there is only one prescription drug although there are several fish oil supplements available over-the-counter.

Lovaza is only good for the one specific indication (very high triglyceride levels) and is not approved for other things that people are using fish oil for. There is no compelling evidence to say we should use this for non-cardiovascular conditions. Thus it was designated as a formulary drug because it is consistent in fatty acid content, unlike various other fish oil products, but only for its FDA-approved indication through a PA. The Committee also agreed there should be no grandfathering; all patients need to go through the PA process to ensure there is no off-label use where there is no evidence to suggest it is beneficial. The dissenting votes came from individuals who felt that Lovaza should be non-formulary.

For bile acid sequestrants the recommendation was to keep Welchol non-formulary with the current medical necessity criteria. The Committee members felt that MHS has plenty of drugs for diabetes and that Welchol didn't need to be on formulary.

ANTILIPIDEMIC-2s (LIP-2s) —PANEL QUESTIONS AND DISCUSSION

Dr. Cohoon asked about the two opposing votes regarding the bile acid sequestrants. Dr. Meade explained the votes. Dr. Cohoon also asked whether a 60-day implementation period would be enough as there is to be no grandfathering. Dr. Meade said it should be.

Ms. LeGette asked what people were using Lovaza for. Dr. Meade said for triglycerides, without trying other agents that would be more cost effective. One field request also indicated Lovaza is being used for behavioral health and cited articles. However, research showed that it was another supplement, not Lovaza, causing the changes.

ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON UF RECOMMENDATION

Without further discussion, the Panel Chair read the P&T Committee's UF recommendations for the antilipidemic-2s (LIP-2s) drug class.

1. **Fibric Acid Derivatives:**
    a) Gemfibrozil, Tricor Triglide, generic fenofibrate micronized/nonmicronized, and Lipofen remain designated with formulary status on the UF; and that Antara, Tricor, Fibricor, and Trilipix will be designated with formulary status on the UF.
    b) Prior authorization for the fenofibrate acid derivatives would require a

trial of gemfibrozil, generic fenofibrate micronized/nonmicronized formulations, or Tricor as step-preferred drugs for new patients.

2. **Omega-3 fatty acids:** Lovaza be designated with formulary status on the UF and subject to PA criteria that allows use in all current and new users, only for FDA-approved indications.
3. **Bile Acid Sequestrants:** Generic Questran, generic Questran Light, generic Colestid remain formulary on the UF; and, Welchol will remain designated with non-formulary status on the UF.

The Panel vote was:

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

The Panel had no comments

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ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON FIBRIC ACID DERIVATIVES PA CRITERIA RECOMMENDATION

Ms. Fryar next read the recommendations regarding fibric acid derivatives PA criteria.

The P&T Committee recommended the following PA criteria should apply to the nonpreferred fibric acid derivatives, Antara, Triglide, Lipofen, Fibricor, Trilipix. Coverage would be approved if the patient met any of the following criteria:

1. Automated PA criteria:
    a) The patient has received a prescription for gemfibrozil, generic fenofibrate micronized/nonmicronized formulations (including Lofibra) or Tricor (at the MTFs, retial network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:

    a) The patient has a contraindication to the preferred fibric acid derivatives that is not expected to occur with the nonpreferred fibric acid derivatives.

Without discussion or comment, the Panel voted:

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

ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON FIBRIC ACID DERIVATIVES PA IMPLEMENTATION PLAN

The Chair read the implementation plan recommendation.

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

The Panel vote was:

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

ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON LOVAZA PA CRITERIA RECOMMENDATION

Dr. Cohoon asked about the distribution of the 40,000 users of Lovaza by point of service. Dr. Meade replied that it is difficult to obtain that information because different data bases are involved.

The Chair then read the Committee's PA recommendation for Lovaza.

The P&T Committee recommended PA criteria should apply to the prescription omega-3 fatty acid product, Lovaza. Lovaza would be approved only for the FDA-approved indications. All current and new users of Lovaza must meet one of the criteria outlined in section 4, subsection, F [of the Committee's recommendations] to pass through the PA process.

That subsection reads as follows:

a) Patients with TG > 500 mg/mL who are receiving statins AND have had an inadequate TG-lowering response to a therapeutic trial of niacin (1-2 g/day) or fibrates, are unable to tolerate niacin or fibrates, or are not candidates for niacin or fibrate therapy.

b) Patients with TG > 500 mg/mL who are not receiving statins AND who have had an inadequateTG-lowering response to a therapeutic trial of monotherapy with both a fibrate and niacin, are unable to tolerate niacin and fibrates, or are not candidates for niacin and fibrate therapy.

c) Coverage is not approved for Lovaza for use in non-FDA approved conditions, including the following: Attention Deficit Hyperactivity Disorder, Alzheimer's disease, bipolar disease, Crohn's disease, cystic fibrosis, dementia, depression, inflammatory bowel disease, intermittent claudication, metabolic syndrome, osteoporosis, post-traumatic stress disorder, renal disease (immunoglobulin A nephropathy), rheumatoid arthritis, schizophrenia, Type 2 diabetes mellitus, and ulcerative colitis.

Without further comment, the BAP voted:

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

ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON LOVAZA PA IMPLEMENTATION PLAN

The Panel next considered the Committee's implementation plan recommendations for the Lovaza PA.

Ms. LeGette commented that it is important to get the letter out as soon as possible on this one. Ms. Fryar asked whether 60 days is a long enough implementation period. Mr. Hutchings said he has been struggling with this question and thinks that 90 days might be better because we are adding a requirement for patients to have to get to their doctor. Dr. Cohoon said she also prefers a longer implementation period. Dr. Schlaifer said that the longer the period is the more problems there will be because the problem is highly marketed so there will be more people using the meds. In addition, she would take into consideration the fact that there would be little or no harm to the patient from missing a dose. There should be no implications at all. She intends to vote to concur. Mr. Hutchings asked about who would get the PA forms, then said that as long as the only form required is a letter, the 60-days would be okay.

Without further discussion, Ms. Fryar read the recommendation.

The P&T Committee recommended an effective date of the first Wednesday after a 60-day implementation period in all points of service; and that TMA send a letter to beneficiaries affected by this UF decision.

The BAP voted:

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

ANTILIPIDEMIC-2s (LIP-2s) —PANEL VOTE ON COLOSEVELAM (WELCHOL) MEDICAL NECESSITY (MN) CRITERIA

To conclude the consideration of this drug class, Ms. Fryar read the recommendation regard Welchol medical necessity criteria.

Based on the clinical evaluation of the bile acid sequestrants and the conditions for establishing MN for a NF medication, the P&T Committee recommended maintaining the current MN criteria for Welchol.

Without discussion or comment, the BAP voted:

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

PANCREATIC ENZYME PRODUCTS (PEPs) DRUG CLASS REVIEW

(PEC Script)

(LCDR Marisol Martinez): *We will now discuss our third UF drug class review, the Pancreatic Enzyme Products.*

PANCREATIC ENZYME PRODUCTS (PEPs) —RELATIVE CLINICAL EFFECTIVENESS

(LCDR Marisol Martinez): The P&T Committee evaluated the relative clinical effectiveness of the drugs in the Pancreatic Enzyme Products (PEP) drug class. The class is comprised of 3 FDA

approved drugs. Please turn to your handout and refer to Table 2 on page 4 for more specifics about drugs in the class. The Pancreatic Enzyme Products class as a whole has not previously been previously reviewed.

Creon and Zenpep were approved for marketing in 2009 and Pancreaze was approved in April 2010. There is one authorized generic PEP formulation, pancrelipase delayed-release capsules, which is equivalent to Zenpep 5,000. All previously marketed non-FDA approved PEPs have been discontinued as of April 28, 2010.

Please look at Figure 4 on Page 4 of your handout. In terms of MHS utilization, Creon, shown in red, is the most utilized (approximately 500,000 units dispensed monthly), followed by Zenpep (100,000 units dispensed monthly), and Pancreaze (100,000 units dispensed monthly). Non-approved PEPs have leveled off on the bottom.

Information regarding the safety, effectiveness, and clinical outcomes of the PEPs was considered.

PEPs—Relative Clinical-Effectiveness

The clinical review focused on use of the PEPs for exocrine pancreatic insufficiency (EPI).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following clinical effectiveness conclusions for the PEP class:

1. There are no head-to-head trials comparing the PEPs. Based on indirect studies Creon, Pancreaze, and Zenpep are superior to placebo for improving fat malabsorption associated with EPI due to cystic fibrosis (CF).
2. For patients with EPI due to CF, the endpoint of the average coefficient of fat absorption (CFA) for Creon, Pancreaze, and Zenpep ranged between 83%–88% in the placebo-controlled trials used to obtain FDA approval. A CFA > 80% is considered clinically relevant for improving fat malabsorption.
3. With regards to safety, the available evidence suggests there are no clinically relevant differences between Creon, Pancreaze, and Zenpep.

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

Dr. Meade will now discuss the PEPs cost effectiveness conclusion and Uniform Formulary recommendations.

PANCREATIC ENZYME PRODUCTS (PEPs) —RELATIVE COST EFFECTIVENESS

(PEC script)

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of the PEPs class. Based on clinical findings that efficacy, safety, tolerability, and other factors found among the PEPs were similar at equipotent doses, Cost Minimization Analyses (CMAs) and Budget Impact

Analyses were performed. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) that Pancreaze was the most cost-effective PEP, followed by Zenpep. Creon was the least cost-effective agent based on weighted average cost per day of therapy. BIA results indicated the scenario that placed all PEPs on the UF was the most cost-effective formulary scenario.

PANCREATIC ENZYME PRODUCTS (PEPs) —COMMITTEE ACTION—UF RECOMMENDATIONS

(PEC script)

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) Creon, Pancreaze, and Zenpep be designated with formulary status on the UF. As a result of this action, no PEPs are designated NF.

(Dave Meade): At this time, COL Lounsbery will provide the physician perspective for the PEPs.

PANCREATIC ENZYME PRODUCTS (PEPs) —COMMITTEE PHYSICIAN PERSPECTIVE

COL Lounsbery told the Panel that there is not a lot to comment on in regard to this class. The budget analysis indicated that it would be beneficial to keep all of the agents on formulary, so the decision was easy.

PANCREATIC ENZYME PRODUCTS (PEPs) —BAP QUESTIONS AND DISCUSSION

The Panel had no questions about the recommendations in this drug class.

PANCREATIC ENZYME PRODUCTS (PEPs) —BAP VOTE ON UF RECOMMENDATION

The BAP Chair read the UF recommendations for the pancreatic enzyme products (PEPs) drug class.

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

with formulary status on the UF. As a result of this action, no PEPs are designated NF.

The Panel vote was as follows:

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

Because all agents are on the UF, no implementation plan is required for this recommendation.

CONSIDERATION OF RECENTLY APPROVED DRUGS

(PEC Script)

(Dave Meade)

For the Newly Approved Drugs, information considered by the Committee for the clinical and cost evaluations included, but were not limited to, the requirements stated in 32 Code of Federal Regulations (CFR) 199.21(e)(1).

1) RENIN ANGIOTENSIN ANTIHYPERTENSIVE AGENTS (RAAs)—ALISKIREN/AMLODIPINE TABLETS (TEKAMLO)

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo)—RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(LCDR Marisol Martinez) Tekamlo is a fixed-dose combination product containing the direct rennin inhibitor aliskirin, also known as Tekturna and calcium channel blocker amlodipine, also known as Norvasc.

Tekamlo is indicated for treating hypertension. No positive clinical outcomes have been reported for Tekamlo or any aliskiren-containing product. Current national guidelines [Joint National Committee (JNC-7)] for treating hypertension have not yet addressed the place in therapy for DRIs, although updated guidelines (JNC-8) are anticipated later this year. The American Society of Hypertension does not list the Tekamlo (or any aliskiren-containing) combination as either preferred or acceptable in their recent position statement. Tekamlo does not contain a thiazide-type diuretic, which is considered first-line for most patients.

Treatment with Tekamlo was shown in one randomized trial to significantly reduce blood pressure (BP) compared to placebo. The adverse reaction profile for Tekamlo reflects that of the individual components.

Relative Clinical Effectiveness Conclusion— The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) that although aliskiren/amlodipine (Tekamlo) has a unique mechanism of action due to the direct rennin inhibitor component and offers the potential for increased medication persistence, it did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over other rennin angiotensin

antihypertensive agents included on the UF.

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —RELATIVE COST EFFECTIVENESS

(PEC Script)

(Dave Meade) The P&T Committee evaluated the cost of Tekamlo in relation to the efficacy, safety, tolerability, and clinical outcomes of the other currently available agents in this subclass. A cost-minimization analysis was performed to evaluate the cost of Tekamlo in relation to the other currently available RAAs, as well as the individual components, aliskiren and amlodipine.

Results from the CMA showed the projected weighted average cost per day for Tekamlo is higher than the other formulary RAAs, including the triple fixed-dose combination drug valsartan/amlodipine/HCTZ (Exforge HCT) and the individual components, Tekturna and amlodipine.

Relative Cost-Effectiveness Conclusion— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) aliskiren/amlodipine (Tekamlo) is not cost-effective relative to the other RAAs in this class

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) aliskiren/amlodipine (Tekamlo) be designated with nonformulary (NF) status on the UF.

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —PRIOR AUTHORIZATION (PA) CRITERIA

(Dave Meade) As a result of UF action, Tekamlo is designated as a non-preferred RAAs. Prior Authorization for the RAAs class requires a trial of one of the following step-preferred drugs for new patients: losartan (Cozaar, generics), losartan/HCTZ (Hyzaar, generics), telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), and valsartan/amlodipine/HCTZ (Exforge HCT). The other RAAs are non-preferred.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) the following PA criteria should apply to aliskiren/amlodipine (Tekamlo):

1. Automated PA criteria:

    a) The patient has received a prescription for losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT),

telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), or valsartan/amlodipine/HCTZ (Exforge HCT) at any Military Health System (MHS) pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:

   a) The patient has tried one of the preferred RAAs and was unable to tolerate treatment due to adverse effects.

   b) The patient has tried one of the preferred RAAs and has had an inadequate response.

   c) The patient has a contraindication to the preferred RAAs, which is not expected to occur with the non-preferred RAAs (e.g., history of angioedema).

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —MEDICAL NECESSITY (MN) CRITERIA

(Dave Meade)

Based on the clinical evaluation of aliskiren/amlodipine (Tekamlo) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Tekamlo.

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —UF IMPLEMENTATION PERIOD

(Dave Meade)

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

(Dave Meade): COL Lounsbery will now give the physician perspective for Tekamlo.

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —COMMITTEE PHYSICIAN PERSEPCTIVE

COL Lounsbery noted that the P&T Committee reviewed the class in August and none of the drugs were made non formulary, but did recommend a Prior Authorization for the direct renin inhibitors at that time. Tekamlo requires comparing a combination to a single agent. TMA already has 30 RAAs on the formulary – combinations of ARBs and other drugs, primarily

diuretics. Given that Tekamlo had data only for treating hypertension, has no data on cardiovascular outcomes such as stroke or death and the role of direct renin inhibitors is unclear, the Committee recommended non-formulary, although it is awaiting further test results which may be helpful.

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —PANEL QUESTIONS AND DISCUSSION

Mr. Hutchings noted that the decision in this case seems to be inconsistent with the Committee's previous review of this class and asked about the basis for it. Dr. Meade replied that the Uniform Formulary rule requires that when a new drug is considered, there has to be a showing of some advantage to the drug. The decision was consistent with that rule. If it were to be reviewed along with all of the drugs in this class instead of by itself, there might be a different outcome, but the class as a whole was reviewed just recently.

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —PANEL VOTE ON UF RECOMMENDATION

Without further discussion Ms. Fryar read the Committee's UF recommendation for Tekamlo.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended Tekamlo be designated with NF status on the UF.

The Panel voted:

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

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —PANEL VOTE ON PA CRITERIA RECOMMENDATION

The Chair next read the recommended PA criteria.

As a result of UF action, Tekamlo is designated as a non-preferred RAA. Prior Authorization for the RAAs class requires a trial of one of the following step-preferred drugs for new patients: generic losartan, generic losartan/HCTZ, Micardis, Micardis HCT, Twynsta, Diovan, Diovan HCT, Exforge, and Exforge HCT. The other RAAs are non-preferred.

The P&T Committee recommended the following PA criteria should apply to aliskiren/amlodipine (Tekamlo):

1. Automated PA criteria:
    a) The patient has received a prescription for a step-preferred RAA — losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), telmisartan/amlodipine (Twynsta), valsartan (Diovan),

valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), or valsartan/amlodipine/HCTZ (Exforge HCT) — at any Military Health System (MHS) pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:

   a) The patient has tried one of the preferred RAAs and was unable to tolerate treatment due to adverse effects.

   b) The patient has tried one of the preferred RAAs and has had an inadequate response.

   c) The patient has a contraindication to the preferred RAAs, which is not expected to occur with the non-preferred RAAs (e.g., history of angioedema).

Without comment or discussion, the BAP voted:

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

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —PANEL VOTE ON MN CRITERIA RECOMMENDATION

The Chair read the MN recommendation.

Based on the clinical evaluation of aliskiren/amlodipine (Tekamlo) and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended MN criteria for Tekamlo.

The BAP vote was:

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

Renin Angiotensin Antihypertensive Agents (RAAs)—Aliskiren/Amlodipine Tablets (Tekamlo) —PANEL VOTE ON UF AND PA IMPLEMENTATION PLAN

The implementation plan recommendation was read.

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

Once again the vote was:

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

2) RENIN ANGIOTENSIN ANTIHYPERTENSIVE AGENTS (RAAs)— OLMESARTAN/AMLODIPINE/HCTZ TABLETS (TRIBENZOR)

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor)—RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(LCDR Marisol Martinez) The second new drug we have to discuss is another RAAs agent. Tribenzor is a fixed-dose combination product containing olmesartan (Benicar), amlodipine (Norvasc, generics), and HCTZ. It is the second three-drug combination product containing an ARB (olmesartan; Benicar), a CCB (amlodipine), and thiazide-type diuretic (HCTZ) to reach the market.

Tribenzor is solely indicated for treating hypertension; it can be substituted for the individual titrated components or used as add-on therapy in patients not adequately controlled on two of the component drugs. It is not approved for initial therapy to control BP. Each of the component drugs is consistent with first-line therapy choices per current national guidelines (JNC-7).

Treatment with Tribenzor was shown in one randomized trial to significantly reduce BP when compared to baseline and to each two-drug combination of the component drugs. There are no trials evaluating clinical outcomes of mortality or morbidity with Tribenzor, although outcomes trials are available with the individual components. The adverse reaction profile for Tribenzor reflects that of the individual components.

Relative Clinical Effectiveness Conclusion— The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 2 absent) that although olmesartan/amlodipine/HCTZ (Tribenzor) offers the potential for increased medication persistence, it did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over other RAAs included on the UF.

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — RELATIVE COST EFFECTIVENESS

(Dave Meade) The P&T Committee evaluated the cost of Tribenzor in relation to the efficacy, safety, tolerability, and clinical outcomes of the RAAs as well as the individual components, olmesartan, amlodipine, and HCTZ.

Results from the cost-minimization analyses showed the projected weighted average cost per day for Tribenzor is higher than the other formulary fixed-dose combination RAAs, including the triple-therapy drug amlodipine/valsartan/hydrochlorothiazide (Exforge HCT) and the individual components olmesartan (Benicar), amlodipine, and HCTZ.

Relative Cost-Effectiveness Conclusion— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained, 2 absent) olmesartan/amlodipine/HCTZ (Tribenzor) is not cost- effective relative to the other RAAs in this class.

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/

Amlodipine/HCTZ Tablets (Tribenzor) — UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 2 absent) olmesartan/amlodipine/HCTZ (Tribenzor) be designated NF on the UF.

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — PRIOR AUTHORIZATION CRITERIA

(Dave Meade) As a result of the UF action, Tribenzor is designated as a non-preferred RAAs. The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) the same automated and manual PA criteria as outlined above for aliskiren/amlodipine (Tekamlo) should apply to olmesartan/amlodipine/HCTZ (Tribenzor).

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — MEDICAL NECESSITY CRITERIA

(Dave Meade) Based on the clinical evaluation of olmesartan/amlodipine/HCTZ (Tribenzor) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Tribenzor.

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — UF IMPLEMENTATION PLAN

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

(Dave Meade): COL Lounsbery will now give the physician perspective for Tribenzor.

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — COMMITTEE PHYSICIAN PERSPECTIVE

COL Lounsbery said the main reason for designating Tribenzor nonformulary is that TMA is trying to steer clinicians to use Exforge HCT. Tribenzor has two of the same components; the third is an ARB – Olmesartan. Exforge is preferred because it has additional indications. Also, Tribenzor is not cost effective.

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — PANEL QUESTIONS AND DISCUSSION

The BAP members had no comments or questions of the presenters concerning this recommendation.

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — PANEL VOTE ON UF RECOMMENDATION

Ms. Fryar read the UF recommendation for Tribenzor.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended olmesartan/amlodipine/HCTZ (Tribenzor) be designated NF on the UF.

The Panel voted as follows:

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

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — PANEL VOTE ON PA CRITERIA

After determining that the BAP members had no questions, comments or concerns about the PA criteria, Ms. Fryar read the P&T Committee's recommendations.

As a result of UF action, Tribenzor is designated as a non-preferred RAA. Prior Authorization for the RAAs class requires a trial of one of the following step-preferred drugs for new patients: generic losartan, generic losartan/HCTZ, Micardis, Micardis HCT, Twynsta, Diovan, Diovan HCT, Exforge, and Exforge HCT. The other RAAs are non-preferred.

The P&T Committee recommended the following PA criteria should apply to aliskiren/amlodipine (Tribenzor):

1. Automated PA criteria:
   a) The patient has received a prescription for a step-preferred RAA — losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), or valsartan/amlodipine/HCTZ (Exforge HCT) — at any Military Health System (MHS) pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:
   a) The patient has tried one of the preferred RAAs and was unable to tolerate treatment due to adverse effects.
   b) The patient has tried one of the preferred RAAs and has had an inadequate response.
   c) The patient has a contraindication to the preferred RAAs, which is not expected to occur with the non-preferred RAAs (e.g., history of angioedema).

Without comment or discussion, the BAP voted:

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

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — PANEL VOTE ON MN CRITERIA

The Chair next read the MN criteria recommendation for Tribenzor.

Based on the clinical evaluation of olmesartan/amlodipine/HCTZ (Tribenzor) and the conditions for establishing MN for a NF medication, the P&T Committee recommended MN criteria for Tribenzor.

Again without discussion or comment, the Panel voted:

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

Renin Angiotensin Antihypertensive Agents (RAAs)—Olmesartan/ Amlodipine/HCTZ Tablets (Tribenzor) — PANEL VOTE ON UF AND PA IMPLEMENTATION PLAN

Ms. Fryar then read the implementation plan.

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

The Panel voted:

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

3) RECENTLY APPROVED DRUGS—ANTIEMETICS—ONDANSETRON SOLUBLE FILM (ZUPLENZ)

(PEC Script)

Antiemetics—Ondansetron Soluble Film (Zuplenz) — RELATIVE CLINICAL EFFECTIVENESS

(LCDR Marisol Martinez)

Zuplenz is a serotonin subtype 3 (5-HT3) receptor antagonist. It is the only newer antiemetic available in an oral soluble film dosage form. Zofran generics are also available in tablets, orally disintegrating tablets (ODT), and an oral solution; these formulations are included on the UF.

If you turn to table 6 on page 12 of the handout, you'll see the list of the Antiemetic drugs. The utilization of some of the Antiemetic drugs is found in Figure 10. The highest utilization is with the generic ondansetron tablets, followed by the ondansetron orally disintegrating tablets.

Ondansetron oral soluble film (Zuplenz) obtained FDA approval via section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act using efficacy and safety data submitted from the ondansetron ODT (Zofran) submission. Bioequivalence studies demonstrated that a single dose of ondansetron oral soluble film 8 mg, taken with or without water and in underfed and fasting conditions, was comparable to ondansetron ODT 8 mg. There are no head-to-head clinical trials comparing ondansetron oral soluble film to the other newer antiemetics. Zuplenz's safety profile reflects that of the other ondansetron products.

Relative Clinical Effectiveness Conclusion— The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) there is no evidence to suggest ondansetron oral soluble film (Zuplenz) has a compelling clinical advantage over ondansetron products currently included on the UF.

Antiemetics—Ondansetron Soluble Film (Zuplenz) — RELATIVE COST EFFECTIVENESS

(Dave Meade) A cost minimization analyses was performed that evaluated the cost of ondansetron oral soluble film (Zuplenz) in relation to other currently available newer antiemetics.

Relative Cost-Effectiveness Conclusion— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) ondansetron oral soluble film (Zuplenz) was more costly than all other oral comparators in the newer antiemetic class.

Antiemetics—Ondansetron Soluble Film (Zuplenz) — UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) ondansetron oral soluble film (Zuplenz) be designated NF on the UF.

Antiemetics—Ondansetron Soluble Film (Zuplenz) — MEDICAL NECESSITY CRITERIA

(Dave Meade) Based on the clinical evaluation of ondansetron oral soluble film (Zuplenz) and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Zuplenz.

Antiemetics—Ondansetron Soluble Film (Zuplenz) — UF IMPLEMENTATION PLAN

(Dave Meade) The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and that TMA send a letter to beneficiaries affected by this UF

decision.

(Dave Meade): COL Lounsbery will now give the physician perspective for Zuplenz.

Antiemetics—Ondansetron Soluble Film (Zuplenz) — COMMITTEE PHYSICIAN PERSPECTIVE

COL Lounsbery informed the BAP that the Committee was unanimous in recommending nonformulary status for Zuplenz. It is a different formulation where TMA already has cost-effective generic agents available. The Ondansetron tablets were the basis for FDA approving the film; the tablets are much more cost effective.

Antiemetics—Ondansetron Soluble Film (Zuplenz) — PANEL QUESTIONS AND DISCUSSION

The Panel had no questions of the presenters.

Antiemetics—Ondansetron Soluble Film (Zuplenz) — PANEL VOTE ON UF RECOMMENDATION

The Chair read the UF recommendation for Zuplenz.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended ondansetron oral soluble film (Zuplenz) be designated NF on the UF.

Without comment, the Panel vote was:

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

Antiemetics—Ondansetron Soluble Film (Zuplenz) — PANEL VOTE ON MN RECOMMENDATION

Ms. Fryar next read the MN recommendation.

Based on the clinical evaluation of ondansetron oral soluble film (Zuplenz) and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended MN criteria for Zuplenz.

The Panel voted:

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

Antiemetics—Ondansetron Soluble Film (Zuplenz) — PANEL VOTE ON IMPLEMENTATION PLAN

The Chair read the implementation plan recommendation for Zuplenz.

The P&T Committee recommended an effective date of the first Wednesday after a 60 days implementation period in all points of service, and that TMA send a letter to beneficiaries affected by this UF decision.

The BAP vote was as follows:

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

4) RECENTLY APPROVED DRUGS —ALZHEIMER'S DRUGS—DONEPEZIL 23 MG TABLETS (ARICEPT 23 MG)

Ms. Fryar, read for the record the following letter received by the DFO concerning Aricept 23 MG before introducing the presentation of P&T Committee recommendations.

Dr. Harry Ramos, MD
Medical Director, Aricept
Eisai Inc.
100 Tice Blvd.
Woodcliff Lake, NJ 07677

LTC Stacia Spridgen
Director, DoD Pharmacoeconomic Center
Bldg 1000
4130 Stanley Rd, Suite 208
Fort Sam Houston, TX 78234

LTC Spridgen:

This letter is in response to the Department of Defense's recent evaluation of Aricept 23 mg and the decision to place Aricept 23 mg on Tier 3 – nonformulary for TRICARE.

After reviewing the Pharmacy & Therapeutic (P&T) committee comments available from the evaluation meeting, it is my desire to clarify for the P&T committee several points regarding the efficacy and safety of Aricept 23mg.

In the comments, it is noted that the P&T committee concluded that Aricept 23mg did not have a significant, clinically meaningful therapeutic advantage in terms of effectiveness or clinical

outcomes over donepezil 10mg.

While the P&T comments correctly note that there was one clinical trial used to gain FDA approval, I think it is important to note that the trial was a large, multinational head-to-head study with over 1,400 patients.

In that clinical trial Aricept 23mg demonstrated statistically significant improvement in cognition, as measured by the Severe Impairment Battery, a validated measure of cognition in moderate to severe patients, as is noted in the P&T comments.

The comments go on to state that Aricept 23mg demonstrated "no benefit in improving global function." Now while it is accurate that Aricept 23mg did not demonstrate statistically significant difference versus Aricept 10mg when measured by the CIBIC+, it should be noted that the majority of patients in both treatment groups experienced no change to minimal worsening in global function.

The P&T comments also make a comparison of the efficacy of Aricept 23 mg to the efficacy of the combination of donepezil 10 mg and memantine. Although it is noted in the comments that the comparison is indirect, the study used to gain approval for Aricept 23mg was not designed to compare Aricept 23mg versus donepezil 10 mg and memantine. Thus, there is no clinical evidence available to support the conclusion that the efficacy of Aricept 23 mg appears similar to the combination of 10 mg of donepezil with memantine.

It is also noted in the P&T comments that "tolerability to the donepezil 23 mg formulation will be limited by the increased incidence of adverse events, particularly gastrointestinal (GI) effects, compared with donepezil 10 mg."

It is accurate that patients titrated to Aricept 23mg experienced a dose-related increase in adverse events versus those patients who remained stable on Aricept 10 mg for greater than three months. It should also be noted that the most common adverse events with ARICEPT 23 mg were often of mild to moderate intensity.

And while the incidence of nausea and vomiting was markedly greater in patients taking ARICEPT 23 mg, in most cases, these effects have been mild and transient, sometimes lasting 1 to 3 weeks, and have resolved during continued use of ARICEPT.

I would welcome the opportunity to discuss the information above with you further. Please feel free to contact me by phone (number redacted) or by e-mail (redacted), if you have any questions.

Sincerely,

Dr. Harry Ramos, MD
Medical Director, Aricept
Eisai, Inc.

(PEC Script)

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — RELATIVE CLINICAL EFFECTIVENESS

(LCDR Marisol Martinez) Donepezil 23 mg (Aricept 23 mg) is a formulation of donepezil (Aricept) in a higher dosage than previously available (5, 10 mg). The Alzheimer's Drug Class was previously reviewed in November 2005; donepezil 5 and 10 mg tablets are the current Extended Core Formulary (ECF) drugs. Generic formulations of donepezil 5 and 10 mg tablets and orally disintegrating tablets (ODTs) entered the market in November 2010.

In Table 5, on page 11 of the handout you will see the list of the Alzheimer's drugs. The utilization is at the bottom of the page, in Figure 10. Aricept has the highest utilization in the MHS.

The pharmacokinetic profile of one donepezil 23 mg tablet shows a delayed and lower peak concentration compared to giving two of the 10 mg tablets. The 23 mg formulation is not an extended-release preparation; the 5 mg, 10 mg, and 23 mg tablets are administered once daily.

The one clinical trial used to gain FDA approval, which compared donepezil 23 mg with 10 mg, showed statistically significant improvement in measures of cognition, but no benefit in improving global functioning. An indirect comparison suggests efficacy of 23 mg donepezil appears similar to giving 10 mg donepezil with memantine, also known as Namenda.

Tolerability of the donepezil 23 mg formulation will be limited by the increased incidence of adverse events, particularly gastrointestinal (GI) effects, compared with donepezil 10 mg.

Relative Clinical Effectiveness Conclusion— The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) donepezil 23 mg (Aricept 23 mg) did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over donepezil 10 mg.

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — RELATIVE COST EFFECTIVENESS

(PEC Script)

(Dave Meade) The P&T Committee evaluated the cost of Aricept in relation to the efficacy, safety, tolerability, and clinical outcomes of the other Alzheimer's drugs. A cost minimization analyses was used to evaluate the relative cost-effectiveness of Aricept 23mg relative to other Alzheimer's drugs.

Relative Cost-Effectiveness Conclusion— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) donepezil 23 mg (Aricept 23 mg) tablets are currently cost competitive with all other comparators in the Alzheimer's Drug Class. However, the current generic manufacturer has

exclusive marketing rights until spring 2011. Once other generic manufacturers enter the market, donepezil 23 mg (Aricept 23 mg) tablets will be more costly than all other drugs in the Alzheimer's Drug Class.

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (13 for, 4 opposed, 1 abstained, 0 absent) donepezil 23 mg tablets (Aricept 23 mg) be designated NF on UF.

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — MEDICAL NECESSITY CRITERIA

(Dave Meade) Based on the clinical evaluation of donepezil 23 mg tablets and the conditions for establishing MN for a NF medication, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Aricept 23 mg.

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — UF IMPLEMENTATION PLAN

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

(Dave Meade): COL Lounsbery will now give the physician perspective for Aricept 23 mg.

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — COMMITTEE PHYSICIAN PERSPECTIVE

COL Lounsbery told the panel that Aricept 23 is another new twist – a higher strength -- on an existing drug. We already have the 5- and 10 milligram formulations and orally disintegrating tablets. The head-to-head trial shows a statistically significant improvement in cognition, but without improvement over the generic in global functioning. Statistically significant improvement is hard to translate to clinical relevance and it is debatable whether it translates at all. The Committee recommended NF, although there were some who wanted it on formulary because Alzheimer's is hard to treat. However, the majority felt that NF placement was justified due to the conflicting results of the trial and because there are more adverse events with the stronger formulation. Additionally, Aricept 23 mg is more costly.

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — PANEL QUESTIONS AND DISCUSSION

Ms. Fryar referenced the smaller doses available and asked what the normal dosage is. COL Lounsbery said the usual is 10 mg. Ms. Fryar asked if the smaller doses could be increased. COL Lounsbery said it could, but it usually doesn't get increased, and justifiably so.

Dr. Cohoon asked if Aricept 23 would be more cost effective. Dr. Meade replied it would be more costly.

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — PANEL VOTE ON UF RECOMMENDATION

The Chair read the UF recommendation for Aricept 23 mg.

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended donepezil 23 mg tablets (Aricept 23 mg) be designated NF on UF.

The BAP vote was as follows:

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

Mr. Chavez commented that his non-concurring vote was because he believes some patients would benefit from having this drug available on the UF.

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — PANEL VOTE ON MN RECOMMENDATION

In discussion, Dr. Crum asked why it is necessary to add a new MN step to the process for each of these new approval items since the NF designation only affects the beneficiaries' co-pay and the MN designation allows them to get the drug at the lower co-pay. Mr. Hutchings said it seems to him like more of a formality – something we have to do. Dr. Cohoon said it seems like the MN provides an avenue for those patients who need it.

Without further discussion, Ms. Fryar read the P&T Committee's MN recommendation for Aricept 23 mg.

Based on the clinical evaluation of donepezil 23 mg tablets and the conditions for establishing MN for a NF medication, the P&T Committee recommended MN criteria for Aricept 23 mg.

The Panel voted:

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

Alzheimer's Drugs—Donepezil 23 mg Tablets (Aricept 23 mg) — PANEL VOTE ON IMPLEMENTATION PLAN

Ms. Fryar read the implementation plan.

The P&T Committee recommended an effective date of the first Wednesday after a 60 days implementation period in all points of service, and that TMA send a letter to beneficiaries affected by this UF decision.

The Panel voted:

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

Ms. Fryar commented for the record that concern has been expressed about who would actually receive the letter: the caretaker or the patient. The PEC Staff commented that they would not have information concerning caretakers, so the letter will have to be sent to the patient. Ms. Fryar also commented that it is important for the MN decisions to be a part of the formal record in each case.

5) RECENTLY APPROVED DRUGS — SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS

(PEC Script)

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — RELATIVE CLINICAL EFFECTIVENESS

(LCDR Heather Helwig) The self-monitoring blood glucose system (SMBGS) test strips were reviewed at the August 2008 P&T Committee meeting. SMBGS test strips designated with formulary status on the UF include Accu-Chek Aviva, Precision Xtra (the BCF SMBGS test strip), Freestyle Lite, Contour and TRUEtest.

If you turn to page 13 of the handout and look at table 7, the self-monitoring blood glucose systems are listed. The utilization is at the bottom of the page, in Figure 11. Precision Xtra has the highest utilization in the MHS.

Glucocard 01, Glucocard Vital, Embrace, and Nova Max SMBGS test strips met the previously determined minimum technical requirements, which were approved at the May 2007 P&T Committee meeting. These 4 test strips also met the operational limitations of the existing Mail Order and Retail contracts, and Federal Government contracting regulations.

With regard to efficacy, the Glucocard 01, Glucocard Vital, Embrace, and Nova Max SMBGS test strips are accurate according to the requirements of the FDA and the International Standard for Organization, do not require manual coding, require only a 0.3–0.6 microliter blood sample size, are approved for at least one alternate testing site, and provide results in 5 to 7 seconds. The Glucocard 01, Glucocard Vital, Embrace, and Nova Max test strips utilize glucose oxidase instead of glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) as the reagent. Test strips with GDH-PQQ have rarely been associated with falsely high blood glucose readings and

potential patient harm when used concurrently with products containing maltose (e.g., dialysis patients receiving icodextrin dialysate solutions).

The following did not meet the minimum technical requirements: Advocate Redi-code, EasyMax, EZ Smart Plus, Fifty50, Microdot, Rightest GS100, Rightest GS300, Ultratrak Ultimate. The following were not in compliance with the Buy American/Trade Agreement Acts: Blood Sugar Diagnostic, Liberty, Wavesense Jazz, Wavesense Presto.

Relative Clinical Effectiveness Conclusion— The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent): 1) Glucocard 01, Glucocard Vital, Embrace, and Nova Max test strips are similar to the other test strips included on the UF, in terms of meeting the minimum technical requirements; 2) Nova Max test strips offer ketone testing on the Nova Max Plus meter (ketone testing is also available with the Precision Xtra meter); 3) Nova Max test strips offer wireless communication with insulin pumps on the Nova Max Link meter; and 4) Embrace test strips used in the Embrace meters offers a talking feature that speaks blood glucose results and instructions for testing.

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — RELATIVE COST EFFECTIVENESS

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of Glucocard 01, Glucocard Vital, Embrace, and Nova Max test strips in relation to efficacy, safety, tolerability, and clinical outcomes of the other test strips in the SMBGS test strip class. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was performed to evaluate the cost-effectiveness of the Glucocard 01, Glucocard Vital, Embrace, and Nova Max SMBGS test strips. The cost-effectiveness of each new test strip was evaluated relative to the following agents: Accu-chek Aviva, Contour, OneTouch Ultra, Precision Xtra, and TRUEtest. CMA results showed the following, in order from most to least cost-effective: Glucocard Vital > Glucocard 01 > TRUEtest > Contour > Precision Xtra > Accu-Chek Aviva > One Touch Ultra > Nova Max.

Relative Cost-Effectiveness Conclusion— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained, 2 absent) 1) Glucocard Vital is the most cost-effective strip in all points of service, 2) Glucocard 01 is the second most cost-effective strip, 3) Embrace test strips fall in the middle of the price range for UF products and 4) Nova Max is the least cost-effective SMBGS test strip.

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 2 absent):

1. Glucocard 01, Glucocard Vital, and Embrace test strips be designated with formulary status on the UF;

2. Nova Max be designated with NF status on the UF; and

3. Advocate Redi-code, Blood Sugar Diagnostic, EasyMax, EZ Smart Plus, Fifty50, Liberty, Microdot, Rightest GS100, Rightest GS300, Ultratrak Ultimate, Wavesense Jazz, and Wavesense Presto be designated with NF status on the UF because they do not meet the minimum technical standards required for inclusion on the UF or Federal Government contracting regulations.

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — MEDICAL NECESSITY CRITERIA

(Dave Meade) Based on the clinical evaluation of the SMBGS and the conditions for establishing medical necessity for a nonformulary medication provided for in the UF rule, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Nova Max SMBGS test strips.

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — UNIFORM FORMULARY IMPLEMENTATION PLAN

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

(Dave Meade): COL Lounsbery will now give the physician perspective for the Test Strips.

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — COMMITTEE PHYSICIAN PERSPECTIVE

COL Lounsbery noted that the PEC staff had made the Committee's job easy by identifying several test strips not meeting minimum technical standards. Of the four that did meet the standards, three were as or more cost effective than test strips already on the UF. One test strip was found to be not cost effective and it was made NF.

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — PANEL QUESTIONS AND DISCUSSION

Several Panel members (Dr. Cohoon, Ms. Fryar) had a brief discussion about the advantages offered by the NF test strip of wireless communication with insulin pumps. LCDR Helwig

explained that the capability is based on the pump. Mr. Hutchings commented on the cost effectiveness.

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — BAP VOTE ON UF RECOMMENDATIONS

The Chair read the P&T Committee's UF recommendations.

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

1. Glucocard 01, Glucocard Vital, and Embrace test strips be designated with formulary status on the UF;

2. Nova Max be designated with NF status on the UF; and

3. Advocate Redi-code, Blood Sugar Diagnostic, EasyMax, EZ Smart Plus, Fifty50, Liberty, Microdot, Rightest GS100, Rightest GS300, Ultratrak Ultimate, Wavesense Jazz, and Wavesense Presto be designated with NF status on the UF because they do not meet the minimum technical standards required for inclusion on the UF or Federal Government contracting regulations.

The BAP voted as follows:

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

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — BAP VOTE ON MN RECOMMENDATIONS

Ms. Fryar then read the MN criteria recommendations for the SMBGS test strips.

Based on the clinical evaluation of the SMBGS and the conditions for establishing medical necessity for a nonformulary medication provided for in the UF rule, the P&T Committee recommended MN criteria for Nova Max SMBGS test strips.

The Panel vote was:

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

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS — BAP VOTE ON UF IMPLEMENTATION PLAN

The Chair read the UF implementation plan recommendation.

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

The Panel voted:

The Panel vote was:

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

UTILIZATION MANAGEMENT —Modification of Prior Authorization

(PEC Script)

(Dave Meade)

A. Quinine Sulfate (Qualaquin) PA

Quinine sulfate, under the trade name Qualaquin, is FDA-approved only for the treatment of malaria. Qualaquin's product labeling states it is not approved for malaria prophylaxis or for persistent malaria. Recommended dosing for treatment of malaria is 2 capsules, 3 times daily, for 7 days. Center for Disease Control recommendations for quinine use include co-administration with tetracycline, doxycycline, or clindamycin, dependent on the type of plasmodium species and the resistance patterns in each malaria-endemic country. In May 2010, the P&T Committee recommended a prior authorization requirement for Qualaquin, limited to treatment of malaria, due to severe adverse events, including death. The PA took effect on October 6, 2010.

B. Quinine Sulfate (Qualaquin) PA Modification—Recommendation for Quantity Limits

To ensure the appropriate use of Qualaquin, consistent with the product labeling, the P&T Committee recommended (16 for, 2 opposed, 0 abstained, 0 absent) implementing a quantity limit of 42 capsules per fill, one fill per prescription, with no refills, which will allow quinine (Qualaquin) use in patients who have a documented diagnosis of malaria.

C. Quinine Sulfate (Qualaquin) PA—Modification of PA Implementation

The quantity limits for Qualaquin become effective the first Wednesday after a 60-day implementation period in all points of service.

Quinine Sulfate — Modification of Prior Authorization — PANEL QUESTIONS AND DISCUSSION

Dr. Cohoon noted that two Committee members were opposed and asked why. Dr. Meade replied he couldn't recall offhand.

Mr. Hutchings indicated he was concerned that 90 days might be too restrictive. He asked how long patients use Qualaquin for and noted he could foresee a loophole from patients going to the doctor each time. Dr. Meade said Qualaquin is a prophylactic treatment and it isn't used for persistent malaria; patients who have persistent malaria ought to be on something different. COL Lounsberry noted that Qualaquin is still being prescribed for leg cramps and practitioners

are writing "malaria" on the PA. The purpose of the modification is so the TMA can decide not to fill it more than once if patients keep coming back with another prescription for malaria. The numbers have decreased since the PA was put on, but it is still happening. Mr. Hutchings said that one year's worth of treatment should be sufficient for malaria.

Further discussion among the Panel Members indicated that they agree with the need for a modification but believe that the time period is too restrictive.

Some concern was also expressed about the precedent being set for what happens when a PA isn't working. Similar situations might come up in the future. Dr. Salom commented that he thinks this is a special case because there is no FDA approval for other than malaria. Mr. Hutchings agreed that there should ne notification that the agent is for malaria and malaria only. Ms. Fryar noted that the medication carries a "black box" warning.

Quinine Sulfate — Modification of Prior Authorization — PANEL VOTE ON PA QUANTITY LIMITS MODIFICATION

Ms. Fryar read the Committee's recommendation.

> To ensure the appropriate use of Qualaquin, consistent with the product labeling, the P&T Committee recommended implementing a quantity limit of 42 capsules per fill, one fill per prescription, with no refills, which will allow quinine (Qualaquin) use in patients who have a documented diagnosis of malaria.

The Panel vote was:

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

Panel Comment: Although the BAP concurs with the need for a modification, several members agree that the time period is too restrictive and recommends that consideration be given to allowing one prescription only with 365 days worth of refills.

Dr. Crum offered a comment to the PEC concerning physicians who are writing prescriptions for leg cramps and putting "malaria" on the PA. He said those practitioners should be investigated and reported for possible criminal action.

Quinine Sulfate — Modification of Prior Authorization — PANEL VOTE ON IMPLEMENTATION PLAN

Ms. Fryar then read the implementation plan.

> The quantity limits for Qualaquin become effective the first Wednesday after a 60-day implementation period in all points of service.

The Panel vote was:

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

ITEMS FOR INFORMATION

(PEC Script)

(Dave Meade) **Propoxyphene Withdrawal from the Market**—Propoxyphene has been

available since the late 1950s, but concerns regarding adverse events, including prolongation of the QT interval have persisted. All propoxyphene products (Darvon, Darvocet, generics) were voluntarily withdrawn from the market in November 2010.

Closing Remarks

The Chair acknowledged the work done by LTC Spridgen, the P&T Committee and the PEC in preparing for the meeting, thanked Panel Members for their efforts and thanked the attendees for coming. Ms. Fryar also suggested that it would be useful to have some kind of an outcome study of how beneficiaries perceive the process and acknowledged the TMA's work in preparing the letters to beneficiaries. She also presented the meeting reporter with a letter thanking him for his efforts in transcribing the minutes.

In closing the meeting, LTC Spridgen also expressed appreciation for the work of the Panel and for their support of TRICARE beneficiaries. She announced that the next meeting is scheduled for June 23.

The meeting was adjourned at 11:30 A.M.

Ms. Deborah Fryar
Chairperson, Uniform Formulary Beneficiary Advisory Panel

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
- ASAs — Aminosalicylates (a drug subclass)
- BAP — Uniform Formulary Beneficiary Advisory Panel (the "Panel" referred to above)
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- BP — Blood pressure
- BPA — Blanket Purchase Agreement
- CEA — Cost-effectiveness analysis
- CFA — Coefficient of Fat Absorption
- C.F.R — Code of Federal Regulations
- CHD — Coronary heart disease
- CMA — Cost-Minimization Analysis
- COPD — Chronic obstructive pulmonary disorder
- CR — Controlled Release (a drug formulation)
- CV — Cardiovascular
- DACON — Daily average consumption
- DEA — U.S. Drug Enforcement Administration
- DFO — Designated Federal Officer
- DM — Diabetes mellitus
- DoD — Department of Defense
- DPP-4 — Dipeptidyl-peptidase 4 inhibitors (a drug subclass)
- ECF — Extended Core Formulary
- ER — Extended Release (a drug formulation)
- ESI — Express-Scripts, Inc.
- FACA — Federal Advisory Committee Act
- FCP — Federal Ceiling Price
- FDA — U.S. Food and Drug Administration
- GI-1 — Gastrointestinal-1s (a drug class)
- HDL — High-density lipoprotein
- IR — Immediate Release (a drug formulation)
- IV — Intravenous

- JNC — Joint National Committee
- LDL — Low-density lipoprotein
- LIP-1s — Antilipidemic-1s (a drug class)
- LIP-2s — Antilipidemic-2s (a drug class)
- MDI — Metered dose inhaler
- MHS — Military Health System
- MI — Myocardial infarction
- MN — Medical Necessity
- MS — Multiple sclerosis
- MTF — Military Treatment Facility
- NDAA — National Defense Authorization Act
- NF — Non-formulary
- NIH — National Institutes of Health
- NNH — Number Needed to Harm
- NNT — Number Needed to Treat
- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DOD Pharmacy and Therapeutics Committee
- PDTS — Pharmacy Data Transaction Service
- PEC — DOD Pharmacoeconomic Center
- PEP — Pancreatic Enzyme Products (a drug class)
- PORT — Pharmacy Outcomes Research Team
- POS — Point of Service
- RAA — Renin Angiotensin Antihypertensive agents (a drug class)
- RCTs — Randomized Control Trials
- SMBGS — Self-Monitoring Blood Glucose System (a drug class)
- SR — Sustained release (a drug formulation)
- SQ — Subcutaneously
- T1DM — Type 1 diabetes mellitus
- T2DM — Type 2 diabetes mellitus
- TG — Triglycerides
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TPHARM — TRICARE Pharmacy Program
- TRRx — TRICARE Retail Pharmacy Program
- UF — DOD Uniform Formulary
- U.S.C. — United States Code
- VA — U.S. Department of Veterans Affairs
- VARR — Voluntary Agreement on Retail Rebates