Executive Summary

UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL COMMENTS
September 22, 2011

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

1. **ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) — 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 (13 for, 0 opposed, 1 abstained, 1 absent) the following remain formulary on the UF without step therapy: diclofenac potassium, diclofenac sodium, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, meloxicam, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, sulindac, tolmetin, naproxen/esomeprazole (Vimovo), diclofenac/misoprostol (Arthrotec), and celecoxib (Celebrex).

   The P&T Committee recommended diclofenac potassium liquid-filled capsules (Zipsor), diclofenac potassium powder packets (Cambia), naproxen sodium ER (Naprelan CR), and mefenamic acid (Ponstel) be designated NF.

   Summary of Panel Vote/Comments:

   Dr. Schlaifer asked whether the generic versions of the drugs made non-formulary will also be NF. Dr. Meade answered that the Naprelan CR generic will be but that they couldn't find a generic for Ponstel.

   Mr. Hutchings asked about the analysis used to decide about not requiring step therapy. He said his experience is that some agents in this class may be used inappropriately. Dr. Meade replied that the cost analysis showed that step therapy wouldn't be cost-effective.

   Mr. Hutchings also asked whether the Committee has discussed the adverse outcomes that might result from the toxicity of some of the medications in this drug class. Maj King said the Committee had explicitly discussed the studies of the cardio-vascular and gastro-intestinal safety factors. He said that there wasn't found to be more risk with one than with the others.

   Mr. Hutchings asked further what was the basis for comparison used in the cost analysis. Dr. Meade replied that it was "cost per day."

   Dr. Salom disclosed that he had designed, supervised and wrote-up for publication and submission to the Food and Drug Administration safety studies for one of the non-steroidal anti-inflammatory drugs on the considered list. This work was performed over 20 years ago.

He denied any conflict-of-interest arising from the work.

- Without further discussion/comment, the Panel voted on the NSAIDs UF recommendation as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

One Panel member commented that he was still concerned about the safety of agents in this drug class and the possibility of their inappropriate use.

No further comments from the Panel.

Director, TMA:

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

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs — 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 TMA send a letter to beneficiaries affected by this UF decision.

- Without further discussion/comment, the Panel voted on the NSAIDs Implementation Plan recommendation as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further comments from the Panel:

Director, TMA:

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

2. **CONTRACEPTIVE AGENTS — 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 the following:

- **OCPs Subclass—**
  - The P&T Committee voted that the Jolessa branded generic formulation of Seasonale should be added to the UF.
  - The P&T Committee voted that the following drugs and their generic equivalents should be retained on the UF:
    - Monophasics with 20 mcg of EE (Yaz, , Sronyx, Loestrin 1/20, Loestrin Fe 1/20)
    - Monphasics with 30 mcg of EE (Levora, Lo/Ovral, Desogen, Loestrin 1.5/30 , Loestrin with iron 1.5/30, 1+35, Yasmin)
    - Monophasics with 35 mcg EE (Mononessa, Modicon, Zovia 1/35)

- Monphasics with 50 mcg EE or mestranol (Zovia 1/50E, Ogestrel)
- Biphasics (Necon 10/11, Mircette)
- Triphasics (Ortho-Tri Cyclen Lo, Trinessa, Trivora, Tri-Norinyl, Ortho-Novum 7/7/7 Cyclessa, Nor-Q-D)

- The following OCPs were designated NF or retained NF status on the UF:
  - norethindrone acetate 1mg/EE 10mcg (Lo Loestrin Fe)
  - levonorgestrel 0.1mg/EE 20mcg + 10mcg (LoSeasonique)
  - drospirenone 3mg/EE 20mcg/levomefolate Ca 0.451mg (Beyaz)
  - drospirenone/EE 30mcg/levomefolate Ca 0.451mg (Safyral)
  - levonorgestrel 90mcg/EE 20mcg, continuous regimen (Lybrel, generic)
  - norethindrone acetate 1mg/EE 20mg, extended regimen (Loestrin 24 Fe)
  - norethindrone 0.4mg/EE 35mcg (Ovcon-35 generics; also includes Femcon Fe chewable and Zeosa chewable)
  - norethindrone 1mg/EE 50mcg (Ovcon-50)
  - levonorgestrel 0.15mg/EE 30mcg + 10mcg, extended regimen (Seasonique, generics)
  - norethindrone 1mg/EE 20mcg/30mcg/35mcg/ferrous fumerate 75mg (Estrostep Fe, generics)
  - dienogest 2mg/3mg/estradiol valerate 3mg/2mg/2mg/1mg, (Natazia)
  - levonorgestrel 0.15mg/EE 30mcg, extended regimen (Seasonale, generics, including Introvale and Quasense), with the exception of Jolessa branded generic

Summary of Panel Vote/Comments:

Mr. Hutchings asked whether the injected contraceptives are covered. Dr. Meade said they are but only after the age of 17, i.e. 18 and over.

Ms. Cohoon referred to previous discussions of contraceptive agents and their safety and asked what steps will be taken to assure that these agents will be appropriately used and will not be harmful. Dr. Meade replied that it is up to the professionals who prescribe the drugs to call the patient's attention to the way in which they should be used.

Dr. Schlaifer noted the Ella was found to be more effective than other emergency contraceptives, but it is also more expensive. She asked if there was any discussion of that by the Committee. The PEC staff replied that there wasn't because the only difference is in the benefit.

- Without further discussion, the Panel voted on the Contraceptive agents UF recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further comments from the Panel:

Director, TMA:

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

- **MISCELLANEOUS CONTRACEPTIVE SUBCLASS**

  The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following drugs remain formulary on the UF: norelgestromin/EE 50 mcg transdermal (Ortho Evra), etonorgestrel/EE vaginal ring (NuvaRing), medroxyprogesterone acetate 150 mg/mL (Depo-Provera IM, generics), and medroxyprogesterone acetate 104 mg/0.65 mL (Depo-SubQ Provera 104). No miscellaneous contraceptive agent was recommended for NF placement.

  - Without further discussion, the Panel voted on the Contraceptive agents UF recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

  No further comments from the Panel:

  Director, TMA:

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

- **EMERGENCY CONTRACEPTIVE SUBCLASS:**

  The P&T Committee recommended (12 for, 0 opposed, 3 abstained, 0 absent) the following drugs remain formulary on the UF: levonorgestrel 0.75mg (Next Choice; Plan B generic), levonorgestrel 1.5mg (Plan B One Step), and that ulipristal (Ella) be designated formulary on the UF. No emergency contraceptive was recommended for NF placement.

  - Without further discussion, the Panel voted on the Contraceptive agents UF recommendations as follows: **Concur: 7 Non-concur: 0 Abstain: 2 Absent: 2**

  No further comments from the Panel:

  Director, TMA:

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

- **CONTRACEPTIVE AGENTS - IMPLEMENTATION PLAN**

  The Chair noted the implementation plan applies to all **THREE** subclasses.

  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) TMA send a letter to beneficiaries affected by this UF decision.

  - Without further discussion, the Panel voted on the Implementation Plan recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

  No further comments from the Panel:

  Director, TMA:

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

  Before proceeding, Mr. Hutchings asked for clarification of which generics are covered and which are not.

3. **PHOSPHODIESTERASE-5 INHIBITOR (PDE-5) FOR ERECTILE DYSFUNCTION — BACKGROUND**

The Chairperson noted that the next drug class involves a partial clinical evaluation perspective presentation and that the Panel will get a full briefing and vote on P&T recommendations for this class at the next BAP meeting.

Dr. Meade introduced the discussion by informing the Panel that over the summer there had been significant price increases and contracts were broken. The Committee had considered this class not too long ago and first thought it could do a quick turnaround. However, legal actions occurring two days before the meeting prevented that. As a result, DoD is going on a national contract with the Veterans Administration. These figures will be used to re-evaluate the cost-effectiveness and develop UF recommendations for the next meeting.

Summary of Panel Comments:

The Chair asked the PEC staff to ensure that the beneficiary comments the Panel heard today be considered by the P&T Committee when it reconsiders this drug class. The PEC staff agreed.

Ms. Cohoon noted that the P&T Committee concluded that reported there was insufficient evidence to conclude that daily therapy for ED was superior to on demand therapy and asked if that would apply to the situation brought before the Panel earlier today. Dr. Meade agreed that it was.

4. **NEWLY DESIGNATED APPROVED DRUGS: RENIN ANGIOTENSIN ANTIHYPERTENSIVES (RAAS)**

- **AZILSARTAN (EDARBI) —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 (13 for, 0 opposed, 1 abstained, 1 absent) azilsartan (Edarbi) remain formulary on the UF.

Summary of Panel Vote/Comments:

Ms. Cohoon asked about the PA for this agent, specifically why it is non-step preferred as it offers a compelling therapeutic advantage over some of the other agents. Dr. Meade answered that it is consistent with the other members of the RAAs class for which there is already a step in place. Also it is more expensive. The need for step therapy will be reconsidered when the class as a whole is re-reviewed.

- Without further discussion, the Panel voted on the Edarbi UF recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further comments from the Panel:

Director, TMA:

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

- **AZILSARTAN (EDARBI)—Prior Authorization Criteria**

The P&T Committee recommended Azilsartan (Edarbi) be designated non-step preferred requiring the following step-therapy/PA criteria. 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 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 Service (MHS) pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

   b) The patient has received a prescription for azilsartan (Edarbi) at any 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 further discussion, the Panel voted on the PA criteria recommendations as follows: **Concur: 8 Non-concur: 1 Abstain: 0 Absent: 2**

Ms. Cohoon commented she didn't believe this drug should be subject to non-step preferred PA criteria because of its clinical effectiveness.

No further comments from the Panel:

Director, TMA:

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

- **AZILSARTAN (EDARBI)—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.

  - Without further discussion, the Panel voted on the Implementation Plan recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further comments from the Panel:

Director, TMA:

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

- **ALISKIREN/AMLODIPINE/HYDROCHLOROTHIAZIDE (AMTURNIDE)**

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 (12 for, 0 opposed, 1 abstained, 2 absent) aliskiren/amlodipine/HCTZ (Amturnide) remain formulary on the UF, as the FDC of DRI/amlodipine/HCTZ may be necessary for hypertensive patients requiring 3 drugs who do not respond to other triple FDC RAAs.

Summary of Panel Vote Comments: **Panel Questions and Discussion**

Mr. Hutchings stated that it might appear as though patients were being pushed into using a triple combination agent. He further pointed out that product was found to be not cost-effective. He also noted that two of the three ingredients in Amturnide were already non-formulary and objected to the inconsistency of making them formulary through their inclusion in a triple combo. He asked for a further explanation of the logic behind the recommended placement.

Dr. Salom stated that he has a bias against triple combination products in general. He believes that the increased gains are not offset by problems from adverse reactions. In this case, where the drug isn't even cost effective, he would think it's not something that should be on the formulary.

Dr. Meade replied that the Committee was looking at the fact that there are so few triple combinations available. They are not used for initial therapy and their utilization in the MHS is quite low. Additionally, there will be a re-review of the entire RAAs class in the near future.

Mr. Hutchings noted that the PA criteria omit mention of whether the patient has been on other agents and questioned the step process in these cases. Dr. Meade answered that they would take that into consideration in the implementation process.

Ms. Fryar asked when this drug class would come up for review again. Dr. Meade replied that they are waiting for certain things to happen, including the launch of another new drug so that they don't have to review that one separately. The objective is to conduct a comprehensive review that includes generic Diovan.

Ms. Cohoon noted that not only was this drug not cost effective, it didn't have a significant therapeutic advantage. She said she might be able to live with the higher cost if it did have a therapeutic advantage.

- Without further discussion, the Panel voted on the UF recommendations as follows:
  Concur: 2 Non-concur: 7 Abstain: 0 Absent: 2

The Panel commented that it was concerned about the inconsistency of including a drug on the UF that contains two NF agents. It was also concerned about placing a drug on the UF that offers no therapeutic advantages and is not cost effective.

No further discussions from the Panel:

Director, TMA:

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

- **ALISKIREN/AMLODIPINE/HYDROCHLOROTHIAZIDE—PA Criteria**

The P&T Committee recommended aliskiren/amlodipine/HCTZ (Amturnide) be designated non-step preferred requiring the following step-therapy/PA criteria. 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 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 MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

   b) The patient has received a prescription for aliskiren/amlodipine/HCTZ (Amturnide) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) 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 further discussion, the Panel voted on the PA Criteria recommendations as follows: **Concur: 8 Non-concur: 1 Abstain: 0 Absent: 2**

Dr. Salom stated that if the drug is to be made UF, these seem to him like reasonable steps.

No further comments from the Panel:

Director, TMA:

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

- **ALISKIREN/AMLODIPINE/HYDROCHLOROTHIAZIDE (AMTURNIDE)—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.

Summary of Panel Vote/Comments:

Mr. Hutchings asked whether it really will require 60 days to implement. Ms. Legette said that the 60 days is necessary to conform to commercial practice and to get letters out to the beneficiaries. Mr. Hutchings said that letters don't have to go out in this case – you just need to flip a switch on the automated system -- and he would recommend something shorter.

- Without further discussion, the Panel voted on the Implementation Plan recommendations as follows: **Concur: 8 Non-concur: 1 Abstain: 0 Absent: 2**

No further comments from the Panel:

Director, TMA:

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

5. **NEWLY APPROVED DRUGS — NON-INSULIN DIABETES MELLITUS DOPAMINE AGONIST**

- **NON-INSULIN DIABETES MELLITUS AGENTS—Bromocriptine mesylate quick release tablets (Cycloset tablets)**

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 (12 for, 1 opposed, 1 abstained, 1 absent) bromocriptine mesylate (Cycloset) be designated NF and non-step preferred.

Summary of Panel Vote/Comments:

Mr. Hutchings asked if there was any discussion of making the step more rigorous. Dr. Meade said there was not.

Dr. Salom expressed the view that this should not even be considered a second line drug and maybe shouldn't even be prescribed at all because its efficacy is so minimal. He believes the PA criteria should be much more rigorous than recommended.

Ms. Cohoon asked about the step preferences. Dr. Meade explained that metformin and sufonylurea are the first line agents. The MHS has not designated second, third or fourth line agents; instead, they trust the prescriber to know where the second line ought to be.

- Without further discussion, the Panel voted on the UF recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further comments from the Panel:

Director, TMA:

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

- **NON-INSULIN DIABETES MELLITUS AGENTS—Bromocriptine mesylate quick release tablets (Cycloset tablets)—PA Criteria:**

Step therapy applies to this new subclass (dopamine agonists) requiring prior trial of metformin or a sulfonylurea. Bromocriptine mesylate (Cycloset) is recommended to be designated as non-step preferred and NF. The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to bromocriptine mesylate (Cycloset).

1. Automated PA criteria:

   a) The patient has received a prescription for metformin or SU at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

   b) The patient has received a prescription for bromocriptine mesylate (Cycloset) at any 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 a confirmed diagnosis of T2DM.

b) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.

c) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.

d) The patient has a contraindication or has had inadequate therapy to both metformin and a SU.

- Without further discussion, the Panel voted on the PA Criteria recommendations as follows: **Concur: 6 Non-concur: 3 Abstain: 0 Absent: 2**

  Comments offered by the Panel members were that the drug is not efficacious and probably shouldn't be used by anyone so the PA criteria should be more rigorous, specifying other agents that should be tried first for contraindications.

No further comments from the Panel:

Director, TMA:

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

- **NON-INSULIN DIABETES MELLITUS AGENTS—Bromocriptine mesylate quick release tablets (Cycloset tablets)—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 2) TMA send a letter to beneficiaries affected by this decision.

- Without further discussion, the Panel voted on the Implementation Plan recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further comments from the Panel:

Director, TMA:

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

6. **NEWLY APPROVED DRUGS — NARCOTIC ANALGESICS**

- **NARCOTIC ANALGESICS —Buprenorphine Transdermal System (Butrans)**

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 (12 for, 2 opposed, 1 abstained, 0 absent) buprenorphine transdermal system (Butrans) remain formulary on the UF with prior authorization to ensure appropriate use of the drug.

Summary of Panel Vote/Comments:

Dr. Salom noted the downside risks of the drug and acknowledged that the PA criteria are intended to address those. However, he also said that it seems like the PA criteria would be difficult to enforce and he is afraid that more harm than good will be done by keeping it on the formulary.

- Without further discussion, the Panel voted on the UF recommendations as follows:
  Concur: 7 Non-concur: 2 Abstain: 0 Absent: 2

  BAP comments were that Butrans has no clinical advantage and is not cost-effective. Additionally, there are sufficient narcotic analgesics on the formulary already.

No further comments from the Panel:

Director, TMA:

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

- **NARCOTIC ANALGESICS—Buprenorphine Transdermal System (Butrans)—PA Criteria**

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to Butrans. Coverage will be approved if the patient met any of the following criteria:

- Manual PA criteria:

  a) Coverage provided for patients ≥18 yrs with moderate-to-severe chronic pain requiring opioid therapy.

     (1) Opioid naïve patients (prior use of <30 mg/day of morphine or equivalent in past 60 days) are limited to Butrans 5 mcg/hr patch.

     (2) Opioid tolerant patients (prior use of 30mg/day to 80 mg/day of morphine or equivalent within past 60 days or Butrans 5 mcg/hr patch) can receive Butrans 10 mcg/hr and 20 mcg/hr patches.

     (3) Maximum dose of Butrans is 20 mcg/hr.

  b) Coverage NOT provided for treatment of opioid-dependence.

  c) Coverage NOT provided for patients:

     (1) Requiring >80 mg/day of morphine or equivalent for pain control;

     (2) With significant respiratory depression or severe bronchial asthma;

(3) With long QT syndrome or family history of long QT syndrome;

(4) On concurrent Class 1A (procainamide, quinidine) or Class III (dofetilide, amiodarone, sotalol) antiarrythmics.

Summary of Panel Vote/Comments:

Dr. Salom repeated that he believes the PA criteria are well meaning but not enforceable, and will lead to inappropriate use of the drug and will do more harm than good.

Ms. Fryar asked Dr. Meade whether the PA criteria are enforceable. Dr. Meade said they are counting on the physicians to honestly answer what they are doing. They are aware of the problem. But even if the drug was made NF, the only effect would be to raise the co-pay to $22. Mr. Hutchings said he really likes the PA on this drug because making it NF wouldn't address the potential problems. Because of the way we are set up, the PA criteria will make it more difficult to abuse the drug.

- Without further discussion, the Panel voted on the PA criteria recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further discussion from the Panel:

Director, TMA:

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

- **NARCOTIC ANALGESICS—Buprenorphine Transdermal System (Butrans)—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.

- Without further discussion, the Panel voted on the Implementation Plan recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further comments from the Panel:

Director, TMA:

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

6. **UTILIZATION MANAGEMENT—SINGULAIR PRIOR AUTHORIZATION**

- **Montelukast (Singulair)—PA Criteria**

The P&T Committee recommended (12 for, 1 opposed, 1 abstained, 1 absent) the following PA criteria should apply to montelukast. Montelukast will be approved only for patients under the

age of 19 and patients 19 or older who show evidence of use for an FDA-approved and guideline-supported indication. All current and new users of montelukast must meet one of the following criteria to pass through the PA process.

Summary of Panel Vote/Comments:

The Chair asked for and received a clarification of the wording of the PA criteria to be voted on.

Dr. Salom asked whether it is correct that a person over the age of 18 would only be able to use the manual PA criteria. Dr. Meade said that patients under 18 get a free pass; patients over 18 have to demonstrate that they have asthma. The automated criteria should read "a" ***or*** "b."

Ms. LeGette asked whether the 91,200 beneficiaries affected by the decision are all adults and whether there will be grandfathering. Dr. Meade replied that these are adults who would not have automated prior authorization. There will be no grandfathering. He also said that there are a significant number of patients that are using the drug for reasons that aren't clear.

Mr. Hutchings said that most patients he knows about are using it for allergies. Dr. Meade said the Committee was aware of that and that steroids are way more cost effective.

Dr. Schlaifer asked what will happen as patients turn 19 and how they would be notified. Dr. Meade said that within 180 days each patient would have other drugs on their profile and will be forced to go through the PA process.

Asked again about the rationale for the age cutoff, Dr. Meade explained that there were unapproved uses of the drugs in kids up to the age of 18 but that 18 was an easily-defined line.

- Without further discussion, the Panel voted on the PA criteria recommendations as follows: **Concur: 7 Non-concur: 2 Abstain: 0 Absent: 2**

No further comments from the Panel:

Corrected recommendation for PA Criteria:

The Chair read the P&T Committee's **corrected PA criteria recommendations** for Singulair.

1. Automated PA criteria:
   a) Patient is ≤18 years of age.
   b) Patient has received an inhaled corticosteroid or inhaled beta agonist or an inhaled combination product during the previous 180 days at a MTF, retail network pharmacy, or the mail order pharmacy.
2. Manual PA criteria:
   a) Coverage approved if:

(1) The patient/provider documents use of montelukast for seasonal allergic rhinitis (or nasal polyposis) with evidence of a inadequate therapy with a nasal corticosteroid dispensed during the previous 180 days at an MTF, a retail network pharmacy, or the mail order pharmacy; or

(2) The patient/provider documents intolerance (due to experienced adverse events) or contraindication to either inhaled or intranasal corticosteroids.

Comments regarding non-concurrence were that the criteria would be difficult to implement from an operational perspective because of the amount of paperwork required. Mr. Hutchings said he would recommend moving manual PA criteria (1a) to the automated category as a way to cut down the amount of paperwork.

Director, TMA:

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

- **Montelukast (Singulair)—PA Implementation Period**

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

- Without further discussion, the Panel voted on the Implementation Plan recommendations as follows: **Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2**

No further comments from the Panel.

Director, TMA:

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

To Beneficiary Advisory Panel September 16, 2011

I believe you should advise the DOD to change their medication policy to include Cialis Daily Treatment as a Formulary Drug.

My husband has hypertension, or high blood pressure. As a result of the medications he has taken for years to combat his blood pressure problems, he has a side effect called erectile dysfunction (E.D.).

Tri-Care pays for only six pills per month of PDE-5 Inhibitor Drugs, such as Viagra, Levitra, or Cialis. I believe that when this policy was established, these drugs were only available on an "as needed" basis. Since that time, Cialis has developed a "daily" treatment for ED.

After my husband and I were married 4 years ago, his urologist prescribed the "as needed" form of a PDE-5 drug. We tried it without success. Sometimes it worked quickly, sometimes it did not work quickly, and sometimes it did not work at all. With only six pills to last a month, we did not have a very successful love life. The doctor suggested that we try the daily Cialis treatment. (I say WE, because even though my husband swallows the pills, the outcome affects both of us.) Our doctor gave us enough samples to try each day for a month. This worked wonders for us.

When the drug stays in the body in a low regular dose it works any time we need it to work. Large doses once in a while are very unpredictable. We wrote to Tri-Care and asked that they allow us to use the daily dose of Cialis, but were denied. We went all the way through the appeal process with the same "rubber-stamped" denial at every level.

On our retirement income (social security and a small National Guard pension), we could not afford to pay for the medication on an on-going basis. Our doctor told us to take the six 20mg tablets that Tri-Care would pay for and cut them into 4 pieces each, and he gave us some samples to make up enough to get through the month. This solved our problem, but is not very accurate. The pills are egg-shaped, and it is impossible to cut them into 4 equal pieces. Therefore, some days he gets more of the drug and some days he gets less. And there are always some chips and powder that fall away in the cutting process. We must gather this up to make one dose and hope we gather up what equals 5 mg.

My husband got another surprising benefit from using the Daily Cialis. His blood pressure was reduced substantially after he began to take Cialis on a daily basis. He had been taking three blood pressure medications, and the doctor took him off one of them, Lotrel. He now takes only 2 blood pressure medications. Blood pressure medications

have some bad side effects, including destruction of the kidneys. My husband's kidneys have been badly damaged by the years of using three blood pressure medications. His kidney function is at 35%. It will never get better, but hopefully we can stop it from getting worse, by keeping him off the third blood pressure medicine. The side effects of Cialis are not nearly as harmful as those of other blood pressure medications.

Most drug companies list the purpose of a drug on the sheet that accompanies every prescription and then adds "OR FOR OTHER CONDITIONS AS PRESCRIBED BY YOUR PHYSICIAN". In every other case, TriCare pays for the drug as prescribed by the physician. WHY NOT IN THE CASE OF DAILY CIALIS? Our doctor prescribes it for two purposes – E.D. AND blood pressure reduction.

I believe there is a term used by Tri-Care and other insurance companies, called "Therapeutic Failure". This means that a certain medication that is prescribed for a condition does not work for certain people, while another similar drug will work. Tri-care will allow a change if the doctor sends a letter stating that the Tri-care preferred drug has met with Therapeutic Failure in a certain patient. This is the case with a pain patch that I wear since I had bone cancer seven years ago. Only one certain brand of the Fentanyl patch worked, the Mylan Brand. My doctor writes on the prescription that the Fentanyl is to be filled with Mylan brand only, and TriCare dispenses that brand. Why then must TriCare refuse this with Cialis? My doctor has sent such a letter to TriCare several times, (SEE ATTACHMENT 1) with no success.

I have checked with all our local pharmacies which are national chains. I have learned that 30 of the 5 mg pills are considerably cheaper than 6 of the 20mg pills consistently in all drug stores I checked with (SEE ATTACHMENT 2). To refuse to allow the Daily Cialis is fiscally irresponsible.

Tri-Care pays for birth-control pills to be taken every day. They pay for OTHER blood pressure pills to be taken every day. Every single other medicine paid for by Tri-Care allows the patient to take his medication daily or as prescribed by his physician. Why then is there a discrimination against the PDE-5 Inhibitors? And how did they come up with the magic number of six pills per month? Even if the PDE-5 "as needed" drugs worked every time, which they don't, six chances monthly to make love with one's spouse is woefully, painfully inadequate. Which person on the BAP wishes to have the government tell him or her when he may or may not enjoy intimacy with his spouse?

During the days when PDE-5 drugs were a "new sensation", when this policy probably was made , many people made jokes about "Viagra"; but the jokes are not funny to men who suffer with high blood pressure side effects. Before ED drugs were invented, these men had to rely on things like penile pumps or implants to deal with impotence. I have no knowledge of the implants, but I can warn you to stay away from the pumps if at all possible. Just to watch my husband trying that procedure made me hurt. Cialis has come a long way in their research, and have discovered that a little medicine each day works better than six major jolts of a quadruple dose of the same medication at random times.

We will continue to use Cialis on a daily basis, whether or not you approve the coverage of daily Cialis. But I believe it would be safer to have the 5 mg. pills that are uniformly manufactured rather than to be forced to use a piece of the chopped up 20 mg pill.

- I ask you again, to advise the approval of Daily Cialis for those patients who wish to use it. If I need to clarify anything in this request, or if you have further questions, please [redacted]. My husband and I have made arrangements to attend the BAP meeting this Thursday, where I will take advantage of the opportunity to speak with you face to face in hopes of getting TriCare's approval of Daily Cialis. I speak for many more people than just my husband, when I say that a policy change to allow this treatment option is way past due.

If, after reading this request, seeing that the daily Cialis is cheaper than the "as needed" drug that you do approve, and seeing that the medical benefits to the patient are superior with daily use, you still decide to deny the approval of daily Cialis, I will be anxious to hear your reasons for the denial when I meet with you Thursday. I will also request to know how to reach the next link in the "chain of command", so that I will know where to appeal next. I am also interested in learning how to become a part of this panel, should a vacancy ever occur – whether or not my request is approved.

From:

[redacted]

ATTACHMENT 1

(For the purpose of e-mailing this to you, I have re-typed the letter from our doctor, [redacted], which I have previously sent to Tri-Care. I will bring the actual letter, signed by the doctor, when I see you on Thursday.)

3/1/2010
To Whom It May Concern:

[redacted] has a history of erectile dysfunction, as well as hypertension. He has tried multiple times to be approved for daily Cialis therapy, 5 mg without success. Using his 20 mg tablets along with samples, he has been splitting his medicines and taking them daily with very good results. The other benefit he has noticed is significant reductions in his blood pressure, and has actually been able to stop one of his previous blood pressure medications due to his improvement with the daily Cialis. Based on this I would again ask you to consider approving this patient for daily Cialis therapy.

Sincerely,

[redacted]

ATTACHMENT 2

Cost Comparison of 6 pills Cialis 20 mg (as needed) to 30 pills of Cialis 5 mg (daily use)

Pharmacy Name	Cost of 6 – 20 mg	Cost of 30 – 5 mg
Rite Aid	$143	$127
Walgreens	$158	$150
CVS	$152	$144
Publix	$162	$150
Bi-Lo	$190	$152

In all 5 companies the cost of daily Cialis is cheaper than 6 "as needed" pills

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
September 22, 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 Family Association, representing The Military Coalition
- Santiago Chavez, Association of Military Surgeons of the United States, representing The Military Coalition
- 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, Geriatrics and Medicine, Mount Sinai School of Medicine
- Marissa Schlaifer, Medical Professional, Academy of Managed Care Pharmacy

Medical professional Panel members Brian Casull (TriWest Healthcare Alliance) and John Crum, (Humana Military Healthcare Services, Inc.) were absent from the meeting.

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. Mr. William H. Blanche, the Alternate Designated Federal Officer (DFO), called the proceedings to order at 9:00 A.M. After introducing himself, Mr. Blanche indicated the Panel has been convened to review and comment on the therapeutic drug class recommendations resulting from the Department of Defense (DoD) Pharmacy and Therapeutic (P&T) Committee meeting held August, 10 and 11, 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*
    - Oral Non-Steroidal Anti-Inflammatory Drugs (NSAID)
    - Contraceptive Agents
      - Oral contraceptive products
      - Miscellaneous agents

        - Emergency contraceptives
    - Phosphodiesterase-5 Inhibitor (PDE-5) for Erectile Dysfunction (Clinical Only)

➢ *Designated Newly Approved Drugs*

- Renin Angiotensin Antihypertensives (RAAs)
    - Azilsartan – (Edarbi Tablets)
    - Aliskiren/amlodipine/Hydrochlorothiazide – (Amturnide Tablets)
- Non-Insulin Diabetes Mellitus Agents — Bromocriptine mesylate quick release tablets (Cycloset Tablets)
- Narcotic Analgesics — Buprenorphine transdermal patch – (Butrans)

➢ *Items for Information —*

- Singulair Prior Authorization

Opening Remarks

Mr. Blanche 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, Mr. Blanche said the role of the BAP is to comment on the UF recommendations made by the P&T Committee at their last meeting. While the Department appreciates that the BAP may be interested in the drug classes selected for review, drugs recommended for the basic core formulary (BCF) or specific pricing data, these topics do not fall under the purview of the BAP.

The P&T Committee met for approximately 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), Mr. Blanche explained housekeeping considerations then turned the meeting over to the Panel Chairperson, Ms. Deborah Fryar.

Chairperson's Opening Remarks

The Chair welcomed the audience and thanked everyone for coming. She reminded the Panel that its function is to represent the beneficiaries by reviewing the P&T Committee's recommendations, asking questions, offering input, voting to concur or not and making comments as appropriate; however the Panel cannot make recommendations on its own. Those must come from the P&T Committee.

Private Citizen Comments

The Chair then opened the meeting for private citizen comments, noting that one individual, [redacted], had signed up to address the Panel. Ms. Fryar indicated that [redacted] had submitted a letter to the Panel and said that it would be included in the record [Note: the letter and its attachments are included as Appendix 1 at the end

of these minutes].

[redacted] stated that she had her husband's permission to discuss his medical condition, informing the BAP that he has high blood pressure and that an unfortunate side effect of his blood pressure medication is erectile dysfunction (ED). The [redacted] have been married for four years and have tried various medications prescribed by their doctor for the problem, including "as needed" Viagra and Levitra, which didn't work. Finally the doctor told them to try daily Cialis. The smaller doses of the daily medication taken regularly were much more effective. As an unexpected benefit, Mr. [redacted] blood pressure readings lowered significantly over a period of several months, allowing him to be taken off one of his blood pressure medications. Mrs. [redacted] also noted that the side effects of taking Cialis were far less serious than the blood pressure medication.

The problem now is the patient is only allowed six pills per month. Mrs. [redacted] said she has a folder full of letters she has written — to Express-Scripts, TRICARE and her Congressmen — about the problem. The only answer she has ever been given is "it is policy that there are only six pills a month." When she inquired further as to who wrote the policy, where are they and when can she see them, she got no answer to her requests.

Mrs. [redacted] said she had recently happened to come across a reference to the Beneficiary Advisory Panel and took steps to address it today. She informed the BAP that six pills per month is a grossly inadequate amount and doesn't understand how the figure was derived. For a person with Mr. [redacted] problem far more than six pills a month are needed. She also noted she had read a report that stress is greatly reduced when you have a satisfactory love life.

Mrs. [redacted] passed around samples showing how they have coped with the problem: they cut each pill into four pieces. That still isn't enough but they have been able to supplement that with samples from their doctor so that they have one for every day of the month. She also noted that it is difficult to get the pieces the same size.

She concluded by saying she was sure that when the policy was established all that was available were the "as needed" pills, but science has come a long way since then and the policy needs to be changed to approve the daily medication in appropriate quantities. She thanked the Panel for the chance to address them and said she would appreciate whatever they could do to help.

Ms. Fryar thanked Mrs. [redacted] for her presentation.

With no other members of the public wishing to address the Panel, Ms. Fryar asked Dr. Meade to begin the drug class review presentations.

DRUG CLASS REVIEW PRESENTATIONS

[PEC Script]

(Dr. Meade): I'm Dave Meade, Director of Clinical Operations at the Pharmacoeconomic Center. Joining me today from the PEC is Lt Col Rey Morales, our Air Force physician consultant. Also joining us today is Maj Jeremy King, one of the DoD P&T Committee

members who will provide the physician perspective and comment on the recommendations made by the P&T Committee. Dr. Kugler, the chairmen of the P&T Committee and a retired Army Colonel and physician, is also here. Joining us from the TMA is CAPT Nita Sood, the TMA Chief of Staff of the Pharmaceutical Operations Directorate.

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 two Uniform Formulary drug classes – the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and the Contraceptives. Additionally, we'll present one clinical effectiveness review for the Phosphodiesterase-5 Inhibitors – the cost and Uniform Formulary recommendations will be presented at a future meeting. The 4 newly approved drugs that were reviewed were Edarbi, Amturnide, Butrans patch and Cycloset.
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.

UNIFORM FORMULARY CLASS REVIEWS — ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)
(Lt Col Morales)

Background Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the oral NSAIDs. There are 26 drugs in the class, comprised of 19 different chemical entities. Generic formulations are available for 21 drugs and there are 5 branded products: Celebrex, Arthrotec, Vimovo, Zipsor, and Cambia. Celecoxib (Celebrex) is the only cyclooxygenase-2 (COX-2) selective inhibitor available in the United States. Two fixed dose combinations (FDCs) of an NSAID with an anti-ulcer drug are available. Arthrotec is a combination of diclofenac and the prostaglandin analog misoprostol. Vimovo is the first FDC of an NSAID and a proton pump inhibitor (PPI) and is comprised of naproxen and esomeprazole. Diclofenac potassium liquid-filled capsules (Zipsor) contains 25 mg of diclofenac potassium, which is the lowest diclofenac dosage strength marketed; it is solely indicated for relief of mild-to-moderate acute pain. Cambia is a formulation of diclofenac potassium in powder packets for suspension. The partially COX-2-selective NSAIDs include meloxicam, nabumetone, and etodolac. The remaining drugs in the class are the non-COX-2-selective NSAIDs: diclofenac potassium tablets (Cataflam, generics), diclofenac sodium (Voltaren, generics), diflunisal, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid (Ponstel, generics), naproxen (Naprosyn, generics), naproxen sodium (Anaprox, generics), naproxen sodium extended release (ER) (Naprelan CR, generics), oxaprozin, piroxicam, sulindac, and tolmetin.

The oral NSAIDs have not previously been reviewed; however, prior to implementation of the Uniform Formulary Rule in 2005, the following drugs were added to the Basic Core Formulary (BCF): ibuprofen, indomethacin, meloxicam, and naproxen. The clinical review focused on use of the oral NSAIDs for adults with chronic pain due to osteoarthritis, rheumatoid arthritis, soft-tissue pain, back pain, or anklylosing spondylitis. The review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness— The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 1absent) the following conclusions for the Oral NSAIDs:

With regards to efficacy,

1. For short-term pain relief (less than 6 months), all of the oral NSAIDs have a similar effect on reducing chronic pain in adults due to osteoarthritis, rheumatoid arthritis, soft-tissue pain, back pain, or ankylosing spondylitis, based on systematic reviews from the Oregon Drug Effectiveness Review Project (DERP), and the Cochrane group.
2. There is no significant difference in efficacy of pain relief with celecoxib (Celebrex) versus the partially COX-2 selective or nonselective NSAIDs, based on results from randomized controlled trials, meta-analyses, and a systematic review from the Agency for Healthcare Research and Quality (AHRQ; Chou 2007).

3. Diclofenac potassium liquid-filled capsules (Zipsor) were superior to placebo for reducing pain following bunionectomy in two trials. There are no head-to-head trials comparing Zipsor to the other NSAIDs.
4. The FDC of naproxen with esomeprazole (Vimovo) was superior to placebo and non-inferior to celecoxib for reducing pain in patients with osteoarthritis of the knee in two trials.

With regard to gastrointestinal (GI) safety,

5. All the NSAIDs increase the risk of serious GI adverse reactions, including bleeding, inflammation, ulceration, and perforation of the stomach or intestines, which can be fatal.
6. Celecoxib showed benefit for short-term (therapy duration less than or equal to 6 months) GI safety versus nonselective NSAIDs based on meta-analyses (DERP and AHRQ) and the SUCCESS trial. However, celecoxib did not show benefit for long-term (therapy duration greater than 6 months) GI safety (CLASS trial; DERP and AHRQ meta-analyses; FDA analysis).
7. In one trial, celecoxib plus aspirin versus naproxen plus the PPI lansoprazole plus aspirin showed no significant difference for development of endoscopically-confirmed ulcers at 12 weeks (short-term) (Goldstein 2007).
8. Celecoxib versus diclofenac plus the PPI omeprazole showed no significant differences in terms of recurrent ulcer bleeding at 6 months (short-term GI safety) (Chan 2002 New England Journal of Medicine).
9. The GI protective effects of celecoxib therapy alone versus NSAID plus PPI were recently evaluated in the CONDOR study. The results showed short-term GI safety benefit for celecoxib for the composite endpoint of upper and lower GI bleeds when compared to diclofenac plus omeprazole. The results were primarily due to a lower risk of a decrease in hemoglobin (due to presumed occult bleeding of GI origin in the small bowel) in the celecoxib group. (Chan 2010 Lancet)
10. For high-risk patients, taking celecoxib with a PPI may provide increased GI protection versus long-term celecoxib monotherapy. The results of one good-quality trial reported that celecoxib plus omeprazole significantly lowered recurrent GI bleeding in very high-risk GI patients (12-month trial) (Chan 2007 Lancet).
11. For the partially selective NSAIDs, nabumetone showed short-term GI safety benefit compared to nonselective NSAIDs in a single meta-analysis of fair quality (Huang 1999). Etodolac and meloxicam showed no consistent differences in conferring GI safety benefit as compared to nonselective NSAIDs, based on randomized controlled trials and observational studies.
12. For the non-COX-2-selective NSAIDs, clinical trial data suggest that all nonselective NSAIDs are associated with relatively similar risks of serious GI events.
13. Further study is needed to determine the comparative GI safety benefits of concomitant use of an NSAID with various gastroprotective agents (misoprostol, H2 blocker, PPI) in preventing clinical GI events. Misoprostol decreases the risk of

clinically relevant GI events, but is associated with a significant increase in nausea, diarrhea, and abdominal pain.

14. In terms of endoscopically visualized gastric ulcers and discontinuation of therapy due to GI adverse events, Vimovo showed short-term GI safety benefit in patients taking low-dose aspirin versus enteric-coated naproxen alone in two trials.
15. There is insufficient data with Zipsor to assess GI risks.

With regard to cardiovascular (CV) safety,

16. NSAIDs may cause an increased risk of serious CV thrombotic events, myocardial infarction (MI), and stroke, which can be fatal.
17. Based on indirect analyses and observational studies, naproxen appears to be risk-neutral with regard to cardiovascular events; however, a black box warning is still present in the package insert for CV events.
18. Celecoxib, partially-selective NSAIDs, and nonselective NSAIDs have an increased risk of CV events, but there are no consistent differences in the incidence of CV events between them (with the exception of naproxen), based on clinical trials, and the DERP and AHRQ analyses.
19. No CV events related to Vimovo and Zipsor were reported in short-term clinical trials, but there is limited data available.

With regard to tolerability,

20. Relative to nonselective NSAIDs, COX-2 selective and partially selective NSAIDs demonstrated improved or similar tolerability profiles. There are no clear differences in tolerability between the nonselective NSAIDs
21. Vimovo showed a significant benefit in tolerability as compared to use of enteric-coated naproxen alone.

With regard to other factors,

22. Two NSAIDs are available over-the-counter without a prescription: ibuprofen and naproxen.
23. Four NSAIDs are formulated as oral suspensions: indomethacin, meloxicam, ibuprofen, and naproxen.

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) — RELATIVE COST EFFECTIVENESS

(PEC Script)
(Dr. Meade)

The P&T Committee evaluated the relative cost-effectiveness of the oral NSAIDs. Based on the clinical findings regarding efficacy, safety, tolerability, and clinical outcomes with NSAIDs, a cost minimization analysis (CMA) was performed to compare the non-COX-2 selective/partially-COX-2 selective NSAIDs and NSAID/anti-ulcer FDCs. A cost-effectiveness analysis (CEA) was conducted to compare celecoxib (Celebrex) with the nonselective NSAIDs for treatment of osteoarthritis, and a budget impact analysis (BIA) was performed to compare competing

formulary scenarios. 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 results for nonselective/partially-selective NSAIDs showed that these products are the most cost-effective option within the oral NSAID class and should be used prior to treatment with NSAID/anti-ulcer FDCs or celecoxib (Celebrex) when clinically appropriate. However, several specific nonselective/partially-selective NSAIDs were recognized as not being cost-effective relative to the other agents in the class, including naproxen sodium ER (Naprelan CR, generic), diclofenac potassium liquid-filled capsules (Zipsor), diclofenac potassium powder packets (Cambia), and mefenamic acid (Ponstel, generic). The NSAID/anti-ulcer FDCs were comparable on costs with other agents in the oral NSAID class.

Results of the CEA demonstrated that celecoxib was more costly than the nonselective/partially-selective NSAIDs. Published clinical evidence suggested lower risk of GI events with celecoxib compared to nonselective NSAIDs in the short-term (less than or equal to 6 months). However, the cost of preventing an additional ulcer complication with celecoxib was high due to the large difference in cost and small risk reduction in the published clinical data with celecoxib compared to nonselective NSAIDs. Longer-term evidence (greater than 6 months) with celecoxib remains inconclusive with regards to GI risk. Based on these findings, celecoxib should be reserved for patients at high risk for adverse GI events.

The BIA compared several formulary scenarios, including a scenario with an automated PA (step therapy) requiring a trial of generic formulations of partially-selective or nonselective NSAIDs prior to use of celecoxib, and a scenario without an automated PA (no step therapy). The BIA results concluded that the no step-therapy scenario was more cost-effective than the scenario with step therapy for new users of celecoxib.

Relative Cost-Effectiveness Conclusion—Based on the results of the economic analysis and other clinical and cost considerations, the P&T Committee concluded (14 for, 0 opposed, 0 abstained, 1 absent) that the most cost-effective scenario designated the following with formulary status on the UF: diclofenac potassium, diclofenac sodium, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, meloxicam, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, sulindac, tolmetin, naproxen/esomeprazole (Vimovo), diclofenac/misoprostol (Arthrotec), and celecoxib (Celebrex).

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) — UF RECOMMENDATION

(PEC Script)
(Dr. Meade)

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (13 for, 0 opposed, 1 abstained, 1 absent) the following remain formulary on the UF without step therapy: diclofenac potassium, diclofenac sodium, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, meloxicam, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, sulindac, tolmetin, naproxen/esomeprazole (Vimovo), diclofenac/misoprostol (Arthrotec), and

celecoxib (Celebrex). The P&T Committee recommended diclofenac potassium liquid-filled capsules (Zipsor), diclofenac potassium powder packets (Cambia), naproxen sodium ER (Naprelan CR), and mefenamic acid (Ponstel) be designated NF.

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) — IMPLEMENTATION PLAN

(PEC Script)
(Dr. Meade)

The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) — COMMITTEE PHYSICIAN'S PERSPECTIVE

(Maj King)

Maj King, representing the members of the P&T Committee, said this was a non-controversial decision for them. The NSAIDs designated non-formulary were either not cost effective or lacked clinical advantages. Regarding Celebrex, Maj King said it isn't clear what its true benefit is beyond six months, although it does have short-term benefits. The Committee discussed a model that would require step therapy before Celebrex but that didn't seem to be cost-effective and the Committee didn't want to affect a lot of beneficiaries under those conditions so decided not to require step therapy is required for Celebrex. The combination product Vimovo was recommended to be on the UF because of the cardiac risk-neutral profile of naproxen and because the combination drug was more effective than using regular naproxen plus a PPI.

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) — BAP QUESTIONS AND DISCUSSION

The Chair opened the floor for Panel questions and discussion of this drug class.

Dr. Schlaifer asked whether the generic versions of the drugs made non-formulary will also be NF. Dr. Meade answered that the Naprelan CR generic will be but that they couldn't find a generic for Ponstel.

Mr. Hutchings asked about the analysis used to decide about not requiring step therapy. He said his experience is that some agents in this class may be used inappropriately. Dr. Meade replied that the cost analysis showed that step therapy wouldn't be cost-effective.

Mr. Hutchings also asked whether the Committee has discussed the adverse outcomes that might result from the toxicity of some of the medications in this drug class. Maj King said the Committee had explicitly discussed the studies of the cardio-vascular and gastro-intestinal safety factors. He said that there wasn't found to be more risk with one than with the others.

Mr. Hutching asked further what was the basis for comparison used in the cost analysis. Dr. Meade replied that it was "cost per day."

Dr. Salom disclosed that he had designed, supervised and wrote-up for publication and submission to the Food and Drug Administration safety studies for one of the non-steroidal anti-inflammatory drugs on the considered list. This work was performed over 20 years ago. He denied any conflict-of-interest arising from the work.

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs — BAP VOTE ON UF RECOMMENDATIONS

There being no further Panel questions or discussion, Ms. Fryar read the P&T Committee's recommendations for the oral non-steroidal anti-inflammatory drugs (NSAIDs) 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 remain formulary on the UF without step therapy: diclofenac potassium, diclofenac sodium, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, meloxicam, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, sulindac, tolmetin, naproxen/esomeprazole (Vimovo), diclofenac/misoprostol (Arthrotec), and celecoxib (Celebrex). The P&T Committee recommended diclofenac potassium liquid-filled capsules (Zipsor), diclofenac potassium powder packets (Cambia), naproxen sodium ER (Naprelan CR), and mefenamic acid (Ponstel) be designated NF.

The Panel vote was follows:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

One Panel member commented that he was still concerned about the safety of agents in this drug class and the possibility of their inappropriate use.

ORAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs — BAP VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

The Chair read the P&T Committee's recommendations for the oral non-steroidal anti-inflammatory drugs (NSAIDs) drug class.

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) TMA send a letter to beneficiaries affected by this UF decision.

Without discussion, the Panel voted as follows:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

CONTRACEPTIVE AGENTS — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)
(Lt Col Morales)

The P&T Committee evaluated the relative clinical effectiveness of the drugs in the Contraceptive Agents class. The clinical review for the contraceptive products included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1). The Contraceptives Agents class is comprised of three subclasses: oral contraceptive products (OCPs), miscellaneous contraceptives (transdermal patch, vaginal ring, medroxyprogesterone injections) and emergency contraceptives.

The Contraceptive Agents were previously reviewed in May 2006 for UF status. Generic formulations are available for several products (See Table 2). Four new OCPs have recently entered the market: drospirenone 3mg/ethinyl estradiol (EE) 20 mcg/levomefolate Ca 0.451mg (Beyaz), norethindrone acetate 1mg/EE 10mcg/ferrous fumerate 75mg (Lo Loestrin Fe), levonorgesterol 0.1mg/EE 20mcg and levonorgesterol 0.1mg/EE 10mcg for extended use (LoSeasonique), and drospirenone 3mg/EE 30mcg/levomefolate Ca 0.451mg (Safyral). One new emergency contraceptive is also available, ulipristal (Ella).

Several OCPs are available on the UF and BCF, and all the miscellaneous contraceptives are currently designated as UF. For the emergency contraceptives, in November 2009, levonorgestrel 0.75 mg (Next Choice, Plan B generic) was designated as BCF and levonorgestrel 1.5 mg (Plan B One Step) was designated formulary on the Uniform Formulary.

The Contraceptive Drug Class accounted for $87 million in MHS expenditures in FY 2010. In terms of MHS utilization, drospirenone 3mg/EE 20mcg (Yaz, generics) is the most utilized contraceptive, followed by norgestimate 0.18mg/0.215mg/0.25mg/EE 25mcg (Ortho Tri-Cyclen Lo).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended the following conclusions for the contraceptives:

- **Oral Contraceptives Subclass**—For the OCPs subclass, the P&T Committee, voted (14 for, 0 against, 0 abstained, 1 absent) the following conclusions were made:
    1. The differences among the OCPs include estrogen content, progestogen content, regimen, phasic formulation, and non-contraceptive benefits (e.g., acne, premenstrual dysmorphic disorder). The most commonly utilized OCPs are the low-estrogen products containing 20-30 mcg of EE. OCPs commonly include an estrogen with a progestin (combined OCP).
    2. There are no clinically relevant differences in contraceptive effectiveness among the different OCPs, as they all have Pearl Indices (pregnancies per 100 woman-years of use) ranging from < 1 to <3. Current literature does not provide sufficient evidence that combined OCs containing ≤ 20 mcg EE differ from those with higher EE dosage in preventing pregnancy. However, combined OCs with ≤ 20 mcg EE are associated with higher rates of changes in bleeding and amenorrhea.

3. The continuous and extended cycle products (Lybrel Seasonale, Seasonique, LoSeasonique), allow for shorter, fewer or no periods, and are very popular. The Cochrane reviewers concluded extended or continuous cycle contraceptives are reasonable options for women without contraindications to therapy. Of note, the same regimen can be reproduced by eliminating the pill-free interval of monophasic combined OCs for 2-3 cycles.
4. Most if not all combined contraceptives offer non-contraceptive benefits, including control of heavy menstrual bleeding or irregular cycles, and reduction of acne, dysmenorrhea, endometriosis pain and menstrual migraines, regardless of FDA approval for uses other than pregnancy prevention.
5. The most commonly reported adverse effects of oral contraceptives include breast tenderness, headache, migraine, nausea, nervousness, vomiting, dizziness, weight gain, fluid retention, tiredness, decline of libido, and increased blood pressure.
6. The use of combined OCs confers an increased risk of VTE. Based on epidemiological data, the risk of VTE with drospirenone (found in Yaz, Yasmin, Sayfral and Beyaz) is about 2-3 times higher than levonorgestrel-containing OCPs; this risk appears similar to the risk with the third-generation progestins (e.g., desogestrel). FDA is currently reviewing all available data regarding the increased VTE risk with drospirenone-containing oral contraceptives.
7. Comments regarding the newest OCPs include the following: dienogest 2mg/3mg/estradiol valerate 3mg/2mg/2mg/1mg, (Natazia) has complicated dosing instructions if a dose is missed, and the benefits of a quadraphasic OCP remain to be determined. For Beyaz and Safyral, these two products are similar to Yaz and Yasmin, respectively, with the exception of folate, which is added to decrease the risk of neural tube defects if a pregnancy occurs during therapy. Efficacy for both Beyaz and Sayfral was based on data with the innovator products, and clinical trial data is not available. Lo Loestrin Fe has the lowest dose of EE available in an OCP, and had a Pearl Index of 2.92 in the open-label trial used to gain FDA approval. LoSeasonique is a low-EE dose extended cycle OCP given for 91 days (84 days of estrogen and progesterone and 7 days of low dose estrogen).

- **Miscellaneous Contraceptives Subclass**—For the miscellaneous contraceptives subclass, the P&T Committee, based upon its collective professional judgment voted (15 for, 0 against, 0 abstained, 1 absent)

1. Contraceptive products offer alternative routes of administration including depot medroxyprogesterone acetate (DMPA) injections, a transdermal patch (Ortho Evra), and a vaginal ring (Nuvaring).
2. Trials have demonstrated similar contraceptive effectiveness for the patch or vaginal ring as the combined OCs. The injectable DMPA contraceptives are

highly effective agents; no pregnancy was reported in the three, year-long trials used to gain FDA approval.

3. Based on a comparative trial, adverse effects of the transdermal patch appear similar to the combined OC comparator, with the exception of a higher incidence of site application reactions, breast symptoms (e.g., breast tenderness), and dysmenorrhea. Other concerns with the Ortho Evra patch include adhesion problems and application site reactions. The OrthoEvra patch has a black box warning with respect to greater risk of VTE than oral contraceptives, and higher consistent estrogen blood levels (systemic exposure ~ 60% higher than combined OCs).
4. The most common adverse effects of the vaginal ring were vaginitis, headache, vaginal secretion, weight gain, and nausea. One concern with Nuvaring is deployment limitations related to storage requirements.
5. Women receiving injectable DMPA may lose significant bone mineral density, an effect which may not be completely reversible. Injectable DMPA products carry a black box warning regarding this risk. Other concerns with injectable DMPA include progressive (and substantial) weight gain, amenorrhea, irregular menses and unpredictable spotting/bleeding; and lack of immediate reversibility (10 months to return to baseline fertility)
6. The miscellaneous contraceptives serve a niche role and are appropriate contraceptive options for select patients.

- **Emergency Contraceptives Subclass**—For the miscellaneous contraceptives subclass, the P&T Committee, (14 for, 1 against, 0 abstained, 0 absent)

1. Levonorgestrel (Next Choice, generic Plan B; Plan B One Step) has a 3-day window of effectiveness following unprotected intercourse or contraceptive failure, and is available over-the-counter (OTC) for women older than 17 years. Ulipristal (Ella) is a new prescription emergency contraceptive which is effective for up to 5 days after unprotected intercourse.
2. Levonorgestrel 0.75 mg taken in 2 doses 12 hours apart has an efficacy rate of about 95% if taken within 24 hours of unprotected intercourse. Efficacy decreases over time; the efficacy rate is 86% if taken within 25-48 hours, and 58% if taken within 49 to 72 hours of unprotected intercourse. The single-dose 1.5-mg levonorgestrel regimen is as effective as the two-dose regimen taken 12 hours apart.
3. Ulipristal (Ella) is effective at preventing pregnancy following unprotected intercourse, based on the two pivotal trials. Additionally, no decrease in efficacy occurred over the 120 hour period. Two head-to-head comparisons of Ella 30 mg with levonorgestrel 1.5mg, are available. In one study Ella was non-inferior to levonorgestrel at preventing pregnancy (Creinin 2006). The other study demonstrated that Ella prevented more unintended pregnancies than levonorgestrel when administered within 72 and 120 hours after unprotected intercourse (observed pregnancy rate with Ella 1.90, 95% CI 1.13-3.12, versus levonorgestrel 2.50, 95% CI 1.68-3.94; p = 0.037; (Glasier 2010).

4. Ella was well tolerated in the clinical trials and its side effect profile is similar to that of levonorgestrel. The most common adverse effects were headache, abdominal pain, nausea and dysmenorrhea. Long term safety with Ella remains unknown.

CONTRACEPTIVE AGENTS — RELATIVE COST EFFECTIVENESS

(PEC Script)
(Dr. Meade)

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the oral contraceptive products (OCPs), the miscellaneous contraceptives (patch, vaginal ring, medroxyprogesterone injections), and the emergency contraceptives. CMAs and BIAs were performed based on clinical findings that the efficacy, safety, tolerability, and other factors among the OCPs were similar with regard to contraception when used correctly. CMAs were used to analyze the miscellaneous contraceptives. CEAs and CMAs were used to analyze the emergency contraceptives, as efficacy differences between the agents were noted in the clinical review. 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 and BIA were used to assess the potential impact of cost scenarios where selected OCPs were designated with formulary or NF status on the UF. Two of the selected products are currently designated with BCF status: Yaz, and Yasmin. Four new agents selected are currently designated with formulary status on the UF: Beyaz, Loestrin Fe, LoSeasonique, and Safyral. Cost scenarios evaluating the impact of designating selected agents on the BCF were also considered.
- CMA alone was performed on the miscellaneous contraceptives (patch, vaginal ring, and medroxyprogesterone intramuscular (IM) and subcutaneous formulations) because there is limited generic competition within the class.
- In the emergency contraceptives subclass, CEA and CMA analyses were used to assess potential impact of pregnancies avoided, based on the clinically reviewed differences between the agents. The relative drug costs of the various treatment regimens were also assessed.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analyses, the P&T Committee concluded the following:

- **Oral Contraceptives Subclass**—For the OCPs subclass, the P&T Committee, based upon its collective professional judgment, voted (14 for, 0 against, 0 abstained, 1 absent) as follows: BIA showed the scenario where all current BCF agents were retained on the BCF, all current UF agents that had been previously reviewed were retained on the UF, and all current NF, as well as the four new agents, were designated with NF status resulted in the lowest cost estimate compared to current MHS expenditures.

- **Miscellaneous Contraceptives Subclass**—For the miscellaneous contraceptives subclass, the P&T Committee, based upon its collective professional judgment, voted (15 for, 0 against, 0 abstained, 0 absent) as follows: CMA results showed that the average weighted price per day of therapy at all three points of service for the miscellaneous contraceptives was comparable to formulary agents included in the OCPs subclass.
- **Emergency Contraceptives Subclass**—For the emergency contraceptives subclass, the P&T Committee, based upon its collective professional judgment, voted (15 for, 0 against, 0 abstained, 0 absent) as follows: CEA results for the emergency contraceptive agents showed that at current costs, the incremental cost effectiveness ratio with ulipristal (Ella) was less than the projected annual median cost of a live birth in the United States and treatment with ulipristal is a cost-effective alternative compared to levonorgestrel in the MHS. The CMA results showed that Next Choice was the most cost-effective agent, followed by Plan B One-Step and Ella.

CONTRACEPTIVE AGENTS — UF RECOMMENDATION

(PEC Script)
(Dr. Mead

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:

- **OCPs Subclass—**
  - The P&T Committee voted that the Jolessa branded generic formulation of Seasonale should be added to the UF.
  - The P&T Committee voted that the following drugs and their generic equivalents should be retained on the UF:
    - Monophasics with 20 mcg of EE (Yaz, , Sronyx, Loestrin 1/20, Loestrin Fe 1/20)
    - Monphasics with 30 mcg of EE (Levora, Lo/Ovral, Desogen, Loestrin 1.5/30 , Loestrin with iron 1.5/30, 1+35, Yasmin)
    - Monophasics with 35 mcg EE (Mononessa, Modicon, Zovia 1/35)
    - Monphasics with 50 mcg EE or mestranol (Zovia 1/50E, Ogestrel)
    - Biphasics (Necon 10/11, Mircette)
    - Triphasics (Ortho-Tri Cyclen Lo, Trinessa, Trivora, Tri-Norinyl, Ortho-Novum 7/7/7 Cyclessa, Nor-Q-D)
  - The following OCPs were designated NF or retained NF status on the UF:
    - norethindrone acetate 1mg/EE 10mcg (Lo Loestrin Fe)
    - levonorgestrel 0.1mg/EE 20mcg + 10mcg (LoSeasonique)

- drospirenone 3mg/EE 20mcg/levomefolate Ca 0.451mg (Beyaz)
- drospirenone/EE 30mcg/levomefolate Ca 0.451mg (Safyral)
- levonorgestrel 90mcg/EE 20mcg, continuous regimen (Lybrel, generic)
- norethindrone acetate 1mg/EE 20mg, extended regimen (Loestrin 24 Fe)
- norethindrone 0.4mg/EE 35mcg (Ovcon-35 generics; also includes Femcon Fe chewable and Zeosa chewable)
- norethindrone 1mg/EE 50mcg (Ovcon-50)
- levonorgestrel 0.15mg/EE 30mcg + 10mcg, extended regimen (Seasonique, generics)
- norethindrone 1mg/EE 20mcg/30mcg/35mcg/ferrous fumerate 75mg (Estrostep Fe, generics)
- dienogest 2mg/3mg/estradiol valerate 3mg/2mg/2mg/1mg, (Natazia)
- levonorgestrel 0.15mg/EE 30mcg, extended regimen (Seasonale, generics, including Introvale and Quasense), with the exception of Jolessa branded generic

- **Miscellaneous Contraceptive Subclass**—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following drugs remain formulary on the UF: norelgestromin/EE 50 mcg transdermal (Ortho Evra), etonorgestrel/EE vaginal ring (NuvaRing), medroxyprogesterone acetate 150 mg/mL (Depo-Provera IM, generics), and medroxyprogesterone acetate 104 mg/0.65 mL (Depo-SubQ Provera 104). No miscellaneous contraceptive agent was recommended for NF placement.

- **Emergency Contraceptive Subclass**—The P&T Committee recommended (12 for, 0 opposed, 3 abstained, 0 absent) the following drugs remain formulary on the UF: levonorgestrel 0.75mg (Next Choice; Plan B generic), levonorgestrel 1.5mg (Plan B One Step), and that ulipristal (Ella) be designated formulary on the UF. No emergency contraceptive was recommended for NF placement.

CONTRACEPTIVE AGENTS — IMPLEMENTATION PLAN
(PEC Script)
(Dr. Mead

The P&T Committee recommended (14 for, 0 against, 0 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

CONTRACEPTIVE AGENTS — COMMITTEE PHYSICIAN'S PERSPECTIVE

(Maj King)

Major King said he personally, as a women's health care professional, was very comfortable

with the NF choices made in this drug class. Relatively few of the agents in this class are NF at this point. Those recommended for NF status offer some new twists on previously available contraceptives but those have only minimally significant clinical improvement. The recommendations were non-controversial. There was some discussion of the extended cycle Jolessa brand generic which was found to pose some unknown health risks and is still undergoing FDA review. The Committee also discussed the newer emergency contraceptives but none were made NF.

CONTRACEPTIVE AGENTS — BAP QUESTIONS AND DISCUSSION

Ms. Fryar opened the floor for questions and discussion of the contraceptive agents drug class. Mr. Hutchings asked whether the injected contraceptives are covered. Dr. Meade said they are but only after the age of 17, i.e. 18 and over.

Ms. Cohoon referred to previous discussions of contraceptive agents and their safety and asked what steps will be taken to assure that these agents will be appropriately used and will not be harmful. Dr. Meade replied that it is up to the professionals who prescribe the drugs to call the patient's attention to the way in which they should be used.

Dr. Schlaifer noted the Ella was found to be more effective than other emergency contraceptives, but it is also more expensive. She asked if there was any discussion of that by the Committee. The PEC staff replied that there wasn't because the only difference is in the benefit.

CONTRACEPTIVE AGENTS — BAP VOTE ON UF RECOMMENDATIONS

Ms. Fryar read the recommendations separately for the three subclasses of agents in this class: oral, miscellaneous and emergency contraceptives.

ORAL CONTRACEPTIVES SUBCLASS

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:

- **OCPs Subclass—**
  - The P&T Committee voted that the Jolessa branded generic formulation of Seasonale should be added to the UF.
  - The P&T Committee voted that the following drugs and their generic equivalents should be retained on the UF:
    - Monophasics with 20 mcg of EE (Yaz, , Sronyx, Loestrin 1/20, Loestrin Fe 1/20)
    - Monphasics with 30 mcg of EE (Levora, Lo/Ovral, Desogen, Loestrin 1.5/30 , Loestrin with iron 1.5/30, 1+35, Yasmin)

- Monophasics with 35 mcg EE (Mononessa, Modicon, Zovia 1/35)
- Monphasics with 50 mcg EE or mestranol (Zovia 1/50E, Ogestrel)
- Biphasics (Necon 10/11, Mircette)
- Triphasics (Ortho-Tri Cyclen Lo, Trinessa, Trivora, Tri-Norinyl, Ortho-Novum 7/7/7 Cyclessa, Nor-Q-D)

- The following OCPs were designated NF or retained NF status on the UF:
  - norethindrone acetate 1mg/EE 10mcg (Lo Loestrin Fe)
  - levonorgestrel 0.1mg/EE 20mcg + 10mcg (LoSeasonique)
  - drospirenone 3mg/EE 20mcg/levomefolate Ca 0.451mg (Beyaz)
  - drospirenone/EE 30mcg/levomefolate Ca 0.451mg (Safyral)
  - levonorgestrel 90mcg/EE 20mcg, continuous regimen (Lybrel, generic)
  - norethindrone acetate 1mg/EE 20mg, extended regimen (Loestrin 24 Fe)
  - norethindrone 0.4mg/EE 35mcg (Ovcon-35 generics; also includes Femcon Fe chewable and Zeosa chewable)
  - norethindrone 1mg/EE 50mcg (Ovcon-50)
  - levonorgestrel 0.15mg/EE 30mcg + 10mcg, extended regimen (Seasonique, generics)
  - norethindrone 1mg/EE 20mcg/30mcg/35mcg/ferrous fumerate 75mg (Estrostep Fe, generics)
  - dienogest 2mg/3mg/estradiol valerate 3mg/2mg/2mg/1mg, (Natazia)
  - levonorgestrel 0.15mg/EE 30mcg, extended regimen (Seasonale, generics, including Introvale and Quasense), with the exception of Jolessa branded generic.

Without further discussion, the BAP vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

MISCELLANEOUS CONTRACEPTIVES SUBCLASS

The P&T Committee recommended the following drugs remain formulary on the UF: norelgestromin/EE 50 mcg transdermal (Ortho Evra), etonorgestrel/EE vaginal ring (NuvaRing), medroxyprogesterone acetate 150 mg/mL (Depo-Provera IM, generics), and medroxyprogesterone acetate 104 mg/0.65 mL (Depo-SubQ Provera 104). No miscellaneous contraceptive agent was recommended for NF placement.

There was no further discussion. The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

EMERGENCY CONTRACEPTIVES SUBCLASS

The P&T Committee recommended the following drugs remain formulary on the UF: levonorgestrel 0.75mg (Next Choice; Plan B generic), levonorgestrel 1.5mg (Plan B One Step), and that ulipristal (Ella) be designated formulary on the UF. No emergency contraceptive was recommended for NF placement.

Without further discussion, the Panel voted as follows:

Concur: 7 Non-concur: 0 Abstain: 2 Absent: 2

IMPLEMENTATION PLAN

The Chair noted the implementation plan applies to all three subclasses. It is:

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) TMA send a letter to beneficiaries affected by this UF decision.

The Committee vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

Before proceeding, Mr. Hutchings asked for clarification of which generics are covered and which are not.

Ms. Fryar noted that the next drug class involves a partial clinical evaluation perspective presentation and that the Panel will get a full briefing and vote on P&T recommendations for this class at the next BAP meeting.

PHOSPHODIESTERASE-5 INHIBITOR (PDE-5) FOR ERECTILE DYSFUNCTION — BACKGROUND

(Dr. Meade)

Dr. Meade introduced the discussion by informing the Panel that over the summer there had been significant price increases and contracts were broken. The Committee had considered this class not too long ago and first thought it could do a quick turnaround. However, legal actions occurring two days before the meeting prevented that. As a result, DoD is going on a national contract with the Veterans Administration. These figures will be used to re-evaluate the cost-effectiveness and develop UF recommendations for the next meeting.

PHOSPHODIESTERASE-5 INHIBITOR (PDE-5) FOR ERECTILE DYSFUNCTION — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)
(Dr. Meade)

Relative Clinical Effectiveness—The P&T Committee evaluated the clinical effectiveness of the PDE-5 Inhibitors for the treatment of ED. The drugs in the class include sildenafil (Viagra), tadalafil (Cialis), vardenafil oral tablets (Levitra), and one new drug—vardenafil orally dissolving tablets (ODT) (Staxyn). The PDE-5s for ED were previously reviewed in August 2009; at that time, vardenafil was designated with BCF status, with an automated PA requiring a trial of vardenafil prior to sildenafil or tadalafil, which were designated NF. Quantity limits are in place for the PDE-5s for ED.

Vardenafil ODT (Staxyn) contains the same chemical ingredient as vardenafil oral tablets (Levitra). It is available in 10 mg ODT tablets, which is the recommended dose for all patients. In contrast, the starting dose for vardenafil oral tablets is 5 mg in patients older than age 65. Pharmacokinetic studies with vardenafil 10 mg ODT show a higher area under the curve compared to vardenafil 10 mg oral tablets. The two placebo-controlled trials used to obtain FDA approval reported superior efficacy with Staxyn in treating ED. Information regarding the safety, effectiveness, and clinical outcomes of the PDE-5s for ED subclass was considered. The clinical review included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 0 absent) the following conclusions for the PDE-5s for ED:
With regards to efficacy,

1. There are no head-to-head comparative trials between the PDE-5 inhibitors assessing efficacy for ED.
2. Based on meta-analyses by AHRQ, Cochrane, and BioMed Central, indirect comparisons suggest that there are similar improvements between vardenafil oral tablets, sildenafil, and tadalafil in the following endpoints: International Index of Erectile Function (IIEF) "EF" domain change, percentage of patients responding "Yes" to Global Assessment question 1 (which asks "Did this treatment improve your erections?"), and percentage of patients reporting improved erections.
3. The improvement in IIEF score with Staxyn appears similar to that seen in the AHRQ review based on indirect comparison.
4. The 2009 PDE-5 UF review reported there was insufficient evidence to conclude that daily therapy for ED was superior to on demand therapy. There is no new evidence to change this conclusion
5. The improvement in IIIEF score with Staxyn appears similar to that seen in the AHRQ review based on indirect comparison.

With regard to safety,

6. There is insufficient evidence to conclude that there are clinically relevant differences in safety between PDE-5 inhibitors for ED.
7. Clinical trials with vardenafil ODT have identified no safety issues that were not previously identified in the studies of the vardenafil film-coated tablets. However, unlike the other PDE-5s, vardenafil ODT is not recommended for use in patients with renal or hepatic impairment.

With regard to other factors,

The PDE-5 inhibitors are highly therapeutically interchangeable, when used for treating ED.

PHOSPHODIESTERASE-5 INHIBITOR (PDE-5) FOR ERECTILE DYSFUNCTION — RELATIVE COST EFFECTIVENESS

Relative Cost-Effectiveness, Relative Cost-Effectiveness Conclusion, UF Recommendation—Due to contract solicitation issues, the cost effectiveness review and P&T Committee conclusions for the PDE-5 inhibitors for ED will be presented at an interim meeting.

PHOSPHODIESTERASE-5 INHIBITOR (PDE-5) FOR ERECTILE DYSFUNCTION — PANEL QUESTIONS AND DISCUSSION

The Chair asked the PEC staff to ensure that the beneficiary comments the Panel heard today be considered by the P&T Committee when it reconsiders this drug class. The PEC staff agreed.

Ms. Cohoon noted that the P&T Committee concluded that reported there was insufficient evidence to conclude that daily therapy for ED was superior to on demand therapy and asked if that would apply to the situation brought before the Panel earlier today. Dr. Meade agreed that it was.

The Chair then called for the presentation of recommendations on new agents recently approved by the FDA.

DESIGNATED NEWLY APPROVED DRUGS

RENIN ANGIOTENSIN ANTIHYPERTENSIVES (RAAs)

A. Azilsartan (Edarbi)

Azilsartan (Edarbi)—Relative Clinical Effectiveness

(PEC Script)
(Lt Col Morales)

Relative Clinical Effectiveness—Azilsartan (Edarbi) is a once daily angiotensin receptor blocker (ARB), the eighth ARB to enter the market. It is classified in the RAAs drug class. The class was last reviewed in August 2010. The clinical evaluation for Edarbi included, but was not limited to, the requirements stated in 32 Code of Federal Regulations (CFR) 199.21(e)(1).

Edarbi is indicated for the management of hypertension, alone or in combination with other agents. It has no other FDA-approved indications and there are no clinical outcomes (e.g., reduction in heart failure hospitalization, death, or type 2 diabetic renal disease) studies completed, in-process, or planned. Because of corresponding published reductions in stroke and all-cause mortality, a reduction of either systolic or diastolic blood pressure (BP) of 2 mm Hg or more is considered clinically meaningful for this review.

In seven clinical trials—two published and five unpublished—Edarbi demonstrated efficacy in treating hypertension. In two studies, it demonstrated superiority to valsartan (Diovan), a step-preferred, BCF agent, at a clinically meaningful reduction in systolic BP of 3-5 mm Hg. Additionally, Edarbi showed non-inferiority and statistical superiority (and a potentially

clinically meaningful systolic BP reduction of 1-2 mm Hg) to olmesartan (Benicar). In terms of safety, there is no evidence that Edarbi is more or less safe, on average, than any of the seven other ARBs.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (14 for, 0 opposed, 0 abstained, 1 absent) azilsartan (Edarbi) offers a compelling therapeutic advantage over valsartan and possibly olmesartan, but does not have clinical outcomes studies available.

Azilsartan(Edarbi)—Relative Cost Effectiveness

(PEC Script)
(Dr. Meade)

Although the clinical review concluded Edarbi produced a clinically relevant reduction in BP compared to other ARBs, CMA was used to compare its cost to the other ARBs, consistent with the cost analysis for the ARBs subclass conducted at the August 2010 UF review for the RAAs. CMA was performed to evaluate Edarbi's cost in comparison to other UF RAAs drugs, including generic losartan, telmisartan (Micardis), valsartan (Diovan), irbesartan (Avapro), olmesartan (Benicar), and candesartan (Atacand). 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 (14 for, 0 opposed, 0 abstained, 1 absent) that Edarbi was more costly than telmisartan (Micardis), valsartan (Diovan), irbesartan (Avapro), olmesartan (Benicar), and less costly than Atacand (candesartan).

Azilsartan(Edarbi)—UF Recommendation

(PEC Script)

(Dr. Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors the P&T Committee, based upon its collective professional judgment, recommended (13 for, 0 opposed, 1 abstained, 1 absent) azilsartan (Edarbi) remain formulary on the UF.

Azilsartan (Edarbi)—Prior Authorization (PA) Criteria

(PEC Script)

(Dr. Meade) The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) that azilsartan (Edarbi) be designated non-step preferred requiring the following step-therapy/PA criteria. 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 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 Service (MHS) pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.
    b) The patient has received a prescription for azilsartan (Edarbi) at any 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).

Azilsartan (Edarbi)—UF and PA Implementation Plan

(PEC Script)

(Dr. Meade) The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

Azilsartan (Edarbi)—Committee Physician's Perspective

(Maj King) Maj King said the class was just reviewed last yer And several agents were put on the UF but adding Edarbi was non-controversial decision and noted that the P&T Committee plans to re-review this entire class again next year because of change in the class.

Azilsartan (Edarbi)—Panel Questions and Discussion

Ms. Cohoon asked about the PA for this agent, specifically why it is non-step preferred as it offers a compelling therapeutic advantage over some of the other agents. Dr. Meade answered that it is consistent with the other members of the RAAs class for which there is already a step in place. Also it is more expensive. The need for step therapy will be reconsidered when the class as a whole is re-reviewed.

Azilsartan (Edarbi)—Panel Vote on UF Recommendation

With no further discussion, Ms. Fryar read the Committee's UF recommendation for Edarbi.

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 azilsartan (Edarbi) remain formulary on the UF.

The Panel voted as follows:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

Azilsartan (Edarbi)—Panel Vote on Prior Authorization Criteria

Ms. Fryar next read the PA criteria for Edarbi:

The P&T Committee recommended Azilsartan (Edarbi) be designated non-step preferred requiring the following step-therapy/PA criteria. 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 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 Service (MHS) pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

   b) The patient has received a prescription for azilsartan (Edarbi) at any 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).

The Panel voted:

Concur: 8 Non-concur: 1 Abstain: 0 Absent: 2

Ms. Cohoon commented she didn't believe this drug should be subject to non-step preferred PA criteria because of its clinical effectiveness.

Azilsartan (Edarbi)—Panel Vote on Implementation Plan

The Chair then read the P&T Committee's implementation plan recommendation.

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

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

NEWLY APPROVED DRUGS — RENIN ANGIOTENSIN ANTIHYPERTENSIVES (RAAs)

B. Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—Relative Clinical Effectiveness

(PEC Script)

(Lt Col Morales) *Relative Clinical Effectiveness*—Amturnide is a once daily triple-FDC antihypertensive product. It contains aliskiren, a direct renin inhibitor (DRI), amlodipine, a dihydropyridine calcium channel blocker (DHP CCB), and hydrochlorothiazide (HCTZ), a thiazide-type diuretic. Amturnide is the third triple-combination antihypertensive to enter the market. It is classified in the RAAs drug class due to the aliskiren (DRI) component. This class was last reviewed in August 2010. The clinical evaluation for Amturnide included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Amturnide is indicated for the management of hypertension as an add-on or switch from two of the components, or as a substitute for all three titrated components, but not for initial therapy. It has no other FDA-approved indications and there are no clinical outcomes studies completed, in-process, or planned. Aliskiren has outcomes studies underway, while amlodipine and HCTZ have well-established published outcomes data.

In three unpublished clinical trials, Amturnide demonstrated efficacy in treating hypertension versus the efficacy demonstrated by dual combinations of the individual component medications. In terms of safety, there is no evidence that Amturnide is more or less safe, on average, than either of the two other triple FDCs, valsartan/amlodipine/HCTZ (Exforge HCT) and olmesartan/amlodipine/HCTZ (Tribenzor). The combination of these three drug classes (DRI, DHP CCB and thiazide diuretic) has no compelling advantage in terms of efficacy over giving other combinations (e.g., ARB/DHP CCB/HCTZ). In terms of safety, the Amturnide FDC partially offsets the peripheral edema common to CCBs, the hypokalemia common to diuretics, and the hyperkalemia sometimes seen with ARBs.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (14 for, 0 opposed, 0 abstained, 1 absent) that Amturnide does not offer a compelling therapeutic advantage in terms of efficacy or safety over other antihypertensive FDCs currently on the UF.

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—Relative Cost Effectiveness

(PEC Script)

(Dr. Meade) CMA was performed to evaluate the cost of aliskiren/amlodipine/HCTZ (Amturnide) in relation to the other UF RAAs drugs, including the following: aliskiren/HCTZ (Tekturna HCT) plus generic amlodipine, benazepril/amlodipine, telmisartan/amlodipine (Twynsta), olmesartan/HCTZ (Benicar HCT), valsartan/amlodipine (Exforge), valsartan/amlodipine/HCTZ (Exforge HCT), olmesartan/amlodipine (Azor), and olmesartan/amlodipine/HCTZ (Tribenzor). 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 (13 for, 0 opposed, 0 abstained, 2 absent) Amturnide was more costly, compared with other RAAs currently designated with BCF or UF status.

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—UF Recommendation

(PEC Script)

(Dr. Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (12 for, 0 opposed, 1 abstained, 2 absent) aliskiren/amlodipine/HCTZ (Amturnide) remain formulary on the UF, as the FDC of DRI/amlodipine/HCTZ may be necessary for hypertensive patients requiring 3 drugs who do not respond to other triple FDC RAAs.

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—PA Criteria

(PEC Script)

(Dr. Meade) The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) aliskiren/amlodipine/HCTZ (Amturnide) be designated non-step preferred requiring the following step-therapy/PA criteria. 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 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 MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the

previous 180 days.

b) The patient has received a prescription for aliskiren/amlodipine/HCTZ (Amturnide) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) 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).

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—UF and PA Implementation Plan

(PEC Script)

(Dr. Meade) The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—Committee Physician's Perspective

(Maj King)

Major King noted that Amturnide was more costly than other RAAs agents on the UF. He told the Panel that the P&T Committee recommended UF placement for this drug because of the importance of treating hypertension and because the triple combination might be beneficial for some patients. He also said that this class is expected to be re-reviewed after new guidelines are issued. There is also a step in place for this class and Amturnide will be behind the step.

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—Panel Questions and Discussion

The members of the Panel engaged in an extensive discussion of the recommendations regarding this agent and the rationale for those recommendations. Mr. Hutchings stated that it might appear as though patients were being pushed into using a triple combination agent. He further pointed out that product was found to be not cost-effective. He also noted that two of the three ingredients in Amturnide were already non-formulary and objected to the inconsistency of making them formulary through their inclusion in a triple combo. He asked for a further

explanation of the logic behind the recommended placement.

Dr. Salom stated that he has a bias against triple combination products in general. He believes that the increased gains are not offset by problems from adverse reactions. In this case, where the drug isn't even cost effective, he would think it's not something that should be on the formulary.

Dr. Meade replied that the Committee was looking at the fact that there are so few triple combinations available. They are not used for initial therapy and their utilization in the MHS is quite low. Additionally, there will be a re-review of the entire RAAs class in the near future.

Mr. Hutchings noted that the PA criteria omit mention of whether the patient has been on other agents and questioned the step process in these cases. Dr. Meade answered that they would take that into consideration in the implementation process.

Ms. Fryar asked when this drug class would come up for review again. Dr. Meade replied that they are waiting for certain things to happen, including the launch of another new drug so that they don't have to review that one separately. The objective is to conduct a comprehensive review that includes generic Diovan.

Ms. Cohoon noted that not only was this drug not cost effective, it didn't have a significant therapeutic advantage. She said she might be able to live with the higher cost if it did have a therapeutic advantage.

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—Panel Vote on UF Recommendations

The Chair noted that there would be three votes for Amturnide: UF, PA criteria and implementation plan. She then read the 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 aliskiren/amlodipine/HCTZ (Amturnide) remain formulary on the UF, as the FDC of DRI/amlodipine/HCTZ may be necessary for hypertensive patients requiring 3 drugs who do not respond to other triple FDC RAAs.

The Panel vote was:

Concur: 2 Non-concur: 7 Abstain: 0 Absent: 2

The Panel commented that it was concerned about the inconsistency of including a drug on the UF that contains two NF agents. It was also concerned about placing a drug on the UF that offers no therapeutic advantages and is not cost effective.

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—Panel Vote on PA Criteria

The Chair then read the PA criteria recommendations.

The P&T Committee recommended aliskiren/amlodipine/HCTZ (Amturnide) be designated non-step preferred requiring the following step-therapy/PA criteria. 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 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 MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

   b) The patient has received a prescription for aliskiren/amlodipine/HCTZ (Amturnide) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) 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).

With no further discussion, the Panel voted on the PA criteria recommendations:

Concur: 8 Non-concur: 1 Abstain: 0 Absent: 2

Dr. Salom stated that if the drug is to be made UF, these seem to him like reasonable steps.

Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)—Panel Vote on UF and PA Implementation Plan

The Chair read the 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.

Mr. Hutchings asked whether it really will require 60 days to implement. Ms. Legette said that the 60 days is necessary to conform to commercial practice and to get letters out to the beneficiaries. Mr. Hutchings said that letters don't have to go out in this case – you just need to flip a switch on the automated system -- and he would recommend something shorter.

The Panel voted as follows:

Concur: 8 Non-concur: 1 Abstain: 0 Absent: 2

NEWLY APPROVED DRUGS — NON-INSULIN DIABETES MELLITUS DOPAMINE AGONIST

- **Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)**

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—Relative Clinical Effectiveness

(PEC Script)

(Lt Col Morales) *Relative Clinical Effectiveness*—The P&T Committee evaluated the relative clinical effectiveness of a newly approved formulation of bromocriptine, bromocriptine mesylate (Cycloset). The clinical review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

Cycloset is a centrally-acting dopamine agonist (DA) and is the only DA approved for the treatment of diabetes. This agent falls into the new DA subclass of the Non-Insulin Diabetes Drugs, which was reviewed for UF placement in November 2010. The other subclasses include dipeptidyl-peptidase 4 inhibitors (DPP-4s), thiazolidinediones (TZDs), glucagon-like peptide-1 receptor agonists biguanides, sulfonylureas (SUs), meglitinides, and alpha-glucosidase inhibitors. Step therapy (automated PA) applies for the Non-Insulin Diabetes Drug Class, which requires a trial of metformin or a sulfonylurea.

Bromocriptine is an old drug with a new use. It was first approved in 1978 for the treatment of Parkinson's disease and has uses in other endocrine-related disorders such as hyperprolactinemia, acromegaly, and prolactin-secreting adenomas. Bromocriptine should not be used to suppress lactation since an increase in stroke and myocardial should not be used to suppress lactation, since myocardial infarction and stroke were reported in postpartum women. The new bromocriptine Cycloset product is a quick release formulation administered in the morning. Other bromocriptine mesylate formulations are available, including immediate release (IR) 2.5 tablets and scored tablets, and 5 mg IR capsules (Parlodel, generics). Decreased levels of dopamine may contribute to insulin resistance, and increasing dopamine activity in the morning is effective at improving glucose dysregulation. Cycloset is indicated as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes mellitus (T2DM).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 1 absent) the following conclusions for bromocriptine mesylate (Cycloset):

- Uptitration of Cycloset is required to achieve the maximum therapeutic benefit. Patients start with 0.8mg (1 tab) daily and increase by 0.8mg in weekly increments to a maximally tolerated dose of 4.8mg daily. The minimum therapeutic dose is 1.6mg daily.

- When used as monotherapy, Cycloset decreased glycosolated hemoglobin or hemoglobin A1c (HbA1c) 0.1% from baseline compared to placebo. Cycloset decreased HbA1c 0.1-

0.4% from baseline when added to a SU and a produced a maximum 0.5% decrease from baseline when combined with both metformin and a SU.

- There are no head-to-head studies to date with other non-insulin diabetes medications and no long-term outcomes studies currently in progress.

- Bromocriptine mesylate is weight neutral; however, as with other medications, more weight gain is likely when administered with a SU or TZD. It may have a beneficial effect on lipid levels and BP.

- Nausea is the primary side effect (~31%) although bromocriptine mesylate is generally well tolerated. The incidence of serious adverse events is similar to placebo.

- There was a statistically significant decrease in major cardiovascular events with Cycloset noted in one 52-week study. However, the clinical relevance of this secondary endpoint is not clear.

- Many potential drug interactions exist with Cycloset, including strong CYP 3A4 inducers or inhibitors; highly protein-bound drugs (e.g. salicylates, sulfonamides, chloramphenicol, probenecid); dopamine receptor antagonists; ergot-related drugs and sympathomimetic drugs.

- According to current T2DM treatment guidelines, the place in therapy for bromocriptine mesylate (Cycloset) remains unknown.

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—Relative Cost Effectiveness

(PEC Script)

(Dr. Meade) The P&T Committee evaluated the cost of bromocriptine mesylate (Cycloset). CMA was 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 (13 for, 0 opposed, 0 abstained, 2 absent) Cycloset was more costly when compared to step-preferred UF agents (metformin, SU, DPP-4 inhibitors, TZDs) and generic bromocriptine mesylate IR.

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—UF Recommendation

(PEC Script)

(Dr. Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (12 for, 1 opposed, 1 abstained, 1 absent) bromocriptine mesylate (Cycloset) be designated NF and non-step preferred.

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—PA Criteria

(PEC Script)

(Dr. Meade) Step therapy applies to this new subclass (dopamine agonists) requiring prior trial of metformin or a sulfonylurea. Bromocriptine mesylate (Cycloset) is recommended to be designated as non-step preferred and NF. The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to bromocriptine mesylate (Cycloset).

1. Automated PA criteria:

    a) The patient has received a prescription for metformin or SU at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

    b) The patient has received a prescription for bromocriptine mesylate (Cycloset) at any 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 a confirmed diagnosis of T2DM.

    b) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.

    c) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.

d) The patient has a contraindication or has had inadequate therapy to both metformin and a SU.

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—UF and PA Criteria Implementation Plan

(PEC Script)

(Dr. Meade) The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this decision.

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—Committee Physician's Perspective

(Maj King)

Maj King said the Committee recommended NF placement for Cycloset because it is more costly than the other diabetic drugs. Also, its clinical effectiveness was to reduce hemoglobin A1c by 0.1 percent alone and 0.4 percent in combination with other agents; in a previous review of this class the Committee had determined that 0.5 percent would be clinically relevant. All of the other diabetic drugs on the UF provide at least a 0.5 percent reduction. The one dissenting vote said that Cycloset should be on the UF because it has a unique mechanism. Metformin or sulfonylurea is the preferred first-line agent for diabetes.

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—Panel Questions and Discussion

The Chair opened the floor to questions and discussion. Mr. Hutchings asked if there was any discussion of making the step more rigorous. Dr. Meade said there was not.

Dr. Salom expressed the view that this should not even be considered a second line drug and maybe shouldn't even be prescribed at all because its efficacy is so minimal. He believes the PA criteria should be much more rigorous than recommended.

Ms. Cohoon asked about the step preferences. Dr. Meade explained that metformin and sufonylurea are the first line agents. The MHS has not designated second, third or fourth line agents; instead, they trust the prescriber to know where the second line ought to be.

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—Panel Vote on UF Recommendation

The Chair read the UF recommendation for Cycloset.

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 bromocriptine mesylate (Cycloset) be designated NF and non-step preferred.

The BAP voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—Panel Vote on PA Criteria

Ms. Fryar then read the Committee's recommended PA criteria for Cycloset.

Step therapy applies to this new subclass (dopamine agonists) requiring prior trial of metformin or a sulfonylurea. Bromocriptine mesylate (Cycloset) is recommended to be designated as non-step preferred and NF. The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to bromocriptine mesylate (Cycloset).

1. Automated PA criteria:

   a) The patient has received a prescription for metformin or SU at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

   b) The patient has received a prescription for bromocriptine mesylate (Cycloset) at any 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 a confirmed diagnosis of T2DM.

   b) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.

   c) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.

   d) The patient has a contraindication or has had inadequate therapy to both metformin and a SU.

The Panel voted as follows:

Concur: 6 Non-concur: 3 Abstain: 0 Absent: 2

Comments offered by the Panel members were that the drug is not efficacious and probably shouldn't be used by anyone so the PA criteria should be more rigorous, specifying other agents that should be tried first for contraindications.

Non-Insulin Diabetes Mellitus Agents—Bromocriptine mesylate quick release tablets (Cycloset tablets)—Panel Vote on UF and PA Criteria Implementation Plan

The Chair read the UF and PA criteria 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 2) TMA send a letter to beneficiaries affected by this decision.

The BAP vote was:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

NEWLY APPROVED DRUGS — NARCOTIC ANALGESICS

- **Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)**

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—Relative Clinical Effectiveness

(PEC Script)

(Lt Col Morales) *Relative Clinical Effectiveness*—Butrans is a transdermal formulation of buprenorphine, a semi-synthetic opioid with mixed agonist/antagonist activity at opioid receptors. It is a Schedule III drug, classified as a low-potency single analgesic agent in the Narcotic Analgesics Drug Class. The class was last reviewed in February 2007. The clinical evaluation for Butrans included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

There are other formulations of buprenorphine commercially available: parenteral formulations for post-operative pain management and sublingual tablets for the management of opioid-dependence. Butrans is indicated for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock, opioid analgesic for an extended period of time. One transdermal system allows for systemic delivery of buprenorphine, continuously over seven days, which offers a convenient regimen for patients.

In two unpublished clinical trials, Butrans demonstrated efficacy in treating chronic low back pain. There are no direct head-to-head studies comparing it to other long-acting narcotic agents of similar potency marketed in the United States. In terms of safety, there are some additional concerns with Butrans compared to other narcotics, particularly the risk of QTc prolongation at doses greater than 20mcg/hr, which will limit its use in patients with unstable cardiac disease.

The major safety issue with Butrans is buprenorphine-induced respiratory depression. This poses a concern for elderly patients or those with impaired pulmonary function since the effects of buprenorphine are not completely reversible with naloxone (an opioid antagonist). Butrans is not intended for patients requiring treatment with high–dose opioids (>80 mg/day of morphine or equivalent), another factor that may limit its use in patients stable on alternative opioid analgesics. Butrans provides an additional treatment option when a long-acting, low-potency analgesic is needed.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 0 absent) that other than the convenience of less frequent dosing, buprenorphine transdermal system (Butrans) offers no other compelling therapeutic advantages over the other low potency narcotic analgesics currently on the UF.

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—Relative Cost Effectiveness

(PEC Script)

(Dr. Meade) The P&T Committee evaluated Butran's cost relative to the other low-potency agents in the Narcotic Analgesics Drug Class. CMA was performed based on clinical findings that efficacy, safety, tolerability, and factors other than patient convenience found among the agents in this class were similar at equipotent doses. 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—The P&T Committee, based upon its collective professional judgment, concluded (15 for, 0 opposed, 0 abstained, 0 absent) that buprenorphine transdermal system (Butrans) was more costly, based on an average weighted cost per day of therapy, than other low-potency single analgesic agents currently on the UF. However, Butrans was less costly than the sublingual formulations of buprenorphine already on the UF.

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—UF Recommendation

(PEC Script)

(Dr. Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (12 for, 2 opposed, 1 abstained, 0 absent) buprenorphine transdermal system (Butrans) remain formulary on the UF with prior authorization to ensure appropriate use of the drug.

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—PA Criteria

(PEC Script)

(Dr. Meade) The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to Butrans. Coverage would be approved if the patient met any of the following criteria:

1. Manual PA criteria:
   a) Coverage provided for patients ≥18 yrs with moderate-to-severe chronic pain requiring opioid therapy.
      (1) Opioid naïve patients (prior use of <30 mg/day of morphine or equivalent in past 60 days) are limited to Butrans 5 mcg/hr patch.
      (2) Opioid tolerant patients (prior use of 30mg/day to 80 mg/day of morphine or equivalent within past 60 days or Butrans 5 mcg/hr patch) can receive Butrans 10 mcg/hr and 20 mcg/hr patches.
      (3) Maximum dose of Butrans is 20 mcg/hr.
   b) Coverage NOT provided for treatment of opioid-dependence.
   c) Coverage NOT provided for patients:
      (1) Requiring >80 mg/day of morphine or equivalent for pain control;
      (2) With significant respiratory depression or severe bronchial asthma;
      (3) With long QT syndrome or family history of long QT syndrome;
      (4) On concurrent Class 1A (procainamide, quinidine) or Class III (dofetilide, amiodarone, sotalol) antiarrythmics.

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—PA Criteria and UF Implementation Plan

(PEC Script)

(Dr. Meade) The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—Committee Physician's Perspective

(Maj King)

Maj King said the Committee recommended UF placement for Butrans primarily because of the convenience it offers of less frequent dosing. There were two dissenting votes from Committee members who recommended NF placement due to the risk of adverse effects and because there are a sufficient number of other narcotics already on the UF. The Committee did recommend Prior Authorization to provide guidance for dosing.

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—Panel Questions and Discussion

The Chair opened the floor for questions and discussion. Dr. Salom noted the downside risks of the drug and acknowledged that the PA criteria are intended to address those. However, he also said that it seems like the PA criteria would be difficult to enforce and he is afraid that more harm than good will be done by keeping it on the formulary.

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—Panel Vote on UF Recommendations

Noting that there will again be a need for three votes, Ms. Fryar read the UF recommendations for Butrans.

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 buprenorphine transdermal system (Butrans) remain formulary on the UF with prior authorization to ensure appropriate use of the drug.

The Panel voted as follows:

Concur: 7 Non-concur: 2 Abstain: 0 Absent: 2

BAP comments were that Butrans has no clinical advantage and is not cost-effective. Additionally, there are sufficient narcotic analgesics on the formulary already.

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—PA Criteria

The Chair asked for discussion on the PA criteria. Dr. Salom repeated that he believes the PA criteria are well meaning but not enforceable, and will lead to inappropriate use of the drug and will do more harm than good.

Ms. Fryar asked Dr. Meade whether the PA criteria are enforceable. Dr. Meade said they are counting on the physicians to honestly answer what they are doing. They are aware of the problem. But even if the drug was made NF, the only effect would be to raise the co-pay to $22. Mr. Hutchings said he really likes the PA on this drug because making it NF wouldn't address the potential problems. Because of the way we are set up, the PA criteria will make it more difficult to abuse the drug.

Ms. Fryar then read the recommended PA criteria before voting.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to Butrans. Coverage would be approved if the patient met any of the following criteria:

1. Manual PA criteria:
   a) Coverage provided for patients ≥18 yrs with moderate-to-severe chronic pain requiring opioid therapy.

      (1) Opioid naïve patients (prior use of <30 mg/day of morphine or equivalent in past 60 days) are limited to Butrans 5 mcg/hr patch.

      (2) Opioid tolerant patients (prior use of 30mg/day to 80 mg/day of morphine or equivalent within past 60 days or Butrans 5 mcg/hr patch) can receive Butrans 10 mcg/hr and 20 mcg/hr patches.

      (3) Maximum dose of Butrans is 20 mcg/hr.

   b) Coverage NOT provided for treatment of opioid-dependence.

   c) Coverage NOT provided for patients:

      (1) Requiring >80 mg/day of morphine or equivalent for pain control;

      (2) With significant respiratory depression or severe bronchial asthma;

      (3) With long QT syndrome or family history of long QT syndrome;

      (4) On concurrent Class 1A (procainamide, quinidine) or Class III (dofetilide, amiodarone, sotalol) antiarrythmics.

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)—UF and PA Criteria Implementation Plan

The Chair read the implementation plan.

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

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

UTILIZATION MANAGEMENT—SINGULAIR PRIOR AUTHORIZATION

Montelukast (Singulair)—PA Criteria

(PEC Script)

(Dr. Meade) PA criteria were proposed for montelukast due to inordinate usage for asthma, sinusitis and pneumo diagnoses. National and international treatment guidelines, as well as pertinent published clinical literature, were used to define supportable indications for use of montelukast. Utilization data from the MHS population was presented to the P&T Committee with respect to indications deemed supportable.

The P&T Committee recommended (12 for, 1 opposed, 1 abstained, 1 absent) the following PA criteria should apply to montelukast. Montelukast will be approved only for patients under the age of 19 and patients 19 or older who show evidence of use for an FDA-approved and guideline-supported indication. All current and new users of montelukast must meet one of the following criteria to pass through the PA process.

1. Automated PA criteria:
   a) Patient is ≤18 years of age.
   b) Patient has received an inhaled corticosteroid or inhaled beta agonist during the previous 180 days at a MTF, retail network pharmacy, or the mail order pharmacy.
2. Manual PA criteria:
   a) Coverage approved if:
      (1) The patient/provider documents use of montelukast for seasonal allergic rhinitis (or nasal polyposis) with evidence of a inadequate therapy with a nasal corticosteroid dispensed during the previous 180 days at a MTF, a retail network pharmacy, or the mail order pharmacy; or

      (2) The patient/provider documents intolerance (due to experienced adverse events) or contraindication to either inhaled or intranasal corticosteroids.

Montelukast (Singulair)—PA Implementation Period *(Dr. Meade)*

The P&T Committee recommended (12 for, 0 opposed, 2 abstained, 1 absent)
1) an effective date of the first Wednesday after a 90-day implementation period in all points of service; and 2) TMA send a letter to beneficiaries affected by this UF decision.

Montelukast (Singulair)—Panel Questions and Discussion

The Chair asked for and received a clarification of the wording of the PA criteria to be voted on.

Dr. Salom asked whether it is correct that a person over the age of 18 would only be able to use

the manual PA criteria. Dr. Meade said that patients under 18 get a free pass; patients over 18 have to demonstrate that they have asthma. The automated criteria should read "a" ***or*** "b."

Ms. LeGette asked whether the 91,200 beneficiaries affected by the decision are all adults and whether there will be grandfathering. Dr. Meade replied that these are adults who would not have automated prior authorization. There will be no grandfathering. He also said that there are a significant number of patients that are using the drug for reasons that aren't clear.

Mr. Hutchings said that most patients he knows about are using it for allergies. Dr. Meade said the Committee was aware of that and that steroids are way more cost effective.

Dr. Schlaifer asked what will happen as patients turn 19 and how they would be notified. Dr. Meade said that within 180 days each patient would have other drugs on their profile and will be forced to go through the PA process.

Asked again about the rationale for the age cutoff, Dr. Meade explained that there were unapproved uses of the drugs in kids up to the age of 18 but that 18 was an easily-defined line.

Montelukast (Singulair)—Panel Vote on PA Criteria

The Chair read the P&T Committee's corrected PA criteria recommendations for Singulair.

The P&T Committee recommended the following PA criteria should apply to montelukast. Montelukast will be approved only for patients under the age of 19 and patients 19 or older who show evidence of use for an FDA-approved and guideline-supported indication. All current and new users of montelukast must meet one of the following criteria to pass through the PA process.

1. Automated PA criteria:
   a) Patient is ≤18 years of age.
   b) Patient has received an inhaled corticosteroid or inhaled beta agonist or an inhaled combination product during the previous 180 days at a MTF, retail network pharmacy, or the mail order pharmacy.
2. Manual PA criteria:
   a) Coverage approved if:
      (1) The patient/provider documents use of montelukast for seasonal allergic rhinitis (or nasal polyposis) with evidence of a inadequate therapy with a nasal corticosteroid dispensed during the previous 180 days at an MTF, a retail network pharmacy, or the mail order pharmacy; or

      (2) The patient/provider documents intolerance (due to experienced adverse events) or contraindication to either inhaled or intranasal corticosteroids.

The BAP voted as follows:

Concur: 7 Non-concur: 2 Abstain: 0 Absent: 2

Comments regarding non-concurrence were that the criteria would be difficult to implement from an operational perspective because of the amount of paperwork required. Mr. Hutchings said he would recommend moving manual PA criteria (1a) to the automated category as a way to cut down the amount of paperwork.

Montelukast (Singulair)—Panel Vote on PA Implementation Period

Ms. Fryar read the implementation plan.

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

The Panel voted:

Concur: 9 Non-concur: 0 Abstain: 0 Absent: 2

CLOSING REMARKS

In closing, Ms. Fryar thanked all the presenters and others who worked on the reviews, the public commenter and members of the audience. She then noted that this was Dr. Marissa Schlaifer's last meeting as a member of the Panel and thanked her for her efforts during the time she has served. Dr. Schlaiffer received a round of applause from those present.

The Chair announced that the next BAP meeting tentatively scheduled for December 15, 2011.

The meeting was adjourned at 11:45 A.M.

Deborah Fryar 3 Oct 2011

Ms. Deborah Fryar,
Chairperson, Uniform Formulary Beneficiary Advisory Panel

To Beneficiary Advisory Panel September 16, 2011

I believe you should advise the DOD to change their medication policy to include Cialis Daily Treatment as a Formulary Drug.

My husband has hypertension, or high blood pressure. As a result of the medications he has taken for years to combat his blood pressure problems, he has a side effect called erectile dysfunction (E.D.).

Tri-Care pays for only six pills per month of PDE-5 Inhibitor Drugs, such as Viagra, Levitra, or Cialis. I believe that when this policy was established, these drugs were only available on an "as needed" basis. Since that time, Cialis has developed a "daily" treatment for ED.

After my husband and I were married 4 years ago, his urologist prescribed the "as needed" form of a PDE-5 drug. We tried it without success. Sometimes it worked quickly, sometimes it did not work quickly, and sometimes it did not work at all. With only six pills to last a month, we did not have a very successful love life. The doctor suggested that we try the daily Cialis treatment. (I say WE, because even though my husband swallows the pills, the outcome affects both of us.) Our doctor gave us enough samples to try each day for a month. This worked wonders for us.

When the drug stays in the body in a low regular dose it works any time we need it to work. Large doses once in a while are very unpredictable. We wrote to Tri-Care and asked that they allow us to use the daily dose of Cialis, but were denied. We went all the way through the appeal process with the same "rubber-stamped" denial at every level.

On our retirement income (social security and a small National Guard pension), we could not afford to pay for the medication on an on-going basis. Our doctor told us to take the six 20mg tablets that Tri-Care would pay for and cut them into 4 pieces each, and he gave us some samples to make up enough to get through the month. This solved our problem, but is not very accurate. The pills are egg-shaped, and it is impossible to cut them into 4 equal pieces. Therefore, some days he gets more of the drug and some days he gets less. And there are always some chips and powder that fall away in the cutting process. We must gather this up to make one dose and hope we gather up what equals 5 mg.

My husband got another surprising benefit from using the Daily Cialis. His blood pressure was reduced substantially after he began to take Cialis on a daily basis. He had been taking three blood pressure medications, and the doctor took him off one of them, Lotrel. He now takes only 2 blood pressure medications. Blood pressure medications have some bad side effects, including destruction of the kidneys. My husband's kidneys

have been badly damaged by the years of using three blood pressure medications. His kidney function is at 35%. It will never get better, but hopefully we can stop it from getting worse, by keeping him off the third blood pressure medicine. The side effects of Cialis are not nearly as harmful as those of other blood pressure medications.

Most drug companies list the purpose of a drug on the sheet that accompanies every prescription and then adds "OR FOR OTHER CONDITIONS AS PRESCRIBED BY YOUR PHYSICIAN". In every other case, TriCare pays for the drug as prescribed by the physician. WHY NOT IN THE CASE OF DAILY CIALIS? Our doctor prescribes it for two purposes – E.D. AND blood pressure reduction.

I believe there is a term used by Tri-Care and other insurance companies, called "Therapeutic Failure". This means that a certain medication that is prescribed for a condition does not work for certain people, while another similar drug will work. Tri-care will allow a change if the doctor sends a letter stating that the Tri-care preferred drug has met with Therapeutic Failure in a certain patient. This is the case with a pain patch that I wear since I had bone cancer seven years ago. Only one certain brand of the Fentanyl patch worked, the Mylan Brand. My doctor writes on the prescription that the Fentanyl is to be filled with Mylan brand only, and TriCare dispenses that brand. Why then must TriCare refuse this with Cialis? My doctor has sent such a letter to TriCare several times, (SEE ATTACHMENT 1) with no success.

I have checked with all our local pharmacies which are national chains. I have learned that 30 of the 5 mg pills are considerably cheaper than 6 of the 20mg pills consistently in all drug stores I checked with (SEE ATTACHMENT 2). To refuse to allow the Daily Cialis is fiscally irresponsible.

Tri-Care pays for birth-control pills to be taken every day. They pay for OTHER blood pressure pills to be taken every day. Every single other medicine paid for by Tri-Care allows the patient to take his medication daily or as prescribed by his physician. Why then is there a discrimination against the PDE-5 Inhibitors? And how did they come up with the magic number of six pills per month? Even if the PDE-5 "as needed" drugs worked every time, which they don't, six chances monthly to make love with one's spouse is woefully, painfully inadequate. Which person on the BAP wishes to have the government tell him or her when he may or may not enjoy intimacy with his spouse?

During the days when PDE-5 drugs were a "new sensation", when this policy probably was made , many people made jokes about "Viagra"; but the jokes are not funny to men who suffer with high blood pressure side effects. Before ED drugs were invented, these men had to rely on things like penile pumps or implants to deal with impotence. I have no knowledge of the implants, but I can warn you to stay away from the pumps if at all possible. Just to watch my husband trying that procedure made me hurt. Cialis has come a long way in their research, and have discovered that a little medicine each day works better than six major jolts of a quadruple dose of the same medication at random times.

We will continue to use Cialis on a daily basis, whether or not you approve the coverage of daily Cialis. But I believe it would be safer to have the 5 mg. pills that are uniformly manufactured rather than to be forced to use a piece of the chopped up 20 mg pill.

- I ask you again, to advise the approval of Daily Cialis for those patients who wish to use it. If I need to clarify anything in this request, or if you have further questions, please [redacted]. My husband and I have made arrangements to attend the BAP meeting this Thursday, where I will take advantage of the opportunity to speak with you face to face in hopes of getting TriCare's approval of Daily Cialis. I speak for many more people than just my husband, when I say that a policy change to allow this treatment option is way past due.

If, after reading this request, seeing that the daily Cialis is cheaper than the "as needed" drug that you do approve, and seeing that the medical benefits to the patient are superior with daily use, you still decide to deny the approval of daily Cialis, I will be anxious to hear your reasons for the denial when I meet with you Thursday. I will also request to know how to reach the next link in the "chain of command", so that I will know where to appeal next. I am also interested in learning how to become a part of this panel, should a vacancy ever occur – whether or not my request is approved.

From:

[redacted]

ATTACHMENT 1

(For the purpose of e-mailing this to you, I have re-typed the letter from our doctor, [redacted], which I have previously sent to Tri-Care. I will bring the actual letter, signed by the doctor, when I see you on Thursday.)

3/1/2010
To Whom It May Concern:

[redacted] has a history of erectile dysfunction, as well as hypertension. He has tried multiple times to be approved for daily Cialis therapy, 5 mg without success. Using his 20 mg tablets along with samples, he has been splitting his medicines and taking them daily with very good results. The other benefit he has noticed is significant reductions in his blood pressure, and has actually been able to stop one of his previous blood pressure medications due to his improvement with the daily Cialis. Based on this I would again ask you to consider approving this patient for daily Cialis therapy.

Sincerely,

[redacted]

ATTACHMENT 2

Cost Comparison of 6 pills Cialis 20 mg (as needed) to 30 pills of Cialis 5 mg (daily use)

Pharmacy Name	Cost of 6 – 20 mg	Cost of 30 – 5 mg
Rite Aid	$143	$127
Walgreens	$158	$150
CVS	$152	$144
Publix	$162	$150
Bi-Lo	$190	$152

In all 5 companies the cost of daily Cialis is cheaper than 6 "as needed" pills

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
- AHRQ — Agency for Healthcare Research and Quality
- APR — Automated Profile Review
- ARB — Angiotensin receptor blocker (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
- CCB — Calcium channel blocker
- CEA — Cost-effectiveness analysis
- CFR — Code of Federal Regulations
- CHD — Coronary heart disease
- CMA — Cost-Minimization Analysis
- COPD — Chronic obstructive pulmonary disorder
- COX-2 — cyclooxygenase-2 selective inhibitor
- CPG — Clinical Practice Guideline
- CR — Controlled Release (a drug formulation)
- CV — Cardiovascular
- DEA — U.S. Drug Enforcement Administration
- DERP — Oregon Drug Effectiveness Review Project
- DFO — Designated Federal Officer
- DM — Diabetes mellitus
- DMPA — Depot medroxyprogesterone acetate (an injectable contraceptive)
- DoD — Department of Defense
- DRI — Direct rennin inhibitor
- ECF — Extended Core Formulary
- ED — Erectile dysfunction
- EE — Estrogen
- 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
- FDC — Fixed dose combination
- GI — Gastrointestinal
- HCTZ — Hydrochlorothiazide
- IR — Immediate Release (a drug formulation)
- IV — Intravenous
- MHS — Military Health System
- MN — Medical Necessity
- MTF — Military Treatment Facility
- NADs — Nasal Allergy Drugs (a drug class)
- NDAA — National Defense Authorization Act
- NF — Non-formulary
- NIH — National Institutes of Health
- NNH — Number Needed to Harm
- NNT — Number Needed to Treat
- NSAID — Non-steroidal anti-inflammatory drug (a drug class)
- OCP — Oral contraceptive products (a drug subclass)
- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DoD Pharmacy and Therapeutics Committee
- PAR — Perennial allergic rhinitis
- PDE-5 — Phosphodiesterase-5 (a drug class)
- PDTS — Pharmacy Data Transaction Service
- PEC — DoD Pharmacoeconomic Center
- PORT — Pharmacy Outcomes Research Team
- POS — Point of Service
- RAAs — Renin angiotensin antihypertensives (a drug class)
- RCTs — Randomized Control Trials
- SAR — Seasonal allergic rhinitis
- SR — Sustained release (a drug formulation)
- SUs — Sulfonylureas (a drug subclass)
- T2DM — Type 2 diabetes mellitus
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TPHARM — TRICARE Pharmacy Program
- TRRx — TRICARE Retail Pharmacy Program
- TZDs — Thiazolidinediones (a drug subclass)
- UF — DoD Uniform Formulary
- USC — United States Code
- VA — U.S. Department of Veterans Affairs
- VTE — Venous thromboembolism