22 January 2011

Executive Summary

UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL COMMENTS
6 January 2011

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy & Therapeutics (P&T) Committee November 2010 meeting.

1. NON-INSULIN DIABETES DRUGS – BIGUANIDE SUBCLASS. The P&T Committee recommended the following:

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

1. The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions for the Biguanides subclass: metformin IR (500 mg, 850 mg,1000 mg), metformin ER (500 mg, 750 mg), and Riomet® liquid (500 mg/5 ml) remain formulary on the UF;
2. Fortamet® (500mg, 1000 mg) and Glumetza® (500 mg, 1000 mg) be designated Non-formulary on the Uniform Formulary.

Summary of Panel Vote/Comments:

Ms. Cohoon noted that her paper showed one person opposed the UF recommendation and asked for clarification. Dr. Meade replied that one person expressed the view that since metformin is the preferred agent, all forms of metformin should be available in front of the step therapy.

Mr. Hutchings asked about the reason for requiring step therapy for these agents. Dr. Meade answered that it has to do with the number of scripts.

Ms. Cohoon noted the distribution of users for the drugs being made non-formulary and asked that the letters to beneficiaries who will no longer be able to get their prescriptions at the MTF include information about switching over to mail order. She also asked whether drugs could be moved off formulary quicker than 60 days in the MTFs, perhaps 30 days with a grace period of an additional 30 days for those who are already on the drugs. In response to her first concern, Ms. Le Gette explained that there already is appropriate verbiage in the letters that go out. Dr, Meade replied to the second question, indicating that when he was running an MTF pharmacy they would always work with the patient and the physician to provide another formulation or, if required, to establish medical necessity. In his view, however, thirty days would be too fast. Ms. Le Gette agreed, noting that her organization has to create the forms and get them approved. She said that the medical necessity forms are often available on the web before the implementation date; in the case of this class, which is a large class, there will be quite a few forms that have to be made. Dr. Meade assured the Panel that the MTFs will start working on the changeover as soon as the minutes are signed. He also noted that MTF patients probably get the most one-on-one attention as far as points of service are concerned.

Ms. Fryar noted that the PEC received over 440 physician responses for this drug class and asked whether any of the diabetic management specialists in DoD were consulted. Ms. Lugo replied that a lot of the responses were from specialists in the field.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

- Without further discussion the Panel voted as follows on the implementation plan as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

Director, TMA:

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

2. NON-INSULIN DIABETES DRUGS - SULFONYLUREAS (SUs) SUBCLASS. The P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) the following remain formulary on the UF:

chlorpropamide (Diabinese®, generics); glimepiride (Amaryl®, generics); glipizide (Glucotrol®, generic); glipizide ER (Glucotrol XL®, generics); glyburide (Diabeta®, Micronase®, generics); glyburide micronized (Glynase Press Tab®, generic); glipizide/metformin (Metaglip®, generics); and glyburide/metformin (Glucovance®, generics)

Summary of Panel Vote/Comments:

Dr. Salom said he was pleased to see that chlorpropamide has very low utilization. He asked why it was considered at all for formulary status since it is likely inappropriate for use in elderly patients. Mr. Hutchings added that the ADA doesn't actually recommend glyburide because of the increased risk for certain patients. He asked the PEC staff to comment on both agents.

Dr. Meade replied that where there is historic utilization, the Military Health System (MHS) keeps the agent available unless there is a recommendation against its use from the level of the U.S. Food and Drug Administration (FDA). Dr. Salom asked for the utilization figures on chlorpropamide as a follow-up to the meeting. Mr. Hutchings asked if there was any discussion about requiring step therapy for those agents, even though they are low utilization. He explained that the majority of the population he deals with are elderly. Dr. Meade answered that step therapy hadn't been considered.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Panel comment:

- Mr. Hutchings commented that he believes step therapy would have been an effective way to deal with chlorpropamide and glyburide and would have been more pleased with the recommendations had they included step because of the elderly nature of the population being treated.

***Director, TMA*:**

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

3. NON-INSULIN DIABETES DRUGS - DIPEPTIDYL-PEPTIDASE- 4 INHIBITORS (DPP-4s) SUBCLASS. The P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) sitagliptin (Januvia®), sitagliptin/metformin (Janumet®), and saxagliptin (Onglyza®) remain formulary on the UF. Prior authorization/step-therapy for the DPP-4 inhibitors would require a trial of metformin or SUs for new patients.

Summary of Panel Vote/Comments:

Dr. Casull noted that as a pediatrician he has always tried to figure out what body part was affected by what. He asked whether the Committee ever considers the mechanism of action when deciding where to place an agent. In this case, the sulfonylureas and the DPP-4s both work at the basal cell and metformin works on the liver the same way as the DPP-4s. He asked if that is taken into account when making a decision. Lt Col Hannah replied that the Committee absolutely does take into consideration the mechanism of action.

Ms. Cohoon noted that the ADA guidelines do not mention the DPP-4s in the information she was given, but that there was an ADA meeting in January and she wonders whether any changes might have come from that meeting. Ms. Lugo answered that ADA Guidelines were updated recently and published on their website on Tuesday. She hasn't finished reviewing all of the updates yet, but she noted that ADA doesn't necessarily update their treatment guidelines annually although they do update their treatment algorithm. She will check further into whether there were any changes affecting the DPP-4s.

Mr. Hutchings said he assumes that the combo products are behind us now. The PEC staff said there was a lot of discussion about that. Dr. Meade said the key thing about the combo drugs is that metformin is in them. Mr. Hutchings said the issue is with the other drugs and whether a patient needs to go through step therapy to use metformin in combination. Ms. Lugo said there were also operational concerns because of the rejections that might occur. For example, if a patient is already using metformin and presented a prescription for one of the other drugs, they would get a rejection. Mr. Hutchings said it sounds to him like the situation is that if the patient had been using metformin all along the prescription for the combo would go through but if they showed up with a new prescription they would get a rejection. A PEC staff member from the audience clarified by indicating that if a patient shows up with prescriptions for the individual items together, if the pharmacy were to fill the metformin first, then the second one would go through. So if the patient can get them individually, there is no reason to reject them as a combo.

Ms. Schlaifer asked whether a patient who presented a prescription for Januvia® would be rejected. The answer was if the patient gets metformin and Januvia®, then it would go through. Mr. Hutchings asked for further clarification of the discussion behind the step therapy requirements. Dr. Meade said there was a lot of debate but the Committee came to the conclusion that with a limited number of beneficiaries it would not be a good thing to make the guidelines too complex. Mr. Hutchings asked whether the entire class would have to be re-bid if the rules were changed. He said he agrees that following the ADA guidelines will be the best thing for the majority of patients. If physicians don't want to do monitoring and just want to be free from any concern about hypoglycemia, they can just put patients on metformin. He also noted that patients who have been on metformin don't necessarily want to try sulfonylurea because of the hypoglycemic affects when in fact the metformin may not work as well as the sulfonylurea. Ms. Schlaifer said it was pointed out to her at the last meeting that the purpose of the actions was not to be the clinical guideline but to point physicians toward the clinical guideline. But the clinical guideline can't be enforced nationwide. Mr. Hutchings said he would vote to concur, but that it was helpful to know what went on behind the scenes.

Dr. Casull asked if it would be possible to require an automated clearance before going to a combo or whether that would cause a lot of difficulty. A PEC staff member in the audience agreed that it would be possible but also said it would be very complicated. Dr. Meade said that when it comes to step therapy, the MHS is fairly new at it with only about a year and half's experience. Therefore they are cautious about what they do and are careful not to do anything that might cause tie-ups or a massive disruption.

Dr. Schlaifer asked whether it comes up in discussion that when you go out in public you can get Janumet® without trying a sulfonylurea or metformin first. She feels that the MHS is kind of opening itself up for allegations of inappropriate marketing. Lt Col Hannah said it absolutely was discussed, but came to the conclusion that at the end of the day the patient is on metformin. Dr. Schlaifer pointed out that the patient could be getting just metformin a whole lot cheaper. Dr. Meade said the main concern was that the patient tries the first-line agent and the second-line agent.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

- Without further discussion, the Panel voted on the PA criteria recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Panel comment:

- Mr. Hutchings offered the comment that he still believes Janumet® should be placed behind the step rather than in front of the step. He views combination therapy as a way to help somebody once they are stable. If a patient gets metformin and Januvia® and becomes stable they should be able to safely use the combo drug. Dr. Schlaifer agreed with the comment.

- Dr. Crum noted that the PA criteria that MHS is trying to develop are for a real world with minimum disruption. Although he acknowledges that the comment may be theoretically correct, he doesn't believe that it is appropriate for this installation.

- The Panel voted on the implementation plan recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

Following the vote, Ms. Lugo offered additional clarification regarding this drug subclass, stating that the ADA guidelines provide no guidance about prescribing two drugs at once. The Committee believes that it is appropriate to do so. However, for the most part, the P&T Committee follows the ADA guidelines. Clinically, the Committee agreed that it did not want Janumet® behind the step. She also stated that the Committee would be keeping an eye on the other combinations in terms of their utilization.

Dr. Meade noted that the concerns about this subclass can be put on a preliminary management document that goes to the MTFs. The Committee will also make them available to physicians in the network to try to communicate what both the P&T Committee and the BAP thought regarding these agents. This will be a first for this procedure.

***Director, TMA*:**

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

4. NON-INSULIN DIABETES DRUGS - GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS (GLP1RAs) SUBCLASS. The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) exenatide (Byetta®) be designated formulary on the UF (step-preferred), and liraglutide (Victoza®) be designated as formulary on the UF (non-preferred). Prior authorization for the GLP1RAs would require a trial of metformin or SUs for new patients. Exenatide (Byetta®) was designated as the preferred drug within the subclass; a trial of exenatide (Byetta®) would be required prior to liraglutide (Victoza®) for new patients.

Summary of Panel Vote/Comments:

Mr. Hutchings said he assumes that if a patient is using metformin they don't need to meet the manual PA that they have diabetes.

Ms. Le Gette asked whether what is required for Victoza® is a two-step step process in which the system looks back first for Byetta® in order to avoid a double rejection. A PEC staff member in the audience agreed that the Byetta® look-back process would ensure that metformin or an SU had been tried first.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

- Without further discussion, the Panel voted on the PA criteria recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Panel Comment:

- Mr. Hutchings, as a clarification to the answer provided to Ms. Fryar's question, noted that the criteria seem to indicate that a patient would have to have Type 2 diabetes AND meet one of the other criteria. He asked if that is a correct reading. The answer given was that it is a correct reading.

  Without further comment, the Panel voted on the implementation plan recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

***Director, TMA*:**

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

5. NON-INSULIN DIABETES DRUGS - THIAZOLIDINEDIONES (TZDs) SUBCLASS.
The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent):

a) pioglitazone (Actos®), pioglitazone/metformin (Actoplus Met®, Actoplus Met XR®), and pioglitazone/glimepiride (Duetact®) remain designated formulary on the UF;

b) rosiglitazone (Avandia®), rosiglitazone/ metformin (Avandamet®), and rosiglitazone/glimepiride (Avandaryl®) be designated NF on the UF.

Summary of Panel Vote/Comments:

Ms. Cohoon asked how the PA process was going to work for the combo drugs in this class, Avandamet® and Avandaryl®. Dr. Meade answered that Actos® products would probably be in front of the step and that Avandia® would be behind the step. But there will be very few new patients going on Avandia® and, in fact, people will be coming off it because of the safety issues. The rest are grandfathered.

Mr. Hutchings said that a very recent study of Actos® had also shown increased cardiovascular risk. He's not sure that he would want someone to get Actos® "straight out of the chute" from a safety standpoint. Dr. Meade assured the Panel that MHS would be keeping an eye on these products in case FDA comes down with additional concerns about Actos® products.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Panel comment: The Panel asked to include a comment regarding the step therapy placement of combination products in this class, noting that it might be preferable to place all of them after the step.

- Without further discussion, the Panel voted on the PA criteria recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

- Without further discussion, the Panel voted on the implementation plan recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

Director, TMA:

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

6. NON-INSULIN DIABETES DRUGS - MEGLITINIDES. The DoD P&T recommended the following:

Based upon its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 2 absent) nateglinide (Starlix, generic), repaglinide (Prandin), and repaglinide/metformin (Prandimet) be designated formulary on the UF.

Summary of Panel Vote/Comments:

Ms. Cohoon, referring to the graph in the handout (figure 7) asked why there had been a drop in the utilization of Starlix. Dr. Meade replied that it is probably due to utilization of its generic equivalent product. He noted that is a typical result when a product goes generic.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

Director, TMA:

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

7. NON-INSULIN DIABETES DRUGS - ALPHA-GLUCOSIDASE INHIBITORS (AGIs). The DoD P&T recommended the following:

Based upon its collective professional judgment, recommended (16 for, 1 opposed, 1 abstained, 0 absent) acarbose (Precose®, generics) and miglitol (Glyset®) be designated formulary on the UF.

Summary of Panel Vote/Comments:

Mr. Hutchings asked about the cost-effectiveness of agents in this subclass compared to other subclasses. Dr. Meade replied that they are more expensive. Dr. Casull asked if this was the reason for the relatively low utilization of Precose® and Glyset®. Dr. Meade said the reason is probably that the MTFs prefer the generic formulation, Acarbose®.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

Director, TMA:

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

8. NON-INSULIN DIABETES DRUGS - AMYLIN AGONISTS (PRAMLINTIDE). The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) pramlintide (Symlin®) injection remain designated as formulary on the UF.

Summary of Panel Vote/Comments:

Dr. Salom said that this is a drug that is off his radar screen. He asked about the vials used to dispense the drug.

Dr. Schlaifer asked about the PA that is already in place for this drug that is being modified, noting that there are safety concerns but she isn't sure what that PA is. Ms. Lugo answered that the PA requirement was adopted in 2005 requiring prior insulin therapy. This one adds the requirement that the patient have a confirmed diagnosis of Type 1 or Type 2 diabetes.

Mr. Hutchings said that the 2005 PA was actually effective. Ms. Lugo explained that the 2005 PA is being retained, but it is being added to.

Mr. Hutchings said his problem is that there is no hard block and that it can be used for weight loss. There are safety concerns stemming from the drug not being able to be mixed with insulin and having to be dosed at separate times. Those safety concerns should be added to the PA form. He is afraid if the PA is automated, those concerns will be bypassed. He would argue against having an automated PA for this subclass.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Panel comment:

- Mr. Hutchings commented that, in the retail world, this medication is not inexpensive, perhaps $1,000 per injection. This is another reason why he would like to see only a non-automated PA. For this reason (he disagrees with the automated PA and thinks it should be manual only) he will vote to non-concur on the PA.

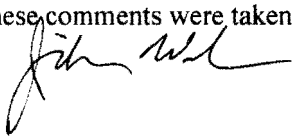
- Without further discussion, the Panel voted on the PA criteria recommendation as follows: Concur: 7 Non-concur: 4 Abstain: 0 Absent: 0

Panel comment:

- The Panel commented that the non-concur votes were due to the automated PA being unsafe. The 2005 PA criteria would be sufficient to address the concerns, which is that someone might be prescribed the drug inadvertently without understanding the risks. Dr. Casull said that he doesn't see what this drug does than insulin doesn't do, plus it has the downside of a safety risk plus high cost.
- Without further comment, the Panel voted on the implementation plan recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

***Director, TMA*:**

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



9. NEW DRUGS IN ALREADY REVIEWED CLASSES.

a. INHALED CORTICOSTEROID (ICS)/LONG-ACTING BETA AGONIST (LABA) - MOMETASONE/FORMOTEROL ORAL INHALER (DULERA®). The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) mometasone/formoterol (Dulera®) be designated formulary on the UF.

Summary of Panel Vote/Comments:

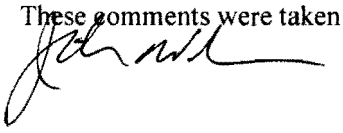
Mr. Hutchings asked when Advair® is expected to go generic, noting that it has been on the market for many years. Dr. Meade replied that he thinks one of the Advair® combinations will go generic in 2012. Generic Advair® is not imminent.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

***Director, TMA*:**

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



b. ANTILIPIDEMIC-1S (LIP-1S) - PITAVASTATIN (LIVALO®). The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) pitavastatin (Livalo) be designated NF on the UF.

Summary of Panel Vote/Comments:

Dr. Salom asked about the graph shown in the handout (Figure 11). He noted that scale of the graph doesn't show how many prescriptions are being issued for Livalo®. He noted that there are a large number of drugs in the class and that they are expensive and asked about the actual utilization of Livalo®. Dr. Meade answered it is between 4,000 and 5,000.

Ms. Fryar asked for clarification of the number of beneficiaries affected and if that number would translate to a total of about 700 beneficiaries affected. Dr. Meade said that the number of patients would be about 700 and the number of 30-day prescriptions is about four-to-five thousand.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0
- Without further discussion, the Panel voted on the PA criteria recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0
- Without further discussion, the Panel voted on the implementation plan recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

Director, TMA:

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

c. NEWER SEDATIVE HYPNOTIC AGENTS (SED-1S) — DOXEPIN TABLETS (SILENOR®). The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) doxepin tablets (Silenor®) be designated formulary on UF, with a PA requiring a trial of zolpidem IR for new users.

Summary of Panel Vote/Comments:

Dr. Casull asked, in terms of the DoD "1:1:1" program, whether the Committee's deliberations included a discussion of why the MHS would not elevate a fairly effective, non-controlled drug with minimum side effects over a controlled substance on the PA. Dr. Meade noted that the subject was discussed and explained that Silenor® isn't really as effective as zolpidem IR in treating insomnia, but it is an option for those who have tried zolpidem IR and can't tolerate it.

Dr. Crum asked if the Committee had evaluated how often the old formulation of doxepin was prescribed. Dr. Meade said it is difficult to get that information out of the data. Dr. Crum noted that there seems to be a clinical advantage to this product versus the old formulation.

Ms. Cohoon said she had concerns about trying to put a PA behind a non-controlled substance given all the recent rhetoric and interest in prescription drug abuse by the White House and others. She said putting a PA on something drives the provider in a certain direction. This seems to be sending a mixed message by putting a non-controlled substance behind a controlled

substance on the PA. She said the White House Task Force is looking specifically at the use of prescription drugs in the military. Dr. Meade noted that Rozerem® is a non-controlled drug and it is behind the step also, an action which dates from 2007.

Dr. Salom noted that he finds it interesting that the manufacturer chose to make the drug in 3 mg and 6 mg tablets; he said they might also have thought about having a 5 mg, with the idea that someone might come out with a generic tablet.

Ms. Le Gette asked about the old generic formulation and whether it would be placed on the first tier, even though it is low utilization. Dr. Meade replied that they would prefer to re-evaluate that after others go generic.

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

Panel comment: The non-concurring Panel member explained that her vote was because of the PA requirement; she has no problem with the drug being on formulary.

- Without further comment, the Committee voted on the PA criteria as follows: Concur: 9 Non-concur: 2 Abstain: 0 Absent: 0

Panel comment: The non-concurring members commented that they disagree with the message being sent by placing the non-controlled Silenor® after a controlled and potentially abusable substance on the step therapy process over one that is not. One member believes that the Committee should reconsider reversing the step process.

Mr. Hutchings asked whether the Committee had discussed those people who have been on doxipin already and will now be behind the step. Dr. Meade answered that it hadn't been discussed but that it can be when the class is reviewed again.

Ms. Fryar asked if her understanding is correct that this class will be coming up for review again soon. Dr. Meade said it's in process, but he isn't sure which month it will come up in. Ms. Fryar said she trusts that the Panel's comments will be reviewed when the class does come up again.

- Without further comment, the Panel voted on the implementation plan recommendations as follows: Concur: 10 Non-concur: 1 Abstain: 0 Absent: 0

No further comment from the Committee.

***Director, TMA*:**

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

d. NARCOTIC ANALGESICS - HYDROMORPHONE EXTENDED RELEASE (ER) TABLETS (EXALGO®). The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (10 for, 6 opposed, 2 abstained, 0 absent) hydromorphone ER tablets (Exalgo®) be designated formulary on the UF.

Summary of Panel Vote/Comments:

Dr. Casull noted that the product has a higher cost, can be broken down on the street even though that would result in a higher incidence of death because of the way the product is manufactured. He did not hear any discussion of why this product is superior to some of the other currently-available long-acting agents, such as oxycontin generics or oxycodone. Lt Col Hannah said that was discussed and Exalgo® is not necessarily more effective. Dr. Casull said since that means we haven't proven it is superior, combined with the other attributes already mentioned, he would vote to non-concur. Dr. Salom said he agrees and for exactly the same reasons. Dr. Casull stated the P&T Committee should be educated on the 1-1-1 program and how it is relevant to the panel's review and comment on the development of the uniform formulary.

Mr. Hutchings said that he views the inability to break down the drug as a plus, because right now Oxycontin® has an extremely high street value and hydromorphone is rarely used on the street. He feels inclined to vote in favor of the agent because there is less likelihood of abusing it and if someone does the result is likely to be fatal. Moreover, there are other narcotics out that aren't widely abused. Dr. Casull replied that street use is the major problem with controlled substances, not prescribed controlled substances. It is prevalent across mainstream America. Illicit drug use and drug seeking behavior are two different issues.

Dr. Salom said that the drug will be broken down, even if that is less likely. We will see fatalities from this and that is a reason not to make it a formulary drug. If a practitioner wants to prescribe it and go through the hoops, that's fine.

Dr. Schlaifer said she concurs with Mr. Hutchings. Although her initial reaction was "why?" she said that was the reason why the FDA approved the drug. She views the fact that it is less lethal as being helpful to her as a prescriber.

Mr. Hutchings said if he was looking only at his population of over-65 patients, he would vote to non-concur, but there are already so many barriers that this one isn't going to matter much.

A PEC staff member in the audience said that a wounded soldier in transition (i.e., going home from an MTF) can be prescribed this drug and take it to a pharmacist. If it is non-formulary, the co-pay will be $22. Federal law does not allow the pharmacist to change the prescription over the telephone. A new, hand-written prescription will be required. That puts the patient in a bind, especially if he needs the high-potency narcotic. That was something that the P&T considered when they were deliberating.

Dr. Casull asked who was consulted with, naming one individual in particular (Dr. Brown, who works with returning wounded warriors). LTC Spridgen said there are providers on the Committee and others who work with the WTUs.
Ms. Fryar asked what types of comments were received from providers on this agent: were they in favor or not in favor. Dr. Meade said that providers are on the Committee but the PEC does not solicit expert opinions regarding wounded warrior care. Dr. Casull commented that when seeking expert opinion on "Wounded Warriors" and controlled substances that only one installation received a "best practice" mention from the 2010 Army Task Force on Pain Management. That was the program run by Dr. Brown at Tripler Army Medical Center.

Ms. Cohoon noted that making a drug non-formulary makes it harder for the MTFs to have it available.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 7 Non-concur: 4 Abstain: 0 Absent: 0

Panel comment: The votes to non-concur were based on the fact that it is higher cost, potentially fatal if abused and was not demonstrated to be clinically superior to other drugs in the class.

Chairman Note: Panel member's concerns are all valid and should be taken into account when this drug class is reviewed in the near future. Upon hearing panel member concerns about potential problems with this drug class I would ask the P&T to consider reviewing this entire drug class sooner rather than later.

No further comment from the Panel.

Director, TMA:

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

e. ANTILIPIDEMIC-2S (LIP-2S) - FENOFIBRIC ACID (FIBRICOR®). The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (15 for, 1 opposed, 1 abstained, 1 absent) fenofibric acid (Fibricor®) be designated NF on the UF.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0
- Without further discussion, the Panel voted on the implementation plan recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

Director, TMA:

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

f. CONTRACEPTIVES - ESTRADIOL VALERATE/DIENOGEST (NATAZIA®). The DoD P&T Committee recommended the following:

Based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) estradiol valerate/dienogest (Natazia®) be designated NF on the UF.

Summary of Panel Vote/Comments:

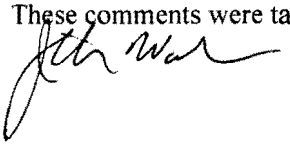
Ms. Cohoon asked how many days or months can patients get this medication in a single refill. Dr. Meade answered up to three months. Ms. Cohoon also asked to verify that the copay will be higher with the drug off the formulary. Dr. Meade said that is correct.

- Without further discussion, the Panel voted on the UF recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0
- Without further discussion, the Panel voted on the implementation plan recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No further comment from the Panel.

Director, TMA:

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



10. UTILIZATION MANAGEMENT.

a. Fentanyl Citrate—Modification of Prior Authorization. The P&T Committee recommended the following:

To ensure the appropriate use of high-potency opioids in opioid-tolerant patients, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) modifying the fentanyl automated PA and including the following drugs:

- morphine sulfate ER (MS Contin® generics 100, 200 mg; Avinza® 45, 60, 75, 90, 120 mg; Kadian® 100, 200 mg);
- morphine sulfate ER/naltrexone (Embeda® 100/4mg);
- fentanyl buccal soluble film (Onsolis® 200, 400, 600, 800, 1200 mcg);
- hydromorphone ER (Exalgo® 8, 12, 16 mg); and oxycodone ER (Oxycontin® 60, 80, 160 mg)

Summary of Panel Vote/Comments:

Dr. Casull asked if there is a non-automated PA for these agents. Mr. Hutchings explained that this is not a PA, it's a safety warning. The pharmacist at the counter at any POS can override the warning if it can be determined that the patient is opioid-tolerant. Dr. Meade explained the process.

Ms. Fryar asked for clarification as to why the action is labeled a PA if it is more of a safety warning. Specifically, she asked if the language presented here is an actual modification of a Prior Authorization. Dr. Meade replied that the MHS calls it a Prior Authorization because the dispensing process is stopped with a warning if there is no previous prescription for a high-potency opioid in the pharmacy profile within the past 60 days. She suggested it might be wise to put in a caveat with the vote.

- Without further discussion, the Panel voted on the modification of the fentanyl citrate PA recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

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

Panel comment: The non-concur vote was based on the need to work out how many patients will be dropping off first.

***Director, TMA*:**

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

b. Fingolimod (Gilenya®) - Prior Authorization. The DoD P&T Committee recommended the following:

To ensure the appropriate use of fingolimod is consistent with the product labeling, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) implementing a PA, which will allow use of fingolimod (Gilenya®) in patients who met the following criteria:

1. a documented diagnosis for relapsing forms of MS

2. no current use of interferon alpha/beta or Copaxone®

- Without further discussion, the Panel voted on the PA recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0
- Without further discussion, the Panel voted on the implementation plan recommendation as follows: Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

***Director, TMA*:**

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

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
January 6, 2011
Washington, D.C.

Panel Members Present:

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

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

LTC Spridgen stated the Panel has been convened to review and comment on the recommendations of the Department of Defense (DoD) Pharmacy and Therapeutic (P&T) Committee meeting held November 16 and 17, 2010 in San Antonio, TX.

Agenda

The agenda for this meeting of the Panel is:

- Welcome and opening remarks
- Public citizen comments
- Review and Panel discussion of P&T Committee recommendations for the following therapeutic drug classes:

  - *Drug Class Reviews*
    - *Non-insulin Diabetes Drugs*
      - *Metformin (Biguanides)*
      - *Sulfonylureas*

        - *Dipeptidyl-peptidase 4 (DPP-4) inhibitors*
        - *Glucagon-like peptide-1 receptor agonists (GLP1RAs)*
        - *Thiazolidinediones (TZDs)*
        - *Meglitinides*
        - *Alpha-glucosidase inhibitors (AGIs)*
        - *Amylin agonists*

- *Designated Newly Approved Drugs*
    - *Inhaled Corticosteroid/Long-Acting Beta Agonists—Dulera (mometasone/formoterol inhaler)*
    - *Antilipidemic-1s —Livalo (pitavastatin tablets)*
    - *Newer Sedative Hypnotic—Silenor (doxepin tablets)*
    - *Narcotic Analgesic—Exalgo (hydromorphone extended release tablets)*
    - *Antilipidemi-2s—Fibricor (fenofibric acid)*
    - *Contraceptive Agents—Natazia (estradiol valerate/dienogest)*

- *Utilization Management—Prior Authorization:*
    - *Expansion of fentanyl prior authorization*
    - *Recommendation for fingolimod (Gilenya) prior authorization*

Opening Remarks

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

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

The duties of the Uniform Formulary Beneficiary Advisory Panel are:

- To review and comment on the recommendations of the P&T Committee concerning the establishment of the UF and subsequent recommended changes. Comments to the Director, TMA, regarding recommended formulary status, pre-authorizations, and the effective dates for changing drugs from "formulary" to "non formulary" status must be reviewed by the Director before making a final decision.
- To hold quarterly meetings in an open forum. The Panel may not hold meetings except

at the call of or with the advance approval of the DFO in consultation with the Chairperson of the Panel.

- To prepare minutes of the proceedings and prepare comments for the Secretary or his designee regarding the Uniform Formulary or changes to the Formulary. The minutes will be available on the website and comments will be prepared for the Director, TMA.

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

The P&T Committee met for approximately 20 hours conducting its reviews of the drug class recommendations presented today. Since this meeting is considerably shorter, the Panel will not receive the same extensive information that is presented to the P&T Committee members. However, the BAP will receive an abbreviated version of each presentation and its discussion. The materials provided to the Panel are available on the TRICARE website.

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

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

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

After introducing the individual Panel members, LTC Spridgen then noted the housekeeping considerations pertaining to the meeting.

Private Citizen Comments

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

Chairperson's Opening Remarks

The Panel Chairperson, Ms. Deborah Fryar, thanked those in attendance for coming and noted that some may have difficulty hearing the proceedings because of problems with the public address system. She especially thanked the Panel members for their advance preparation and

noted that she is expecting an interesting meeting with a lot of discussion. She also reminded the Panel members that the BAP cannot make recommendations and when it votes it is voting on the recommendations brought forth by the P&T Committee. However, the Panel is free to comment and all of its comments are actually reviewed and taken into account before any action is final. She also encouraged Panel members to ask questions; its input is very important as the members represent the beneficiaries.

Ms. Fryar then asked for clarification on the record of a point raised at the last meeting concerning whether commanders can divert pharmacy funds for other uses. LTC Spridgen provided the requested information. She said while it's true that commanders have discretion, the pharmacy bill must be paid.

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

DRUG CLASS REVIEW PRESENTATIONS

[PEC Script]

(Dave Meade)*:* I'm Dave Meade, Director of Clinical Operations at the Pharmacoeconomic Center. Joining me today from the PEC are Amy Lugo, one of the PEC clinical pharmacists, and LCDR Ola Ojo, another PEC clinical pharmacist. Also joining us today is Lt Col William Hannah, one of the DoD P&T Committee members who will provide the physician perspective and comment on the recommendations made by the 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 Pharmaceutical Operations Directorate are CAPT Nita Sood, and LT Nguyen.

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 based upon its collective professional judgment when considering the analyses from both the relative clinical and relative cost-effectiveness evaluations of one Uniform Formulary drug class – the Non-Insulin Diabetes Drugs, which is comprised of 8 drug subclasses; and 6 newly approved drugs. The newly approved drugs include Dulera oral Inhaler, Livalo, Silenor, Exalgo extended release tablets, Fibricor), and Natazia. Lastly two prior authorizations will also be discussed.
4) The DoD P&T Committee's recommendation as to the effective date of the agents being changed from formulary tier to the non-formulary tier of the Uniform Formulary. Based on 32 C.F.R. 199.21, such change will not be longer than 180 days from the final decision date but may be less.

We've given you a handout which includes the Uniform Formulary recommendations for all the drugs discussed today; these are found on pages 2 through 15. 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.

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

UNIFORM FORMULARY CLASS REVIEWS — NON-INSULIN DIABETES DRUGS

(Amy Lugo): *We will now discuss our first UF drug class review, the* **NON-INSULIN DIABETES DRUGS – RELATIVE CLINICAL EFFECTIVENESS.**

(Amy Lugo): The P&T Committee evaluated the relative clinical effectiveness of the drugs in the Non-insulin Diabetes drug class. The class is comprised of 8 subclasses. Please turn to your handout and refer to Table 1 on page 2 for more specifics about drugs in each class. The Non-insulin Diabetes drug class as a whole has not previously been reviewed.

The Non-insulin Diabetes drug class is ranked in the top 5 most costly MHS drug classes, with expenditures exceeding $311 million annually. For the individual subclasses, Fiscal Year 2010 expenditures for the DPP-4 inhibitors were approximately $124 million, followed by the TZDs ($108 million), GLP1RAs ($28 million), biguanides ($23 million), SUs ($15 million), meglitinides ($9 million), amylin agonists ($3 million), and AGIs ($800,000).

Please look at Figure 1 on Page 3 of your handout. In terms of MHS utilization, the biguanides, shown in turquoise, are the most utilized (approximately 225,000 30-day equivalent prescriptions (Rxs) dispensed monthly), followed by the sulfonylureas (SUs) (160,000 30-day equivalent Rxs), thiazolidinediones (TZDs) (100,000 30-day equivalent Rxs), and dipeptidyl peptidase-4 (DPP-4) inhibitors (60,000 30-day equivalent Rxs); the glucagon like-peptide-1 receptor agonists (GLP1RAs), meglitinides, alpha glucosidase inhibitors (AGIs), and amylin agonists each account for less than 10,000 30-day equivalent Rxs dispensed monthly.

The current American Diabetes Association (ADA) guidelines recommend metformin in addition to lifestyle modification as first-line therapy, followed by SUs, as tier one, well-validated

therapies for type 2 diabetes mellitus (T2DM). Based on the ADA guidelines and the Military Health System (MHS) providers' responses, an automated Prior Authorization/step-therapy was considered for the Non-insulin Diabetes drug class, which would require a trial of metformin or a SU prior to using another Non-insulin Diabetes subclass. Step-therapy was also considered for the TZDs, GLP1RAs, and DPP-4 inhibitors within each subclass (e.g., requiring a trial of a step-preferred drug before using the other drugs in the subclass).

Information regarding the safety, effectiveness, and clinical outcomes of the Non-Insulin Diabetes Drugs was considered.

Biguanides—Relative Clinical-Effectiveness

Now we'll dig deeper and review each non-insulin diabetes drug subclass, starting with the Biguanides, which is Metformin. Take a look at Figure 2 on page 3.

Metformin immediate release (IR) has the highest utilization, with over 200,000 30-day equivalent Rxs dispensed monthly in the MHS, followed by generic metformin ER products (40,000 30-day equivalent Rxs dispensed monthly). There were <1,000 30-day equivalent Rxs dispensed monthly for the branded metformin ER products Fortamet and Glumetza.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions for the Biguanides subclass:

1. The ADA guidelines recommend metformin as the first-line, tier one (well-validated therapy) for the treatment of T2DM.
2. When used as monotherapy, metformin decreases HbA1c by 1.5%–2%.
3. Metformin reduced the risk for diabetes-related death and all-cause mortality, when compared to dietary modification, in one large study, the United Kingdom Prospective Diabetes Study (UKPDS).
4. There is no evidence to suggest that differences in the ER formulations of Glumetza and Fortamet confer clinically relevant benefits in efficacy or safety when compared to the generic metformin ER preparations.

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

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

The Chair, Ms. Fryar asked Dr. Meade to clarify matters regarding Prior Authorizations (PAs) and step therapy before starting his briefing. Specifically, she asked for clarification regarding these two procedures and "preferred" versus "non-preferred" drug status.

Dr. Meade explained that with this class, the Committee established a requirement that metformin must be tried before using the other subclasses in the group. This was done because of the ADA guidelines referred to earlier, which are very specific on how they should be used. The class has a whole has eight subclasses and within each, there can be a preferred and a non-

preferred agent. In these cases, the Committee not only established the metformin step therapy requirement but also established a requirment to try the preferred agent before the non-preferred agent. As a practical matter, there are only three subclasses where this might occur. How the system would work in these cases is if a patient comes in who has already been on metformin or sulfonylurea, there would be an automatic lookback of 180 days and the patient would get the drug right away. If the patient has not been on the agents, there would be a 180-day lookback that would result in a hard stop. In those cases the patient or the pharmacist would have to contact the physician to get a trial or a reason why the patient couldn't have a trial of metformin or sulfonylurea. One of those would have to happen before the patient could get the drug being sought. The concern is that if a drug is made non-formulary it won't be available at the MTFs. Because MTFs are the most cost-effective point of service, TMA tries to avoid that situation. To guide therapy, the designations "preferred" versus "non-preferred" are used. Patients who wish a non-preferred agent have to try a preferred agent first.

In response to a question about why the automated PA is used, Dr. Meade said it's because, first, the automated system looks back 180 days, and second, most patients who want to try a non-preferred drug do try the preferred drug first. It's not usually a problem.

At this point in the meeting, an unidentified individual joined the proceedings by phone but did not comment.

(Resume PEC Script)

Biguanides—Relative Cost-Effectiveness

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of the Biguanides (metformin) subclass. Metformin combination products were evaluated with the parent compound (e.g., Janumet (sitagliptin/metformin) was evaluated with the DPP-4s subclass). Cost Minimization Analyses (CMAs) were performed.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) all generic formulations of metformin and the branded drug Riomet liquid were more cost-effective than Fortamet and Glumetza.

Biguanides—Uniform Formulary Recommendation

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 1 opposed, 1 abstained, 0 absent):

1. metformin IR (500 mg, 850 mg,1000 mg), metformin ER (500 mg, 750 mg), and Riomet liquid (500 mg/5 ml) remain formulary on the UF;
2. Fortamet (500mg, 1000 mg) and Glumetza (500 mg, 1000 mg) be designated Non-formulary on the Uniform Formulary.

Biguanides—Uniform Formulary Implementation Plan

(Dave Meade) The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 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.

(Dave Meade): At this time, Lt Col Hannah will provide the physician perspective for the biguanides.

BIGUANIDES — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah informed the Panel that there was no controversy about the biguanides subclass. Metformin is the preferred drug and will remain on formulary along with its generic formulations. The two drugs recommended for non-formulary were not cost effective compared to those recommended for formulary placement.

BIGUANIDES — BAP QUESTIONS AND DISCUSSION

Ms. Cohoon noted that her paper showed one person opposed and asked for clarification. Dr. Meade replied that one person expressed the view that since metformin is the preferred agent, all forms of metformin should be available in front of the step therapy.

Mr. Hutchings asked about the reason for requiring step therapy for these agents. Dr. Meade answered that it has to do with the number of scripts.

Ms. Cohoon noted the distribution of users for the drugs being made non-formulary and asked that the letters to beneficiaries who will no longer be able to get their prescriptions at the MTF include information about switching over to mail order. She also asked whether drugs could be moved off formulary quicker than 60 days in the MTFs, perhaps 30 days with a grace period of an additional 30 days for those who are already on the drugs. In response to her first concern, Ms. Le Gette explained that there already is appropriate verbiage in the letters that go out. Dr, Meade replied to the second question, indicating that when he was running an MTF pharmacy they would always work with the patient and the physician to provide another formulation or, if required, to establish medical necessity. In his view, however, thirty days would be too fast. Ms. Le Gette agreed, noting that her organization has to create the forms and get them approved. She said that the medical necessity forms are often available on the web before the implementation date; in the case of this class, which is a large class, there will be quite a few forms that have to be made. Dr. Meade assured the Panel that the MTFs will start working on the changeover as soon as the minutes are signed. He also noted that MTF patients probably get the most one-on-one attention as far as points of service are concerned.

Ms. Fryar noted that the PEC received over 440 physician responses for this drug class and asked whether any of the diabetic management specialists in DoD were consulted. Ms. Lugo replied that a lot of the responses were from specialists in the field.

BIGUANIDES — BAP VOTE ON UF RECOMMENDATIONS

There being no further Panel questions or discussion, Ms. Fryar read the P&T Committee's recommendations for the biguanides subclass of the non-insulin diabetic 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:

1. metformin IR (500 mg, 850 mg,1000 mg), metformin ER (500 mg, 750 mg), and Riomet liquid (500 mg/5 ml) remain formulary on the UF;
2. Fortamet (500mg, 1000 mg) and Glumetza (500 mg, 1000 mg) be designated Non-formulary on the Uniform Formulary.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

No Panel comments were offered.

BIGUANIDES — BAP VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

The Chair asked for questions, comments or discussion on the Committee's implementation plan recommendations. There was no further discussion, so Ms. Fryar read the implementation plan recommendation to be voted on.

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 Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Again there were no comments.

NON-INSULIN DIABETES DRUGS — SULFONYLUREAS (SUs)

The Chair asked for the presentation on the next drug subclass, the SUs.

(PEC Script)

SUs—Relative Clinical Effectiveness

(Amy Lugo): Let's review our second subclass, the Sulfonylureas, and their relative clinical effectiveness.

The P&T Committee evaluated the relative clinical effectiveness of the SU subclass. All the SU products are available in generic formulations. In the MHS, glipizide is the highest utilized sulfonylurea agent as you can see in Figure 3 on Page 4. For the individual SUs agents, refer to Table 1 on Page 2 of your handout about half-way down.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions for the SUs:

1. The ADA guidelines recommend SUs as the second-line of tier one, well-validated therapies for the treatment of T2DM.
2. The SUs decrease HbA1c 1.5% to 2% when used as monotherapy.
3. One UKPDS sub-study showed beneficial outcomes in diabetes-related endpoints and microvascular endpoints, in patients receiving a SU or insulin.
4. For adverse effects, the SUs are well known to cause hypoglycemia and weight gain.
5. With regard to renal dysfunction, glipizide may be used in patients who have creatinine clearance <50 mL/min if the dose is reduced.

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

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

SUs—Relative Cost-Effectiveness

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of the SUs subclass. SUs and SU combination products were evaluated with the parent compound (e.g., Duetact (pioglitazone/glimepiride) was evaluated with the TZDs subclass). Chlorpropamide was not evaluated due to its extremely low utilization in the MHS. Cost-minimization analyses (CMA's) were performed.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) all agents in the SUs subclass were cost-effective.

SUs—Uniform Formulary Recommendation

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

chlorpropamide (Diabinese, generic); glimepiride (Amaryl, generic); glipizide (Glucotrol, generic); glipizide ER (Glucotrol XL, generic); glyburide (Diabeta, Micronase, generic); glyburide micronized (Glynase Press Tab, generic); glipizide/metformin (Metaglip, generic); and glyburide/metformin (Glucovance, generic)

(Dave Meade) Lt Col Hannah will now provide the physician perspective for the sulfonylureas.

SULFONYLUREAS — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah provided the BAP with the physician's perspective on the review of this drug

subclass.

He said there is not much to add to what has been covered in the presentation. All the agents in this subclass are generic and all are cost-effective, so all were recommended for formulary placement.

SULFONYLUREAS — BAP QUESTIONS AND DISCUSSION

Dr. Salom said he was pleased to see that chlorpropamide has very low utilization. He asked why it was considered at all for formulary status since it is likely inappropriate for use in elderly patients. Mr. Hutchings added that the ADA doesn't actually recommend glyburide because of the increased risk for certain patients. He asked the PEC staff to comment on both agents.

Dr. Meade replied that where there is historic utilization, the Military Health System (MHS) keeps the agent available unless there is a recommendation against its use from the level of the U.S. Food and Drug Administration (FDA). Dr. Salom asked for the utilization figures on chlorpropamide as a follow-up to the meeting. Mr. Hutchings asked if there was any discussion about requiring step therapy for those agents, even though they are low utilization. He explained that the majority of the population he deals with are elderly. Dr. Meade answered that step therapy hadn't been considered.

The Panel had no further questions or comments on this subclass.

SULFONYLUREAS — BAP VOTE ON UF RECOMMENDATIONS

Ms. Fryar read the P&T Committee's UF recommendations for the agents in the sulfonylurea 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 remain formulary in the UF:

chlorpropamide (Diabinese, generic); glimepiride (Amaryl, generic); glipizide (Glucotrol, generic); glipizide ER (Glucotrol XL, generic); glyburide (Diabeta, Micronase, generic); glyburide micronized (Glynase Press Tab, generic); glipizide/metformin (Metaglip, generic); and glyburide/metformin (Glucovance, generic).

The BAP vote on the UF recommendations was as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Comment: Mr. Hutchings commented that he believes step therapy would have been an effective way to deal with chlorpropamide and glyburide and would have been more pleased with the recommendations had they included step because of the elderly nature of the population being treated.

Ms. Lugo thanked the Panel for their comments, noting that the Committee appreciates this kind

of input.

As there was no need for an implementation plan in this subclass, the Chair called for the presentation on the next subclass.

NON-INSULIN DIABETES DRUGS — DPP-4 (DIPEPTIDYL-PEPTIDASE- 4) INHIBITORS

(PEC Script)

DPP-4 INHIBITORS — RELATIVE CLINICAL EFFECTIVENESS

(Amy Lugo) The P&T Committee evaluated the relative clinical effectiveness of the DPP-4 inhibitors subclass. The DPP-4 inhibitors subclass includes sitagliptin (Januvia), sitagliptin/metformin (Janumet), and saxagliptin (Onglyza).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following clinical effectiveness conclusions for the DPP-4 inhibitors subclass:

1. The ADA guidelines do not mention DPP-4 inhibitors. However, the guidelines are updated annually, and DPP-4 inhibitors may be mentioned in the future, given wider clinical use and concerns regarding the TZD safety profile.
2. There are no completed long-term studies assessing cardiovascular (CV) outcomes, although 2 studies are under way.
3. Monotherapy with Januvia reduced HbA1c on average by 0.6%–0.79%; whereas, Onglyza monotherapy reduced HbA1c approximately 0.4%–0.7%.
4. The one published head-to-head trial comparing Januvia with Onglyza reported Januvia lowered HbA1c by approximately 0.1% more from baseline than Onglyza. Although the results were statistically significant, the difference between the two agents is not clinically significant.
5. Overall, DPP-4 inhibitors are considered weight neutral and lipid neutral.
6. DPP-4 inhibitors have very few reported adverse events and there are no clinically relevant differences between agents. Drug interaction profiles are also similar between agents.
7. In terms of serious adverse events, 88 cases of acute pancreatitis have been reported to the FDA as of September 2009. The majority of cases occurred with Januvia, but Januvia has a longer marketing history than Onglyza.
8. Results from a request for MHS providers' input showed the majority of responders stated at least one DPP-4 inhibitor was necessary on the UF. Providers would be willing to use either Januvia or Onglyza, but acknowledged more familiarity with Januvia.
9. There is a high degree of therapeutic interchangeability between Januvia and Onglyza.

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

Dr. Meade will now discuss the DPP-4 Inhibitors cost effectiveness conclusion, Uniform Formulary, and Automated Prior Authorization recommendations.

DPP-4 INHIBITORS — RELATIVE COST-EFFECTIVENESS

(*Dave Meade*) The P&T Committee evaluated the relative cost-effectiveness of the DPP-4 inhibitors. CMAs and budget impact analyses (BIAs) were performed based on findings that there were no clinically relevant differences in efficacy, safety, tolerability, and other factors among the DPP-4 inhibitors.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

- BIA was used to assess the potential impact of cost scenarios where selected DPP-4 inhibitors and DPP-4 inhibitor fixed drug combinations were designated as formulary or NF on the UF. BIA results for the DPP-4 inhibitors subclass showed that all investigated scenarios resulted in lower cost estimates than current MHS expenditures. Sensitivity analysis results supported the above conclusion.

DPP-4 INHIBITORS — UNIFORM FORMULARY RECOMMENDATION

(*Dave Meade*) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) sitagliptin (Januvia), sitagliptin/metformin (Janumet), and saxagliptin (Onglyza) remain formulary on the UF. Prior authorization/step-therapy for the DPP-4 inhibitors would require a trial of metformin or SUs for new patients.

DPP-4 INHIBITORS—PRIOR AUTHORIZATION CRITERIA

(*Dave Meade*) The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) the following PA criteria should apply to the DPP-4 inhibitors subclass. Coverage would be approved if the patient met any of the following criteria:

a) Automated PA criteria:

   (1) The patient has 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.
   (2) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, or Onglyza) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

   (1) 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.

(2) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.
(3) The patient has a contraindication to both metformin and a SU.

DPP-4 INHIBITORS — UNIFORM FORMULARY AND PRIOR AUTHORIZATION IMPLEMENTATION PLAN

(*Dave Meade*) The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

(Dave Meade) Lt Col Hannah will now give the physician perspective for the DPP-4 inhibitors.

DPP-4 INHIBITORS — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah informed the Panel that the use of DPP-4 inhibitors is increasing, particularly since they don't cause weight gain or adversely affect the lipid profile and have a relatively benign adverse affect profile. The one head-to-head study available showed similar efficacy between Januvia with Onglyza; while results were statistically significant, they were not clinically significant. No clinical outcomes are available in this subclass. In contrast, positive clinical outcomes are available for metformin and the sufonylureas. The ADA does recommend metformin as first-line therapy followed by the sufonylureas. Having the step therapy requirement that a patient try metformin or a sulfonylurea before using a DPP-4 is consistent with the ADA guidelines. All three DPP-4 age3nts remain on the formulary.

DPP-4 INHIBITORS — PANEL QUESTIONS AND DISCUSSION

Dr. Casull noted that as a pediatrician he has always tried to figure out what body part was affected by what. He asked whether the Committee ever considers the mechanism of action when deciding where to place an agent. In this case, the sulfonylureas and the DPP-4s both work at the basal cell and metformin works on the liver the same way as the DPP-4s. He asked if that is taken into account when making a decision. Lt Col Hannah relied that the Committee absolutely does take into consideration the mechanism of action.

Ms. Cohoon noted that the ADA guidelines do not mention the DPP-4s in the information she was given, but that there was an ADA meeting in January and she wonders whether any changes might have come from that meeting. Ms. Lugo answered that ADA Guidelines were updated recently and published on their website on Tuesday. She hasn't finished reviewing all of the updates yet, but she noted that ADA doesn't necessarily update their treatment guidelines annually although they do update their treatment algorithm. She will check further into whether there were any changes affecting the DPP-4s.

Mr. Hutchings said he assumes that the combo products are behind us now. The PEC staff said there was a lot of discussion about that. Dr. Meade said the key thing about the combo drugs is that metformin is in them. Mr. Hutchings said the issue is with the other drugs and whether a patient needs to go through step therapy to use metformin in combination. Ms. Lugo said there were also operational concerns because of the rejections that might occur. For example, if a

patient is already using metformin and presented a prescription for one of the other drugs, they would get a rejection. Mr. Hutchings said it sounds to him like the situation is that if the patient had been using metformin all along the prescription for the combo would go through but if they showed up with a new prescription they would get a rejection. A PEC staff member from the audience clarified by indicating that if a patient shows up with prescriptions for the individual items together, if the pharmacy were to fill the metformin first, then the second one would go through. So if the patient can get them individually, there is no reason to reject them as a combo. Ms. Schlaifer asked whether a patient who presented a prescription for Januvia would be rejected. The answer was if the patient gets metformin and Januvia, then it would go through. Mr. Hutchings asked for further clarification of the discussion behind the step therapy requirements. Dr. Meade said there was a lot of debate but the Committee came to the conclusion that with a limited number of beneficiaries it would not be a good thing to make the guidelines too complex. Mr. Hutchings asked whether the entire class would have to be re-bid if the rules were changed. He said he agrees that following the ADA guidelines will be the best thing for the majority of patients. If physicians don't want to do monitoring and just want to be free from any concern about hypoglycemia, they can just put patients on metformin. He also noted that patients who have been on metformin don't necessarily want to try sulfonylurea because of the hypoglycemic affects when in fact the metformin may not work as well as the sulfonylurea. Ms. Schlaifer said it was pointed out to her at the last meeting that the purpose of the actions was not to be the clinical guideline but to point physicians toward the clinical guideline. But the clinical guideline can't be enforced nationwide. Mr. Hutchings said he would vote to concur, but that it was helpful to know what went on behind the scenes.

Dr. Casull asked if it would be possible to require an automated clearance before going to a combo or whether that would cause a lot of difficulty. A PEC staff member in the audience agreed that it would be possible but also said it would be very complicated. Dr. Meade said that when it comes to step therapy, the MHS is fairly new at it with only about a year and half's experience. Therefore they are cautious about what they do and are careful not to do anything that might cause tie-ups or a massive disruption.

Dr. Schlaifer asked whether it comes up in discussion that when you go out in public you can get Janumet without trying a sulfonylurea or metformin first. She feels that the MHS is kind of opening itself up for allegations of inappropriate marketing. Lt Col Hannah said it absolutely was discussed, but came to the conclusion that at the end of the day the patient is on metformin. Dr. Schlaifer pointed out that the patient could be getting just metformin a whole lot cheaper. Dr. Meade said the main concern was that the patient try the first-line agent and the second-line agent.

The BAP had no further questions or discussion.

DPP-4 INHIBITORS — BAP VOTE ON UF RECOMMENDATION

Ms. Fryar read the P&T Committee's UF recommendation for the dipeptidyl-peptidase- 4 (DPP-4) 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 sitagliptin (Januvia), sitagliptin/metformin

(Janumet), and saxagliptin (Onglyza) remain formulary on the UF. Prior authorization/step-therapy for the DPP-4 inhibitors would require a trial of metformin or SUs for new patients.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

There were no Panel comments on the UF recommendation.

DPP-4 INHIBITORS — BAP VOTE ON PRIOR AUTHORIZATION RECOMMENDATION

The Chair asked whether any Panel members had further questions or comments on the PA recommendations. There being no further discussion. Ms. Fryar read the P&T Committee's PA recommendation.

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

a) Automated PA criteria:

(1) The patient has 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.
(2) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, or Onglyza) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

(1) 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.
(2) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.
(3) The patient has a contraindication to both metformin and a SU.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Panel comments:

Mr. Hutchings offered the comment that he still believe Janumet should be placed behind the step rather than in front of the step. He views combination therapy as a way to help somebody once they are stable. If a patient gets metformin and Januvia and becomes stable they should be able to safely use the combo drug. Dr. Schlaifer agreed with the comment.

Dr. Crum noted that the PA criteria that MHS is trying to develop are for a real world with minimum disruption. Although he acknowledges that the comment may be theoretically correct, he doesn't believe that it is appropriate for this installation.

DPP-4 INHIBITORS — BAP VOTE ON UF AND PRIOR AUTHORIZATION IMPLEMENTATION PLAN

Without further questions or comment, the Chair read the 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 as follows:
Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Following the vote, Ms. Lugo offered additional clarification regarding this drug subclass, stating that the ADA guidelines provide no guidance about prescribing two drugs at once. The Committee believes that it is appropriate to do so. However, for the most part, the P&T Committee follows the ADA guidelines. Clinically, the Committee agreed that it did not want Janumet behind the step. She also stated that the Committee would be keeping an eye on the other combinations in terms of their utilization.

Dr. Meade noted that the concerns about this subclass can be put on a preliminary management document that goes to the MTFs. The Committee will also make them available to physicians in the network to try to communicate what both the P&T Committee and the BAP thought regarding these agents. This will be a first for this procedure.

The Chair then asked for the next subclass presentation.

NON-INSULIN DIABETES DRUGS — GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS (GLP1RAs)

GLP1RAs — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)
(Amy Lugo) The P&T Committee evaluated the relative clinical effectiveness of the GLP1RAs subclass which includes exenatide (Byetta) injection and liraglutide (Victoza) injection. See Figure 5 on page 5 for utilization information. Prior authorization currently applies to the class, which excludes off-label use of the drugs for obesity in patients who do not have DM.

(Amy Lugo) *Relative Clinical Effectiveness Conclusion*—The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following clinical effectiveness conclusions for the GLP1RAs:

1. The ADA guidelines for T2DM place GLP1RAs in tier 2, (less well-validated therapy) after therapeutic lifestyle modification plus metformin.
2. Both Byetta and Victoza are indicated for use in patients with T2DM as monotherapy, and in combination with metformin, SUs, or TZDs. Off-labels uses of

the GLP1RAs include weight loss in patients without DM; weight loss is not a benefit covered by TRICARE.

3. Byetta is dosed twice daily with meals, whereas Victoza is dosed once daily 30–60 minutes prior to meals. The titration schedule and maximum doses differ between the two drugs.
4. There are no long-term studies assessing CV outcomes. However, two trials are underway.
5. GLP1RAs offer another option for add-on therapy when oral agents no longer provide adequate glycemic control. When combined with metformin, SU, or both metformin and SU, Byetta 10mcg twice daily lowered HbA1c 0.77%–0.86% from baseline, compared to Victoza 1.8mg once daily, which lowered HbA1c 1.3% from baseline.
6. Both Byetta and Victoza improve fasting plasma glucose (FPG) and postprandial glucose (PPG) concentrations; however, Victoza has a greater effect on lowering FPG than PPG due to its longer duration of action. In contrast, Byetta has a greater effect on PPG than FPG.
7. GLP1RAs offer no clinically significant reduction in HbA1c compared to basal insulin.
8. In the one published head-to-head trial between Byetta and Victoza, Victoza showed a greater decrease in HbA1c compared to Byetta (1.16% versus 0.87%), respectively. While the difference of 0.29% was statistically significant, it was not clinically significant. Limitations to the study included the open-label and non-inferiority study design and sponsorship by the manufacturer of Victoza.
9. Patients using a GLP1RA as monotherapy, or in combination with metformin, can expect a 2 kg to 3 kg weight loss.
10. Lipid parameters improve or remain neutral with Byetta or Victoza.
11. There are no clinically relevant differences among the GLP1RAs in common adverse events (nausea and hypoglycemia) and drug interactions.
12. Serious adverse events reported with the GLP1RAs include altered renal function with Byetta, and rare pancreatitis with both Byetta and Victoza. Both agents may cause formation of antibodies to the GLP1RA. Victoza has a black box warning in the product labeling for risk of developing a certain type of thyroid tumors.
13. Both agents are available in prefilled pen devices. Byetta requires two different pens to titrate patients to the target dose. Conversely, all three doses of Victoza are available in one dial-a-dose pen.
14. Results from a request for MHS providers' input showed that 49% of responders replied a GLP1RA was required on the UF, 21% were undecided, and 30% replied a GLP1RA was not required on the UF.
15. With the exception that Victoza offers patient convenience of a decreased dosing frequency compared to Byetta (once daily versus twice daily, respectively), and that Victoza targets FPG while Byetta targets PPG, there is a high degree of therapeutic interchangeability between the two products in terms of glycemic control. There is a lower degree of therapeutic interchangeability between the two products in terms of serious adverse events of endocrine system tumors.

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

Dr. Meade will now discuss the GLP1RA cost effectiveness conclusion, Uniform Formulary, and Automated Prior Authorization recommendations.

GLP1RAs—Relative Cost-Effectiveness

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of the GLP1RAs subclass. CMAs and BIAs were performed.

(Dave Meade) *Relative Cost-Effectiveness Conclusion*—Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 1 abstained, 1 absent) the following:

- BIA was used to assess the potential impact of cost scenarios where selected GLP1RAs were designated as formulary or NF on the UF.
- Victoza (liraglutide) pens are less costly than Byetta (exenatide) pens when comparing price per pen. However, Victoza patients require 2 or 3 pens per 30 days of therapy. Byetta patients only require 1 pen for 30 days of therapy. From a perspective examining cost-per-day of therapy, Byetta is significantly less costly than Victoza. The scenario where Byetta was step-preferred on the UF while Victoza was non-preferred and remained on the UF was determined to be the most cost-effective scenario. A sensitivity analysis was performed on the percentage of new users receiving a Victoza prescription. Sensitivity analysis results showed that market share gains by Victoza will result in additional costs to the MHS.

GLP1RAs—Uniform Formulary Recommendation

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) exenatide (Byetta) be designated formulary on the UF (step-preferred), and liraglutide (Victoza) be designated as formulary on the UF (non-preferred). Prior authorization for the GLP1RAs would require a trial of metformin or SUs for new patients. Exenatide (Byetta) was designated as the preferred drug within the subclass; a trial of exenatide (Byetta) would be required prior to liraglutide (Victoza) for new patients.

GLP1RAs—Prior Authorization Criteria

(Dave Meade) The P&T Committee recommended the following PA criteria should apply to the GLP1RAs. The prior PA criteria for the GLP1RAs would be replaced by the new criteria. Coverage would be approved if the patient met the following criteria:

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) the following PA criteria would apply to both exenatide (Byetta) and liraglutide (Victoza):

a) Automated PA criteria:

(1) 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.
AND

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria would apply to liraglutide (Victoza):

(1) Automated PA criteria:
The patient has received a prescription for exenatide (Byetta) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

The following would apply to exenatide (Byetta) and liraglutide (Victoza):

(1) The patient has a confirmed diagnosis of T2DM.

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

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

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

In addition to the above criteria regarding metformin and SU, the following PA criteria would apply specifically to liraglutide (Victoza):

(1) The patient has a contraindication to exenatide (Byetta).

(2) The patient has had inadequate response to exenatide (Byetta).

(3) The patient has experienced an adverse event with exenatide (Byetta), which is not expected to occur with liraglutide (Victoza).

GLP1RAs—Uniform Formulary and Prior Authorization Implementation Plan

(Dave Meade) The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

(Dave Meade): LT Col Hannah will now provide the physician perspective for the GLP1s.

GLP1RAs — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah stated that the efficacy is similar for Byetta and Victoza in terms of dosing frequency and safety profiles. The convenience of the once-daily dosing for Victoza did not offset the increased cost. Step therapy requiring a trial of metformin or a sulfonylurea also

applies to this subclass. Additionally, there is also a requirement for a trial of Byetta prior to using Victoza as it is the preferred drug in this subclass. There was already a PA requirement for this subclass, which is being replaced by the new PA recommendations.

GLP1RAs — PANEL QUESTIONS AND DISCUSSION

Mr. Hutchings said he assumes that if a patient is using metformin they don't need to meet the manual PA that they have diabetes.

Ms. Le Gette asked whether what is required for Victoza is a two-step step process in which the system looks back first for Byetta in order to avoid a double rejection. A PEC staff member in the audience agreed that the Byetta lookback process would ensure that metformin or an SU had been tried first.

GLP1RAs — PANEL VOTE ON COMMITTEE UF RECOMMENDATIONS

Without further discussion, the Chair read the P&T Committee's UF recommendations for the glucagon-like peptide-1 receptor agonists GLP1RAs 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 exenatide (Byetta) be designated formulary on the UF (step-preferred), and liraglutide (Victoza) be designated as formulary on the UF (non-preferred). Prior authorization for the glucagon-like peptide-1 receptor agonists would require a trial of metformin or SUs for new patients. Exenatide (Byetta) was designated as the preferred drug within the subclass; a trial of exenatide (Byetta) would be required prior to liraglutide (Victoza) for new patients.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

GLP1RAs — PANEL VOTE ON COMMITTEE PA CRITERIA RECOMMENDATIONS

Regarding the multiple PA criteria, Ms. Fryar asked whether a patient has to meet all of the criteria or just one. The answer provided was that a patient only has to meet one of the criteria.

The Chair then read the recommendations for the glucagon-like peptide-1 receptor agonists (GLP1RAs) PA criteria.

The P&T Committee recommended the following PA criteria should apply to the GLP1RAs. The prior PA criteria for the GLP1RAs would be replaced by the new criteria. Coverage would be approved if the patient met the following criteria:

The P&T Committee recommended the following PA criteria would apply to both exenatide

(Byetta) and liraglutide (Victoza):

a) Automated PA criteria:
(1) 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.
AND

The P&T Committee recommended the following PA criteria would apply to liraglutide (Victoza):

(1) Automated PA criteria:
The patient has received a prescription for exenatide (Byetta) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

The following would apply to exenatide (Byetta) and liraglutide (Victoza):

(1) The patient has a confirmed diagnosis of T2DM.

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

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

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

In addition to the above criteria regarding metformin and SU, the following PA criteria would apply specifically to liraglutide (Victoza):

(1) The patient has a contraindication to exenatide (Byetta).

(2) The patient has had inadequate response to exenatide (Byetta).

(3) The patient has experienced an adverse event with exenatide (Byetta), which is not expected to occur with liraglutide (Victoza).

The Panel voted as follows:
Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Mr. Hutchings, as a clarification to the answer provided to Ms. Fryar's question, noted that the criteria seem to indicate that a patient would have to have Type 2 diabetes AND meet one of the other criteria. He asked if that is a correct reading. The answer given was that it is a correct reading.

GLP1RAs — PANEL VOTE ON COMMITTEE UF AND PA IMPLEMENTATION PLAN RECOMMENDATIONS

The Chair opened the floor for Panel questions and discussion on the implementation plan

recommendations. There were none, so Ms. Fryar read the recommendation for the record.

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 as follows:
Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Note: following the vote Ms. Lugo offered a clarifying comment that was not audible on the recorded transcript.

NON-INSULIN DIABETES DRUGS — THIAZOLIDINEDIONES (TZDs)

TZDs — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(Amy Lugo) The P&T Committee evaluated the relative clinical effectiveness of the TZDs subclass. The subclass is comprised of rosiglitazone (Avandia) and pioglitazone (Actos), and fixed drug combination products with metformin or SU. None of the TZDs are available in generic formulations; the patent for Actos is expected to expire in 2012. The TZDs were reviewed previously for UF placement. Currently all the TZDs are designated formulary on the UF.

(Amy Lugo) *Relative Clinical Effectiveness Conclusion*—The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 2 absent) the following clinical effectiveness conclusions for the TZDs subclass:

1. ADA guidelines list Actos (but not Avandia) as a step 2, tier 2, (less well-validated) therapy for the treatment of T2DM.
2. At maximal doses, Actos and Avandia both reduce HbA1c by 0.6% to 1.6%. The differences between the two drugs for HbA1C reduction are not clinically relevant.
3. Outcomes studies are available with Actos from the PROactive trial where there was a significant decrease in all-cause mortality, non-fatal myocardial infarction (MI), stroke, and above the knee major leg amputation. In contrast, there is no direct evidence that Avandia prevents vascular events in patients with T2DM.
4. The TZDs differ in their effects on the lipid profile. Actos has a less unfavorable effect on lipids than rosiglitazone.
5. Safety and tolerability profiles are similar between Avandia and Actos in terms of incidence of heart failure, weight gain, edema, and hypoglycemia.
6. Avandia is associated with an increase in adverse CV events that is not seen with Actos. The Avandia product labeling includes a black box warning regarding increased risk of MI.

7. The FDA has allowed Avandia to remain on the U.S. market, but the manufacturer must develop a restricted access program that will limit Avandia use to patients unable to achieve goal HbA1c levels with other drugs.
8. The FDA released a safety communication regarding a potential increase in risk of bladder cancer with Actos. Studies are ongoing to further assess this risk.
9. The Pharmacy Outcomes Research Team analyzed TZD prescription trends in the MHS that showed a sharp decrease in use of Avandia, and an overall decrease in TZD use. New users of Avandia fell from 274 during June 2010, to 34 during October 2010. New users of Actos also decreased, with 2,202 new users in June 2010 compared to 1,372 during October 2010.
10. Results from a request for MHS providers' input showed that 69% of responders would prefer Actos over Avandia; 75% of the responders stated a TZD/metformin fixed dose combination product was not required on the UF.
11. In terms of glycemic control, there is a high degree of therapeutic interchangeability between Actos and Avandia. However, there is a lower degree of therapeutic interchangeability with regard to safety profiles.

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

Dr. Meade will now discuss the cost effectiveness conclusion of the TZD's, Uniform Formulary, and Automated Prior Authorization recommendations.

TZDs—Relative Cost-Effectiveness

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of the TZDs subclass. CMAs were performed.

(Dave Meade) *Relative Cost-Effectiveness Conclusion*—Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 1 abstained, 1 absent) rosiglitazone and rosiglitazone fixed dose combinations [rosiglitazone (Avandia), rosiglitazone/ metformin (Avandamet), and rosiglitazone/glimepiride (Avandaryl)] are more cost-effective than pioglitazone and pioglitazone fixed dose combinations [pioglitazone (Actos), pioglitazone/metformin (Actoplus Met, Actoplus Met XR), and pioglitazone/glimepiride (Avandaryl)]. Additionally, increased safety concerns for Avandia, Avandamet, and Avandaryl outweigh their apparent cost efficiency.

TZDs—Uniform Formulary Recommendation

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent):

a) pioglitazone (Actos), pioglitazone/metformin (Actoplus Met, Actoplus Met XR), and pioglitazone/glimepiride (Avandaryl) remain designated formulary on the UF;

b) rosiglitazone (Avandia), rosiglitazone/ metformin (Avandamet), and rosiglitazone/glimepiride (Avandaryl) be designated NF on the UF.

Off Script: Mr. Hutchings asked if the recommendations as worded are correct, noting an apparent error in the agents included in a) those designated formulary. Dr. Meade agreed and corrected the record to read:

a) pioglitazone (Actos), pioglitazone/metformin (Actoplus Met, Actoplus Met XR), and Duetact remain designated formulary on the UF;
b) rosiglitazone (Avandia), rosiglitazone/ metformin (Avandamet), and rosiglitazone/glimepiride (Avandaryl) be designated NF on the UF.

TZDs—Prior Authorization Criteria

(Dave Meade) The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) the following PA criteria should apply to the TZDs subclass. Coverage would be approved if the patient met any of the following criteria:

a) Automated PA criteria:

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

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

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

(1) 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.

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

(3) The patient has a contraindication to metformin and SUs.

TZDs—Uniform Formulary and Prior Authorization Implementation Plan

(Dave Meade) The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 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.

(Dave Meade): Lt Col. Hannah will now give the physician perspective for the TZDs.

TZDs — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah noted that there are safety concerns with this subclass, particularly with Avandia, which now includes a black box warning regarding myocardial infarction, but also with Actos,

which is being investigated in relation to bladder cancer. The number of new users of both drugs have decreased.

TZDs — PANEL QUESTIONS AND DISCUSSION

Ms. Fryar pointed out that Table 1 of the handout lists "Rosiglitazone (Actos)" as being recommended for non-formulary placement. That entry should read, "Rosiglitazone (Avandia)."

Ms. Cohoon asked how the PA process was going to work for the combo drugs in this class, Avandamet and Avandaryl. Dr. Meade answered that Actos products would probably be in front of the step and that Avandia would be behind the step. But there will be very few new patients going on Avandia and, in fact, people will be coming off it because of the safety issues. The rest are grandfathered.

Mr. Hutchings said that a very recent study of Actos had also shown increased cardiovascular risk. He's not sure that he would want someone to get Actos "straight out of the chute" from a safety standpoint. Dr. Meade assured the Panel that MHS would be keeping an eye on these products in case FDA comes down with additional concerns about Actos products.

Ms. Fryar asked if there were any more questions, comments or discussion about the presentation. There were none.

THIAZOLIDINEDIONES (TZDs) — PANEL VOTE ON UF RECOMMENDATIONS

The Chair then read the P&T Committee's UF recommendations for the TZDs 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:

a) pioglitazone (Actos), pioglitazone/metformin (Actoplus Met, Actoplus Met XR), and glimepiride/pioglitazone (Duetact) remain designated formulary on the UF;
b) rosiglitazone (Avandia), rosiglitazone/ metformin (Avandamet), and rosiglitazone/glimepiride (Avandaryl) be designated NF on the UF.

The Panel vote on the UF recommendations was as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Panel comment: The Panel asked to include a comment regarding the step therapy placement of combination products in this class, noting that it might be preferable to place all of them after the step.

TZDs — PANEL VOTE ON PA RECOMMENDATIONS

Without further discussion, the Chair read the recommendations on the PA criteria for this subclass.

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

a) Automated PA criteria:

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

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

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

(1) 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.

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

(3) The patient has a contraindication to metformin and SUs.

The BAP vote on the PA criteria recommendations was:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

TZDs — PANEL VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

The Chair then read the P&T Committee's implementation plan recommendations for the TZD subclass.

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 UF decision.

The Panel vote was:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

NON-INSULIN DIABETES DRUGS — MEGLITINIDES

MEGLITINIDES — RELATIVE CLINICAL EFFECTIVENESS

(PEC script)

(Amy Lugo) The P&T Committee evaluated the relative clinical effectiveness of the Meglitinides subclass. The subclass includes nateglinide (Starlix, generic), repaglinide (Prandin), and repaglinide/metformin (Prandimet). Prandin has the highest MHS utilization in this subclass as you can see in Figure 7 on page 6.

(Amy Lugo) *Relative Clinical Effectiveness Conclusion*—The P&T Committee recommended

(18 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions for the Meglitinides subclass:

1. The ADA guidelines consider the meglitinides as "other therapies," and the subclass is not considered in the tier one (well-validated) or tier two (less well-validated) therapies. Joint guidelines from the DoD/Veterans Affairs (VA) list the meglitinides as alternative agents, which may be used after therapy with metformin or the SUs.
2. Average HbA1c reductions for the subclass range from 0.1% to 2.1% with Prandin, 0.2% to 0.6% Starlix, and 1.4% with Prandimet.
3. Weight gain ranging from 0.7 kg to 2.1 kg has occurred with both agents.
4. In terms of efficacy or safety/tolerability, there are no clinically relevant differences between Starlix and Prandin overall.

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

Dr. Meade will now discuss the cost effectiveness conclusion of the Meglitinide class, Uniform Formulary, and Automated Prior Authorization recommendations.

Meglitinides—Relative Cost-Effectiveness

(Dave Meade) P&T Committee evaluated the relative cost-effectiveness of the Meglitinides subclass. CMAs were performed.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained, 2 absent) that all meglitinides in this subclass were cost-effective.

Meglitinides—Uniform Formulary Recommendation

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 2 absent) nateglinide (Starlix, generic), repaglinide (Prandin), and repaglinide/metformin (Prandimet) be designated formulary on the UF.

(Dave Meade) **Meglitinides—Uniform Formulary Implementation Plan: Not Applicable**

(Dave Meade): Lt Col. Hannah will now provide the physician perspective for the meglitinides.

MEGLITINIDES - COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah said the meglitinide subclass is not commonly used. It is mainly prescribed for patients with postprandial hypoglycemia. All three agents are to remain on formulary. Patients are not required to have metformin or a sulfolylurea first; they are not part of step therapy.

MEGLITINIDES – BAP QUESTIONS AND DISCUSSION

Ms. Cophoon, referring to the graph in the handout (figure 7) asked why there had been a drop in the utilization of Starlix. Dr. Meade replied that it is probably due to utilization of its generic equivalent product. He noted that is a typical result when a product goes generic.

MEGLITINIDES – BAP VOTE ON UF RECOMMENDATIONS

Without further discussion, the Chair read the P&T Committee's UF recommendations for the meglitinides 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 nateglinide (Starlix, generic), repaglinide (Prandin), and repaglinide/metformin (Prandimet) be designated formulary on the UF.

The Panel then voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

As no implementation plan was necessary in the subclass, the Chair called for the next presentation.

NON-INSULIN DIABETES DRUGS — ALPHA-GLUCOSIDASE INHIBITORS (AGIs*)*

AGIs — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(Amy Lugo) The P&T Committee evaluated the relative clinical effectiveness of the AGIs subclass. The subclass is comprised of acarbose (Precose, generics) and miglitol (Glyset). The subclass has very low utilization in the MHS as seen in Figure 8 on page 6.

(Amy Lugo) *Relative Clinical Effectiveness Conclusion*—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions for the AGIs subclass:

1. The ADA guidelines consider the AGIs as "other therapies," and the subclass is not considered in the tier one (well-validated) or tier two (less well-validated) therapies. Joint guidelines from the DoD/VA list the AGIs as alternative agents, which may be used after therapy with metformin or the SUs.
2. The AGIs reduce HbA1c by less than 1%; acarbose reduces HbA1c by 0.77% and miglitol reduces HbA1c by 0.68%. A decrease in HbA1c by 0.5% is considered clinically relevant.
3. In terms of efficacy or safety/tolerability, there were no clinically relevant differences between acarbose and miglitol overall. The significant GI adverse effects caused by AGIs, the requirement for multiple-daily dosing, and the minimal reduction in HbA1c limit the clinical usefulness of this subclass when compared to

the other non-insulin diabetes drug subclasses.

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

Dr. Meade will now discuss the cost effectiveness conclusion of the alpha-glucosidase inhibitors and Uniform Formulary recommendations.

AGIs—Relative Cost-Effectiveness

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of the AGIs subclass. CMAs were performed.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) that acarbose (Precose, generic) and miglitol (Glyset) were cost-effective.

AGIs—Uniform Formulary Recommendation

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 1 opposed, 1 abstained, 0 absent) acarbose (Precose, generics) and miglitol (Glyset) be designated formulary on the UF.

(Dave Meade) AGIs—Uniform Formulary Implementation Plan: Not Applicable

(Dave Meade): Lt Col Hannah will now provide the physician perspective for the AGIs.

AGIs — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah informed the panel that the drugs in this subclass are rarely used in the United States, largely because of the adverse side effects. Within the subclass, there were no clinically relevant differences between acarbose and miglitol. Both are on formulary and patients are not required to have metformin or a sulfonylurea before taking them; they are not part of step therapy.

AGIs — BAP QUESTIONS AND DISCUSSION

The Chair opened the floor for Panel questions.

Mr. Hutchings asked about the cost-effectiveness of agents in this subclass compared to other subclasses. Dr. Meade replied that they are more expensive. Dr. Casull asked if this was the reason for the relatively low utilization of Precose and Glyset. Dr. Meade said the reason is probably that the MTFs prefer the generic formulation, Acarbose.

ALPHA-GLUCOSIDASE INHIBITORS (AGIs*)* — BAP VOTE ON UF RECOMMENDATION

Lacking further discussion, the Chair read the P&T Committee's UF recommendation for the AGI 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 acarbose (Precose, generics) and miglitol (Glyset) be designated formulary on the UF.

The BAP vote was:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Again, no implementation plan was required for this subclass as all of the agents are to remain on formulary.

Ms. Fryar then asked for the next presentation.

NON-INSULIN DIABETES DRUGS — AMYLIN AGONISTS (PRAMLINTIDE)

AMYLIN AGONISTS (PRAMLINTIDE) — RELATIVE CLINICAL EFFECTIVENESS

(PEC Script)

(Amy Lugo) The P&T Committee evaluated the relative clinical effectiveness of the Amylin Agonists subclass. Pramlintide (Symlin) injection is the only amylin agonist currently on the market. Due to safety concerns, a PA was implemented in 2005 to ensure appropriate dosing of Symlin, which is consistent with the product labeling.

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

1. The ADA guidelines for T2DM do not mention the place in therapy for Symlin.
2. Symlin is indicated as add-on therapy to insulin for the treatment of Type 1 diabetes (T1DM) and T2DM when patients are inadequately controlled on intensive insulin regimens. Off-label uses of Symlin include weight loss in patients without DM; weight loss is not a benefit covered by TRICARE.
3. In patients with T1DM, Symlin lowers HbA1C -0.1% to -0.39%. In patients with T2DM, Symlin lowers HbA1c -0.3% to -0.62%.
4. There are no outcomes studies with pramlintide.
5. Symlin causes weight loss of 1 to 2.3 kg.
6. Symlin is available in multidose vials and a prefilled pen device. The prefilled pen device includes a dial-a-dose feature which decreases the risk of dosing errors.
7. Symlin is efficacious in lowering HbA1c and improving glycemic control, and patients can expect a 1 kg to 2 kg weight loss. However, its clinical utility is limited because it cannot be mixed with insulin, patients require multiple injections of insulin and Symlin at separate times, there is an increased risk of dosing errors when vials are used, and insulin doses must be decreased by 50% on initiation of therapy to reduce the risk of hypoglycemia.

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

Dr. Meade will now discuss the cost effectiveness conclusion of pramlintide, our Amylin agonist, Uniform Formulary, and Automated Prior Authorization recommendations.

Amylin Agonists (Pramlintide)—Relative Cost-Effectiveness

(Dave Meade) The P&T Committee evaluated the relative cost-effectiveness of the Amylin Agonists subclass. A CMA was performed.

(Dave Meade) *Relative Cost-Effectiveness Conclusion*—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) that pramlintide is cost-effective as an adjunct treatment in T1DM and T2DM patients who cannot achieve desired glucose control despite optimal insulin.

Amylin Agonists (Pramlintide)—Uniform Formulary Recommendation

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) pramlintide (Symlin) injection remain designated as formulary on the UF.

Amylin Agonists (Pramlintide)—Prior Authorization Criteria

(Dave Meade) The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following PA criteria should apply to the pramlintide (Symlin). Coverage would be approved if the patient met any of the following criteria:

a) Automated PA criteria:
   (1) The patient has received a prescription for bolus insulin at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

The current PA for pramlintide (Symlin) does not exclude use in obese patients who do not have DM. The P&T Committee recommended adding the following to the existing manual PA:

b) Manual PA criteria, if automated criteria are not met:
   (1) The patient has a confirmed diagnosis of T1DM or T2DM.

Amylin Agonists (Pramlintide)—Prior Authorization Implementation Plan

(Dave Meade) The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of

service.

(Dave Meade): Lt Col Hannah will provide the physician perspective for pramlintide.

AMYLIN AGONISTS (PRAMLINTIDE) — COMMITTEE PHYSICIAN PERSPECTIVE

Lt. Col Hannah noted that symlin is used in addition to insulin for both Type 1 and Type 2 diabetes patients who have difficulty controlling glucose levels. In addition to the multi-dose vials, a pen device is also now available. It is recommended to stay on the formulary with Prior Authorization. Patients are not required to have metformin or a sulfonylurea first; it is not part of step therapy.

AMYLIN AGONISTS (PRAMLINTIDE) — BAP QUESTIONS AND DISCUSSION

Dr. Salom said that this is a drug that is off his radar screen. He asked about the vials used to dispense the drug.

Dr. Schlaifer asked about the PA that is already in place for this drug that is being modified, noting that there are safety concerns but she isn't sure what that PA is. Ms. Lugo answered that the PA requirement was adopted in 2005 requiring prior insulin therapy. This one adds the requirement that the patient have a confirmed diagnosis of Type 1 or Type 2 diabetes.

Mr. Hutchings said that the 2005 PA was actually effective. Ms. Lugo explained that the 2005 PA is being retained, but it is being added to.

Mr. Hutchings said his problem is that there is no hard block and that it can be used for weight loss. There are safety concerns stemming from the drug not being able to be mixed with insulin and having to be dosed at separate times. Those safety concerns should be added to the PA form. He is afraid if the PA is automated, those concerns will be bypassed. He would argue against having an automated PA for this subclass.

AMYLIN AGONISTS (PRAMLINTIDE) — BAP VOTE ON UF RECOMMENDATION

There being no further questions, the Chair read the P&T Committee's UF recommendation for the amylin agonists 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 pramlintide (Symlin) injection remain designated as formulary on the UF.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

AMYLIN AGONISTS (PRAMLINTIDE) — BAP VOTE ON PA CRITERIA RECOMMENDATIONS

The Chair next read the PA criteria recommendations for this subclass.

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following PA criteria should apply to the pramlintide (Symlin). Coverage would be approved if the patient met any of the following criteria:

a) Automated PA criteria:
   (1)The patient has received a prescription for bolus insulin at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

The current PA for pramlintide (Symlin) does not exclude use in obese patients who do not have DM. The P&T Committee recommended adding the following to the existing manual PA:

b) Manual PA criteria, if automated criteria are not met:
   (1) The patient has a confirmed diagnosis of T1DM or T2DM.

Mr. Hutchings commented that, in the retail world, this medication is not inexpensive, perhaps $1,000 per injection. This is another reason why he would like to see only a non-automated PA. For this reason (he disagrees with the automated PA and thinks it should be manual only) he will vote to non-concur on the PA.

The Panel vote on the PA criteria recommendations was:

Concur: 7 Non-concur: 4 Abstain: 0 Absent: 0

Panel comment: The Panel commented that the non-concur votes were due to the automated PA being unsafe. The 2005 PA criteria would be sufficient to address the concerns, which is that someone might be prescribed the drug inadvertently without understanding the risks. Dr. Casull said that he doesn't see what this drug does that insulin doesn't do, plus it has the downside of a safety risk plus high cost.

AMYLIN AGONISTS (PRAMLINTIDE) — BAP VOTE ON PA IMPLEMENTATION PLAN

The Chair read the implementation plan for this subclass.

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 comment or discussion, the Panel voted:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

NEWLY APPROVED DRUGS

(PEC script)

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

INHALED CORTICOSTEROID (ICS)/LONG-ACTING BETA AGONIST (LABA) - MOMETASONE/FORMOTEROL ORAL INHALER (DULERA)

(LCDR Olaitan Ojo)

DULERA — RELATIVE CLINICAL EFFECTIVENESS

Dulera contains the ICS mometasone (Asmanex) and the LABA formoterol (Foradil) in an oral metered-dose inhaler (MDI). It is the third FDA-approved ICS/LABA combination inhaler to reach the market. The Pulmonary 1 class, which includes the ICS/LABA combinations, was reviewed at the February 2009 P&T Committee meeting.

If you turn to table 2 on page 8 of the handout, you'll see the list of the Inhaled Corticosteroid/Long-Acting Beta Agonists drugs. The utilization of these agents can be found below, in Figure 10. As you can see, the highest utilization is Advair diskus.

Dulera is FDA-approved for treating patients older than 12 years with asthma. Advair is approved for treating asthma in patients older than 4 years, and is also approved for treating chronic obstructive pulmonary (COPD).

There are no head-to-head trials between Dulera and the other ICS/LABA combinations inhalers, but clinically relevant differences in efficacy are not expected, if equivalent doses are used.

The product labeling contains the same black box warning as Advair and Symbicort regarding increased risk of death in patients with asthma who receive unopposed LABA therapy.

- *Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (18 for, 0 opposed, 0 abstained) Dulera offers no clinically meaningful therapeutic advantage over other ICS/LABA combinations in terms of efficacy, safety, or tolerability. However, it does provide a third ICS/LABA option for the treatment of asthma.

Inhaled Corticosteroid (ICS)/Long-Acting Beta Agonist (LABA) - Mometasone/formoterol Oral Inhaler (Dulera) — RELATIVE COST EFFECTIVENESS

(Dave Meade) The P&T Committee evaluated the cost of Dulera in relation to the efficacy, safety, tolerability, and clinical outcomes of the other currently available agents in this subclass. CMA was performed to evaluate the cost of Dulera in relation to the other currently available ICS/LABAs.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) Dulera was less costly than the other ICS/LABA combination agents on the UF.

Inhaled Corticosteroid (ICS)/Long-Acting Beta Agonist (LABA) - Mometasone/formoterol Oral Inhaler (Dulera) — UNIFORM FORMULARY RECOMMENDATION

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

UNIFORM FORMULARY IMPLEMENTATION PLAN — NOT APPLICABLE

(Dave Meade): Lt Col Hannah will now give the physician perspective for Dulera.

DULERA — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah told the BAP that there shouldn't be any controversy with respect to Dulera. It is a combination ICS/LABA inhaler that is effective for treating both children and adults. The FDA has approved treatment for young children using the long-lasting beta agonist alone. Dulera provides a third option for the treatment of asthma using the combination.

DULERA — BAP QUESTIONS AND DISCUSSION

Mr. Hutchings asked when Advair is expected to go generic, noting that it has been on the market for many years. Dr. Meade replied that he thinks one of the Advair combinations will go generic in 2012. Generic Advair is not imminent.

DULERA — BAP VOTE ON UF RECOMMENDATION

With no further discussion, the Chair read the UF recommendation for the newly approved drug Dulera.

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 mometasone/formoterol (Dulera) be designated formulary on the UF.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

The Chair noted that the implementation plan does not apply.

NEWLY APPROVED DRUGS

2) ANTILIPIDEMIC-1S (LIP-1S) — PITAVASTATIN (LIVALO)

(PEC Script)

LIVALO — RELATIVE CLINICAL EFFECTIVENESS

(LCDR Ojo) The second new drug we have to discuss is a statin drug. Pitavastatin (Livalo) is the seventh statin to reach the U.S. market. It lowers low-density lipoprotein (LDL) by less than 45%. The statins are classified in the LIP-1s drug class, which were reviewed in May 2010. Automated PA/step-therapy now applies to the LIP-1s; generic statins (simvastatin, pravastatin, lovastatin) or atorvastatin (Lipitor) are the preferred drugs.

If you turn to page 9 of the handout and look at table 3, the LIP-1s drugs are listed. The utilization is at the bottom of the page, in Figure 11. Simvastatin has the highest utilization in the MHS, followed by Atorvastatin (Lipitor).

There are no published or planned studies evaluating clinical outcomes (such as mortality, CV events, acute coronary syndromes) with Livalo. Short-term clinical trials lasting less than 12 weeks show efficacy comparable to other low-to-moderate dose statins (those that lower LDL <45%) in terms of effects on the lipid parameters.

Livalo's safety profile appears similar to the other statins but more long-term safety data is required. Livalo undergoes minimal CYP 450 metabolism and is similar to Pravachol and Crestor, but has a more favorable drug interaction profile than simvastatin. However, Livalo is metabolized by the transporter system and has unique drug interactions not seen with the other statins, including contraindications with cyclosporine and reduced dosage requirements with erythromycin.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) that pitavastatin (Livalo) does not have a significant, clinically meaningful therapeutic advantage in terms of effectiveness, safety, and tolerability over other LIP-1s included on the UF, which have evidence for positive effects on CV clinical outcomes.

Antilipidemic-1s (LIP-1s) Pitavastatin (Livalo) - RELATIVE COST EFFECTIVENESS

(Dave Meade) A CMA was performed that evaluated the cost of pitavastatin (Livalo) in relation to other available LIP-1s.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) pitavastatin (Livalo) was more costly than all other low-to-moderate LDL-lowering LIP-1s included on the UF.

Livalo - UNIFORM FORMULARY RECOMMENDATION

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

Livalo — PRIOR AUTHORIZATION CRITERIA

(Dave Meade) Prior authorization for the LIP-1s requires a trial of a step-preferred drug [simvastatin, lovastatin, lovastatin or atorvastatin (Lipitor)] prior to a non-step preferred LIP-1 [other UF LIP-1s, including rosuvastatin (Crestor), simvastatin/ezetimibe (Vytorin)]. Pitavastatin (Livalo) would be designated as non-step preferred and NF. The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to pitavastatin (Livalo).

a) Automated PA criteria:

(1) The patient has received a prescription for a preferred agent targeting

similar LDL reduction at any MHS pharmacy point of service (MTFs, retail network pharmacies, or home delivery) during the previous 180 days.

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

(1) The patient has a known contraindication to the preferred LIP-1 drugs.

(Off script) Dr. Meade paused here to ask if the Panel had any questions about the fact that Livalo is recommended as both non-formulary and non-preferred. There were no questions.

(PEC Script)

Livalo UNIFORM FORMULARY AND PRIOR AUTHORIZATION IMPLEMENTATION PLAN

(Dave Meade) The P&T Committee recommended (17 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; and 2) TMA send a letter to beneficiaries affected by this UF decision.

(Dave Meade): Lt Col Hannah will now give the physician perspective for Livalo.

LIVALO — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah noted that safety profiles of mini-trials of drugs in this class indicate their use may increase the risk of death, TMI or stroke. Long-term adverse effect trials indicate there is a similar applicability to the population as a whole. The statin class was reviewed in May 2010 and made generic statins (simvastatin, pravastatin and lovastatin) and Lipitor the preferred agents. Prior to this meeting a PA has been implemented to ensure use of the preferred drugs. The primary reason to make Livalo non-formulary is that it is more powerful and doesn't have outcomes data. Other statins (Crestor and Vytorin) are available on the UF.

LIVALO — BAP QUESTIONS AND DISCUSSION

Dr. Salom asked about the graph shown in the handout (Figure 11). He noted that scale of the graph doesn't show how many prescriptions are being issued for Livalo. He noted that there are a large number of drugs in the class and that they are expensive and asked about the actual utilization of Livalo. Dr. Meade answered it is between 4,000 and 5,000.

Ms. Fryar asked for clarification of the number of beneficiaries affected and if that number would translate to a total of about 700 beneficiaries affected. Dr. Meade said that the number of patients would be about 700 and the number of 30-day prescriptions is about four-to-five thousand.

LIVALO — BAP VOTE ON UF RECOMMENDATION

The Chair next read the P&T Committee's UF recommendation for the newly-approved LIP-1 drug, Livalo.

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 pitavastatin (Livalo) be designated NF on the UF.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

The Panel offered no comments.

LIVALO — BAP VOTE ON PA RECOMMENDATION

The Panel also had no questions or comments on the PA recommendation, so the Chair read it for the record.

Prior authorization for the LIP-1s requires a trial of a step-preferred drug [simvastatin, lovastatin, lovastatin or atorvastatin (Lipitor)] prior to a non-step preferred LIP-1 [other UF LIP-1s, including rosuvastatin (Crestor), simvastatin/ezetimibe (Vytorin)]. Pitavastatin (Livalo) would be designated as non-step preferred and NF. The P&T Committee recommended the following PA criteria should apply to pitavastatin (Livalo).

a) Automated PA criteria:

(1) The patient has received a prescription for a preferred agent targeting similar LDL reduction at any MHS pharmacy point of service (MTFs, retail network pharmacies, or home delivery) during the previous 180 days.

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

(1) The patient has a known contraindication to the preferred LIP-1 drugs.

Without comment, the Panel voted was:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

LIVALO — BAP VOTE ON IMPLEMENTATION PLAN RECOMMENDATION

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

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

The Panel vote was:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

NEWLY APPROVED DRUGS

3) NEWER SEDATIVE HYPNOTIC AGENTS (SED-1S) — DOXEPIN TABLETS (SILENOR)

(PEC Scritpt)

SILENOR — RELATIVE CLINICAL EFFECTIVENESS

(LCDR Ojo) The next drug is Silenor. Silenor is a new low-dose (3 mg and 6 mg) tablet formulation of doxepin (Sinequan, generics). The product is FDA-approved for treatment of insomnia characterized by difficulty with sleep maintenance. The SED-1s class was reviewed in February 2007. The current BCF/UF drug is zolpidem IR (generic Ambien). Automated Prior Authorization (PA)/step-therapy applies to this class: a trial of zolpidem IR (generic Ambien) prior to use of the other drugs in the class is required.

Page 10 of the handout and table 4 has the list of Newer Sedative Hypnotic Agents. The utilization is at the bottom of the page, in Figure 12. Generic zolpidem IR (Ambien) by far has the highest utilization in the MHS.

Silenor differs from the other SED-1s because it selectively binds the histamine H1 receptor to reduce wakefulness. It is not a controlled substance; all other agents in the class are classified as schedule IV, except ramelteon (Rozerem).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) doxepin tablets (Silenor) are superior to placebo in the treatment of sleep maintenance insomnia. Silenor's adverse event profile is more favorable that those of formulary agents on the UF. It provides an option for patients with sleep maintenance problems where a controlled substance is not warranted.

Newer Sedative Hypnotic Agents (SED-1s) — Doxepin Tablets (Silenor) RELATIVE COST EFFECTIVENESS

(Dave Meade) The P&T Committee evaluated the cost of Silenor in relation to the efficacy, safety, tolerability, and clinical outcomes of the other Newer Sedative Hypnotic Agents. CMA was used to evaluate the relative cost-effectiveness of Silenor relative to other Newer Sedative Hypnotic Agents.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) doxepin tablets (Silenor) was less costly than the other sleep maintenance agents included on the UF.

Newer Sedative Hypnotic Agents (SED-1s) — Doxepin Tablets (Silenor) UNIFORM FORMULARY RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) doxepin tablets (Silenor) be designated formulary on UF, with a PA requiring a trial of zolpidem IR for new users.

Newer Sedative Hypnotic Agents (SED-1s) — Doxepin Tablets (Silenor) PRIOR

AUTHORIZATION CRITERIA

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to doxepin (Silenor). Coverage would be approved if the patient met any of the following criteria:

a) Automated PA criteria:

(1) The patient has received a prescription for zolpidem IR at any Military Health Service (MHS) pharmacy point of service (Military Treatment Facilities (MTFs), retail network pharmacies, or home delivery) during the previous 180 days.

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

(1) The patient has tried zolpidem IR and was unable to tolerate treatment due to adverse effects.
(2) The patient has tried zolpidem IR and has had an inadequate response.
(3) The patient has a known contraindication to zolpidem IR.
(4) The patient requires a nonscheduled agent for sleep maintenance.

Newer Sedative Hypnotic Agents (SED-1s) — Doxepin Tablets (Silenor) UNIFORM FORMULARY AND PRIOR AUTHORIZATION IMPLEMENTATION PLAN

(Dave Meade) The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service.

(Dave Meade): Lt Col Hannah will now give the physician perspective for Silenor.

SILENOR — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah noted that Silenor is a new formulation of an old drug used to treat insomnia. The MHS can't use the old formulation, which is a 10 mg capsule. The primary advantage of Silenor is that it is not a Schedule IV (Controlled substance). Additionally, its adverse event profile is more favorable than other drugs in this class. Accordingly it is recommended for formulary placement.

SILENOR — BAP QUESTIONS AND DISCUSSION

Dr. Casull asked, in terms of the DoD 1:1:1 (one provider/one pharmacy/one facility for controlled substances) program, whether the Committee's deliberations included a discussion of why the MHS would not elevate a fairly effective, non-controlled drug with minimum side effects over a controlled substance on the PA. Dr. Meade noted that the subject was discussed and explained that Silenor isn't really as effective as zolpidem IR in treating insomnia, but it is

an option for those who have tried zolpidem IR and can't tolerate it.

Dr. Crum asked if the Committee had evaluated how often the old formulation of doxepin was prescribed. Dr. Meade said it is difficult to get that information out of the data. Dr. Crum noted that there seems to be a clinical advantage to this product versus the old formulation.

Ms. Cohoon said she had concerns about trying to put a PA behind a non-controlled substance given all the recent rhetoric and interest in prescription drug abuse by the White House and others. She said putting a PA on something drives the provider in a certain direction. This seems to be sending a mixed message by putting a non-controlled substance behind a controlled substance on the PA. She said the White House Task Force is looking specifically at the use of prescription drugs in the military. Dr. Meade noted that Riverem is a non-controlled drug and it is behind the step also, an action which dates from 2007.

Dr. Salom noted that he finds it interesting that the manufacturer chose to make the drug in 3 mg and 6 mg tablets; he said they might also have thought about having a 5 mg, with the idea that someone might come out with a generic tablet.

Ms. Le Gette asked about the old generic formulation and whether it would be placed on the first tier, even though it is low utilization. Dr. Meade replied that they would prefer to re-evaluate that after others go generic.

SILENOR — BAP VOTE ON UF RECOMMENDATION

There being no further discussion, the Chair read the P&T Committee's UF recommendation for Silenor.

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 doxepin tablets (Silenor) be designated formulary on UF, with a PA requiring a trial of zolpidem IR for new users.

The Panel voted as follows:

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

Panel comment: the non-concurring Panel member explained that her vote was because of the PA requirement; she has no problem with the drug being on formulary.

SILENOR — BAP VOTE ON PA CRITERIA RECOMMENDATION

The Chair next read the Committee's recommended PA criteria.

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to doxepin (Silenor). Coverage would be approved if the patient met any of the following criteria:

a) Automated PA criteria:

(1) The patient has received a prescription for zolpidem IR at any Military Health Service (MHS) pharmacy point of service (Military Treatment Facilities (MTFs), retail network pharmacies, or home delivery) during the previous 180 days.

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

(1) The patient has tried zolpidem IR and was unable to tolerate treatment due to adverse effects.
(2) The patient has tried zolpidem IR and has had an inadequate response.
(3) The patient has a known contraindication to zolpidem IR.
(4) The patient requires a nonscheduled agent for sleep maintenance.

The Panel vote on the PA criteria was:

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

Panel Comment: The non-concurring members commented that they disagree with the message being sent by placing the non-controlled Silenor after a controlled and potentially abusable substance on the step therapy process over one that is not. One member believes that the Committee should reconsider reversing the step process.

Mr. Hutchings asked whether the Committee had discussed those people who have been on doxitin already and will now be behind the step. Dr. Meade answered that it hadn't been discussed but that it can be when the class is reviewed again.

Ms. Fryar asked if her understanding is correct that this class will be coming up for review again soon. Dr. Meade said it's in process, but he isn't sure which month it will come up in. Ms. Fryar said she trusts that the Panel's comments will be reviewed when the class does come up again.

SILENOR — BAP VOTE ON IMPLEMENTATION PLAN RECOMMENDATION

The Chair read the Committee's implementation plan recommendations.

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 as follows:

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

Panel comment: The non-concurring member explained that her reason is the same: she disagrees with the PA requirement.

NEWLY APPROVED DRUGS

4) NARCOTIC ANALGESICS — HYDROMORPHONE EXTENDED RELEASE (ER) TABLETS (EXALGO)

(PEC Script)

EXALGO — RELATIVE CLINICAL EFFECTIVENESS

(LCDR Ojo) Hydromorphone ER (Exalgo) is a potent opioid agonist that is FDA-approved for the treatment of moderate-to-severe pain in opioid-tolerant patients requiring continuous, around-the-clock opioid analgesia for an extended period of time. Exalgo is classified as a high-potency single analgesic agent in the Narcotic Analgesics drug class, which was reviewed in February 2007.

If you turn to table 5 on page 11 of the handout, you'll see the list of the Narcotic Analgesic drugs. Exalgo falls into the category of a long-acting agent with a duration of action that is more than 12 hours. The utilization of some of the Narcotic Analgesics is found on the next page, in Figure 13. For Figure 13, the highest utilization is with Oxycontin, followed by morphine sulfate tablet, followed by Oxymorphone Hydrochloride Extended Release (Opana ER).

The delivery mechanism for Exalgo allows for once daily dosing of hydromorphone, which offers a convenient regimen for patients as opposed to the four times a day dosing with the IR formulation.

There are no direct comparative clinical trials between Exalgo and the other high- potency extended release narcotic analgesics; however, it is unlikely that there are clinically relevant differences in pain relief if equianalgesic doses are administered. Exalgo's safety and tolerability profile is consistent with the known profile of narcotic analgesics. Exalgo's hard tablet shell makes it difficult to crush and attempts to dissolve the particles result in a viscous substance that is potentially fatal if injected. These features, though unproven, may decrease the abuse liability of the drug.

Relative Clinical Effectiveness Conclusion—Despite the fact that there are several other high-potency controlled-release narcotics available on the UF and BCF (many are available in generic formulations), the P&T Committee concluded (17 for, 0 opposed, 1 abstained, 0 absent) that Exalgo is the only extended-release hydromorphone product on the market. With the exception that Exalgo provides an option for patients who do not respond to or cannot tolerate other high-potency agents, Exalgo does not offer compelling clinical advantages over the other high-potency long-acting narcotic analgesics included on the UF.

Narcotic Analgesics— Hydromorphone ER Tablets (Exalgo) – RELATIVE COST EFFECTIVENESS

(Dave Meade) A CMA was performed that evaluated the cost of Exalgo in relation to other currently available agents in Narcotic Analgesic drug class.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 1 abstained, 0 absent) Exalgo was more costly than the other high-potency narcotic analgesics with sustained-release formulations currently on the UF.

Narcotic Analgesics — Hydromorphone ER Tablets (Exalgo) UNIFORM FORMULARY

RECOMMENDATION

(Dave Meade) Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (10 for, 6 opposed, 2 abstained, 0 absent) hydromorphone ER tablets (Exalgo) be designated formulary on the UF.

UNIFORM FORMULARY IMPLEMENTATION PLAN – NOT APPLICABLE

(Dave Meade): Lt Col Hannah will now give the physician perspective for Exalgo.

EXALGO — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah indicated that this agent was a controversial subject for the P&T Committee in terms of whether to maker it non-formulary or keep it on the formulary. This medication is the only other long-acting once daily narcotic on the market besides morphine. There is concern for abuse. The main reasons for making it non-formulary were: (1) it has a higher cost than the other narcotics; (2) several other alternatives are already available on the UF; and (3) the current special order/medical necessity process at the MTFs would ensure that patients who truly need this drug can get it. The main reasons for not making it non-formulary are: (1) the MTFs use immediate release hydromorphone to break through pain and a patient could easily adjust to an ER hydromorphone tablet; and (2) portability (active duty patients are frequently referred to outside physicians for surgery). Ultimately, the Committee took notes of several different products in the pipeline that will result in a re-review of this class once these new products reach the market.

EXALGO — BAP QUESTIONS AND DISCUSSION

Dr. Casull noted that the product has a higher cost, can be broken down on the street even though that would result in a higher incidence of death because of the way the product is manufactured. He did not hear any discussion of why this product is superior to some of the other currently-available long-acting agents, such as oxycontin generics or oxycodone. Lt Col Hannah said that was discussed and Exalgo is not necessarily more effective. Dr. Casull said since that means we haven't proven it is superior, combined with the other attributes already mentioned, he would vote to non-concur. Dr. Salom said he agrees and for exactly the same reasons. Dr. Casull also stated that the Panel should be educated on the "one-one-one" program and its relevance to the Panel's review and comment on the development of the uniform formulary.

Mr. Hutchings said that he views the inability to break down the drug as a plus, because right now oxycontin has an extremely high street value and hydromorphone is rarely used on the street. He feels inclined to vote in favor of the agent because there is less likelihood of abusing it and if someone does the result is likely to be fatal. Moreover, there are other narcotics out that aren't widely abused. Dr. Casull replied that street use is the major problem with controlled substances, not prescribed controlled substances. It is prevalent across mainstream America. Illicit drug use and drug seeking behavior are two different issues.

Dr. Salom said that the drug will be broken down, even if that is less likely. We will see fatalities from this and that is a reason not to make it a formulary drug. If a practitioner wants to prescribe it and go through the hoops, that's fine.

Dr. Schlaifer said she concurs with Mr. Hutchings. Although her initial reaction was "why?" she said that was the reason why the FDA approved the drug. She views the fact that it is less lethal as being helpful to her as a prescriber.

Mr. Hutchings said if he was looking only at his population of over-65 patients, he would vote to non-concur, but there are already so many barriers that this one isn't going to matter much.

A PEC staff member in the audience said that a wounded soldier in transition (i.e., going home from an MTF) can be prescribed this drug and take it to a pharmacist. If it is non-formulary, the co-pay will be $22. Federal law does not allow the pharmacist to change the prescription over the telephone. A new, hand-written prescription will be required. That put the patient in a bind, especially if he needs the high-potency narcotic. That was something that the P&T considered when they were deliberating.

Dr. Casull asked who was consulted with, naming one individual in particular (Dr. Brown, who works with returning wounded warriors). LTC Spridgen said there are providers on the Committee and others who work with it.

Ms. Fryar asked what types of comments were received from providers on this agent: were they in favor or not in favor. Dr. Meade said that providers are on the Committee but the PEC does not solicit expert opinions regarding wounded warrior care. Dr. Casull commented that when seeking expert opinion on "Wounded Warriors" and controlled substances that only one installation received a "best practice" mention from the 2010 Army Task Force on Pain Management. That was the program run by Dr. Brown at Tripler Army Medical Center.

Ms. Cohoon noted that making a drug non-formulary makes it harder for the MTFs to have it available.

EXALGO — BAP VOTE ON UF RECOMMENDATION

Ms. Fryar then read the Committee's UF recommendation for the hydromorphone ER tablets (Exalgo).

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 hydromorphone ER tablets (Exalgo) be designated formulary on the UF.

The Panel voted as follows:

Concur: 7 Non-concur: 4 Abstain: 0 Absent: 0

Panel comments. The votes to non-concur were based on the fact that it is higher cost, potentially fatal if abused and was not demonstrated to be clinically superior to other drugs in the class.

Chairman Note: Panel members concerns are all valid and should be taken into account when this drug class is reviewed in the near future. Upon hearing panel member concerns about potential problems with this drug class I would ask the P&T to consider reviewing this entire drug class sooner rather than later.

An implementation plan is not required for Exalgo.

NEWLY APPROVED DRUGS

5) ANTILIPIDEMIC-2S (LIP-2S) — FENOFIBRIC ACID (FIBRICOR)

(PEC Script)

ANTILIPIDEMIC-2S (LIP-2S) — FENOFIBRIC ACID (FIBRICOR) — RELATIVE CLINICAL EFFECTIVENESS

(LCDR Ojo) The next new drug we have to discuss is Fibricor. Fibricor is the second fenofibric acid marketed in the United States; Trilipix, the choline salt of fenofibric acid, was marketed first. The fenofibrates are classified in the LIP-2s drug class, which was reviewed in May 2007. The entire LIP-2s drug class (Fibrates, omega-3/fish oil, and bile acid sequestrants) is scheduled for review at the February 2011 P&T Committee meeting.

If you turn to page 13 of the handout and look at table 6, the LIP-2 drugs are listed. Fibricor is subclassified as a fibrate. The utilization is at the bottom of the page, in Figure 14. Tricor has the highest utilization in the MHS.

Fibricor is approved for use as monotherapy to reduce TG levels in patients with severe hypertriglyceridemia (>500 mg/dl). In contrast to Trilipix, Fibricor is not FDA-approved for concomitant use with a statin.

Fibricor obtained FDA approval via section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act using efficacy and safety data submitted from the original fenofibrate nanocrystallized (Tricor) submission. Pharmacokinetic studies comparing Fibricor 105mg with Tricor 145mg demonstrated bioequivalence between the two products. There are no head-to-head clinical trials comparing Fibricor and the other LIP-2s. Fibricor's safety profile reflects that of the other fenofibrate products.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) there is no evidence to suggest a compelling clinical advantage over the fenofibrate products on the UF.

Antilipidemic-2s (LIP-2s)— Fenofibric Acid (Fibricor) RELATIVE COST EFFECTIVENESS

(Dave Meade) A CMA was performed that evaluated the cost of fenofibric acid (Fibricor) in relation to other currently available LIP-2s.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) that fenofibric acid (Fibricor) was more costly than all other comparators in the fenofibrate subclass of LIP-2s, except for Trilipix or Tricor.

Antilipidemic-2s (LIP-2s)— Fenofibric Acid (Fibricor)UNIFORM FORMULARY RECOMMENDATION

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

Antilipidemic-2s (LIP-2s) — Fenofibric Acid (Fibricor) UNIFORM FORMULARY IMPLEMENTATION PLAN

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

(Dave Meade): Lt Col Hannah will now give the physician perspective for Fibricor.

ANTILIPIDEMIC-2S (LIP-2S) — FENOFIBRIC ACID (FIBRICOR) — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah said the Committee viewed Fibicor as just another fibrate similar to Tricor and Trilipix. Tricor's patent is expected to expire in 2012. The subclass will be reviewed in its entirety in February 2011.

ANTILIPIDEMIC-2S (LIP-2S) — FENOFIBRIC ACID (FIBRICOR) — BAP QUESTIONS AND DISCUSSION

The Panel had no questions for the presenters.

ANTILIPIDEMIC-2S (LIP-2S) — FENOFIBRIC ACID (FIBRICOR) — BAP VOTE ON UF RECOMMENDATIONS

The Chair read the Committee's UF recommendation for the antilipidemic-2s (LIP-2s), fenofibric acid (Fibracor).

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 fenofibric acid (Fibricor) be designated NF on the UF.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

ANTILIPIDEMIC-2S (LIP-2S) — FENOFIBRIC ACID (FIBRICOR) — BAP VOTE ON IMPLEMENTATION PLAN RECOMMENDATIONS

Ms. Fryar then read the implementation plan recommendations for Fibricor.

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 or comment, the BAP voted:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

NEWLY APPROVED DRUGS

6) CONTRACEPTIVES — ESTRADIOL VALERATE/DIENOGEST (NATAZIA)

(PEC Script)

CONTRACEPTIVES — ESTRADIOL VALERATE/DIENOGEST (NATAZIA) — RELATIVE CLINICAL EFFECTIVENESS

(LCDR Ojo) The last new drug we have to discuss is a contraceptive agent. Natazia is a combination oral contraceptive containing a new dosage form of estradiol valerate (which was previously only available in an injectable form) and a new progestin (dienogest). It utilizes a 4-phasic active drug regimen with 2 hormone-free days. Estradiol valerate/dienogest is solely indicated for the prevention of pregnancy. It is included in the Contraceptive drug class, which was reviewed in May 2006.

If you turn to page 14 of the handout and look at table 7, the Contraceptive drugs are listed. The utilization is found on the next page, in Figure 15. Yaz has the highest utilization in the MHS, followed by Ortho Tri-Cyclen Lo.

A head-to-head comparison between Natazia and 20 mcg ethinyl estradiol/100 mg levonorgestrel (Lessina, Sronyx equivalent) found significantly fewer days of withdrawal (scheduled) bleeding with Natazia but a similar incidence of intracyclic (unscheduled) bleeding, due to the shorter number of hormone-free days (2 with Natazia versus 7 with the comparator). Spotting or breakthrough bleeding is still common, especially when therapy is first started.

The adverse event profile for Natazia is similar to that of other oral contraceptives. The patient instructions for missed doses are significantly more complicated than those for other oral contraceptives. The purported benefits of 4-phasic contraceptive regimens remain to be established and Natazia's long-term safety remains unknown.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 1 abstained, 1 absent) estradiol valerate/dienogest (Natazia) does not have a significant, clinically

meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over the other oral contraceptives on the UF.

Contraceptives — Estradiol Valerate/Dienogest (Natazia) RELATIVE COST EFFECTIVENESS

(Dave Meade) CMA was performed that evaluated the cost of estradiol valerate/dienogest (Natazia) in the Contraceptive Agents drug class.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) estradiol valerate/dienogest (Natazia) was more costly than all other contraceptive agents on the UF.

Contraceptives — Estradiol Valerate/Dienogest (Natazia) UNIFORM FORMULARY RECOMMENDATION

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

Contraceptives — Estradiol Valerate/Dienogest (Natazia) UNIFORM FORMULARY IMPLEMENTATION PLAN

(Dave Meade) The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 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.

(Dave Meade): Lt Col Hannah will now give the physician perspective for Natazia.

CONTRACEPTIVES — ESTRADIOL VALERATE/DIENOGEST (NATAZIA) — COMMITTEE PHYSICIAN PERSPECTIVE

Lt Col Hannah noted that Natazia is a new contraceptive which utilizing two hormone-free days, which decreases the number of bleeding days. He said this medication has the most complicated instructions of any in the class requiring the patient to be dependent on what day of the cycle the tablet was used. Several other contraceptives are available on the UF.

CONTRACEPTIVES — ESTRADIOL VALERATE/DIENOGEST (NATAZIA) — BAP QUESTIONS AND DISCUSSION

Ms. Cohoon asked how many days or months can patients get this medication in a single refill. Dr. Meade answered up to three months. Ms. Cohoon also asked to verify that the copay will be higher with the drug off the formulary. Dr. Meade said that is correct.

CONTRACEPTIVES — ESTRADIOL VALERATE/DIENOGEST (NATAZIA) — BAP VOTE ON UF RECOMMENDATION

There being no further questions or discussion, the Chair read the P&T Committee's UF recommendation for Natazia.

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 estradiol valerate/dienogest (Natazia) be designated NF on the UF.

The Panel voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

CONTRACEPTIVES — ESTRADIOL VALERATE/DIENOGEST (NATAZIA) — BAP VOTE ON IMPLEMENTATION PLAN RECOMMENDATION

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

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

Without further discussion, the BAP voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

UTILIZATION MANAGEMENT

(PEC Script)

Fentanyl Citrate—Modification of Prior Authorization - Background
(Dave Meade) In August 2007, an automated PA was implemented for transdermal fentanyl (Duragesic, generics) to ensure patients are not opioid-naïve. The dispensing process is stopped with a warning if there is no previous prescription for a high-potency opioid in the pharmacy profile within the past 60 days. This automated PA is available at the retail and mail order points of service. Pharmacists at all points of service have the ability to override the system warning after determining that the patient could be presumed to be opioid-tolerant. Fentanyl transmucosal tablets (Fentora) and lozenges (Actiq, generic) were added to the automated PA in May 2009.

The P&T Committee discussed expanding the fentanyl citrate automated PA to include high-potency opioids with specific labeling that restricts their use to opioid-tolerant patients.

The specific automated PA criteria that will apply to the proposed drugs, as well as all fentanyl prescriptions, is:

- Patient is likely to be opioid-tolerant based on receiving at least one prescription for one of the following strong opioids (fentanyl transdermal, fentanyl transmucosal, morphine,

oxycodone (not including combination products), hydromorphone, methadone, or oxymorphone) during the last 60 days.

After reviewing estimates of the number of utilizers affected by this expanded PA, the P&T Committee agreed to incorporate the high-potency opioids labeled for use in opioid-tolerant patients to the existing fentanyl citrate PA. The impact was estimated to be relatively small compared to the number of current fentanyl utilizers.

Fentanyl Citrate—Modification of Prior Authorization Recommendation

(Dave Meade) To ensure the appropriate use of high-potency opioids in opioid-tolerant patients, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) modifying the fentanyl automated PA and including the following drugs:

- morphine sulfate ER (MS Contin generics 100, 200 mg; Avinza 45, 60, 75, 90, 120 mg; Kadian 100, 200 mg);
- morphine sulfate ER/naltrexone (Embeda 100/4mg);
- fentanyl buccal soluble film (Onsolis 200, 400, 600, 800, 1200 mcg);
- hydromorphone ER (Exalgo 8, 12, 16 mg); and oxycodone ER (Oxycontin 60, 80, 160 mg)

Fentanyl Citrate — Modification of Prior Authorization Implementation
(Dave Meade) The expanded fentanyl PA becomes effective the first Wednesday after a 60-day implementation period in all points of service.

FENTANYL CITRATE — BAP QUESTIONS AND DISCUSSION

Dr. Casull asked if there is a non-automated PA for these agents. Mr. Hutchings explained that this is not a PA, it's a safety warning. The pharmacist at the counter at any POS can override the warning if it can be determined that the patient is opioid-tolerant. Dr. Meade explained the process.

Ms. Fryar asked for clarification as to why the action is labeled a PA if it is more of a safety warning. Specifically, she asked if the language presented here is an actual modification of a Prior Authorization. Dr. Meade replied that the MHS calls it a Prior Authorization because the dispensing process is stopped with a warning if there is no previous prescription for a high-potency opioid in the pharmacy profile within the past 60 days. She suggested it might be wise to put in a caveat with the vote.

FENTANYL CITRATE — BAP VOTE ON PA MODIFICATION

The Chair read the Committee's recommendation regarding the fentanyl citrate PA modification.

To ensure the appropriate use of high-potency opioids in opioid-tolerant patients, the P&T Committee recommended modifying the fentanyl automated PA and including the following drugs:

- morphine sulfate ER (MS Contin generics 100, 200 mg; Avinza 45, 60, 75, 90, 120 mg; Kadian 100, 200 mg);
- morphine sulfate ER/naltrexone (Embeda 100/4mg);
- fentanyl buccal soluble film (Onsolis 200, 400, 600, 800, 1200 mcg);
- hydromorphone ER (Exalgo 8, 12, 16 mg); and oxycodone ER (Oxycontin 60, 80, 160 mg)

The BAP voted as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

Panel comment: Although the Panel voted to concur in the recommendation, it commented that, pursuant to its discussion, that it understands the action is more of a safety recommendation than a true PA and that the pharmacist can override the warning at the POS.

FENTANYL CITRATE — BAP VOTE ON PA MODIFICATION IMPLEMENTATION

The Chair read the implementation plan.

The expanded fentanyl PA becomes effective the first Wednesday after a 60-day implementation period in all points of service.

The BAP vote was:

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

The non-concur vote was based on the need to work out how many patients will be dropping off first.

UTILIZATION MANAGEMENT

(PEC Script)

Fingolimod (Gilenya)—Prior Authorization - Background

(Dave Meade) Fingolimod is an oral disease-modifying agent for multiple sclerosis (MS). It is FDA-approved for treating patients with relapsing forms of MS to reduce the frequency of clinical exacerbations and delay the accumulation of physical disability. Fingolimod is the first oral agent marketed for the treatment of relapsing MS and its cost per month of therapy is considerably more than that of injectable interferon agents on the UF. The fingolimod product labeling states it is not approved for concurrent use with the injectable interferons or glatiramer injection (Copaxone).

Fingolimod (Gilenya)—Prior Authorization Recommendation

(Dave Meade) To ensure the appropriate use of fingolimod is consistent with the product labeling, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) implementing a PA, which will allow use of fingolimod (Gilenya) in patients who met the following criteria:

1. a documented diagnosis for relapsing forms of MS

2. no current use of interferon alpha/beta or Copaxone

Fingolimod (Gilenya)—Prior Authorization Implementation

(Dave Meade) The fingolimod PA becomes effective the first Wednesday after a 60-day implementation period in all points of service.

FINGOLIMOD (GILENYA) — BAP QUESTIONS AND DISCUSSION

Dr. Meade was asked whether this drug is on formulary. He said that now it is but it will come up for review soon.

FINGOLIMOD (GILENYA) — BAP VOTE ON PA

The Chair read the Committee's PA recommendation for fingolimod (Gilenya).

To ensure the appropriate use of fingolimod is consistent with the product labeling, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) implementing a PA, which will allow use of fingolimod (Gilenya) in patients who met the following criteria:

1. a documented diagnosis for relapsing forms of MS

2. no current use of interferon alpha/beta or Copaxone

The BAP voted without comment as follows:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

FINGOLIMOD (GILENYA) — BAP VOTE ON IMPLEMENTATION PLAN

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

The fingolimod PA becomes effective the first Wednesday after a 60-day implementation period in all points of service.

Again the BAP voted without comment:

Concur: 11 Non-concur: 0 Abstain: 0 Absent: 0

CLOSING REMARKS

Dr. Meade announced that the DoD Uniform Formulary will now be available for PDAs and that an official announcement will be made shortly.

LTC Spridgen announced that the next meeting of the BAP is scheduled for 24 March, 2011. The DFO then closed the meeting at 12:30 P.M.

Deborah Fryar

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

Brief Listing of Acronyms Used in This Summary

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

- AE — Adverse event
- AGIs — Alpha-glucosidase inhibitors (a drug subclass)
- APR — Automated Profile Review
- BAP — Uniform Formulary Beneficiary Advisory Panel (the "Panel" referred to above)
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- BP — Blood pressure
- BPA — Blanket Purchase Agreement
- CEA — Cost-effectiveness analysis
- C.F.R — Code of Federal Regulations
- CHD — Coronary heart disease
- CMA — Cost-Minimization Analysis
- COPD — Chronic obstructive pulmonary disorder
- CR — Controlled Release (a drug formulation)
- CV — Cardiovascular
- DACON — Daily average consumption
- DEA — U.S. Drug Enforcement Administration
- DFO — Designated Federal Officer
- DM — Diabetes mellitus
- DoD — Department of Defense
- DPP-4 — Dipeptidyl-peptidase 4 inhibitors (a drug subclass)
- ECF — Extended Core Formulary
- ER — Extended Release (a drug formulation)
- ESI — Express-Scripts, Inc.
- FACA — Federal Advisory Committee Act
- FCP — Federal Ceiling Price
- FDA — U.S. Food and Drug Administration
- FPG — Fasting plasma glucose
- GLP1RAs — Glucagon-like peptides 1 receptor agonists (a drug subclass)
- HbA1c — Glycated hemoglobin
- ICS — Inhaled corticosteroid (a drug class)
- IR — Immediate Release (a drug formulation)

- IV — Intravenous
- LABA — Long-acting beta agonist (a drug class)
- LDL — Low-density lipoprotein
- LIP-1s — Antilipidemic-1s (a drug class)
- LIP-2s — Antilipidemic-2s (a drug class)
- MDI — Metered dose inhaler
- MHS — Military Health System
- MI — Myocardial infarction
- MN — Medical Necessity
- MS — Multiple sclerosis
- MTF — Military Treatment Facility
- NDAA — National Defense Authorization Act
- NF — Non-formulary
- NIH — National Institutes of Health
- NNH — Number Needed to Harm
- NNT — Number Needed to Treat
- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DOD Pharmacy and Therapeutics Committee
- PDTS — Pharmacy Data Transaction Service
- PEC — DOD Pharmacoeconomic Center
- PORT — Pharmacy Outcomes Research Team
- POS — Point of Service
- PPG — Postprandial glucose
- RCTs — Randomized Control Trials
- SED-1s — Newer sedative hypnotic agents (a drug class)
- SR — Sustained release (a drug formulation)
- SQ — Subcutaneously
- SUs — Sulfonylureas (a drug subclass)
- T1DM — Type 1 diabetes mellitus
- 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
- U.S.C. — United States Code
- VA — U.S. Department of Veterans Affairs
- VARR — Voluntary Agreement on Retail Rebates