DOD PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

INFORMATION FOR THE UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL

I. UNIFORM FORMULARY REVIEW PROCESS

Under 10 United States Code § 1074g, as implemented by 32 Code of Federal Regulations (CFR) 199.21, the DoD Pharmacy and Therapeutics (P&T) Committee is responsible for developing the Uniform Formulary (UF). Recommendations to the Director, TMA, on formulary status, pre-authorizations, and the effective date for a drug's change from formulary to non-formulary (NF) status receive comments from the Beneficiary Advisory Panel (BAP), which must be reviewed by the Director before making a final decision.

II. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. Non-insulin Diabetes Drug Class—Background

Background Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the drugs in the Non-insulin Diabetes drug class.

The class is comprised of the following 8 subclasses: dipeptidyl-peptidase 4 (DPP-4) inhibitors, glucagon-like peptide-1 receptor agonists (GLP1RAs), biguanides (metformin), thiazolidinediones (TZDs), sulfonylureas (SUs), meglitinides, alpha-glucosidase inhibitors (AGIs), and amylin agonists (pramlintide; Symlin), and their FDC products with metformin or SU. 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), amlyin agonists ($3 million), and AGIs ($800,000).

In terms of MHS utilization, the biguanides are the most utilized (approximately 225,000 30-day equivalent prescriptions (Rxs) dispensed monthly), followed by the SUs (160,000 30-day equivalent Rxs), TZDs (100,000 30-day equivalent Rxs), and DPP-4 inhibitors (60,000 30-day equivalent Rxs); the GLP1RAs, meglitinides, AGIs, and amylin agonists each account for less than 10,000 30-day equivalent Rxs dispensed monthly.

American Diabetes Association (ADA) Guidelines (Diabetes Care, 2009, 32:193-203) recommend metformin, in addition to lifestyle modification, as first-line therapy for Type 2 Diabetes Mellitus (T2DM) and is considered in tier 1 (well-validated therapy). SUs or basal insulin are recommended next in the hierarchy (second-line, tier one). Tier two or less well-validated therapies include the TZDs and GLP1RAs. No recommendation is made for DPP-4 inhibitors, but the algorithm is updated annually in January.

A request for MHS providers' opinions solicited over 440 responses. When asked which subclass was most appropriate for first-line therapy for T2DM, over 98% of the responders selected metformin, followed by the SUs (62% of responders), TZDs (39%), DPP-4 inhibitors (36%), and GLP1RAs (23%).

Based on recommendations from the current ADA guidelines (metformin first-line, followed by SUs as tier one, well-validated therapies for T2DM) and the MHS providers' responses, an automated PA/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).

An analysis by the DoD Pharmacy Outcomes Research Team (PORT) estimated that approximately 102,000 new users of diabetes medications are expected annually across all points of service in the MHS. For the DPP-4 inhibitors, an estimated 35,364 new users are expected each year; 17% of the new users may start first-line on a DPP-4 inhibitor, and are not expected to have had a prior prescription for metformin or a SU. There are 12,024 estimated new users for the GLP1RAs; 10% are anticipated to have no prior prescription for metformin or a SU.

Background Relative Cost Effectiveness—Cost-effectiveness analysis (CEA) was conducted to provide an overall assessment of the relative cost-effectiveness among the subclasses used for second-line therapy (when added to metformin.

Relative Cost Effectiveness Conclusion—For subclasses added as second-line therapy to metformin, the SU subclass were considered to be dominant (e.g., providing the largest reduction in HbA1c at the lowest cost), in terms of cost per HbA1c reduction. GLP1RAs and TZDs were more expensive therapies than the SUs with relatively little difference in HbA1c efficacy. The DPP-4 inhibitors were similar in efficacy to the SUs but were less cost effective.

B. Biguanides—Relative Clinical Effectiveness

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of Biguanides subclass. Metformin is the only biguanide drug currently on the market. The Biguanides subclass has not previously been reviewed; all the drugs are currently designated with formulary status on the UF.

The individual metformin formulations are:

- **Metformin IR:** 500 mg, 850 mg, 1000 mg tablets (Glucophage, generics); 500 mg/5 ml liquid (Riomet)
- **Metformin ER:** 500 mg, 750 mg (Glucophage XL, generics); 500 mg, 1000 mg (Fortamet); and 500 mg, 1000 mg (Glumetza)

Metformin 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. With regard to efficacy, the results of one large prospective sub-study of the United Kingdom Prospective Diabetes Study (UKPDS) reported beneficial effects of metformin on improving clinical outcomes, including a risk reduction for diabetes-related death and all-cause mortality, when compared to dietary modification.
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.

C. Biguanides—Relative Cost-Effectiveness

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the Biguanides subclass. Metformin and metformin combination products were evaluated with the parent compound (e.g., Janumet (sitagliptan/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 were more cost-effective than Fortamet and Glumetza.

D. Biguanides—Uniform Formulary Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (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 (500 mg/5 ml) remain formulary on the UF;
2. Fortamet (500mg, 1000 mg) and Glumetza (500 mg, 1000 mg) be designated NF on the UF.

E. Biguanides—Uniform Formulary Implementation Plan

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.

III. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. Biguanides—Uniform Formulary Recommendation

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

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Biguanides—Uniform Formulary Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

IV. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. SUs—Relative Clinical Effectiveness

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the SUs subclass. The sulfonylurea agents have not previously been reviewed; all the drugs are currently designated with formulary status on the UF. All the SU products are available in generic formulations. In the MHS, glipizide is the highest utilized sulfonylurea agent.

The individual SUs agents are:

- **First generation :** chlorpropamide (Diabinese, generic)

- **Second generation:** glimepiride (Amaryl, generic), glipizide (Glucotrol, generic), glipizide ER (Glucotrol XL, generic), glyburide (Diabeta, Micronase, generic), glyburide, micronized (Glynase Press Tab, generic)
- **Combination products:** glipizide/metformin (Metaglip, generic), glyburide/metformin (Glucovance, generic)

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. In a UKPDS sub-study, patients receiving a SU or insulin had a lower risk of developing any diabetes-related endpoint and microvascular endpoints than patients receiving dietary modification. Diabetes-related mortality and all-cause mortality did not differ between the two groups.
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.
6. With regard to special populations, glyburide crosses the placenta in minimal amounts. In one retrospective review of more than 500 women with gestational diabetes, glyburide treatment resulted in achievement of target HbA1c.

B. SUs—Relative Cost-Effectiveness

Relative Cost-Effectiveness—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. 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 agents in the SUs subclass were cost-effective.

C. SUs—Uniform Formulary Recommendation

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

a) 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)

D. SUs—Uniform Formulary Implementation Plan: Not Applicable

V. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. SUs—Uniform Formulary Recommendation

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

a) 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)

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. SUs—Uniform Formulary Implementation Plan: Not Applicable

VI. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. DPP-4 Inhibitors—Relative Clinical Effectiveness

Relative Clinical Effectiveness—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). A FDC product saxagliptin/metformin ER (Kombiglyze XR) recently received FDA approval and will be reviewed an upcoming meeting. The DPP-4 inhibitors have not previously been reviewed.

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; 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 CV outcomes, although 2 studies are under way.
3. Monotherapy with sitagliptin 100mg daily reduced HbA1c on average by 0.6%–0.79%; whereas, saxagliptin monotherapy reduced HbA1c approximately 0.4%–0.7%. Adding sitagliptin to metformin or pioglitazone (Actos) reduced HbA1c 0.5%–0.9%. The FDC sitagliptin 50mg plus metformin 1000mg (Janumet) given twice daily reduced HbA1c by 1.9% from baseline.
4. There is one published head-to-head non-inferiority trial evaluating glycemic control between the two DPP-4 inhibitors when added to stable metformin therapy. Sitagliptin lowered HbA1c by approximately 0.1% more from baseline than saxagliptin. Saxagliptin was considered non-inferior to sitagliptin. While statistical significance was achieved, the difference between the two agents is not clinically significant.

5. When used as monotherapy or when combined with metformin, DPP-4 inhibitors may provide weight loss; typically less than -0.7 kg from baseline with sitagliptin and metformin and -1.8 kg from baseline with saxagliptin and metformin. When the DPP-4s are combined with SUs or TZDs, weight gain may occur, which is a known adverse effect of the SUs and TZDs subclasses. Therefore, DPP-4 inhibitors are generally considered to be weight-neutral.
6. Effects on lipid parameters were assessed in some but not all studies with the DPP-4 inhibitors. Most studies showed minor improvements in lipid parameters. Therefore, DPP-4 inhibitors are generally considered to have neutral effects on lipids.
7. In terms of commonly reported adverse events, there are no clinically relevant differences between sitagliptin and saxagliptin. Drug interaction profiles are also similar between agents.
8. 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 sitagliptin, but sitagliptin has a longer marketing history than saxagliptin.
9. 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 sitagliptin or saxagliptin, but acknowledged more familiarity with sitagliptin.
10. There is a high degree of therapeutic interchangeability between sitagliptin and saxagliptin.

B. DPP-4 Inhibitors—Relative Cost-Effectiveness

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 FDCs 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.

C. DPP-4 Inhibitors—Uniform Formulary Recommendation

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

D. DPP-4 Inhibitors—Prior Authorization Criteria

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.

E. DPP-4 Inhibitors—Uniform Formulary and Prior Authorization Implementation Plan

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.

VII. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. DPP-4 Inhibitors—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. DPP-4 Inhibitors—Prior Authorization Criteria

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.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. DPP-4 Inhibitors—Uniform Formulary and Prior Authorization Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

VIII. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. GLP1RAs—Relative Clinical Effectiveness

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the GLP1RAs subclass. The GLP1RAs subclass includes exenatide (Byetta) injection and liraglutide (Victoza) injection. The GLP1RAs have not previously been reviewed. Prior authorization currently applies to the class, which excludes off-label use of the drugs for obesity in patients who do not have DM.

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 exenatide and liraglutide 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. Exenatide is dosed twice daily with meals, whereas liraglutide 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: the EXSCEL trial (using an investigational formulation of exenatide dosed once weekly), and the LEADER trial (with liraglutide). Results are expected in 2016–2017.
5. GLP1RAs offer another option for add-on therapy when oral agents (e.g., metformin, SUs, TZDs) no longer provide adequate glycemic control. When combined with metformin, SU, or both metformin and SU, exenatide 10mcg twice daily lowered HbA1c 0.77%–0.86% from baseline. Liraglutide 1.8mg once daily, when combined with metformin and SU, lowered HbA1c 1.3% from baseline.
6. Both exenatide and liraglutide improve fasting plasma glucose (FPG) and postprandial glucose (PPG) concentrations; however, liraglutide has a greater effect on lowering FPG than PPG due to its longer duration of action. In contrast, exenatide has a greater effect on PPG than FPG.
7. Exenatide and liraglutide have been compared to insulin glargine (Lantus); both trials were non-inferiority in design. GLP1RAs offer no clinically significant reduction in HbA1c compared to basal insulin.
8. LEAD-6 is the only head-to-head trial between exenatide and liraglutide. Using the maximum doses of each agent, liraglutide showed a greater decrease in HbA1c compared to exenatide (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 liraglutide.

9. The relationship between weight loss and HbA1C was assessed in the LEAD-6 trial. The difference in HbA1C reduction between patients with and without weight loss was not statistically significant. Patients using a GLP1RA as monotherapy, or in combination with metformin, can expect a 2 kg to 3 kg weight loss.
10. Lipid parameters improved or remained neutral in the exenatide and liraglutide trials; changes in the lipid levels were not statistically significant.
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 exenatide, and rare pancreatitis with both exenatide and liraglutide. Both agents may cause formation of antibodies to the GLP1RA. Liraglutide has a black box warning for risk of developing thyroid C-cell tumors and is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2.
13. Both agents are available in prefilled pen devices. Exenatide requires two different pens to titrate patients to the target 10mcg twice daily dose. Conversely, all three doses of liraglutide 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. Providers had little to no experience with liraglutide; however, 63% were willing to prescribe the drug if efficacy and cost were similar to exenatide.
15. With the exception that liraglutide offers patient convenience of a decreased dosing frequency compared to exenatide (daily versus twice daily, respectively), and that liraglutide targets FPG while exenatide 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.

B. GLP1RAs—Relative Cost-Effectiveness

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

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 (liraglutide) patients require 2 or 3 pens per 30 days of therapy. Byetta (exenatide) patients only require 1 pen for 30 days of therapy. From a perspective examining cost-per-day of therapy, Byetta (exenatide) is significantly less costly than Victoza (liraglutide). The scenario where Byetta (exenatide) was step-preferred on the UF while Victoza (liraglutide) 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 (liraglutide) prescription. Sensitivity analysis results showed that market share gains by Victoza (liraglutide) will result in additional costs to the MHS.

C. GLP1RAs—Uniform Formulary Recommendation

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

D. GLP1RAs—Prior Authorization 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 (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):

b) Automated PA criteria:

(1) 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.

c) 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).

E. GLP1RAs—Uniform Formulary and Prior Authorization Implementation Plan

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.

IX. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. GLP1RAs—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. GLP1RAs—Prior Authorization 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):

b) Automated PA criteria:

(1) 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.

c) 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).

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. GLP1RAs—Uniform Formulary and Prior Authorization Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

X. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. TZDs—Relative Clinical Effectiveness

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the TZDs subclass. The subclass is comprised of rosiglitazone and pioglitazone, and FDC products with metformin or SU. The individual TZDs are:

- **Rosiglitazone drugs:** rosiglitazone (Avandia), rosiglitazone/metformin (Avandamet), rosiglitazone/glimepiride (Avandaryl)
- **Pioglitazone drugs:** pioglitazone (Actos), pioglitazone/metformin (Actoplus Met), pioglitazone/metformin ER (Actoplus Met XR), pioglitazone/glimepiride (Duetact)

None of the TZDs are available in generic formulations; the patent for pioglitazone is expected to expire in 2012.

The TZDs were reviewed previously for UF placement. Currently all the TZDs are designated formulary on the UF.

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 pioglitazone (but not rosiglitazone) as a step 2, tier 2, (less well-validated) therapy for the treatment of T2DM.
2. Based on meta-analyses and head-to-head trials, rosiglitazone and pioglitazone at maximal doses reduce HbA1c by 0.6% to 1.6%. The differences between the two drugs for HbA1C reduction are not clinically relevant, when used as monotherapy or when combined with metformin, SUs, or insulin.
3. Outcomes studies are available with the TZDs. Pioglitazone in the PROactive trial resulted in a statistically significant reduction in the composite endpoint, including all-cause mortality, non-fatal myocardial infarction (MI) (including silent MI), stroke, and above the knee major leg amputation. In contrast, there is no direct evidence that rosiglitazone prevents vascular events in patients with T2DM.
4. The TZDs differ in their effects on the lipid profile. Pioglitazone has a less unfavorable effect on lipid parameters than rosiglitazone.

5. Safety and tolerability profiles are similar between rosiglitazone and pioglitazone in terms of incidence of heart failure, weight gain, edema, and hypoglycemia.
6. Rosiglitazone is associated with an increase in adverse CV events that is not seen with pioglitazone, based on results of meta-analyses, an open label, non-inferiority trial (RECORD), and a retrospective study using the Medicare database (Graham, JAMA 2010). The rosiglitazone product labeling includes a black box warning regarding increased risk of MI.
7. The FDA has allowed rosiglitazone to remain on the U.S. market, but the manufacturer must develop a restricted access program under a Risk Evaluation and Mitigation Strategy (REMS) with measures limiting rosiglitazone use to patients unable to attain glycemic control with other drugs. An ongoing head-to-head trial (TIDE) comparing CV events between rosiglitazone and pioglitazone has been halted. In Europe, rosiglitazone has been removed from the market.
8. The FDA released a safety communication regarding a potential increase in risk of bladder cancer with pioglitazone. Studies are ongoing to further assess this risk.
9. The DoD PORT analyzed the effects of discontinuing TZDs and switching between pioglitazone and rosiglitazone. Observations from the analysis suggest that TZDs were discontinued, rather than substituted with another non-insulin diabetes drug subclass or insulin. Of the 24,683 patients total who received rosiglitazone in the analysis timeframe, 73% of these patients continued with rosiglitazone, 8% switched to pioglitazone, 13% received (or continued to receive) other diabetes medications, but not TZDs, and 6% did not fill a Rx for any diabetes medication (including insulin). Changes in utilization patterns are likely to accelerate with implementation of the REMS program for rosiglitazone.
10. The PORT also commented on trends that show a sharp decrease in use of rosiglitazone and an overall decrease in TZD use. New users of rosiglitazone fell from 274 during June 2010 to 34 during October 2010, MHS-wide. New users of pioglitazone also decreased month-by-month, with 2,202 new users in June 2010 compared to 1,372 during October 2010.
11. Results from a request for MHS providers' input showed that 69% of responders would prefer pioglitazone over rosiglitazone; 75% of the responders stated a TZD/metformin FDC product was not required on the UF.
12. In terms of glycemic control, there is a high degree of therapeutic interchangeability between rosiglitazone and pioglitazone. However, there is a lower degree of therapeutic interchangeability with regard to safety profiles.

B. TZDs—Relative Cost-Effectiveness

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

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 FDCs [rosiglitazone (Avandia), rosiglitazone/ metformin (Avandamet), and rosiglitazone/glimepiride (Avandaryl)] are more cost-effective than pioglitazone and pioglitazone FDCs [pioglitazone (Actos), pioglitazone/metformin (Actoplus Met, Actoplus Met RX), and pioglitazone/glimepiride (Avandaryl)]. Additionally, increased safety concerns for rosiglitazone and rosiglitazone FDCs outweigh their apparent cost efficiency.

C. TZDs—Uniform Formulary Recommendation

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

a) pioglitazone (Actos), pioglitazone/metformin (Actoplus Met, Actoplus Met RX), 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.

D. TZDs—Prior Authorization Criteria

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.

E. TZDs—Uniform Formulary and Prior Authorization Implementation Plan

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.

XI. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. TZDs—Uniform Formulary Recommendation

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

a) pioglitazone (Actos), pioglitazone/metformin (Actoplus Met, Actoplus Met RX), 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.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. TZDs—Prior Authorization Criteria

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.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. TZDs—Uniform Formulary and Prior Authorization Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XII. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. Meglitinides—Relative Clinical Effectiveness

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the Meglitinides subclass. The subclass includes nateglinide (Starlix, generic), repaglinide (Prandin), and the FDC product repaglinide/metformin (Prandimet). The Meglitinides subclass has not previously been reviewed. Repaglinide has the highest MHS utilization in this subclass.

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 repaglinide (Prandin), 0.2% to 0.6% with nateglinide, and 1.4% with repaglinide/metformin (Prandimet).
3. In a systematic review by the Cochrane group, repaglinide and nateglinide both reduced HBA1c >0.5% versus placebo (range for nateglinide 0.2%–0.6%; range for repaglinide 0.1%–2.1%).
4. In terms of adverse events, nateglinide and repaglinide can cause hypoglycemia; assistance is rarely required. In the Cochrane systematic review, weight gain ranging from 0.7 kg to 2.1 kg occurred with both agents.
5. In terms of efficacy or safety/tolerability, there were no clinically relevant differences between nateglinide and repaglinide overall.

B. Meglitinides—Relative Cost-Effectiveness

Relative Cost-Effectiveness—The 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.

C. Meglitinides—Uniform Formulary Recommendation

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

D. Meglitinides—Uniform Formulary Implementation Plan: Not Applicable

XIII. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. Meglitinides—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Meglitinides—Uniform Formulary Implementation Plan: Not Applicable

XIV. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. AGIs—Relative Clinical Effectiveness

Relative Clinical Effectiveness—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 AGIs have not previously been reviewed. The subclass has very low utilization in the MHS.

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.

B. AGIs—Relative Cost-Effectiveness

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

C. AGIs—Uniform Formulary Recommendation

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

D. AGIs—Uniform Formulary Implementation Plan: Not Applicable

XV. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. AGIs—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. AGIs—Uniform Formulary Implementation Plan: Not Applicable

XVI. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. Amylin Agonists (Pramlintide)—Relative Clinical Effectiveness

Relative Clinical Effectiveness—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. Pramlintide has not previously been reviewed; it is currently designated with formulary status on the UF. Due to safety concerns, a PA was implemented in 2005 to ensure appropriate dosing of pramlintide, 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 pramlintide.
2. Pramlintide is indicated as adjunctive therapy for the treatment of Type 1 diabetes (T1DM) and T2DM when patients are inadequately controlled on intensive insulin regimens (e.g., bolus insulin doses with meals). Off-label uses of pramlintide include weight loss in patients without DM; weight loss is not a benefit covered by TRICARE.
3. Patients with T1DM showed an average decrease in HbA1c from baseline ranging from -0.1% to -0.39% with pramlintide compared to -0.12% to +0.09% with placebo. In patients withT2DM, the average change in HbA1c ranged from -0.3% to -0.62% with pramlintide versus -0.15% to -0.25% with placebo.
4. There are no outcomes studies with pramlintide.
5. Pramlintide causes weight loss. Mean weight loss with pramlintide ranged from -1.0 kg to -2.3 kg in patients with T1DM compared to a weight gain of 0.3 kg with placebo.
6. Pramlintide is available in multi-dose vials and a prefilled pen device. Because the product is dosed in mcg, dosing errors are a concern when vials are used but drawn up in insulin syringes marked with units. The prefilled pen device includes a dial-a-dose feature which decreases the risk of dosing errors.
7. Results from a request for providers' input showed over 90% of respondents do not prescribe pramlintide.
8. Pramlintide 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 pramlintide 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.

B. Amylin Agonists (Pramlintide)—Relative Cost-Effectiveness

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

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.

C. Amylin Agonists (Pramlintide)—Uniform Formulary Recommendation

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

D. Amylin Agonists (Pramlintide)—Prior Authorization Criteria

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.

E. Amylin Agonists (Pramlintide)—Prior Authorization Implementation Plan

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. The effective date is Mo Day, 2011.

XVII. UNIFORM FORMULARY CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. Amylin Agonists (Pramlintide)—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Amylin Agonists (Pramlintide)—Prior Authorization Criteria

The P&T Committee recommended 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.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. Amylin Agonists (Pramlintide)—Uniform Formulary and Prior Authorization Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XVIII. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—INHALED CORTICOSTEROID (ICS)/LONG-ACTING BETA AGONIST (LABA)

P&T Comments

A. Mometasone/formoterol Oral Inhaler (Dulera)—Relative Clinical Effectiveness

Relative Clinical Effectiveness—Dulera is a fixed-dose combination (FDC) product containing the ICS mometasone (Asmanex) and the LABA formoterol (Foradil) in an oral metered-dose inhaler (MDI). It represents the third FDA-approved ICS/LABA combination inhaler. The Pulmonary 1 class, which includes the ICS/LABA combinations, was reviewed at the February 2009 P&T Committee meeting.

Dulera is FDA-approved for treating patients older than 12 years with moderate-to- persistent asthma who are not controlled on moderate-to-high dose ICS. Advair is approved for treating asthma in patients older than 4 years, and is also approved for treating chronic obstructive pulmonary (COPD). All three ICS/LABA products (Advair, Symbicort and Dulera) have dose counters.

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.

The mometasone component of Dulera is available on the Basic Core Formulary (BCF) as a single inhaler (Asmanex). For patients who are receiving mometasone and require step-up/step-down therapy to or from a combination ICS/LABA inhaler, maintaining Dulera on the UF allows this population an option to return to their initial ICS.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (18 for, 0 opposed, 0 abstained) mometasone/formoterol (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.

B. Mometasone/formoterol Oral Inhaler (Dulera)—Relative Cost-Effectiveness

CMA was performed to evaluate the cost of mometasone/formoterol (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) mometasone/formoterol (Dulera) was less costly than the other ICS/LABA combination agents on the UF.

C. Mometasone/formoterol Oral Inhaler (Dulera)—Uniform Formulary Recommendation

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

D. Mometasone/formoterol Oral Inhaler (Dulera)—Uniform Formulary Implementation Plan: Not Applicable

XIX. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—INHALED CORTICOSTEROID (ICS)/LONG-ACTING BETA AGONIST (LABA)

BAP Comments

C. Mometasone/formoterol Oral Inhaler (Dulera)—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

D. Mometasone/formoterol Oral Inhaler (Dulera)—Uniform Formulary Implementation Plan: Not Applicable

XX. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—ANTILIPIDEMIC-1s (LIP-1s)

P&T Comments

A. Pitavastatin (Livalo)—Relative Clinical Effectiveness

Relative Clinical Effectiveness—Pitavastatin (Livalo) is the seventh statin to reach the U.S. market. At the maximum 4 mg dose, 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.

There are no published or planned studies evaluating clinical outcomes with pitavastatin (e.g., mortality, cardiovascular (CV) events, acute coronary syndromes, etc.). Short-term clinical trials lasting less than 12 weeks show efficacy comparable to other low-to-moderate dose statins (those that lower LDL <45%) for lowering LDL and triglyceride (TG), and raising high-density lipoprotein (HDL).

Livalo's safety profile appears similar to the other statins but more long-term safety data is required. Pitavastatin undergoes minimal CYP 450 metabolism and is similar to pravastatin and rosuvastatin, but has a more favorable drug interaction profile than simvastatin. However, pitavastatin 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.

B. Pitavastatin (Livalo)—Relative Cost-Effectiveness

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.

C. Pitavastatin (Livalo)—Uniform Formulary Recommendation

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

D. Pitavastatin (Livalo)—Prior Authorization Criteria

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.

E. Pitavastatin (Livalo)—Uniform Formulary and Prior Authorization Implementation Plan

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.

XXI. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—ANTILIPIDEMIC-1s (LIP-1s)

BAP Comments

A. Pitavastatin (Livalo)——Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Pitavastatin (Livalo)—Prior Authorization Criteria

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.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. Pitavastatin (Livalo)—Uniform Formulary and Prior Authorization Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XXII. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—NEWER SEDATIVE HYPNOTIC AGENTS (SED-1s)

P&T Comments

A. Doxepin Tablets (Silenor)—Relative Clinical Effectiveness

Relative Clinical Effectiveness—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 (Ambien, generic). Automated Prior Authorization (PA)/step-therapy applies to this class: a trial of zolpidem immediate release (IR) prior to use of the other drugs in the class is required. Eszopiclone (Lunesta) is designated with formulary status on the UF; the other SED-1s are nonformulary (NF); zolpidem controlled release (Ambien CR), zaleplon (Sonata), and ramelteon (Rozerem).

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).

There are no head-to-head trials with the other SED-1s. Silenor's adverse event profile and discontinuation rate were similar to placebo. There were no reports of aberrant sleep behaviors, increased suicidality, or amnesia that has been noted with the other UF agents. However, a patient medication guide is dispensed with each prescription that details risk of these events.

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.

B. Doxepin Tablets (Silenor)—Relative Cost-Effectiveness

Relative Cost-Effectiveness—The P&T Committee evaluated the cost of doxepin (Silenor) in relation to the other available newer sedative hypnotics in this drug class. CMA was 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) doxepin tablets (Silenor) was less costly than the other sleep maintenance agents included on the UF.

C. Doxepin Tablets (Silenor)—Uniform Formulary Recommendation

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

D. 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.

E. Doxepin Tablets (Silenor)—Prior Authorization Implementation Plan

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.

XXIII. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—NEWER SEDATIVE HYPNOTIC AGENTS (SED-1s)

BAP Comments

A. Doxepin Tablets (Silenor)—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Doxepin Tablets (Silenor)—Prior Authorization Criteria

The P&T Committee recommended 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.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. Doxepin Tablets (Silenor)—Uniform Formulary and Prior Authorization Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XXIV. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—NARCOTIC ANALGESICS

P&T Comments

A. Hydromorphone Hydrochloride (HCl) Extended Release (ER) Tablets (Exalgo)—Relative Clinical Effectiveness

Relative Clinical Effectiveness—Hydromorphone HCl 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. Exalgo utilizes the osmotic controlled release oral delivery system (OROS) to confer its extended release properties. The delivery mechanism 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. The OROS formulation does not appear to potentiate the known gastrointestinal (GI) effects of hydromorphone (constipation, nausea, and vomiting). 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.

B. Hydromorphone Hydrochloride (HCl) Extended Release (ER) Tablets (Exalgo)—Relative Cost-Effectiveness

Relative Cost-Effectiveness— A CMA was performed that evaluated the cost of hydromorphone HCl ER (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) hydromorphone HCl ER (Exalgo) was more costly than the other high-potency narcotic analgesics with sustained-release formulations currently on the UF. Exalgo is still a necessary agent because it is the only currently marketed extended-release formulation of hydromorphone HCl in the United States.

C. Hydromorphone Hydrochloride (HCl) Extended Release (ER) Tablets (Exalgo)—Uniform Formulary Recommendation

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

D. Hydromorphone Hydrochloride (HCl) Extended Release (ER) Tablets (Exalgo)—Uniform Formulary Implementation Plan: Not Applicable

XXV. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—NARCOTIC ANALGESICS

BAP Comments

A. Hydromorphone Hydrochloride (HCl) Extended Release (ER) Tablets (Exalgo)—Uniform Formulary Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended hydromorphone HCl ER (Exalgo) be designated formulary on the UF.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Hydromorphone Hydrochloride (HCl) Extended Release (ER) Tablets (Exalgo)—Uniform Formulary Implementation Plan: Not Applicable

XXVI. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—ANTILIPIDEMIC-2s (LIP-2s)

P&T Comments

A. Fenofibric Acid (Fibricor)—Relative Clinical Effectiveness

Relative Clinical Effectiveness—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 (fenofibrates, omega-3/fish oil, and bile acid sequestrants) is scheduled for review at the February 2011 P&T Committee meeting.

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.

B. Fenofibric Acid (Fibricor)—Relative Cost-Effectiveness

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.

C. Fenofibric Acid (Fibricor)—Uniform Formulary Recommendation

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

D. Fenofibric Acid (Fibricor)—Uniform Formulary Implementation Plan

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

XXVII. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—ANTILIPIDEMIC-2s (LIP-2s)

BAP Comments

A. Fenofibric Acid (Fibricor)—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Fenofibric Acid (Fibricor)—Uniform Formulary Implementation Plan

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

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissentions:

XXVIII. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—CONTRACEPTIVES

P&T Comments

A. Estradiol Valerate/Dienogest (Natazia)—Relative Clinical Effectiveness

Relative Clinical Effectiveness—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 Agents drug class, which was reviewed in May 2006.

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.

B. Estradiol Valerate/Dienogest (Natazia)—Relative Cost-Effectiveness

Relative Cost-Effectiveness— 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.

C. Estradiol Valerate/Dienogest (Natazia)—Uniform Formulary Recommendation

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

D. Estradiol Valerate/Dienogest (Natazia)—Uniform Formulary Implementation Plan

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.

XXIX. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—CONTRACEPTIVES

BAP Comments

A. Estradiol Valerate/Dienogest (Natazia)—Uniform Formulary Recommendation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Estradiol Valerate/Dienogest (Natazia)—Uniform Formulary Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XXX. UTILIZATION MANAGEMENT—MODIFICATION OF PRIOR AUTHORIZATION FOR FENTANYL CITRATE

P&T Comments

A. Fentanyl Citrate—Modification of Prior Authorization

In August 2007, an automated PA was implemented for transdermal fentanyl 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.

B. Fentanyl Citrate—Modification of Prior Authorization Recommendation

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)

C. Fentanyl Citrate—Modification of Prior Authorization Implementation

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

XXXI. UTILIZATION MANAGEMENT—MODIFICATION OF PRIOR AUTHORIZATION FOR FENTANYL CITRATE

BAP Comments

A. Fentanyl Citrate—Modification of Prior Authorization Recommendation

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)

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. Fentanyl Citrate—Modification of Prior Authorization Implementation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XXXII. UTILIZATION MANAGEMENT—FINGOLIMOD (GILENYA) PRIOR AUTHORIZATION

P&T Comments

A. Fingolimod (Gilenya)—Prior Authorization

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).

B. Fingolimod (Gilenya)—Prior Authorization Recommendation

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

C. Fingolimod (Gilenya)—Prior Authorization Implementation

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

XXXIII. UTILIZATION MANAGEMENT—FINGOLIMOD (GILENYA) PRIOR AUTHORIZATION

BAP Comments

A. Fingolimod (Gilenya)—Prior Authorization Recommendation

To ensure the appropriate use of fingolimod is consistent with the product labeling, the P&T Committee recommended 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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. Fingolimod (Gilenya)—Prior Authorization Implementation

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions: