DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS
February 2010

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on February 17, 2010, and February 18, 2010, at the DoD Pharmacoeconomic Center (PEC), Fort Sam Houston, Texas.

II. ATTENDANCE

The attendance roster is found in Appendix A.

A. Review Minutes of Last Meetings

1. **Approval of February minutes**—Allen W. Middleton, Acting Director, approved the minutes of the November 2009 DoD P&T Committee meeting on February 3, 2010.
2. **Corrections to August minutes**—The P&T Committee clarified that the Prior Authorization (PA) for Phosphodiesterase-5 (PDE-5) inhibitors for erectile dysfunction is not subject to a one-year expiration. Minutes from the May 2005 and August 2009 P&T Committee meetings revealed a discrepancy that required corrective action.
   a) ***COMMITTEE ACTION***—The P&T Committee voted (15 for, 0 opposed, 1 abstained, 0 absent) that the PA for the PDE-5 inhibitors is not subject to the one-year expiration.

   Acting Director, TMA, Decision: ■ Approved □ Disapproved

   Approved, but modified as follows:

III. REVIEW OF RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS

A. Narcotic Analgesics—Morphine sulfate extended release (ER)/naltrexone capsules (Embeda)

Relative Clinical Effectiveness—Embeda is the first abuse-deterrent formulation of morphine to reach the market. Each capsule contains round pellets of morphine sulfate ER that surround a naltrexone core. Morphine sulfate ER/naltrexone is a Schedule II controlled substance and is classified as a high-potency single analgesic agent in the narcotic analgesic drug class, which was last reviewed in February 2007. Embeda is

indicated for the treatment of moderate to severe pain in adults when continuous, around-the-clock analgesia is required for an extended period of time.

Morphine is a pure opioid agonist selective for the mu receptor, while naltrexone is a mu antagonist that reverses the effects of the mu agonists. When the capsules are taken whole as directed, the morphine provides analgesia with no clinical effects from the naltrexone. Attempts to tamper with the pellets either by crushing or dissolving will cause a rapid release and absorption of the naltrexone, antagonizing the effects of the morphine released.

The unpublished trial used to gain FDA approval reported that Embeda was superior to placebo in relieving pain in patients with osteoarthritis. A study in recreational opioid users reported reduced drug liking for crushed Embeda capsules and whole Embeda capsules, when compared to immediate release morphine solution. The clinical significance of reduction in drug liking is unknown. The product labeling states, "There is no evidence that the naltrexone in Embeda reduces the abuse liability of Embeda." There are no other abuse deterrent opioids on the market, though several are currently in development.

The safety profile for Embeda reflects that of other morphine sulfate ER products and narcotic analgesics on the Uniform Formulary (UF). Crushing, chewing or dissolving pellets can cause fatal release of morphine or precipitate withdrawal in opioid-tolerant individuals.

The clinical evaluation for Embeda included, but was not limited to, requirements stated in 32 Code of Federal Regulations (CFR) 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) there was a potential benefit, though not yet proven, that morphine sulfate ER/naltrexone (Embeda) has a blunted drug-liking response, compared to other UF high-potency narcotic analgesics.

Relative Cost-Effectiveness—The P&T Committee evaluated the costs of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the other currently available narcotic analgesics. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Cost minimization analysis (CMA) was used to evaluate the relative cost-effectiveness of the agent. Results from the CMA showed the projected weighted average cost per day for Embeda is higher than the other formulary narcotic analgesics, including transdermal fentanyl, morphine sulfate ER (Avinza and MS Contin), oxycodone (OxyContin), and oxymorphone (Opana ER). However, the projected weighted average cost per day for Embeda was lower than the UF agent morphine sulfate (Kadian).

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (16 for, 0 opposed, 0 abstained, 0 absent) morphine sulfate ER/naltrexone (Embeda) was cost effective relative to the other UF agents in the narcotic analgesics drug class.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (12 for, 3 opposed, 1 abstained, 0 absent) morphine sulfate ER/naltrexone capsules (Embeda) be designated formulary on the UF.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

2. ***COMMITTEE ACTION: BASIC CORE FORMULARY (BCF) RECOMMENDATION***—The P&T Committee considered the BCF status of morphine sulfate ER/naltrexone (Embeda). Based on the results of the clinical and economic evaluations presented, the P&T Committee voted (15 for, 0 opposed, 1 abstained, 0 absent) morphine sulfate ER/naltrexone (Embeda) would not be added to the BCF.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

B. Attention Deficit/Hyperactivity Disorder (ADHD)—Guanfacine extended release (ER) tablets (Intuniv)

Relative Clinical Effectiveness—Intuniv is indicated for the treatment of ADHD in children and adolescents aged 6 to 17 years. Intuniv is included in the ADHD/Narcolepsy drug class, which was reviewed in November 2006.

Guanfacine immediate release (IR) (Tenex, generics) is FDA-approved for treating hypertension, but is well accepted for off-label use in ADHD. Intuniv is dosed once daily for ADHD and is approved as monotherapy. Guanfacine IR is usually dosed twice daily for ADHD. Guanfacine is an alpha-2A agonist and is not a scheduled substance, unlike the stimulants (methylphenidate and amphetamine). Clonidine is another alpha-2A agonist used off-label for ADHD. Clonidine is available in tablets and transdermal formulations. Intuniv has a longer half-life than clonidine and causes less sedative and hypotensive effects.

Atomoxetine (Strattera), another nonstimulant, is FDA-approved as monotherapy for children with ADHD and has a different mechanism of action (norepinephrine reuptake inhibitor) than guanfacine. Strattera has more established efficacy data than Intuniv, but safety concerns include suicidal ideation and hepatotoxicity.

There are no direct comparative trials with Intuniv and other ADHD nonstimulants (guanfacine IR or Strattera). In two 8-week studies, Intuniv was superior to placebo in reducing symptoms associated with ADHD. Its efficacy in adolescents and the optimal dose for heavier adolescents remain to be determined. The duration of action of Intuniv ranged between 8 to 12 hours and was dose-dependent. Longer-term trials are necessary to delineate its place in therapy.

The clinical evaluation for Intuniv included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) that guanfacine ER (Intuniv) has a different mechanism of action and adverse effect profile than Strattera. The P&T Committee acknowledged that Intuniv offers the convenience of once-daily dosing and a defined dosing regimen compared to guanfacine IR and clonidine, but there is insufficient data to suggest whether there are additional clinical advantages compared to the other UF nonstimulants.

Relative Cost-Effectiveness—The P&T Committee evaluated the cost of guanfacine ER (Intuniv) in relation to the efficacy, safety, tolerability, and clinical outcomes of the ADHD agents in the ADHD/Narcolepsy UF drug class. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of Intuniv relative to other UF ADHD agents. Results from the CMA showed the projected weighted average cost per day for Intuniv is higher than other formulary ADHD agents except the clonidine transdermal formulation.

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstained, 1 absent) that guanfacine ER (Intuniv) is comparable in cost to branded stimulant and nonstimulant products in the ADHD/Narcolepsy drug class. In comparison to generics in this class, the P&T Committee determined that the higher daily cost for Intuniv was offset by its FDA-approved dosing regimen and once-daily administration.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness, relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (11 for, 3 opposed, 1 abstained, 1 absent) guanfacine ER tablets (Intuniv) be designated formulary on the UF.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee considered the BCF status of guanfacine ER (Intuniv). Based on the results of the clinical and economic evaluations presented, the P&T Committee voted (14 for, 0 opposed, 1 abstained, 1 absent) guanfacine ER (Intuniv) would not be added to the BCF.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

C. Newer Sedative Hypnotics—Zolpidem sublingual tablets (Edluar)

Relative Clinical Effectiveness—Zolpidem sublingual (SL) tablets (Edluar) is a newer sedative hypnotic approved for the short-term treatment of insomnia characterized by difficulties in sleep initiation. The newer sedative hypnotics were last reviewed in February 2007. Generic zolpidem immediate release (IR) oral tablets are currently included on the BCF.

Edluar was approved under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act by demonstrating bioequivalence to zolpidem IR (Ambien) tablets. The SL tablets disintegrate when placed under the tongue and are not swallowed. The pharmacokinetic profiles of Edluar, Ambien, and zolpidem extended release (Ambien CR) tablets are similar with regard to bioavailability, time to reach maximal concentration, half-life, protein binding, and elimination. There are no direct comparative trials evaluating the final commercially-marketed formulation of Edluar

with zolpidem IR tablets or other newer sedative hypnotics. Two small studies comparing an early zolpidem SL formulation with Ambien reported sleep onset measures were 6 to 7 minutes faster with the SL product than Ambien; however, the clinical relevance of this difference is unknown The safety profile for Edluar reflects that of other zolpidem formulations (e.g., Ambien and Ambien CR).

The clinical evaluation for Edluar included, but was not limited to, the requirements stated in 32 CFR 199.21(3)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee voted (16 for, 0 against, 0 abstained, 0 absent) that although zolpidem SL tablets (Edluar) offer an alternative sedative hypnotic formulation for patients with swallowing difficulties, there is insufficient data to conclude it offers improved efficacy, safety, or tolerability in the treatment of insomnia compared to zolpidem IR tablets.

Relative Cost-Effectiveness—The P&T Committee evaluated the costs of zolpidem SL tablets (Edluar) in relation to the efficacy, safety, tolerability, and clinical outcomes of the other newer sedative hypnotics. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of Edluar tablets. Results from the CMA showed the projected weighted average cost per day for Edluar is higher than the UF newer sedative hypnotic zolpidem IR and nonformulary (NF) newer sedative hypnotics, ramelteon (Rozerem) and zaleplon (Sonata).

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (16 for, 0 opposed, 0 abstained, 0 absent) zolpidem SL (Edluar) was not cost effective relative to the other UF and NF agents in the newer sedative hypnotics drug class.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness, 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, 0 absent) that zolpidem SL tablets (Edluar) be designated NF on the UF.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

2. ***COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA***—Based on the clinical evaluation of zolpidem SL tablets (Edluar) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Edluar. (See Appendix B for full MN criteria).

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday 1 week after the minutes are signed, following a 60-day implementation period in the retail network and mail order, and at Military Treatment Facilities (MTFs) no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval of the DoD P&T Committee minutes.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

D. Renin Angiotensin Antihypertensive Agents (RAAs)—Telmisartan/ amlodipine tablets (Twynsta)

Relative Clinical Effectiveness—Twynsta is a fixed-dose combination product containing telmisartan (Micardis) and amlodipine (Norvasc, generics). It is the third two-drug combination product containing an angiotensin receptor blocker (ARB; Micardis) and dihydropyridine calcium channel blocker (DHP CCB; amlodipine) to reach the market. Azor (olmesartan [Benicar]/amlodipine) and Exforge (valsartan [Diovan]/amlodipine) were the first entrants on the market. Twynsta is solely indicated for treating hypertension; it can be substituted for the individual titrated components or used as initial therapy in patients likely to require two or more drugs to control blood pressure (BP). Current national guidelines for treating hypertension recommend when more than one drug is needed for BP control, one of the components should comprise a diuretic.

Telmisartan is currently designated as formulary on the UF; amlodipine is designated as BCF. Twynsta is included in the RAAs drug class, which is comprised of several

subclasses (ARBs, angiotensin-converting enzyme (ACE) inhibitors, direct renin inhibitors and their combinations with CCBs or diuretics). The RAAs class will be re-evaluated at an upcoming meeting.

Treatment with various combinations of telmisartan/amlodipine was shown in one randomized trial to significantly reduce BP compared to baseline and placebo. There are no trials evaluating clinical outcomes of mortality or morbidity with Twynsta, although outcomes trials are available with the individual components.

The adverse reaction profile for Twynsta reflects that of the individual components. Although no studies are available specifically addressing the potential for increased compliance with Twynsta over the individual components administered together, other studies have shown an increase in persistence with fixed-dose antihypertensive combination products.

The clinical evaluation for Twynsta included, but was not limited to the requirements stated in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) telmisartan/amlodipine (Twynsta) did not have a significant, clinically meaningful, therapeutic advantage in terms of safety, effectiveness, or clinical outcome over other antihypertensive drugs included on the UF.

Relative Cost-Effectiveness—The P&T Committee evaluated the cost of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the combination antihypertensive agents in this class as well as the individual components, telmisartan and amlodipine. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of Twynsta relative to other UF agents in this class. Results from the CMA showed the projected weighted average cost per day for Twynsta is higher than the other formulary combination antihypertensive agents, including triple-therapy oral agent amlodipine/valsartan/hydrochlorothiazide (Exforge HCT) and the individual components amlodipine and telmisartan (Micardis).

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (15 for, 1 opposed, 0 abstained, 0 absent) telmisartan/amlodipine (Twynsta) is not cost effective relative to the other combination antihypertensive agents in this class.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (15

for, 0 opposed, 1 abstained, 0 absent) telmisartan/amlodipine (Twynsta) be designated NF on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluation for telmisartan/amlodipine (Twynsta) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Twynsta. (See Appendix B for full MN criteria).

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday 1 week after the minutes are signed, following a 60-day implementation period in the retail network and mail order, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval of the DoD P&T Committee minutes.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

E. RAAs—Aliskiren/valsartan tablets (Valturna)

Relative Clinical Effectiveness—Valturna is a fixed-dose combination product containing the ARB valsartan (Diovan) and aliskiren (Tekturna), a direct renin inhibitor. Tekturna is also available in a fixed-dose combination tablet containing the diuretic hydrochlorothiazide (HCTZ); both Tekturna and Tekturna HCT are designated as formulary on the UF. Valsartan (Diovan) is designated NF. Valturna is included in the RAAs drug class, which will be re-evaluated at an upcoming meeting.

Valturna is indicated for treating hypertension. It has other indications based on clinical trials showing positive clinical outcomes; outcomes trials with Tekturna are currently underway. Current national guidelines for treating hypertension have not yet addressed the place in therapy for direct renin inhibitors, although updated guidelines are anticipated later this year.

Treatment with Valturna was shown in one randomized trial to significantly reduce BP compared to placebo or administering the components individually. However, the BP reduction seen with Valturna in this study was not as large as that seen in other studies evaluating fixed-dose antihypertensive combination products. The adverse reaction profile for Valturna reflects that of the individual components.

The clinical evaluation for Valturna included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) that although aliskiren/valsartan (Valturna) has a unique mechanism of action due to the direct renin inhibitor component and offers the potential for increased persistence, it did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over other antihypertensive drugs included on the UF.

Relative Cost-Effectiveness—The P&T Committee evaluated the cost of the agent in relation to the efficacy, safety, tolerability, and clinical outcomes of the combination antihypertensive agents in this class as well as the individual components, aliskiren and valsartan. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of Valturna compared to other UF agents. Results from the CMA showed the projected weighted average cost per day for Valturna is higher than the other formulary combination antihypertensive agents, including triple-therapy oral agent Exforge HCT and the individual components, Tekturna and Diovan.

Relative Cost-Effectiveness Conclusion—The P&T Committee voted (16 for, 0 opposed, 0 abstained, 0 absent) that aliskiren/valsartan (Valturna) is not cost effective relative to the other combination antihypertensive agents in this class.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (14 for, 0 opposed, 2 abstained, 0 absent) aliskiren/valsartan (Valturna) be designated NF on the UF.

   Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved

   Approved, but modified as follows:

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluation of aliskiren/valsartan (Valturna) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Valturna. (See Appendix B for full MN criteria).

   Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved

   Approved, but modified as follows:

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday 1 week after the minutes are signed, following a 60-day implementation period in the retail network and mail order, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval of the DoD P&T Committee minutes.

   Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved

   Approved, but modified as follows:

IV. UF DRUG CLASS REVIEWS

A. Basal Insulins

Relative Clinical Effectiveness—The P&T Committee evaluated the clinical effectiveness of the long-acting basal insulin analogues (e.g., basal insulins) for the treatment of diabetes mellitus (DM). Insulin detemir (Levemir) and insulin glargine (Lantus) were FDA approved on June 16, 2005, and April 30, 2000, respectively. Lantus and Levemir are available in both vials and prefilled pen devices (Lantus SoloStar and Levemir FlexPen). Lantus vials are currently on the BCF. Information regarding the safety, effectiveness, and clinical outcomes of the long-acting basal insulin analogues was considered. Neutral Protamine Hagedon (NPH) is an intermediate-acting basal insulin. NPH is not classified in the long-acting basal insulins UF drug class; it remains a BCF drug. The clinical review included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

MHS expenditures for the long-acting basal insulin analogues exceeded $4M per month at the retail, mail order, and MTF points of service (POS) from January 2008 to December 2009. In the MHS, Lantus is the highest utilized basal insulin. Lantus vials were dispensed three times more frequently than the next highest utilized drug, Lantus SoloStar, followed by Levemir FlexPen.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions regarding the basal insulin drug class:

1. With regard to efficacy, the following conclusions were made:
   a) In pivotal trials, both Levemir and Lantus produced similar reductions in glycosylated hemoglobin A1c (HbA1c), when compared to NPH insulin in subjects with type-1 or type-2 DM.

      In head-to-head studies, there was no clinically relevant difference in the reduction in HbA1c between Levemir and Lantus in subjects with type-1 or type-2 DM. The absolute HbA1c difference was <0.4% between the two drugs.

   b) In head-to-head studies, there was a statistically significant difference in the reduction in fasting plasma glucose (FPG) values between Levemir and Lantus in subjects with type-1 DM; larger FPG reductions were seen with Lantus. This difference was not observed in subjects with type-2 DM. The clinical significance of this finding is unknown.

   c) In head-to-head studies, the total Levemir dose required to achieve goal HbA1C levels (<7%) was larger than the dose of Lantus used to achieve goal HbA1C levels in subjects with type-1 DM. Levemir was dosed twice-daily more often

2. With regard to safety and tolerability, the following conclusions were made:
   a) Existing evidence does not support clinically relevant differences concerning hypoglycemia or weight gain between Levemir and Lantus. In subjects with type-2 DM, the difference in weight gain between Levemir (daily and twice daily dosing) vs. Lantus (once daily dosing) was 0.9 kg ($p=0.01$). Once daily dosing of Levemir caused less weight gain than twice daily dosing (absolute difference 1.4 kg; $p<0.001$). Once daily dosing of Levemir caused less weight gain than once daily dosing of Lantus (absolute difference 1.6 kg; $p<0.001$). The difference in weight gain was similar when twice daily dosing of Levemir was compared to once daily dosing of Lantus (absolute difference 0.2 kg).
   b) There is insufficient evidence to determine if there are clinically relevant differences between Levemir and Lantus with respect to cancer risk. Observational studies raised concerns of an association between the use of Lantus and cancer incidence. These studies had inconsistent findings and many study design flaws. FDA is uncertain of this association.
3. With regard to other factors
   a) There are no clinically relevant differences between the pen devices for Lantus SoloStar and Levemir FlexPen in terms of refrigeration requirements and expiration date after opening, with the exception that Levemir is stable for 42 days and Lantus is stable for 28 days.
   b) Patient preference studies report that patients overall prefer using insulin pen devices compared to insulin vials. Most studies have shown no patient preferences among various pen devices.
   c) A request for input from MTF providers revealed that the majority of responders ranked Lantus as their first preference for a basal insulin, followed by Levemir as the second choice, primarily due to perceived differences in efficacy and availability on the local formulary. The majority of responders stated that availability of one basal insulin on the local formulary was adequate to meet their prescribing needs.

Relative Cost-Effectiveness—In considering the relative cost-effectiveness of the basal insulins, the P&T Committee evaluated the costs in relation to the efficacy, safety, tolerability, and clinical outcomes. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA and budget impact analysis (BIA) were used to evaluate the cost-effectiveness of the basal insulins.

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, 0 abstained, 0 absent) the following:

a) CMA results of the basal insulins revealed that Lantus vials were more cost effective than Levemir vials based on cost per ml of treatment. CMA results of the basal insulins revealed that Lantus SoloStar pen devices were more cost effective than Levemir FlexPen pen devices based on cost per ml of treatment. Cost per ml of treatment was calculated using average quarterly consumption rates for Lantus vials and Lantus SoloStar pen devices and Levemir vials and Levemir FlexPen pen devices.

b) The potential impact of scenarios with selected basal insulins designated formulary or NF on the UF was evaluated using BIA. Scenarios evaluating the impact of designating basal insulins on the BCF were also considered. Results from the BIA for the basal insulins revealed that placing Lantus vials and Lantus SoloStar pen devices on the BCF and UF, with Levemir vials on the UF, and designating Levemir FlexPen pen devices NF was the most cost-effective scenario overall.

c) BIA results showed that Levemir vials and Levemir FlexPen pen devices were more costly than Lantus vials and Lantus SoloStar pen devices in all scenarios that do not require automated prior authorization. Lantus vials and Lantus SoloStar pen devices were more costly than Levemir vials and Levemir FlexPen pen devices in one scenario involving an automated prior authorization. However, The P&T Committee decided that an automated prior authorization was not clinically appropriate for the basal insulin class.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 1 abstained, 0 absent) to recommend the following:

    a) Insulin glargine vials (Lantus), insulin glargine pen devices (Lantus SoloStar) and insulin detemir vials (Levemir) remain classified as formulary on the UF.

    b) Insulin detemir pen devices (Levemir FlexPen) be designated NF on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluation of insulin detemir pen devices (Levemir FlexPen) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Levemir FlexPen. (See Appendix B for full MN criteria).

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday 1 week after the minutes are signed, following a 60-day implementation period in the retail network and mail order, and at MTFs no later than a 60-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval of the DoD P&T Committee minutes.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: BCF 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, voted (15 for, 0 opposed, 1 abstained, 0 absent) that insulin glargine vials (Lantus) remain BCF, and insulin glargine pen devices (Lantus SoloStar) be added to the BCF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

B. Antihemophilic Agents—Plasma-derived/Recombinant Factor VIII and Factor IX products

Relative Clinical Effectiveness—The P&T Committee evaluated the clinical effectiveness of the antihemophilic agents. The class was divided into the factor VIII and factor IX concentrates; and the factor VIII/von Willebrand (vWF) factor complexes; human prothrombin concentrate complexes (PCCs); and inhibitor bypassing products. The antihemophilic agents have not previously been reviewed for UF placement; they are an extended core formulary (ECF) drug class.

Purified factor VIII drugs are used to treat hemophilia A and are manufactured from two sources: plasma-derived (human) and recombinant. The human factor VIII products include Hemofil M, Koate-DVI, and Monoclate-P. The recombinant factor VIII products include Advate, Helixate FS, Kogenate FS, Recombinate, Refacto, and Xyntha. Although Refacto is still available for use, it was no longer manufactured at the time of this review and, therefore, not considered for ECF status.

Purified factor IX drugs used to treat hemophilia B are likewise derived from two sources: human and recombinant. The human factor IX concentrates include AlphaNine SD and MonoNine. There is only one recombinant factor IX product: BeneFIX. Information was considered regarding the safety, effectiveness, and clinical outcomes of the factor VIII and factor IX subclasses of the antihemophilic agents. Only uses that pertain to the outpatient pharmacy benefit were considered. The clinical review included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Military Health System (MHS) expenditures for the all antihemophilic agents (factor VIII, factor IX, factor VIII/vWF complexes, PCCs, and inhibitor bypassing products) exceeded $39M from December 2008 to November 2009 predominantly at the retail POS. There are approximately 190 unique utilizers in the MHS. There were no MHS utilizers of Monoclate-P or AlphaNine SD during this time period.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions regarding purified factor VIII and IX concentrates:

1. With regard to efficacy, the following conclusions were made:

a) There are no head-to-head comparative trials evaluating the factor VIII or factor IX products. Efficacy studies were limited to open-label clinical trials with no active comparators.

b) Many products obtained FDA approval based on pharmacokinetic demonstration of bioequivalence to previously approved (e.g., earlier generation) products following improvements in production and viral depletion or inactivation methods.

c) There is no evidence to conclude that there are clinically relevant differences in efficacy between the respective factor VIII and factor IX concentrates.

2. With regard to safety and tolerability, the P&T Committee agreed that, although the overall risk is small, there is a lower risk of viral transmission with recombinant products than with plasma-derived products. There is insufficient evidence to conclude there are clinically relevant differences in safety between the recombinant factor VIII products.

3. With regard to other factors, the following conclusions were made:

   a) National professional group guidelines and national hemophilia patient advocacy groups caution against switching between products once a patient is stabilized, due to potentially detrimental outcomes, including development of immunogenicity.

   b) There are differences among the factor VIII and factor IX products with regard to viral deactivation/depletion methods, storage and refrigeration requirements, vial sizes available, reconstitution and administration kits, patient support programs, and stabilizers/cell culture media used in recombinant products.

Relative Cost-Effectiveness—In considering the relative cost-effectiveness of pharmaceutical agents in the antihemophilic plasma-derived/recombinant factor VIII and factor IX subclass, the P&T Committee evaluated the costs of the agents in relation to the efficacy, safety, tolerability, and clinical outcomes. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMAs were used to evaluate the cost-effectiveness of the plasma-derived/recombinant factor VIII and factor IX subclass.

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, 0 abstained, 0 absent) the following:

a) CMA results for the antihemophilic factor VIII agents revealed that Xyntha was the most cost-effective recombinant factor VIII product based on cost per unit of treatment. Cost per unit of treatment was calculated using the

b) CMA results for the antihemophilic factor IX agents revealed that BeneFIX was the most cost-effective antihemophilic recombinant factor IX product based on the cost per unit of treatment. Cost per unit of treatment was calculated using average drug price per unit rates for the recombinant factor IX products AlphaNine SD and MonoNine.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (11 for, 1 opposed, 3 abstained, 1 absent):

   a) All factor VIII and factor IX products recommended for inclusion on the UF had existing Uniform Formulary Voluntary Agreement for Retail Refunds (UF VARR) submissions at or below the Federal Ceiling Price (FCP) or a required Mandatory Agreement for Retail Refunds (MARR). No products recommended for NF designation on the UF have required pricing agreements.

   b) The factor VIII products Koate-DVI, Kogenate FS, Refacto, and Xyntha, and the factor IX products AlphaNine SD and BeneFIX remain classified as formulary on the UF.

   c) The factor VIII products Advate, Hemofil M, Helixate FS, Monoclate-P, and Recombinate, and the factor IX product MonoNine be designated NF on the UF.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluation of the plasma-derived and recombinant factor VIII and factor IX products and the conditions for establishing MN for a NF medication, the P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1

absent) MN criteria for Advate, Hemofil M, Helixate FS, Monoclate-P, Recombinate, and MonoNine. (See Appendix B for full MN criteria.)

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday 1 week after the minutes are signed, following a 180-day implementation period in the retail network and mail order, and at MTFs no later than a 180-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval of the DoD P&T Committee minutes.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

4. ***COMMITTEE ACTION: ECF 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, voted (15 for, 0 opposed, 1 abstained, 0 absent):

   a) The factor VIII product Xyntha be designated as ECF on the UF.

   b) The factor IX product BeneFIX be designated as ECF on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

C. Antihemophilic Agents—Human Factor VIII/vWF, PCCs, and Inhibitor Bypassing products (Recombinant VIIa Factor and Human Activated PCC) Products

Relative Clinical Effectiveness—The P&T Committee evaluated the clinical effectiveness of the remainder of the antihemophilic drug class, comprised of the human factor VIII/vWF complexes, the human PCCs, and the inhibitor bypassing products.

Humate-P and Alphanate are the two human factor VIII products containing a measured amount of vWF that are used to treat certain types of von Willebrand disease and to replace factor VIII in patients with hemophilia A. Human PCCs were formerly the treatment of choice for hemophilia B before highly purified products became available and now are used to treat factor II and factor X deficiency. The PCCs include Bebulin VH and Profilnine SD. The inhibitor bypassing products include one recombinant activated factor VII, NovoSeven RT, and one human activated PCC, Feiba VH. These two products are indicated for use in patients with hemophilia A or hemophilia B who have developed inhibitors, and are used to treat bleeding episodes, or to prevent bleeding episodes during surgical interventions.

Information was considered regarding the safety, effectiveness, and clinical outcomes of the factor VIII/vWF complexes, the PCCs, and the inhibitor bypassing subclass of the antihemophilic agents. Only uses that pertain to the outpatient drug benefit were considered. The clinical review included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1). There were no MHS utilizers of Humate-P or Profilnine SD from December 2008 to November 2009.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) the following clinical effectiveness conclusions:

1. With regard to efficacy, the following conclusions were made:
    a) There is no evidence to conclude that there are clinically relevant differences in efficacy between NovoSeven RT and Feiba VH in the outpatient treatment of bleeding episodes in hemophilia patients who have inhibitors.

b) There is no evidence to conclude that there are clinically relevant differences in efficacy between Bebulin VH and Profilnine SD in the outpatient treatment of factor II or factor X deficiency.

c) There is no evidence to conclude that there are clinically relevant differences in efficacy between Humate-P and Alphanate in the outpatient treatment of von Willebrand disease or hemophilia A.

2. With regard to safety and tolerability, the P&T Committee agreed that:

a) Although the risk is small, there is a lower risk of viral transmission with a recombinant product (NovoSeven RT) than with a plasma-derived product (Feiba VH). Feiba VH may also cause an anamnestic response in patients with inhibitors who are classified as high responders to therapy, and can cause anaphylaxis or nephrotic syndrome in hemophilia B patients who have developed inhibitors. Both products carry a very low risk of thrombotic complications. Feiba VH has a warning advising extreme caution when using in patients with hepatic impairment.

b) Bebulin VH contains heparin and may not be appropriate to use in patients with a history of type II heparin induced thrombocytopenia (HIT); otherwise, there is no evidence that there are clinically relevant differences in safety between Bebulin VH and Profilnine SD.

c) Alphanate contains heparin and may not be appropriate to use in patients with a history of type II HIT; otherwise, there is no evidence that there are clinically relevant differences in safety between Humate-P and Alphanate.

3. With regard to other factors:

a) Feiba VH has a longer half-life than Novoseven RT and may be more appropriate when considering prophylactic treatment in a hemophilia patient who has developed inhibitors and is classified as a high responder to therapy.

c) National professional group guidelines and national hemophilia patient advocacy groups caution against switching between products once a patient is stabilized, due to potentially detrimental outcomes, including development of immunogenicity.

There are differences among the factor VIII/vWF concentrates, the human PCCs, and the inhibitor bypassing products with regard to viral deactivation/depletion methods, storage and refrigeration requirements, vial sizes available, reconstitution and administration kits, and patient support programs.

Relative Cost-Effectiveness—In considering the relative cost-effectiveness of pharmaceutical agents in the human factor VIII/vWF, PCCs, and inhibitor bypassing products subclass, the P&T Committee evaluated the costs of the agents in relation to the efficacy, safety, tolerability, and clinical outcomes. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMAs were used to evaluate the cost-effectiveness of the human factor VIII/vWF, PCCs, and inhibitor bypassing products subclass.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (13 for, 0 opposed, 2 abstained, 1 absent) the following:

a) CMA results for the Factor VIII/vWF subgroup revealed that Alphanate was the most cost-effective agent based on cost per patient per year of treatment. Cost per patient per year of treatment was calculated using yearly consumption rates for Alphanate and Humate-P.

b) CMA results for the PCCs subgroup revealed that Profilnine SD was the most cost-effective agent based on cost per patient per year of treatment. Cost per patient per year of treatment was calculated using yearly consumption rates for Bebulin VH and Profilnine SD.

c) CMA results for the inhibitor bypassing products subgroup revealed that NovoSeven RT was the most cost-effective agent based on a cost per patient per year of treatment. Cost per patient per year of treatment was calculated using yearly consumption rates for NovoSeven RT and Feiba VH.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, voted (13 for, 0 opposed, 2 abstained, 1 absent):

    a) All factor VIII and factor IX products recommended for inclusion on the UF had existing UF VARR submissions at or below the FCP or a required MARR. No products recommended for NF designation on the UF have required pricing agreements.

    b) The factor VIII/vWF product Alphanate, the human PCC product Profilinine SD, and the inhibitor bypassing product NovoSeven RT remain classified as formulary on the UF.

c) The factor VIII/vWF product Humate-P, the human PCC product Bebulin VH, and the inhibitor bypassing product Feiba VH be designated NF on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluation of the factor VIII/vWF complexes, the human PCCs, and the inhibitor bypassing products subclass of the antihemophilic agents, and the conditions for establishing MN for a NF medication, the P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Humate-P, Bebulin VH, and Feiba. (See Appendix B for full MN criteria).

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday 1 week after the minutes are signed, following a 180-day implementation period in the retail network and mail order, and at MTFs no later than a 180-day implementation period; and 2) TMA send a letter to beneficiaries affected by this UF decision. The implementation period will begin immediately following approval of the DoD P&T Committee minutes.

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

V. UTILIZATION MANAGEMENT—PA/QUANTITY LIMITS (QL)

A. PDE-5 Inhibitors—PA post-prostatectomy: At the August 2009 P&T Committee meeting, PA criteria for the PDE-5 inhibitors were expanded to include restoration/preservation of erectile function following prostatectomy. Clarification regarding the length of therapy and other issues was requested in order to fully operationalize this criterion at the retail network and mail order pharmacy. The P&T Committee reviewed the clinical evidence regarding the use of PDE-5 inhibitors following prostatectomy, including duration of therapy, and also reviewed the requirements from other civilian health plans.

1. ***COMMITTEE ACTION: PA***—The P&T Committee voted (13 for, 0 opposed, 1 abstained, 2 absent) to recommend limiting the length of therapy to one year for the PDE-5s when used following prostatectomy.

   Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved

   Approved, but modified as follows:

B. Sumatriptan needle-free injection (Sumavel DosePro)—QL: A new needle-free sumatriptan injection (Sumavel DosePro) has been marketed. Sumavel DosePro will be reviewed as a new FDA-approved drug in the triptan drug class at an upcoming DoD P&T Committee meeting. QLs are currently in place for both oral and other injectable formulations of sumatriptan (Imitrex, generics) and the other oral triptans, which are consistent with the product labeling.

1. ***COMMITTEE ACTION: QL***—The P&T Committee voted (13 for, 0 opposed, 1 abstained, 2 absent) to recommend QLs of 9 mL (18 units)/90 days in the mail order pharmacy and 3 mL (6 units)/30 days in the retail network, which is

consistent with the recommended dosing from the product labeling and avoids breaking apart packages.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

VI. ITEMS FOR INFORMATION

A. **Pharmacy Outcomes Research Team (PORT)**—The PORT briefed the P&T Committee on study results concerning the automated PA program for the proton pump inhibitors.

B. **Department of Veterans Affairs (VA)/DoD Joint Contracting Initiatives**

BCF/ECF Issues—The P&T Committee was briefed regarding the VA National Acquisition Center contract for insulin needles. In March 2009, the VA/DoD joint national contract for insulin needles was changed to include the 30 ½" and 31 5/16" gauge/length needle sizes with 0.3, 0.5, and 1 ml volumes. The current DoD BCF insulin needles are 28 ½" gauge/length needles with 0.5 and 1ml volumes. DoD anticipates increased availability of the 31 5/16" gauge/length needle. Historical utilization from DoD prime vendor data shows a significant usage of the 0.3 ml volume syringes.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Based on the results of the information presented, the P&T Committee voted (14 for, 0 opposed, 1 abstained, 1 absent) to recommend: 1) 31 5/16" gauge/length needle sizes with the 0.3, 0.5, and 1 ml volumes be added to the BCF; 2) 28 ½" gauge/length needles with 0.5 and 1 ml volumes be deleted from the BCF; and 3) 30 ½" gauge/length needles with 0.5 and 1 ml volumes will be maintained as formulary on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

C. **Exenatide injection (Byetta)—PA:** Due to a new FDA indication for Byetta for use as monotherapy in patients with type-2 DM, the P&T Committee received a request to re-

criteria were established by the P&T Committee in August 2006, based on Byetta's potential use for indications not covered by TRICARE (i.e., weight loss) and/or not supported by clinical evidence. Since the original establishment of the PA, there have been updates to the product labeling due to safety concerns, including pancreatitis. The injectable drugs for DM, including Byetta and a similar product recently approved by the FDA, liraglutide injection (Victoza), will be reviewed at an upcoming meeting. The P&T Committee agreed to defer action until the class is reviewed.

VII. NATIONAL DEFENSE AUTHORIZATION ACT, SECTION 703—INCLUSION OF TRICARE RETAIL PHARMACY PROGRAM IN FEDERAL PROCUREMENT OF PHARMACEUTICALS UPDATE

The P&T Committee reviewed drugs that were not included on a DoD Retail Refund Pricing Agreement; these drugs are not compliant with Fiscal Year 2008 National Defense Authorization Act, Section 703. The law stipulates that if a drug is not compliant with Section 703, these drugs will be designated NF on the UF and will require pre-authorization prior to use in the retail POS and medical necessity in MTFs. These NF drugs will remain available in the mail order POS without pre-authorization. Pre-authorization criteria will be determined at a future DoD P&T Committee meeting. Drugs with and without pricing agreements were systematically classified according to therapeutic and pharmacologic lines. The classification system was based on the American Hospital Formulary System Classification and First Data Bank classification. See Appendix C for the full list of affected medications.

A. ***COMMITTEE ACTION—DRUGS RETAINING UF STATUS***: The P&T Committee recommended by consensus the drugs listed in Appendix C, Section A, retain formulary status on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

B. ***COMMITTEE ACTION—DRUGS RETAINING OR DESIGNATED NF:*** The P&T Committee recommended by consensus the drugs listed in Appendix C, Section B to retain NF status or be designated NF on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

C. ***COMMITTEE ACTION—IMPLEMENTATION DATE FOR PA:*** The P&T Committee recommended by consensus the implementation date will not be prior to July 1, 2010, and not later than 180 days after the minutes of this meeting are signed.

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

D. ***COMMITTEE ACTION—TRANSITION DATE AT THE MTF POS:*** The P&T Committee recommended by consensus a transition period at the MTF POS as ending no later than January 1, 2011.

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

VIII. CLASS OVERVIEWS

Class overviews for the antilipidemic-1s, which includes the statins, niacin and ezetimibe; benign prostatic hyperplasia drugs; the RAAs; and the ophthalmologic-1s class, which includes the ocular antihistamines, mast cell stabilizers and combination antihistamines/mast cell stabilizers, were presented to the P&T Committee. The P&T Committee provided expert opinion regarding those clinical outcomes considered most important for the PEC to use in completing the clinical effectiveness reviews and developing the appropriate cost effectiveness models. The clinical and economic analyses of these classes will be completed at upcoming meetings.

IX. ADJOURNMENT

The meeting adjourned at 1700 hours on February 17, 2010, and at 1200 hours on February 18, 2009. The next meeting will be in May 2010.

Appendix A—Attendance

Appendix B—Table of Medical Necessity Criteria for Newly Approved Drugs

Appendix C—National Defense Authorization Act, Section 703 Affected Medications

Appendix D—Table of Implementation Status of UF Recommendations/Decisions

Appendix E—Table of Abbreviations

SUBMITTED BY:

CDR James Ellzy, MC, USN
DoD P&T Committee Chair

DECISION ON RECOMMENDATIONS

Director, TMA, decisions are as annotated above.

Charles L. Rice, MD

Dr. Charles L. Rice
Acting Director

3 May 2010
(Date)

Appendix A—Attendance

Voting Members Present	
CDR James Ellzy, MC	DoD P&T Committee Chair
LTC Stacia Spridgen, MSC	Director, DoD Pharmacoeconomic Center, (Recorder)
Col Everett McAllister, BSC	Deputy Director, Pharmaceutical Operations Directorate
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Major Jeremy King, MC	Air Force, OB/GYN Physician
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
CAPT David Tanen, MC	Navy, Physician at Large
Col Mike Spilker, BSC	Air Force, Pharmacy Officer
Lt Col Brian Crownover, MC	Air Force, Physician at Large
CDR Phil Blaine *for CAPT Stephanie Simon, MSC*	Navy, Pharmacy Officer
COL Doreen Lounsbery, MC	Army, Internal Medicine Physician, Alternate
LTC Bruce Lovins, MC	Army, Family Practice Physician, Alternate
COL Ted Cieslak, MC	Army, Physician at Large
COL Peter Bulatao *for COL Carole Labadie, MSC*	Army, Pharmacy Officer, Alternate
CAPT Vernon Lew	Coast Guard, Pharmacy Officer
Mr. Joe Canzolino	Department of Veterans Affairs
Nonvoting Members Present	
Mr. David Hurt	Assistant General Counsel, TMA
CDR Francis Williams	Defense Supply Center, Philadelphia
COL Kent Maneval, MS	Defense Medical Standardization Board
Guests	
CDR Rob Hayes	United States Public Health Service/ Indian Health Service
Maj Pete Trang	Lackland AFB
LTC Paula Doulaveris	Army Pharmacovigilence Center
Capt Emily Fusco	Air Force Pharmacy Resident
Dr. Vincent Calabrese	Department of Veteran Affairs

Appendix A—Attendance (continued)

Others Present	
LCDR Joe Lawrence	DoD Pharmacoeconomic Center
Lt Col James McCrary, MC	DoD Pharmacoeconomic Center
Lt Col Cynthia Lee, BSC	DoD Pharmacoeconomic Center
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
CPT Brian Haney, MC	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Eugene Moore	DoD Pharmacoeconomic Center
Dr. Angela Allerman	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe	DoD Pharmacoeconomic Center
Dr. Jeremy Briggs	DoD Pharmacoeconomic Center
Dr. Libby Hearin	DoD Pharmacoeconomic Center
Mr. Stephen Yarger	DoD Pharmacy Outcomes Research Team contractor
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor
Dr. Roger Potyk	DoD Pharmacy Outcomes Research Team contractor
Dr. Dean Valibhai	DoD Pharmacy Operations Center contractor
Dr. Brian Beck	DoD Pharmacy Operations Center contractor
Ms. Jeanette Cosby	DoD Pharmacy Operations Center contractor

Appendix B—Table of Medical Necessity Criteria for Newly Approved Drugs

Drug / Drug Class	Medical Necessity Criteria
Detemir pens (Levemir) **Basal Insulins**	• The patient previously responded to nonformulary agent and changing to a formulary agent would incur unacceptable risk (for patients requiring BID dosing with manual dexterity or visual limitations)
Monoclate-P, Hemofil M, Recombinate, Helixate FS, and Advate **Antihemophilic Agents**	• The patient has experienced or is likely to experience significant adverse effects from formulary alternatives. • Formulary agents have resulted or are likely to result in therapeutic failure. • The patient previously responded to nonformulary agent and changing to a formulary agent would incur unacceptable risk
Humate-P, Bebulin VH, and Feiba VH **Antihemophilic Agents**	• The patient has experienced or is likely to experience significant adverse effects from formulary alternatives. • Formulary agents have resulted or are likely to result in therapeutic failure. • The patient previously responded to nonformulary agent and changing to a formulary agent would incur unacceptable risk • No alternative formulary agent available (if using Feiba VH for prophylaxis and longer half-life is desired)
Zolpidem sublingual tablets (Edluar) **Newer Sedative Hypnotic Agents**	• No alternative formulary agent available (if patients have swallowing difficulties)
Telmisartan/Amlodipine tablets (Twynsta) **Renin Angiotensin Aldosterone Agents**	• No alternative formulary agent available (if patients have swallowing difficulties)
Aliskiren/Valsartan tablets (Valturna) **Renin Angiotensin Aldosterone Agents**	• No alternative formulary agent available (if patients have swallowing difficulties)

Appendix C—National Defense Authorization Act, Section 703 Affected Medications

A. Drugs Retained as Formulary on the Uniform Formulary

Product Name	Subclass	Manufacturer	Num
TARCEVA	Antineoplastic systemic enzyme inhibitors	GENENTECH, INC.	
TARGRETIN	Oral oncological agents	EISAI INC.	

B. Drugs moved to or retained as nonformulary on the Uniform Formulary

Product Name	Subclass	Manufacturer	Num
FLUOROPLEX	Topical antineoplastic & premalignant lesion medic	ALLERGAN INC.	
PANRETIN	Topical antineoplastic & premalignant lesion medic	EISAI INC.	
SUBOXONE	Narcotic analgesics & combos	RECKITT BENCKIS	
SUBUTEX	Narcotic analgesics & combos	RECKITT BENCKIS	
TAZORAC	Psoriasis medications	ALLERGAN INC.	

Appendix D—Table of Implementation Status of UF Recommendations/Decisions

Date	DoD PEC Drug Class	Type of Action*	BCF/ECF Medications MTFs must have BCF meds on formulary	UF Medications MTFs may have on formulary	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Original Review and Updates	Comments
Feb 2010	Basal Insulins	UF Review	▪ Insulin glargine (Lantus) vials ▪ Insulin glargine (Lantus Solostar) pens	▪ Insulin levemir (Detemir) vials	▪ Insulin Levemir (Detemir) pens	Pending 60 days			
Feb 2010	Anti-hemophilic Agents	UF Review	▪ Factor VIII: Xyntha ▪ Factor IX: Benefix	▪ Factor VIII: Koate-DVI, Kogenate FS, Refacto, Alphanate ▪ Factor IX: AlphaNine, Profilnine ▪ Inhibitor bypassing product: Novoseven RT	▪ Factor VIII: Advate, Helixate, Hemofil M, Humate-P, Monoclate-P, Recombinate ▪ Factor IX: Mononine; Bebulin VH ▪ Inhibitor bypassing product: Feiba VH	Pending 60 days			
Feb 2010	ADHD Drugs	New Drug Guanfacine ER (Intuniv)	▪ methylphenidate OROS (Concerta) ▪ mixed amphetamine salts ER ▪ methylphenidate IR	▪ **Guanfacine ER (Intuniv)** ▪ Atomoxetine (Strattera) ▪ Methylphenidate OROS (Concerta ▪ Methylphenidate 30% IR/70% ER (Metadate CD) ▪ Methylphenidate SODAS, SR (Ritalin LA; Ritalin SR) ▪ Mixed Amphetamine salts IR ▪ Dexamphetamine IR ▪ Methamphetamine IR (Desoxyn, generics)	▪ dexmethylphenidate IR, SODAS (Focalin; Focalin SR) ▪ methylphenidate transdermal system (Daytrana) ▪ Lisdexamfetamine (Vyvanse) (Nov 07)	Not applicable		Nov 07 Nov 06	▪ Guanfacine ER (Intuniv) recommended to remain UF (pending)

Date	DoD PEC Drug Class	Type of Action*	BCF/ECF Medications MTFs must have BCF meds on formulary	UF Medications MTFs may have on formulary	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Original Review and Updates	Comments
Feb 2010	RAAs	New Drug ▪ Telmisartan / amlodipine (Twynsta) ▪ Aliskiren / valsartan (Valturna)	ACE inhibitor ▪ captopril ▪ lisinopril ▪ lisinopril / HCTZ ▪ ramipril ACE/CCB ▪ amlodipine/benazepril (Lotrel, generics)	ACE Inhibitor ▪ benazepril, HCTZ ▪ enlapril, HCTZ ▪ fosinopril, HCTZ ▪ quinapril, HCTZ ▪ trandolapril (Mavik) ARB ▪ telmisartan, HCTZ (Micardis, Micardis HCT) ▪ losartan, HCTZ (Cozaar, Hyzaar) ▪ candesartan, HCTZ (Atacand, Atacand HCT) ARB/CCB/diuretic ▪ valsartan/ amlodipine/HCTZ (Exforge HCT) Nov 09 DRI ▪ aliskiren, HCTZ (Tekturna; Tekturna HCT)	DRI/CCB ▪ **Aliskiren/valsartan (Valturna)** ARB/CCB ▪ **telmisartan / amlodipine (Tywnsta)** ▪ olmesartan / amlodipine (Azor) ▪ valsartan amlodipine (Exforge) ACE inhibitor ▪ moexipril, HCTZ (Univasc; Uniretic) ▪ perindopril (Aceon) ACE/CCB combos ▪ verapamil / trandolapril (Tarka) ARB ▪ eprosartan, HCTZ (Teveten; Teveten HCT) ▪ irbesartan, HCTZ (Avapro, Avalide) ▪ olmesartan, HCTZ (Benicar; Benicar HCT) ▪ valsartan, HCTZ (Diovan, Diovan HCT)	Pending 60 days		Nov 09 Jun 08 Nov 07 Aug 07 May 07 Feb 06 Aug 05	▪ Telmisartan / amlodipine (Twynsta) and Aliskiren / valsartan (Valturna) recommended for NF (pending)
Feb 2010	Newer Insomnia	New Drug Zolpidem sublingual (Edluar)	▪ Zolpidem IR	▪ Eszopiclone (Lunesta)	▪ Zolpidem CR (Ambien CR) ▪ Zaleplon (Sonata) ▪ Ramelteon (Rozerem) ▪ **Zolpidem sublingual (Edluar)**	Pending 60 days		Feb 07	▪ Zolpidem sublingual (Edluar) recommended for NF (pending) ▪ Step therapy requiring trial of zolpidem IR applies to class

Date	DoD PEC Drug Class	Type of Action*	BCF/ECF Medications MTFs must have BCF meds on formulary	UF Medications MTFs may have on formulary	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Original Review and Updates	Comments
Feb 2010	Narcotic Analgesics	New Drug Morphine sulfate ER / naltrexone (Embeda)	▪ morphine sulfate IR 15, 30 mg ▪ morphine sulfate 12-hour ER (MS Contin or equivalent) 15, 30, 60 mg ▪ oxycodone/APAP 5/325 mg ▪ hydrocodone/APAP 5/500 mg ▪ codeine/APAP 30/300 mg ▪ codeine/APAP elixir 12/120 mg/5 mL ▪ tramadol IR	▪ **Morphine sulfate ER / naltrexone (Embeda)** ▪ Codeine ▪ Fentanyl transdermal, transmucosal (Actiq), buccal (Fentora) tablets ▪ Hydromorphone (Dilaudid) ▪ Levorphanol ▪ Meperidine ▪ Methadone ▪ Morphine products (other than BCF selections), Kadian and Avinza (ER products) ▪ Opium tincture ▪ Opium/belladonna alkaloids(suppositories) ▪ Oxycodone (Oxycontin) ▪ Oxymorphone (Opana) ▪ Oxycodone/ASA ▪ Oxycodone/APAP other than BCF selections ▪ Buprenorphine injection ▪ Butorphanol ▪ Pentazocine/naloxone ▪ Propoxyphene ▪ Nalbuphine ▪ Codeine / APAP (other than BCF selections) ▪ Codeine / ASA ▪ Codeine / ASA / carisoprodol ▪ Codeine / caffeine / butalbital / APAP or ASA ▪ Dihydrocodeine / caffeine / APAP or ASA ▪ Hydrocodone / APAP ▪ Pentazocine / APAP ▪ propoxyphene / APAP ▪ Propoxyphene / ASA / caffeine ▪ Tramadol / APAP	▪ Tramadol ER (Ultram ER) Feb 07 ▪ Tramadol ER (Ryzolt) Nov 09 ▪ Tapendatol (Nucynta) Nov 09	Not applicable		Feb 07 Nov 09	▪ Morphine sulfate ER / naltrexone (Embeda) to remain UF (pending)

* New Drug—refers to a new FDA-approved drug in a class previously reviewed for Uniform Formulary (UF) status
ACE: angiotensin converting enzyme
ADHD: Attention Deficit / Hyperactivity Disorder drug class
ARB: angiotensin receptor blocker
CCB: calcium channel blocker
DRI: direct rennin inhibitor
HCTZ: hydrochlorothiazide
ER: extended release
IR: immediate release
RAAs: Renin Angiotension Antihypertensive Agents drug class

Appendix E—Table of Abbreviations

ACE	angiotensin converting enzyme
ADHD	attention deficit / hyperactivity disorder drug class
ARB	angiotensin receptor blocker
BAP	Beneficiary Advisory Panel
BCF	Basic Core Formulary
BIA	budget impact analysis
BP	blood pressure
CCB	calcium channel blocker
CEA	Cost-effectiveness analysis
CFR	Code of Federal Regulations
CMA	cost minimization analysis
DHP	dihydropyridine CCB
DM	diabetes mellitus
DoD	Department of Defense
ECF	Extended Core Formulary
ED	erectile dysfunction
ER	extended release
ESI	Express Scripts, Inc
FCP	Federal Ceiling Price
FDA	Food and Drug Administration
FPG	fasting plasma glucose
FSS	Federal Supply Schedule Price
FY	fiscal year
HA	Health Affairs
HbA1c	hemoglobin A1c
HCTZ	hydrochlorothiazide
HIT	heparin-induced thrombocytopenia
IR	immediate release
MARR	Mandatory Agreement for Retail Refunds
MHS	Military Health System
MN	medical necessity
MTF	Military Treatment Facility
NDAA	National Defense Authorization Act
NPH	neutral protamine hagedon insulin
OMB	Office of Management and Budget
P&T	Pharmacy and Therapeutics
PA	prior authorization
PCC	prothromin complex concentrate
PDE-5	phosphodiesterase-type 5 inhibitor drug class
PEC	Pharmacoeconomic Center
PORT	Pharmaceutical Outcomes Research Team
POS	point of service
QL	quantity limit
RAAs	renin-angiotensin antihypertensive drug class
SL	sublingual
TMA	TRICARE Management Activity
TMOP	TRICARE Mail Order Pharmacy
TPHARM	TRICARE Pharmacy Benefit Program
TRRx	TRICARE Retail Pharmacy Network
UF VARR	Uniform Formulary Voluntary Agreement for Retail Refunds
vWF	von Willebrand factor