DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS
November 2010

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on November 16 and 17, 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 August Minutes**—George Peach Taylor, Jr., M.D. MPH, Acting Director, approved the minutes for the August 2010 DoD P&T Committee meeting on November 8, 2010.
2. **Reanalysis of Antihemophilic Agents**—The P&T Committee evaluated the relative clinical and cost effectiveness of the Antihemophilic Factors at the February 17–18, 2010, meeting. The minutes were subsequently signed by the Acting Director, TMA, on May 3, 2010. The following Antihemophilic Agents were returned to formulary status on the UF, per execution of the required DoD Retail Refund Pricing Agreement, as signed by George Peach Taylor, Jr., M.D., MPH, Acting Director, on November 8, 2010:
    - Human Factor VIII: Hemofil M
    - Recombinant Factor VIII: Recombinate, Advate
    - Prothrombin Complex Concentrates: Bebulin VH, Feiba VH

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

A. Inhaled Corticosteroid (ICS)/Long-acting Beta Agonist (LABA)—Mometasone/formoterol Oral Inhaler (Dulera)

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. The

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

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.

Relative Cost-Effectiveness— Cost-minimization analysis (CMA) was performed to evaluate the cost of mometasone/formoterol (Dulera) in relation to the other currently available ICS/LABAs. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

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

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 (17 for, 0 opposed, 1 abstained, 0 absent) mometasone/formoterol (Dulera) be designated formulary on the UF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (17 for, 0 opposed, 1 abstained, 0 absent) mometasone/formoterol (Dulera) be excluded from the BCF.

Director, TMA, Decision : ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: QUANTITY LIMTS (QL)***—ICS/LABA combination inhalers on the UF are subject to QLs, which are consistent with the recommended dosing from the product labeling and safety concerns. The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) QLs for mometasone/formoterol (Dulera), consistent with the other products in the class: 3 inhalers/90-day supply in the mail order pharmacy and 1 inhaler/30-day supply in the retail point of service.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

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

Relative Clinical Effectiveness—Silenor is a new low-dose 3mg 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). The clinical evaluation for Silenor included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

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.

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

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

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 (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.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (17 for, 0 opposed, 1 abstained, 0 absent) doxepin tablets (Silenor) be excluded from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

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

   a) Automated PA criteria:
      (1) The patient has received a prescription for zolpidem IR at any Military Health Service (MHS) pharmacy point of service

(Military Treatment Facilities (MTFs), retail network pharmacies, or home delivery) during the previous 180 days.

b) Manual (paper) PA criteria, if automated criteria are not met:
   (1) The patient has tried zolpidem IR and was unable to tolerate treatment due to adverse effects.
   (2) The patient has tried zolpidem IR and has had an inadequate response.
   (3) The patient has a known contraindication to zolpidem IR.
   (4) The patient requires a nonscheduled agent for sleep maintenance.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: PA IMPLEMENTATION PERIOD***—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. Based on the committee's recommendation, the effective date is April 13, 2011.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

C. Antilipidemic-1s (LIP-1s)—Pitavastatin (Livalo)

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

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.

Relative Cost-Effectiveness—CMA was performed that evaluated the cost of pitavastatin (Livalo) in relation to other available LIP-1s. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (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.

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 (17 for, 0 opposed, 1 abstained, 0 absent) pitavastatin (Livalo) be designated NF on the UF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA***—Based on the clinical evaluation of pitavastatin (Livalo) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) MN criteria for pitavastatin (Livalo). (See Appendix B for full MN criteria).

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: PA 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.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—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. Based on the committee's recommendation, the effective date is April 13, 2011.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

D. Narcotic Analgesics—Hydromorphone Hydrochloride (HCl) Extended Release (ER) Tablets (Exalgo)

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

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.

Relative Cost-Effectiveness—CMA was performed that evaluated the cost of hydromorphone HCl ER (Exalgo) in relation to other currently available agents in Narcotic Analgesic 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).

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.

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 (10 for, 6 opposed, 2 abstained, 0 absent) hydromorphone HCl ER (Exalgo) be designated formulary on the UF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (14 for, 2 opposed, 2 abstained, 0 absent) hydromorphone HCl ER (Exalgo) be excluded from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

F. Antilipidemic-2s (LIP-2s)—Fenofibric Acid (Fibricor)

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

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 Fibricor has a compelling clinical advantage over the fenofibrate products on the UF.

Relative Cost-Effectiveness—CMA was performed that evaluated the cost of fenofibric acid (Fibricor) in relation to other currently available LIP-2s. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

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

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, 1 opposed, 1 abstained, 1 absent) fenofibric acid (Fibricor) be designated NF on the UF.

   Director, TMA, Decision: ☒ Approved ☐ Disapproved

   Approved, but modified as follows:

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluation of fenofibric acid (Fibricor) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) MN criteria for fenofibric acid (Fibricor). (See Appendix B for full MN criteria).

   Director, TMA, Decision: ☒ Approved ☐ Disapproved

   Approved, but modified as follows:

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—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. Based on the committee's recommendation, the effective date is April 13, 2011.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

G. Contraceptives—Estradiol Valerate/Dienogest (Natazia)

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. The clinical evaluation for estradiol valerate/dienogest (Natazia) included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

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.

Relative Cost-Effectiveness— CMA was performed to evaluate the cost of estradiol valerate/dienogest (Natazia) in the Contraceptive Agents 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).

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.

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 (16 for, 0 opposed, 1 abstained, 1 absent) estradiol valerate/dienogest (Natazia) be designated NF on the UF.

   Director, TMA, Decision: ☒ Approved ☐ Disapproved

   Approved, but modified as follows:

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

   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, 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. Based on the committee's recommendation, the effective date is April 13, 2011.

Director, TMA, Decision: ☒ Approved □ Disapproved

Approved, but modified as follows:

IV. UF DRUG CLASS REVIEWS

A. Non-Insulin Diabetes Drugs

Background Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the drugs in the Non-insulin Diabetes drug class. The clinical review for the non-insulin diabetes drugs included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

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 (SU), 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).

DoD Pharmacy Outcomes Research Team (PORT) Analysis: MHS Patterns of Use of Diabetes Drugs—The PORT analyzed data for new users of insulin and non-insulin diabetes drugs. Overall, 619,993 unique DoD beneficiaries received one or more Rxs for a diabetes medication (including insulin) during the one-year period from July 1, 2009–June 30, 2010.

The breakdown of classes is:

- 68% metformin/metformin FDC products
- 36% SU/SU FDC products
- 30% insulin
- 22% TZD/TZD FDC products
- 15% DPP-4 inhibitors
- 4% GLP1RAs
- 3% meglitinides, AGIs or pramlintide

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 following subclasses used for second-line therapy (when added to metformin): AGIs,

basal insulins, DPP-4 inhibitors, GLP1RAs, meglitinides, SUs, and TZDs. The Basal Insulin drug class was reviewed in February 2010 but is included in the CEA due to its inclusion in the ADA guidelines.

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, followed by the basal insulins. 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. Non-insulin Diabetes Drugs—Biguanides

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the 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 BCF includes all strengths of generic metformin IR and ER; BCF metformin products were selected prior to implementation of the UF Rule in 2005. The clinical review focused on use of metformin for T2DM (non-DM uses were not considered) and included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

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.

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

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (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.

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 (16 for, 1 opposed, 1 abstained, 0 absent):

   a) 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;

   b) Fortamet (500mg, 1000 mg) and Glumetza (500 mg, 1000 mg) be designated NF on the UF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (17 for, 0 opposed, 1 abstained, 0 absent) metformin IR (500 mg, 850 mg, 1000 mg), and metformin ER (500 mg, 750 mg) remain on the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

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

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—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. Based on the committee's recommendation, the effective date is April 13,, 2011.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

B. Non-insulin Diabetes Drugs—SUs

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the SUs subclass. The SUs have not previously been reviewed; all the drugs are currently designated with formulary status on the UF. The BCF includes glipizide (Glucotrol, generics), glyburide (Diabeta, Micronase, generics), and glyburide micronized (Glynase Pres Tab, generics). BCF SU products were selected prior to implementation of the UF Rule in 2005. All the SU products are available in generic formulations. In the MHS, glipizide is the highest utilized sulfonylurea agent. The clinical review for the SUs included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

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 alone. 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.

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

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

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 (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)

Director, TMA, Decision: ☑ Approved □ Disapproved

Approved, but modified as follows:

2. ***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, recommended (17 for, 0 opposed, 1 abstained, 0 absent) the following remain on the BCF:

a) glipizide (Glucotrol, generic); glyburide (Diabeta, Micronase, generic); and glyburide micronized (Glynase Press Tab, generic)

Director, TMA, Decision: ☒ Approved □ Disapproved

Approved, but modified as follows:

D. Non-insulin Diabetes Drugs—DPP-4 Inhibitors

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. The clinical review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

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 DPP-4 inhibitors may be mentioned when the guidelines are updated next year, 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; the TECOS trial with sitagliptin and the SAVOR-TIMI 53 trial with saxagliptin. Results are expected in 2014–2015.
3. Monotherapy with sitagliptin 100mg daily reduced HbA1c on average by 0.6%–0.79% (mean difference from placebo); 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. 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.

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

Relative Cost-Effectiveness Conclusion—Based on the results of the cost 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. Cost scenarios evaluating the impact of designating selected agents on the BCF were also considered. 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.

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 (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.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (15 for, 1 opposed, 1 abstained, 1 absent) sitagliptin (Januvia) and sitagliptin/ metformin (Janumet) be added to the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: PA 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.

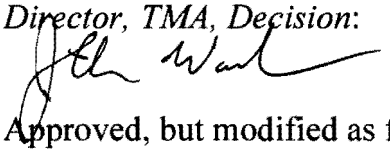
   b) Manual PA criteria, if automated criteria are not met:

      (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.

Director, TMA, Decision: ☑ Approved ☐ Disapproved



Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—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. Based on the committee's recommendation, the effective date is April 13, 2011.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

E. Non-insulin Diabetes Drugs—GLP1RAs

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. The clinical review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

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-label 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 30–60 minutes prior to meals whereas liraglutide is dosed once daily without regard 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.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the GLP1RAs subclass. CMAs and BIAs were performed. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost 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. Cost scenarios evaluating the impact of designating selected agents on the BCF were also considered.

- 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.

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 (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.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (14 for, 1 opposed, 2 abstained, 1 absent) excluding exenatide (Byetta) and liraglutide (Victoza) from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

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

The P&T Committee recommended (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).

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—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. Based on the committee's recommendation, the effective date is April 13, 2011.

Director, TMA, Decision: ☒Approved □ Disapproved

Approved, but modified as follows:

F. Non-insulin Diabetes Drugs—TZDs

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 and there are no BCF drugs. The clinical review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

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.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the TZDs subclass. CMAs were performed. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost 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.

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 (16 for, 0 opposed, 1 abstained, 1 absent):

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

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

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (16 for, 0 opposed, 1 abstained, 1 absent) pioglitazone, pioglitazone FDC products, rosiglitazone, and rosiglitazone FDC products be excluded from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

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

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: PA 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.

   Director, TMA, Decision: ☒ Approved ☐ Disapproved

   Approved, but modified as follows:

5. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—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. Based on the committee's recommendation, the effective date is April 13, 2011.

   Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows

G. Non-insulin Diabetes Drugs—Meglitinides

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. The clinical review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

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.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the Meglitinides subclass. CMAs were performed. Information

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

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

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, 2 absent) nateglinide (Starlix, generic), repaglinide (Prandin), and repaglinide/metformin (Prandimet) be designated formulary on the UF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (15 for, 0 opposed, 1 abstained, 2 absent) nateglinide (Starlix, generic), repaglinide (Prandin), and repaglinide/metformin (Prandimet) be excluded from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

H. Non-insulin Diabetes Drugs—AGIs

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. The clinical review included, but was not

limited to, sources of information listed in 32 CFR 199.21(e)(1).

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.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the AGIs subclass. CMAs were performed. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) acarbose (Precose, generics) and miglitol (Glyset) were cost-effective for the subset of patients who could tolerate the frequent GI side effects and multidose regimens required by these agents.

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 (16 for, 1 opposed, 1 abstained, 0 absent) acarbose (Precose, generics) and miglitol (Glyset) be designated formulary on the UF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (17 for, 0 opposed, 1 abstained, 0 absent) acarbose (Precose, generics) and miglitol (Glyset) be excluded from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

I. Non-insulin Diabetes Drugs—Amylin Agonists (Pramlintide)

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. The clinical review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

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 multidose 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.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the Amylin Agonists subclass. A CMA was performed. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (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.

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 (16

for, 0 opposed, 1 abstained, 1 absent) pramlintide (Symlin) injection remain designated as formulary on the UF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***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, recommended (16 for, 0 opposed, 1 abstained, 1 absent) excluding pramlintide (Symlin) from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: PA 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.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: PA IMPLEMENTATION PERIOD***—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. Based on the committee's recommendation, the effective date is April 13, 2011.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

V. BASIC CORE FORMULARY ISSUES—FENOFIBRATE MELTDOSE (FENOGLIDE) BCF DELETION

The LIP-2s drug class was previously reviewed for UF placement in May 2007. At that time, fenofibrate insoluble drug delivery micro-particle (Triglide) was added to the BCF. In June 2008, fenofibrate meltdose (Fenoglide) replaced Triglide on the BCF, and a $3.00 co-pay was implemented. Changes in licensing and manufacturing agreements have disrupted the availability of Fenoglide, and MTFs are unable to obtain the product. Due to the back order situation, the P&T Committee recommended removing fenofibrate meltdose (Fenoglide) from the BCF. The LIP-2 drug class will be re-reviewed at an upcoming meeting.

1. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee voted (16 for, 0 opposed, 1 abstained, 1 absent) to:
   a) remove Fenoglide from the BCF;
   b) maintain Fenoglide with formulary status on the UF;
   c) raise the co-pay from $3.00 to $9.00; and
   d) notify beneficiaries of the change in formulary status.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

Based on the manufacturer's (Shore Therapeutics) refusal to sign a Master Agreement with the VA and participate in the drug discount program required by 38 U.S.C. 8126, and on the manufacturer's voluntary removal of Fenoglide from the TRICARE Pharmacy Benefits Program on November 24, 2010, Fenoglide is no longer covered by TRICARE.

VI. UTILIZATION MANAGEMENT—PA

A. Fingolimod (Gilenya)—PA: 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).

1. ***COMMITTEE ACTION: PA CRITERIA AND IMPLEMENTATION***—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:

    a) a documented diagnosis for relapsing forms of MS;

    b) no current use of interferon alpha/beta or Copaxone;

    The fingolimod PA becomes effective the first Wednesday after a 60-day implementation period in all points of service. Based on the committee's recommendation, the effective date is April 13, 2011.

    Director, TMA, Decision: ☒ Approved ☐ Disapproved

    Approved, but modified as follows:

B. Fentanyl Citrate—Expansion of PA: 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. 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.

1. ***COMMITTEE ACTION: MODIFICATION OF FENTANYL PA AND IMPLEMENTATION***—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)

The expanded fentanyl PA becomes effective the first Wednesday after a 60-day implementation period in all points of service. Based on the committee's recommendation, the effective date is April 13, 2011.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

VII. ITEMS FOR INFORMATION

A. Effects of Formulary Changes—PORT: The PORT presented data on the effects of formulary changes in two drug classes: the LIP-1s, last reviewed in May 2010, and the Phosphodiesterase-5 Inhibitors (PDE-5s), last reviewed in November 2009. The P&T Committee requested further analysis as more data becomes available.

B. Simvastatin/Niacin ER (Simcor) Automated PA Update—Simvastatin/niacin ER (Simcor) is now available in 40/500 mg and 40/1000 mg tablets, with a maximum dose of 40 mg/2000 mg daily. P&T Committee was informed that the automated PA was updated to include the new simvastatin/niacin ER dosage strengths.

C. Clopidogrel-Proton Pump Inhibitor (PPI) Drug Interaction Update—The P&T Committee was briefed on the most recent information regarding a drug interaction between clopidogrel (Plavix) and PPIs. A previous update was provided to the P&T Committee in May 2009. Joint guidelines from the American College of Cardiology/American Heart Association/American College of Gastroenterology, published in November 2010, address concomitant use of PPIs with clopidogrel and other anti-platelet drugs. The P&T Committee recommended maintaining the current PPI MN and automated PA criteria, continued monitoring of literature and the FDA for new updates, and revisiting the issue when significant new developments occur.

D. Process For New Drug Pharmacy Benefit Determination—A proposed algorithm to determine whether a newly-marketed FDA-approved drug falls under the pharmacy benefit was presented. The proposed algorithm will be reviewed by the TRICARE Office of General Counsel.

VIII. FUTURE CLASS OVERVIEWS

Overviews for three drug classes were presented to the P&T Committee. The LIP-2s drug class is comprised of the fenofibric acid derivatives (gemfibrozil and the fenofibrates), prescription omega-3 fatty acids, and bile acids sequestrants. The nasal corticosteroids were previously reviewed by the P&T Committee in November 2005 and November 2008; they will be re-reviewed at an upcoming meeting. Information regarding the atypical antipsychotics drug class was also presented. 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 presented at an upcoming meeting.

IX. ADJOURNMENT

The meeting adjourned at 1700 hours on November 16, 2010, and at 1600 hours on November 17, 2010. The next meeting will be in February 2011.

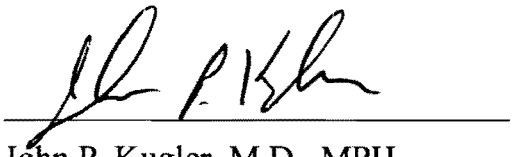
Appendix A—Attendance

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

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

Appendix D—Table of Abbreviations

SUBMITTED BY:



John P. Kugler, M.D., MPH
DoD P&T Committee Chair

DECISION ON RECOMMENDATIONS

Director, TMA, decisions are as annotated above.

, MD.

Jonathan Woodson, M.D.
Director

2/4/2011
(Date)

Appendix A—Attendance

Voting Members Present	
John Kugler, COL (Ret), MC, USA	DoD P&T Committee Chair
LTC Stacia Spridgen, MSC	Director, DoD Pharmacoeconomic Center (Recorder)
Col George Jones, BSC	Deputy Chief, Pharmaceutical Operations Directorate
COL Carole Labadie, MSC	Army, Pharmacy Officer
Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CAPT Stephanie Simon, MSC	Navy, Pharmacy Officer
CAPT Vernon Lew	Coast Guard, Pharmacy Officer
LTC Jack Lewi, MC for COL Doreen Lounsbery, MC	Army, Internal Medicine Physician
COL Ted Cieslak, MC	Army, Physician at Large
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Major Bart Staat, MC for Major Jeremy King, MC	Air Force, OB/GYN Physician
CAPT David Tanen, MC	Navy, Physician at Large
Lt Col Brian Crownover, MC	Air Force, Physician at Large
LTC Mike Wynn, MC for LTC Bruce Lovins, MC	Army, Family Practice Physician
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
CDR Eileen Hoke, MC	Navy, Pediatrics
Mr. Joe Canzolino	Department of Veterans Affairs
Dr. Miguel Montalvo	TRICARE® Regional Office-South Chief of Clinical Operations Division and Medical Director
Nonvoting Members Present	
Mr. David Hurt	Assistant General Counsel, TMA
LCDR Joe Lawrence, MSC	DoD PEC/TMA POD
CDR Michele Hupp, MSC	Defense Medical Standardization Board
Guests	
Brittany Martinez	Student, University of Incarnate Word Feik School of Pharmacy

Appendix A—Attendance (continued)

Guests	
Dr. Todd Semla	Veterans Affairs, Pharmacy Benefits Management Services
LCDR Kailee Fretland	United States Public Health Service/Indian Health Service
Others Present	
COL Cynthia Clagett, MC	DoD Pharmacoeconomic Center
Lt Col Rey Morales, MC	DoD Pharmacoeconomic Center
Lt Col Cynthia Lee, BSC	DoD Pharmacoeconomic Center
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
LCDR Ola Ojo, MSC	DoD Pharmacoeconomic Center
HM1 Trishonya Mcmihelk	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. Joshua Devine	DoD Pharmacoeconomic Center
Dr. Brian Beck	DoD Pharmacoeconomic Center
Dr. Amy Lugo	DoD Pharmacoeconomic Center
Dr. Dean Valibhai	DoD Pharmacoeconomic Center
Dr. Libby Hearin	DoD Pharmacoeconomic Center
Dr. 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

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

Drug / Drug Class	Medical Necessity Criteria
Metformin ER (Fortamet) Metformin ER (Glumetza) **Non-insulin Diabetes Drugs: Biguanides**	• Use of formulary agents contraindicated • The patient has experienced or is likely to experience significant adverse effects from formulary alternatives
Rosiglitazone (Avandia) Rosiglitazone/metformin (Avandamet) Rosiglitazone/glimepiride (Avandaryl) **Non-insulin Diabetes Drugs: Thiazolidinediones (TZDs)**	• Use of formulary agents contraindicated • The patient previously responded to a nonformulary agent, and changing to a formulary agent would incur unacceptable risk
Pitavastatin (Livalo) **Antilipidemics-1s**	• Use of formulary agents contraindicated
Fenofibrate (Fibricor) **Antilipidemics-2s**	• Use of formulary agents contraindicated
Estradiol valerate / dienogest (Natazia) **Contraceptive Agents**	• Use of formulary agents contraindicated • No alternative formulary agent available (if other oral contraceptive agents do not provide adequate bleeding and cycle control)

Appendix C—Table of Implementation Status of UF Recommendations/Decisions Summary Table

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	Comments
Nov 2010	**Non-Insulin Diabetes Drugs** Biguanides	UF Review	▪ Metformin IR 500, 850, 1000 mg (generics) ▪ Metformin ER 500, 750 mg (generics)	▪ Metformin 500 mg/5mL liquid (Riomet)	▪ Metformin ER 500, 1000 mg (Fortamet) ▪ Metformin ER 500, 1000 mg (Glumetza) (Nov 2010)	Pending 60 days	Not applicable	Trial of metformin and/or sulfonylurea is mandated before TZDs, DPP-4 inhibitors or GLP-1 agonists can be used
Nov 2010	**Non-Insulin Diabetes Drugs** Sulfonylureas	UF Review	▪ Glipizide (generics) ▪ Glyburide (generics) ▪ Glyburide micronized tabs (generics)	▪ Chlorpropamide (generics) ▪ Glimepiride (generics) ▪ Glipizide ER (generics) ▪ Glipizide/metformin (generics) ▪ Glyburide/metformin (generics)	Not applicable (no drug designated nonformulary)	Pending 60 days	Not applicable	Trial of metformin and/or sulfonylurea is mandated before TZDs, DPP-4 inhibitors or GLP-1 agonists can be used
Nov 2010	**Non-Insulin Diabetes Drugs** Alpha Glucosidase Inhibitors	UF Review	Not applicable (no drug designated BCF)	▪ Acarbose (generics) ▪ Miglitol	Not applicable (no drug designated nonformulary)	Not applicable	Not applicable	-
Nov 2010	**Non-Insulin Diabetes Drugs** Meglitinides	UF Review	Not applicable (no drug designated BCF)	▪ Nateglinide (generics) ▪ Repaglinide (Prandin) ▪ Repaglinide/metformin (Prandimet)	Not applicable (no drug designated nonformulary)	Not applicable	Not applicable	-
Nov 2010	**Non-Insulin Diabetes Drugs** Thiazolidinediones	UF Review	Not applicable (no drug designated BCF)	▪ Pioglitazone (Actos) ▪ Pioglitazone/metformin (Actoplus Met) ▪ Pioglitazone/metformin XL (Actoplus Met XR) ▪ Pioglitazone/glimepiride (Duetact)	▪ Rosiglitazone (Avandia) ▪ Rosiglitazone/ metformin (Avandamet) ▪ Rosiglitazone/ glimepiride (Avandaryl) (Nov 2010)	Pending 60 days	Step Therapy (Automated PA)	Step Therapy (automated PA) with metformin and sulfonylureas as step preferred agents

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	Comments
Nov 2010	**Non-Insulin Diabetes Drugs** DPP-4 Inhibitors	UF Review	▪ Sitagliptin (Januvia) ▪ Sitagliptin/Metformin (Janumet)	▪ Saxagliptin (Onglyza)	Not applicable (no drug designated nonformulary)	Pending 60 days	Not applicable	Step Therapy (automated PA) with metformin and sulfonylureas as step preferred drugs
Nov 2010	**Non-Insulin Diabetes Drugs** GLP-1 Receptor Agonists	UF Review	Not applicable (no drug designated BCF)	▪ Exenatide (Byetta) ▪ Liraglutide (Victoza)	Not applicable (no drug designated nonformulary)	Pending 60 days	Step Therapy (Automated PA) Manual PA precluding use of GLP-1s for obesity	-Step Therapy (automated PA) with metformin and sulfonylureas as step preferred drugs -Exenatide (Byetta) is step preferred for the GLP-1 subclass
Nov 2010	**Non-Insulin Diabetes Drugs** Amylin Agonist	UF Review	Not applicable (no drug designated BCF)	▪ Pramlintide (Symlin)	Not applicable (no drug designated nonformulary)	Pending 60 days	Manual PA expanded to preclude the use of Symlin for obesity	
Nov 2010	Newer Insomnia	New Drug Doxepin (Silenor)	▪ Zolpidem IR	▪ **Doxepin (Silenor) (Nov 2010)** ▪ Eszopiclone (Lunesta)	▪ Zolpidem CR (Ambien CR) ▪ Zaleplon (Sonata) ▪ Ramelteon (Rozerem) ▪ Zolpidem sublingual (Edluar)	Not applicable	Step Therapy (Automated PA)	Doxepin (Silenor) remains UF Step Therapy applies with zolpidem IR preferred
Nov 2010	Pulmonary-1 ICS/LABA	New Drug Formoterol/ mometasone (Dulera)	▪ Fluticasone/salmeterol (Advair Diskus and HFA)	▪ **Formoterol/ mometasone (Dulera) (Nov 2010)** ▪ Budesonide/formoterol (Symbicort)	Not applicable (no drug designated nonformulary)	Not applicable	QLs apply Retail: 1 MDI/30 d Mail order: 3 MDIs/90 d	

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	Comments
Nov 2010	Antilipidemic Agents I	• *New Drug* Pitavastatin (Livalo)	▪ Atorvastatin (Lipitor) ▪ Pravastatin (Pravachol, generics) ▪ Simvastatin (Zocor, generics)	▪ Atorvastatin / amlodipine (Caduet) ▪ Ezetimibe (Zetia) ▪ Ezetimibe / simvastatin (Vytorin) ▪ Fluvastatin IR/ER (Lescol) ▪ Lovastatin IR ▪ Lovastatin ER (Altoprev) ▪ Lovastatin / niacin ER (Advicor) ▪ Niacin ER (Niaspan) ▪ Rosuvastatin (Crestor) ▪ Simvastatin/ niacin ER (Simcor)	▪ **Pitavastatin (Livalo) (Nov 2010)**	Pending 60 days	Step Therapy (Automated PA)	▪ Pitavastatin (Livalo) designated non-formulary ▪ Step therapy (automated PA) with generics or atorvastatin as the preferred drugs (note: step therapy doe apply to ezetimibe or ni
Nov 2010	Antilipidemic Agents II	• *New Drug* Fenofibric acid (Fibricor) ▪ *BCF removal* Fenofibrate meltdose (Fenoglide)	▪ Gemfibrozil (Lopid)	▪ Fenofibrate meltdose (Fenoglide) ▪ Fenofibrate IDD-P (micronized) (Triglide) ▪ Fenofibrate micronized/nonmicronized (Lofibra) ▪ Cholestyramine / aspartame (Questran Light, Prevalite Locholest Light) ▪ Cholestyramine / sucrose (Questran) ▪ Colestipol (Colestid)	▪ **Fenofibric acid (Fibricor) (Nov 2010)** ▪ Fenofibrate nanocrystallized (Tricor) ▪ Fenofibrate micronized (Antara) ▪ Fenofibric acid (Trilipix) ▪ Omega-3 fatty acids (Lovaza) ▪ Colesevelam (Welchol)	Pending 60 days	Not applicable	▪ Fenofibric acid (Fibricor) recommended for NF (pending) ▪ Fenofibrate meltdose (Fenoglide) removed from BCF and recommended for UF(pending)
Nov 2010	Contraceptive Agents	• *New Drug* Estradiol valerate/ dienogest (Natazia)	▪ See TRICARE formulary search tool*	▪ See TRICARE formulary search tool*	▪ **Estradiol valerate/dienogest (Natazia) (Nov 2010)** ▪ See TRICARE formulary search tool* for remainder of NF drugs	Pending 60 days	Not applicable	▪ Estradiol valerate/dienogest (Natazia) recommended for NF (pending) ▪ Contraceptives update in 2011

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	Comments
Feb 2010	Narcotic Analgesics	• *New Drug* Hydromorphone ER (Exalgo)	▪ 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	▪ **Hydromorphone ER (Exalgo) (Nov 2010)** ▪ Fentanyl buccal soluble film (Onsolis) ▪ Fentanyl transdermal system, transmucosal tablet (Fentora); & transmucosal lozenge ▪ Codeine ▪ Hydromorphone (Dilaudid) ▪ Levorphanol ▪ Meperidine ▪ Methadone ▪ Morphine products (other than BCF), Kadian and Avinza (ER products) ▪ Morphine sulfate ER / naltrexone (Embeda) ▪ Opium tincture ▪ Opium/belladonna alkaloids(suppositories) ▪ Oxycodone IR ▪ Oxycodone ER(Oxycontin) ▪ Oxymorphone (Opana) ▪ Oxycodone/ASA ▪ Oxycodone/APAP not BCF ▪ Buprenorphine injection ▪ Butorphanol ▪ Pentazocine/naloxone ▪ Propoxyphene ▪ Nalbuphine ▪ Codeine / APAP(not BCF) ▪ 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	Not applicable	Hydromorphone ER remains UF (pending)

ASA: aspirin
APA: acetaminophen
DPP-4: dipeptidyl peptidase-4
ER: extended release
ECF: Extended Core Formulary
GLP-1: glucagon-like peptide 1
ICS/LABA: inhaled corticosteroid/long-acting beta agonist
IDD-P: insoluble drug deliver particle
IR: immediate release
MDI: metered dose inhaler
*TRICARE Formulary Search tool: http://www.pec.ha.osd.mil/formulary_search.php

Appendix D—Table of Abbreviations

ADA	American Diabetes Association
AGIs	alpha-glucosidase inhibitors
Avg CER	average cost effectiveness ratio
BAP	Beneficiary Advisory Panel
BCF	Basic Core Formulary
BIA	budget impact analysis
CEA	cost-effectiveness analysis
CFR	Code of Federal Regulations
CI	confidence interval
CMA	cost minimization analysis
CV	Cardiovascular
DM	diabetes mellitus
DPI	dry powder inhaler
DPP-4	dipeptidyl-peptidase 4 inhibitor subclass
DoD	Department of Defense
ECF	Extended Core Formulary
ED	erectile dysfunction
ER	extended release
ESI	Express Scripts, Inc
FCP	Federal Ceiling Price
FDA	U.S. Food and Drug Administration
FDC	fixed-dose combination
FSS	Federal Supply Schedule Price
FPG	fasting plasma glucose
GI	gastrointestinal
GLP1RA	glucagon-like peptide-1 receptor agonist subclass
HA	Health Affairs
HDL	high density lipoprotein cholesterol
HbA1c	glycosolated hemoglobin or hemoglobin A1c
ICS/LABA	inhaled corticosteroid / long-acting beta agonist
IR	immediate release
LDL	low density lipoprotein cholesterol
LIP-1	Antilipidemic-1s drug class
MARR	Mandatory Agreement for Retail Refunds
MHS	Military Health System
MI	myocardial infarction
MDI	metered dose inhaler
MEN2	Endocrine Neoplasia syndrome type 2
MS	multiple sclerosis
MN	medical necessity
MTF	Military Treatment Facility
NDAA	National Defense Authorization Act
OMB	Office of Management and Budget
OROS	osmotic controlled release oral delivery system
P&T	Pharmacy and Therapeutics
PA	prior authorization
PEC	Pharmacoeconomic Center
P1	Period 1
PPG	post prandial glucose

Appendix D—Table of Abbreviations (continued)

PPI	proton pump inhibitor drug class
PORT	Pharmaceutical Outcomes Research Team
QL	quantity limit
Rxs	prescriptions
SED-1	sedative hypnotic-1 drug class
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TCA	tricyclic antidepressant
TG	triglyceride
SR	sustained release
TZD	thiazolidinedione subclass
UKPDS	United Kingdom Prospective Diabetes Study
VA	Veteran's Affairs

DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS
August 2010

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on August 11, and 12, 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 May minutes**—Dr. Charles Rice, Acting Director, approved the minutes for the May 2010 DoD P&T Committee meeting on July 23, 2010.
2. **Clarification of May minutes**—The Basic Core Formulary (BCF) recommendation for the alpha blocker terazosin was clarified to specify generic formulations—not proprietary formulations—are included on the BCF.
3. **Clarifications of February 2010 Minutes**—The clinical effectiveness conclusion for the antihemophilic agents regarding purified factor VIII and IX concentrates was clarified to state:

> "National professional group guidelines, including the National Hemophilia Foundation Medical and Scientific Advisory Committee (MASAC 159) and national hemophilia patient advocacy groups caution against switching between products once a patient is stabilized."

III. UNIFORM FORMULARY (UF) DRUG CLASS REVIEWS

A. Renin Angiotensin Antihypertensive Agents (RAAs)

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the RAAs drug class. The class is comprised of the Angiotensin Converting Enzyme (ACE) Inhibitors, Angiotensin II Receptor Blockers (ARBs), the Direct Renin Inhibitors (DRIs), and their fixed-dose combination (FDC) products with hydrochlorothiazide (HCTZ), calcium channel blockers (CCBs), or other RAAs. The ARBs were previously reviewed by the P&T Committee in May 2007 and February 2005; ACE Inhibitors were previously reviewed in August 2005; and the fixed-dose combination ACE Inhibitor/CCB products were previously reviewed in February 2006.

The clinical review included, but was not limited to, sources of information listed in 32 Code of Federal Regulations (CFR) 199.21(e)(1).

The individual RAAs are listed below:

- **ACE Inhibitors:** benazepril (Lotensin, generic), benazepril/HCTZ (Lotensin HCT, generic), captopril (Capoten, generic), captopril/HCTZ (Capozide, generic), enalapril (Vasotec, generic), enalapril/HCTZ (Vasoretic, generic), fosinopril (Monopril, generic), fosinopril/HCTZ (Monopril HCT, generic), lisinopril (Prinvil, Zestril, generic), lisinopril HCT (Prinzide, Zestoretic, generic), moexipril (Univasc, generic), moexipril/HCTZ (Uniretic generic), perindopril (Aceon, generic), quinapril (Accupril, generic) quinapril/HCTZ (Accuretic, generic), trandolapril (Mavik, generic), and ramipril (Altace, generic)
- **ARBs:** candesartan (Atacand), candesartan/HCTZ (Atacand HCT), eprosartan, (Teveten), eprosartan/ HCTZ (Teveten HCT), irbesartan (Avapro), irbesartan/HCTZ (Avalide), losartan (Cozaar, generic), losartan/HCTZ (Hyzaar, generic), olmesartan (Benicar), olmesartan/HCTZ (Benicar HCT), telmisartan (Micardis), telmisartan/ HCTZ (Micardis HCT), valsartan (Diovan), and valsartan/HCTZ (Diovan HCT)
- **DRIs:** aliskiren (Tekturna), aliskiren/HCTZ (Tekturna HCT), and valsartan/aliskiren (Valturna)
- **Fixed dose combinations:** (RAAs/CCBs): benazepril/amlodipine (Lotrel, generic), trandolapril/verapamil sustained release (SR) (Tarka, generic), olmesartan/amlodipine (Azor), telmisartan/amlodipine (Twynsta), valsartan/amlodipine (Exforge), and valsartan/amlodipine/HCTZ (Exforge HCT)

The current BCF products are lisinopril, lisinopril/HCTZ, ramipril, and benazepril/amlodipine. The nonformulary (NF) agents include perindopril, moexipril +/- HCTZ, trandolapril/verapamil sustained release (SR), eprosartan +/- HCTZ, irbesartan +/-HCTZ, olmesartan +/- HCTZ, valsartan +/-HCTZ, olmesartan/amlodipine, telmisartan/amlodipine, valsartan/amlodipine, and aliskiren/valsartan. The remaining drugs are classified as UF drugs. Generic formulations are available for all the ACE inhibitors and the ACE inhibitor/diuretic products; generic formulations of losartan and losartan/HCTZ entered the market in April 2010. Generic formulations of candesartan, irbesartan, and valsartan are expected in 2012.

The RAAs class is ranked within the top 5 most costly Military Health System (MHS) drug classes, with expenditures exceeding $300 million annually. In terms of utilization, the ACE inhibitors comprise 58% of the RAAs market share, with the ARBs comprising 36%, and the fixed-dose combinations comprising 6%. For expenditures, the ARBs account for 66% of the annual MHS cost for the RAAs.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following conclusions for the RAAs:

1. For treating hypertension, the results of one systematic review reported the ARBs reduce blood pressure (BP) to a similar degree; at maximum recommended doses, the average trough systolic blood pressure reduction is -8 mmHg and the average trough diastolic blood pressure reduction is -5 mmHg.
2. The ACE inhibitors, ARBs, and the DRI aliskiren (Tekturna) reduce BP to a similar degree, based on the conclusions from two systematic reviews.
3. The addition of HCTZ increases the BP-lowering efficacy of the RAAs. The current Joint National Committee (JNC) 7 hypertension guidelines recommend multidrug regimens include a thiazide diuretic (e.g., HCTZ).
4. Hypertension studies show that the FDC products produce significantly greater BP reductions than their individual components. Additional benefits of FDC products include potential enhanced medication compliance, and simplified medication regimens. Disadvantages include loss of flexibility for dosage initiation and titration.
5. All the ARBs are U.S. Food and Drug Administration (FDA)-approved for treating hypertension; some of the ARBS have shown evidence for positive clinical outcomes. Telmisartan (Micardis) is FDA-approved to reduce the risk of cardiovascular (CV) mortality and morbidity in patients who are at high risk for CV events and are intolerant of ACE inhibitors (ON-TARGET and TRANSCEND trials). Candesartan (Atacand) and valsartan (Diovan) are FDA-approved for reducing the risk of death and hospitalization in patients with chronic heart failure. Losartan (Cozaar, generic) and irbesartan (Avapro) are FDA-approved to reduce the risk of delaying progression to end-stage renal disease (ESRD), doubling of serum creatinine, or death in patients with Type 2 diabetes mellitus (DM).
6. Although losartan (Cozaar, generic) is currently not FDA-approved for treating chronic heart failure, data from one trial (HEAAL, Lancet

2010) reported losartan 150 mg reduced the risk of death or hospitalization due to heart failure.

7. One unpublished trial (ORIENT) with olmesartan in patients with Type 2 DM did not find a delayed progression to ESRD, doubling of serum creatinine, or death. Another unpublished trial (ROADMAP) evaluating olmesartan in Type 2 DM patients did find a benefit in the surrogate outcome of delaying progression to microabluminuria.
8. For the RAA/CCB products, benazepril/amlodipine (Lotrel, generic) was superior to benazepril/HCTZ (Lotensin HCT, generic) in reducing the composite of CV mortality and morbidity in patients with hypertension who are at high risk for CV events (ACCOMPLISH trial). Benazepril/amlodipine is the only RAA/CCB FDC product with evidence for positive clinical outcomes, in addition to reducing BP.
9. There is no data to suggest that there are clinically relevant differences in the BP-reducing efficacy of the ARB/CCB FDC products olmesartan/amlodipine (Azor), telmisartan/amlodipine (Twynsta), or valsartan/amlodipine (Exforge). Adding an ARB to amlodipine results in a lower incidence of peripheral edema than that reported with CCB monotherapy.
10. Valsartan/amlodipine/HCTZ (Exforge HCT) is the first triple FDC antihypertensive drug to obtain FDA approval. It is more effective at reducing BP than administering two antihypertensive drugs, but has a higher incidence of orthostatic hypotension and dizziness than two-drug regimens.
11. The DRI aliskiren (Tekturna) reduces BP by suppressing plasma renin activity, which is unique among the RAAs. Aliskiren is effective at reducing BP when used as monotherapy or in combination with other antihypertensive drugs, but the BP effects are similar to that achieved with the diuretics, ARBs, or ACE inhibitors. Aliskiren is approved solely for treating hypertension; clinical outcomes trials are ongoing. Current JNC guidelines do not address the place in therapy for the DRIs. The adverse event profile for aliskiren appears similar to the ARBs.
12. Adding HCTZ to aliskiren (Tekturna HCT) provides enhanced BP reduction and is consistent with JNC guidelines, due to the diuretic component. There is limited published information for aliskiren/ HCTZ.

13. Aliskiren/valsartan (Valturna) is the first DRI/ARB that is FDA-approved for hypertension; it provides another option for patients requiring multidrug antihypertensive regimens. However, there are only limited published studies available, it is approved solely for treating hypertension, and the benefits of dual RAA inhibition are debatable, due to an increased risk of adverse events.
14. For the ACE inhibitors, with the exception of moexipril (Univasc, generics), evidence exists for positive clinical outcomes (e.g., decreased risk of major CV events or death in high-CV risk patients, those with heart failure, in patients with Type 2 diabetic renal disease, or in the post-myocardial (MI) setting), in addition to lowering BP.
15. For the ARBs, it is unlikely that there are clinically relevant differences in their adverse event profiles. Clinical trials show similar adverse event rates as with placebo.
16. The FDA is evaluating the association of ARBs and an increased risk of cancer, which was reported in a recent meta-analysis (Sipahi, et al., Lancet Oncology 2010). The FDA maintains the benefits of ARBs currently outweigh their risk.
17. The FDA is evaluating the risk of increased CV death with olmesartan reported in Type 2 DM patients from the ROADMAP and ORIENT trials. FDA is currently reviewing the data for olmesartan and has not concluded that it increases the risk of death.
18. For the ACE inhibitors, the major adverse events are hyperkalemia, increased serum creatinine, and cough. One systematic review comparing the ARBs with the ACE inhibitors reported the overall incidence of ACE inhibitor-induced cough as ranging between 0%–23% (mean 10%).
19. The DoD Pharmacy Outcomes Research Team (PORT) provided an analysis of RAAs MHS prescription data and reported that ARBs are initiated as first-line therapy in the majority of patients, instead of ACE inhibitors. Additionally, it does not appear that patients with comorbidities (chronic heart failure, DM, left ventricular hypertrophy, post-MI) are prescribed an ARB based on the evidence for positive outcomes data and hypertension.
20. A survey of Military Treatment Facility (MTF) providers regarding the place in therapy using RAAs for hypertension revealed the ACE inhibitors are considered first-line, the ARBs are second-line, and the DRIs are third-line. The majority of providers responded that ARBs are interchangeable for

treating hypertension. Most respondents did not agree that FDC products were necessary to treat the majority of their hypertensive patients.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the RAAs. Cost-minimization analyses (CMAs) and budget impact analyses (BIAs) were performed based on clinical findings that the efficacy, safety, tolerability, and other factors among the RAAs subclasses of ACE inhibitors, ARBs, DRIs, and FDC products with HCTZ, CCBs, or other RAAs were similar with regard to treating hypertension. For the cost effectiveness analysis, the FDC products were compared with their parent RAA. Products containing aliskiren were analyzed and incorporated into the CMA and BIA used to evaluate the ARB subclass.

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

- **ACE Inhibitors and their combinations with HCTZ and/or CCBs:** Because all ACE inhibitors are now available in generic formulations, comparisons were made against the ARBs, ARB/combinations, DRIs, and DRI/combinations in the form of an ACE inhibitor step-therapy model. BIA was used to assess the potential impact of cost scenarios where ACE inhibitors or their combination agents were designated as the step-preferred agents on the UF prior to filling a prescription for ARBs, DRIs, or their respective combination products. Cost scenarios evaluating the impact of designating ACE inhibitors or ACE inhibitors/combinations as BCF agents prior to the use of ARBs, DRIs, or their respective combinations were also considered. BIA results showed that requiring an ACE inhibitor prior to using any ARB, DRI, or their respective combinations would be cost effective. Due to existing prescribing practices in the MHS, the P&T Committee agreed that use of an ACE inhibitor as a required step-preferred therapy could not be operationalized in an Automated Prior Authorization (PA).
- **ARBs, ARB/combinations, DRIs, and DRI/combinations:** BIA was used to assess the potential impact of cost scenarios where selected ARBs, ARB/combinations, DRIs, and DRI/combinations were designated as formulary or NF on the UF. Cost scenarios evaluating the impact of designating selected agents on the BCF were also considered. BIA results for the ARBs and DRIs showed the scenario placing losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/ HCTZ (Micardis HCT), telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), and valsartan/amlodipine/HCTZ (Exforge HCT) as step-preferred agents, while

placing all other ARBs, ARB/combinations, DRIs, and DRI/combinations on the UF was the most cost-effective scenario and operationally-appropriate choice.

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 1 abstained, 0 absent) to accept the relative cost-effectiveness analysis of the RAAs.

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

    a) losartan, losartan/HCTZ, telmisartan (Micardis), and telmisartan/HCTZ (Micardis HCT), remain classified as formulary on the UF, and that telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge) and valsartan/amlodipine/HCTZ (Exforge HCT) be designated formulary on the UF. Prior authorization (PA) for the RAAs drug class would require a trial of one of these step-preferred drugs for new patients (15 for, 0 opposed, 1 abstained, 0 absent);

    b) aliskiren (Tekturna), aliskiren/HCTZ (Tekturna HCT), candesartan (Atacand), candesartan/HCTZ (Atacand HCT), eprosartan (Teveten), eprosartan/HCTZ (Teveten HCT), irbesartan (Avapro), irbesartan/HCTZ (Avalide), olmesartan (Benicar), olmesartan/HCTZ (Benicar HCT), olmesartan/amlodipine (Azor), and valsartan/aliskiren (Valturna), be designated formulary on the UF (non-preferred) (15 for, 0 opposed, 1 abstained, 0 absent);

    c) benazepril, benazepril HCTZ, benazepril/amlodipine, captopril, captopril HCTZ, enalapril, enalapril HCTZ, fosinopril, fosinopril HCTZ, lisinopril, lisinopril HCTZ, quinapril, quinapril HCTZ, ramipril, and trandolapril remain formulary on the UF (15 for, 0 opposed, 1 abstained, 0 absent);

    d) The following four ACEs previously designated NF on the UF are now available in cost-effective generic formulations and will be designated formulary on the UF: moexipril (Univasc), moexipril HCTZ (Uniretic), perindopril (Aceon), and trandolapril/verapamil (Tarka) (15 for, 0 opposed, 1 abstained, 0 absent).

e) As a result of the above recommendations, there are no RAAs designated as nonformulary on the UF.

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved 11/10/10

Approved, but modified as follows:

2. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 2 absent) the following PA criteria should apply to the non-preferred RAAs, aliskiren (Tekturna), aliskiren/HCTZ (Tekturna HCT), aliskiren/valsartan (Valturna), candesartan (Atacand), candesartan/HCTZ (Atacand HCT), eprosartan (Teveten), eprosartan/HCTZ (Teveten HCT), irbesartan (Avapro), irbesartan/HCTZ (Avalide), olmesartan (Benicar), olmesartan/HCTZ (Benicar HCT), and olmesartan/amlodipine (Azor). 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 losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT) telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), or valsartan/amlodipine/HCTZ (Exforge HCT) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

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

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

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

Acting Director, TMA, Decision: ☒ *Approved* □ *Disapproved*

11/10/10

Approved, but modified as follows:

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 2 absent) an effective date an effective date of first Wednesday after a 60 days implementation period in all points of service. The effective date is 12 Jan 2011.

Acting Director, TMA, Decision: ☒ Approved □ Disapproved

11/8/10

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, recommended:
   a) losartan, losartan HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), valsartan (Diovan), valsartan/HCTZ (Diovan HCT) be designated with BCF status (15 for, 0 opposed, 1 abstained, 0 absent);
   b) captopril, benazepril/amlodipine (Lotrel generics), lisinopril, lisinopril HCTZ, ramipril remain on the BCF (15 for, 0 opposed, 1 abstained, 0 absent).

Acting Director, TMA, Decision: ☒ Approved □ Disapproved

11/8/10

Approved, but modified as follows:

B. Ophthalmic-1s

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the agents in the Ophthalmic-1 drug class. The class is comprised of the ophthalmic antihistamines (AHs), mast cell stabilizers (MCS), dual action AH/MCS, and the nonsteroidal anti-inflammatory drugs (NSAIDs). The Ophthalmic-1s have not previously been reviewed for UF placement; all the drugs are currently designated with formulary status on the UF, and there are no BCF or NF drugs. The clinical review focused on use of the Ophthalmic-1s for allergic conjunctivitis (AC) and included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

The individual Ophthalmic-1s are listed below:

- **Antihistamines:** emedastine (Emadine)
- **Dual Action Antihistamine/Mast Cell Stabilizers:** azelastine (Optivar, generics), bepotastine (Bepreve), epinastine (Elestat), olopatadine 0.1% (Patanol), and olopatadine 0.2% (Pataday)
- **Mast Cell Stabilizers:** pemirolast (Alamast), nedocromil (Alocril), cromolyn (Crolom/Opticrom, generic), and lodoxamide (Alomide)
- **NSAIDs:** ketorolac 0.4% (Acular LS, generic), ketorolac 0.45% (Acuvail), ketorolac 0.5% (Acular, generic), bromfenac (Xibrom), diclofenac (Voltaren, generic), flurbiprofen (Ocufen, generics), and nepafenac (Nevanac)

MHS expenditures for the Ophthalmic-1s exceed $19 million annually. In the MHS, olopatadine 0.2% (Patanol) is the highest utilized Ophthalmic-1 agent.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions for the Ophthalmic-1s:

1. With regard to mechanism of action and pharmacokinetic properties, the antihistamines provide relief of ocular itching, hyperemia, and edema, while MCS have anti-inflammatory effects. The dual action AH/MCS exhibit both properties. MCS have a slower onset of action for providing relief of ocular symptoms than AH/MCS (days to weeks, vs. minutes, respectively). NSAIDs relieve pain and reduce erythema.
2. With regard to FDA-approved indications, dual action AH/MCS and the MCS are approved for treating AC. For the NSAIDs, ketorolac 0.5% (Acular, generic) is approved for AC, and clinical trial data supports use of bromfenac (Xibrom) for this indication.

3. With regard to place in therapy, professional guidelines from the American Academy of Ophthalmology and the American Optometric Association recommend use of AHs or AH/MCS as first-line topical therapy for relief of AC symptoms.
4. With regard to efficacy for the treatment of AC, the results of one meta-analysis reported the following: MCS and AHs are superior to placebo in relieving symptoms of AC; there is no significant difference between the AHs and MCS in terms of proportion of patients with perceived benefit; there is insufficient evidence to demonstrate superiority of agents within each subclass; and convenience of use, cost and patient preference should guide treatment choice.
5. Interpretation of clinical efficacy differences between the individual dual action AH/MCS and individual MCS is difficult due to small patient enrollment, short-term treatment, use of single-dose studies, and acute course of symptoms. There are no head-to-head trials comparing bepotastine (Bepreve) with another Ophthalmic-1 agent. Overall, for relief of ocular itching, there does not appear to be clinically relevant differences between the dual action AH/MCS and the MCS.
6. With regard to safety and tolerability, published data does not suggest there are clinically relevant differences concerning burning/stinging, headaches, taste perversion, and hyperemia between the individual dual action AH/MCS and individual MCS in treating AC. The only published available meta-analysis did not assess adverse events, and the head-to-head trials were too small to determine clinically relevant differences individual dual action AH/MCS and individual MCS. The overall adverse event rate is low.
7. Data from the product labeling reports the dual action AH/MCS bepotastine (Bepreve) is associated with taste perversion in 25% of patients. For the MCS, nedocromil (Alocril) has an incidence of burning/stinging on instillation, plus taste perversion in 10%–30% of patients. The 0.5% concentration of ketorolac (Acular) is associated with burning/stinging in up to 40% of patients.
8. With regard to dosing frequency, olopatadine 0.2% (Pataday) is the only dual action AH/MCS that is dosed once daily; the other AH/MCS are dosed twice daily. For the MCS, nedocromil (Alocril) is dosed twice daily, while the other MCS are dosed 4–6 times daily. The NSAID ketorolac 0.5% (Acular) is dosed four times daily for AC.
9. With regard to preservatives, it remains to be determined whether the presence of carboxymethylcellulose instead of benzalkonium chloride

(BAK) in ketorolac 0.45% (Acuvail) or the reduced BAK concentration in bepotastine (Bepreve) are associated with a lower risk of adverse events.

10. A request for input from MTF providers revealed that the majority of responders ranked olopatadine 0.2% (Patanol) as the preferred Ophthalmic-1 agent to treat AC and olopatadine 0.1% (Pataday) as the second preference. The majority of responders chose cromolyn (Crolom/Opticrom, generic) as the preferred MCS, and ketorolac 0.5% (Acular, generic) as the preferred NSAID for treating AC.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the agents in the Ophthalmic-1 drug class used in the treatment of AC. CMAs and BIAs were performed based on clinical findings that the efficacy, safety, tolerability, and other factors among the Ophthalmic-1 subclasses were similar. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

- **Antihistamines and Dual Action AH/MCS:** Emedastine (Emadine) was analyzed with the dual action AH/MCS subclass. CMA results showed olopatadine 0.1% (Patanol) to be the most cost-effective agent for the treatment of AC, based on the cost per day of treatment. BIA was used to assess the potential impact of cost scenarios where Emedastine (Emadine) and/or dual action AH/MCS were designated formulary or NF on the UF. Cost scenarios evaluating the impact of designating agents on the BCF were also considered. BIA results from this analysis showed the most cost-effective scenario designated bepotastine (Bepreve) and epinastine (Elestat) NF on the UF, and the remaining dual action AH/MCS as formulary on the UF. Follow-up P&T Committee discussion considered the potential for MTF recapture of bepotastine (Bepreve) and epinastine (Elestat) from the retail sector to recommend formulary status for all other antihistamines and dual action AH/MCS agents.

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstained, 1 absent) to accept the relative cost-effectiveness analysis of the Antihistamines and Dual Action AH/MCS subclass.

- **Mast Cell Stabilizers:** BIA was used to assess the potential impact of cost scenarios where selected MCS were designated formulary or NF on the UF.

Cost scenarios evaluating the impact of designating agents on the BCF were also considered. BIA results showed the most cost-effective scenario designated cromolyn 0.4% (generic) with formulary status on the UF, with all other MCS designated as NF on the UF. However, P&T Committee discussion recommended that all MCS should remain formulary on the UF because they are primarily prescribed by specialists and have low MHS low utilization.

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (16 for, 0 opposed, 0 abstained, 0 absent) to accept the relative cost-effectiveness analysis of the Mast Cell Stabilizers subclass.

- **Ophthalmic-1 NSAIDs:** BIA was used to assess the potential impact of cost scenarios where selected Ophthalmic-1 NSAIDs were designated formulary or NF on the UF. Cost scenarios evaluating the impact of designating agents with BCF status were also considered. This subclass is more commonly used in the treatment of post-surgical procedures than in the treatment of AC. BIA results showed that the most cost-effective scenario designated ketorolac 0.5% (generic Acular) with BCF status, with all other Ophthalmic-1 NSAIDs designated formulary on the UF. After discussion, the P&T Committee recommended against designating a BCF Opthmalic-1 NSAID because the majority of use is by ophthalmologic specialists for post-surgical procedures rather than primary care providers for AC.

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (16 for, 0 opposed, 0 abstained, 0 absent) to accept the relative cost-effectiveness analysis of the Ophthalmic-1 NSAIDs subclass.

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

    a) **Antihistamines and Dual Action AH/MCS:** azelastine (Optivar, generics), bepotastine (Bepreve), emedastine (Emadine), epinastine (Elestat), olopatadine 0.1% (Patanol), and olopatadine 0.2% (Pataday) remain designated formulary on the UF (15 for, 0 opposed, 1 abstained, 0 absent);

b) **Mast Cell Stabilizers:** cromolyn (generic), lodoxamide (Alomide), nedocromil (Alocril), and pemirolast (Alamast) remain designated formulary on the UF (15 for, 0 opposed, 1 abstained, 0 absent);

c) **NSAIDs:** bromfenac 0.09% (Xibrom), diclofenac 0.1% (Voltaren, generic), flurbiprofen 0.03% (Ocufen, generic), ketorolac 0.4% (Acular LS, generic), ketorolac 0.45% (Acuvail), ketorolac 0.5% (Acular, generic), and nepafenac 0.1% (Nevanac) remain designated formulary on the UF (15 for, 0 opposed, 1 abstained, 0 absent).

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved 11/10/10

Approved, but modified as follows:

2. ***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, recommended upon signing of the minutes:

   a) **Antihistamines and Dual Action AH/MCS:** olopatadine 0.1% (Patanol) be added to the BCF (15 for, 0 opposed, 1 abstained, 0 absent).

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved 11/10/10

Approved, but modified as follows:

IV. UTILIZATION MANAGEMENT—QUANTITY LIMITS (QL)

A. Tramadol ODT (Rybix)—QL: A new orally disintegrating formulation (ODT) of tramadol (Rybix) has been marketed. Tramadol ODT will be reviewed for UF status at an upcoming P&T Committee meeting as a newly-approved drug in the narcotic analgesic drug class. QLs are currently in place for both immediate and extended-release tramadol (Ultram, Ultram ER, generics).

1. ***COMMITTEE ACTION: QL***—The P&T Committee voted (14 for, 0 opposed, 1 abstained, 1 absent) to recommend QLs for tramadol ODT of 720 tablets/90 days in the mail order pharmacy and 240 tablets/30 days in the retail network, which is consistent with the recommended dosing from the product labeling and safety concerns.

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved 11/10/10

Approved, but modified as follows:

B. Ondansetron soluble film (Zuplenz)—QL: An oral soluble film of ondansetron (Zuplenz) is now on the market. Zuplenz will be reviewed as a new FDA-approved drug in the anti-emetic drug class at an upcoming P&T Committee meeting. QLs are currently in place for other formulations of ondansetron and the remainder of the 5-HT3 receptor antagonists in the class.

1. ***COMMITTEE ACTION: QL***— The P&T Committee voted (14 for, 0 opposed, 1 abstained, 1 absent) to recommend QLs for ondansetron soluble film of 180 tablets/90 days in the mail order pharmacy and 60 tablets/30 days in the retail network, which is consistent with the recommended dosing from the product labeling and avoids breaking apart packages for dispensing.

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved 11/10/10

Approved, but modified as follows:

C. Certolizumab Pegol Injection (Cimzia Starter Kit)—QL: A new starter kit of certolizumab pegol pre-filled syringes (Cimzia) for Crohn's disease has been marketed. Cimzia was reviewed as a new FDA-approved drug in the targeted immunomodulatory biologics (TIB) drug class in August 2009. This starter kit provides for a loading dose required at initiation of therapy. QLs are currently in place for the other formulations of certolizumab pegol and the remainder of the TIBs products.

1. ***COMMITTEE ACTION: QL***—The P&T Committee voted (15 for, 0 opposed, 1 abstained, 0 absent) to recommend QLs for certolizumab pegol of 1 kit (6 syringes) with no refills in the mail order pharmacy and 1 kit (6 syringes) with no refills 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 11/10/10

Approved, but modified as follows:

D. Nilotinib Capsules (Tasigna)—QL: Nilotinib (Tasigna) is a kinase inhibitor that is approved for treating Philadelphia chromosome-positive chronic myeloid leukemia. QLs are currently in place for imatinib (Gleevec) and oral antineoplastic agents, due to the potential for drug discontinuations or dosage changes due to adverse effects, drug interactions, or patient response to therapy.

1. ***COMMITTEE ACTION: QL***— The P&T Committee voted (15 for, 0 opposed, 1 abstained, 0 absent) to recommend QLs for nilotinib of 224 capsules/56 days in the mail order pharmacy and 112 capsules/28 days in the retail network, which is consistent with the recommended dosing from the product labeling and safety concerns.

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved 11/10/10

Approved, but modified as follows:

V. ITEMS FOR INFORMATION

A. Pharmacy Outcomes Research Team—The PORT briefed the P&T Committee on the utilization and expenditures for several of the UF drug classes previously reviewed by the P&T Committee. Additional updates will be provided at upcoming meetings.

B. Thiazolidinedione (TZD) Safety Update—The P&T Committee reviewed updated safety information for rosiglitazone. Additional information will be provided when the TZD drug class review is presented at the November 2010 P&T Committee Meeting.

C. **PA for Quinine Sulfate Safety Update**—The P&T Committee reviewed new FDA-mandated safety requirements for quinine sulfate (Qualaquin). Prior Authorization for Qualaquin restricting use for malaria was recommended at the May 2010 P&T Committee Meeting. In July 2010, an FDA safety communication stated Qualaquin should only be used for malaria, warned of safety issues when used off-label for leg cramps; and required the manufacturer to develop a risk evaluation and mitigation strategy program.

D. **BCF Consensus Statement** —The P&T Committee stated its position that BCF-designated drugs will be stocked in the Pharmacy or readily available on the next duty day for MTFs located in the continental United States (CONUS), and be readily available on the next available order for MTFs located outside the continental United States (OCONUS).

VI. CLASS OVERVIEWS

Overviews for two drug classes were presented to the P&T Committee. The inflammatory bowel disease/irritable bowel syndrome drug class is comprised of the 5-aminosalicylates, gastrointestinal steroids, and the 5-HT3 antagonists. The pancreatic enzymes were also reviewed. 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 presented at an upcoming meeting.

VII. ADJOURNMENT

The meeting adjourned at 1620 hours on August 11, 2010, and at 0945 hours on August 12, 2009. The next meeting will be in November 2010.

Appendix A—Attendance

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

Appendix C—Table of Abbreviations

SUBMITTED BY:

Actual Signing date was 8 NOV 2010

John P. Kugler, MD, MPH
DoD P&T Committee Chair

DECISION ON RECOMMENDATIONS

Director, TMA, decisions are as annotated above.

George Peach Taylor, Jr., MD, MPH
Acting Director

11/18/2010
(Date)

Appendix A—Attendance

Voting Members Present	
Dr. John Kugler, COL (Ret), USA, MC	DoD P&T Committee Interim Chair
LTC Stacia Spridgen, MSC	Director, DoD Pharmacoeconomic Center (Recorder)
Col Everett McAllister, BSC	Deputy Chief, Pharmaceutical Operations Directorate
COL Carole Labadie, MS	Army, Pharmacy Officer
Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CAPT Stephanie Simon, MSC	Navy, Pharmacy Officer
CAPT Vernon Lew	Coast Guard, Pharmacy Officer
COL Doreen Lounsbery, MC	Army, Internal Medicine Physician
COL Ted Cieslak, MC	Army, Physician at Large
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Major Jeremy King, MC	Air Force, OB/GYN Physician
CAPT David Tanen, MC	Navy, Physician at Large
Lt Col Brian Crownover, MC	Air Force, Physician at Large
LTC Bruce Lovins, MC	Army, Family Practice Physician
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
CDR Eileen Hoke, MC	Navy, Pediatrics
Mr. Joe Canzolino	Department of Veterans Affairs
Nonvoting Members Present	
Mr. David Hurt	Assistant General Counsel, TMA
CDR Michele Hupp, MSC	Defense Medical Standardization Board
Guests	
Col George Jones, BSC	Pharmaceutical Operations Directorate
Major Achilles Hamilothoris	Defense Logistics Agency Troop Support
Dr. David Trang	University of Incarnate Word Pharmacy School
Melinda Neuhauser	Veterans Affairs, Pharmacy Benefits Management Services
CDR Tamara Close	United States Public Health Service/Indian Health Service

Appendix A—Attendance (continued)

Others Present	
COL Cynthia Clagett	DoD Pharmacoeconomic Center
Lt Col Rey Morales	DoD Pharmacoeconomic Center
Lt Col Cynthia Lee, BSC	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
LCDR Ola Ojo	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. Brian Beck	DoD Pharmacoeconomic Center
Dr. Amy Lugo	DoD Pharmacoeconomic Center
Dr. Dean Valibhai	DoD Pharmacy Operations Center contractor
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

Appendix B—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	Comments
Aug 2010	Renin Angiotensin Anti-Hypertensives (RAAs)	UF Review	**ACE Inhibitors** ▪ Lisinopril (Prinvil, Zestril, generic) ▪ lisinopril HCT (Prinzide, Zestoretic generic) ▪ Captopril (Capoten, generic) ▪ Ramipril (Altace, generic) **ACE-Inhibitor/CCB** ▪ Benazepril/amlodipine (Lotrel, generic) **ARBs** ▪ Losartan (Cozaar, generic) ▪ Losartan/HCTZ (Hyzaar, generic) ▪ Telmisartan (Micardis) ▪ Telmisartan/ HCTZ (Micardis HCT) ▪ Valsartan (Diovan) ▪ Valsartan/HCTZ (Diovan HCT)	**ACE Inhibitors** ▪ Benazepril +/- HCTZ (Lotensin, Lotensin HCT generic) ▪ Captopril/HCTZ (Capozide, generic) ▪ Enalapril, Enalapril/HCTZ (Vasotec, Vasoretic, generic) ▪ Fosinopril, fosinopril HCTZ (Monopril, Monopril HCT generic) ▪ Moexipril +/- HCTZ (Univasc, Uniretic generic) ▪ Perindopril (Aceon, generic) ▪ Quinapril+/- HCTZ (generic) ▪ Trandolapril (Mavik, generic) **ACE Inhibitor/CCB** ▪ Verapamil SR/trandolapril (Tarka, generic) **ARBs** ▪ Candesartan, Candesartan/HCTZ (Atacand, Atacand HCT) ▪ Eprosartan, Eprosartan/ HCTZ (Teveten, Teveten HCT) ▪ Irbesartan, Irbesartan/HCTZ (Avapro, Avalide) ▪ Olmesartan, Olmesartan/HCTZ (Benicar, Benicar HCT) **RAAs/CCB** ▪ Telmisartan/amlodipine (Twynsta) ▪ Olmesartan/amlodipine (Azor) ▪ Valsartan/amlodipine (Exforge) ▪ Valsartan/amlodipine/HCTZ (Exforge HCT) **DRIs** ▪ Aliskiren (Tekturna) ▪ Aliskiren/HCTZ (Tekturna HCT) ▪ Valsartan/aliskiren (Valturna)	▪ Not applicable (no drug designated non-formulary)	Pending 60 days	Step therapy (Automated PA)	**Step-therapy (automated PA)** with the following as the step-preferred drugs: ▪ losartan ±HCTZ ▪ telmisartan ±HCTZ ▪ telmisartan/amlodipine ▪ valsartan ±HCTZ ▪ valsartan/amlodipine ▪ valsartan/amlodipine/ HCTZ Note: telmisartan/amlodipine valsartan/amlodipine & valsartan/amlodipine/HCTZ are step-preferred but not on the BCF

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	Comments
Aug 2010	Ophthalmic-1	UF Review	**Antihistamine/Mast Cell Stabilizers** ▪ Olopatadine 0.1% (Patanol)	**Antihistamines** ▪ Emedastine (Emadine) **Mast Cell Stabilizers** ▪ Pemirolast (Alamast) ▪ Nedocromil (Alocril) ▪ Cromolyn (Crolom/Opticrom, generic) ▪ Lodoxamide (Alomide) **Dual Action Antihistamine/Mast Cell Stabilizers** ▪ Bepotastine (Bepreve) ▪ Olopatadine 0.2% (Pataday) ▪ Azelastine (Optivar, generics) ▪ Epinastine (Elestat) **NSAIDs** ▪ Ketorolac 0.4% (Acular LS, generic) ▪ Ketorolac 0.45% (Acuvail) ▪ Ketorolac 0.5% (Acular, generic) ▪ Bromfenac (Xibrom) ▪ Diclofenac (Voltaren, generic) ▪ Flurbiprofen (Ocufen, generics ▪ Nepafenac (Nevanac)	▪ Not applicable (no drug designated non-formulary)	Pending signing of minutes	Not applicable	▪ Ketotifen (Zaditor, generics) is available OTC
May 2010	Antilipidemic-1s	UF Review	▪ Atorvastatin (Lipitor) ▪ Pravastatin(Pravachol, generics) ▪ Simvastatin (Zocor, generics)	▪ Atorvastatin / amlodipine (Caduet) ▪ Ezetimibe (Zetia) ▪ Ezetimibe / simvastatin (Vytorin) ▪ Fluvastatin IR (Lescol) ▪ Fluvastatin ER (Lescol XL) ▪ Lovastatin IR (Mevacor; generics) ▪ Lovastatin ER (Altoprev) ▪ Lovastatin / niacin ER (Advicor) ▪ Niacin IR ▪ Niacin ER (Niaspan) ▪ Rosuvastatin (Crestor) ▪ Simvastatin / niacin ER (Simcor)	▪ Not applicable (no drug designated non-formulary)	Pending 60 days	Step therapy (Automated PA)	Step therapy (automated PA) with generics, or atorvastatin as the preferred agents (note: step- therapy does not apply to ezetimibe or niacin)

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	Comments
May 2010	Alpha Blockers for BPH	UF Review	▪ Alfuzosin (Uroxatral) ▪ Tamsulosin (Flomax, generics) ▪ Terazosin (Hytrin; generics)	▪ Doxazosin IR (Cardura; generics)	▪ Silodosin (Rapaflo) ▪ Doxazosin ER (Cardura XL)	Pending 60 days	Step therapy (Automated PA)	Step therapy (automated PA) with tamsulosin (Flomax, generics) or alfuzosin as the preferred agents (note: step- therapy does not apply to terazosin, doxazosin, or doxazosin ER)

ACE: angiotensin converting enzyme
CCB: calcium channel blocker
DRI: direct renin inhibitor
HCTZ: hydrochlorothiazide
NSAID: nonsteroidal anti-inflammatory drug
SR: sustained release

Appendix C—Table of Abbreviations

AC	allergic conjunctivitis
ACE-I	angiotensin converting enzyme inhibitor
AH	Antihistamine
AH/MCS	antihistamines/mast cell stabilizers
ARB	angiotensin receptor blocker
BAK	benzalkonium chloride
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
CV	Cardiovascular
DBP	diastolic blood pressure
DM	diabetes mellitus
DoD	Department of Defense
DRI	direct renin inhibitor
ECF	Extended Core Formulary
ESI	Express Scripts, Inc
ESRD	end stage renal disease
FCP	Federal Ceiling Price
FDA	U.S. Food and Drug Administration
FDC	fixed-dose combination
FSS	Federal Supply Schedule Price
FY	fiscal year
HA	Health Affairs
HCTZ	Hydrochlorothiazide
IR	immediate release
JNC	Joint National Commission
MARR	Mandatory Agreement for Retail Refunds
MHS	Military Health System
MI	myocardial infarction
mmHg	millimeters mercury
MN	medical necessity
MTF	Military Treatment Facility
NDAA	National Defense Authorization Act
NSAIDs	non-steroidal anti-inflammatory drugs
ODT	orally disintegrating tablet
OMB	Office of Management and Budget
Opth-1	Opthalmic-1 drug class
P&T	Pharmacy and Therapeutics
PA	prior authorization
PEC	Pharmacoeconomic Center
PORT	Pharmaceutical Outcomes Research Team
QL	quantity limit
SBP	systolic blood pressure
SR	sustained release
TIB	targeted immunomodulatory biologics drug class

DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS
May 2010

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on May 12, 2010, and May 13, 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**—Dr. Charles Rice, Acting Director, approved the minutes for the February 2010 DoD P&T Committee meeting on May 3, 2010.
2. **Correction to February minutes**—The P&T Committee recommended by consensus the following Factor VIII and Factor IX drugs be returned to formulary status on the Uniform Formulary (UF) upon execution of the DoD Retail Refund Pricing Agreement:

   Human Factor VIII: Humate-P, Monoclate-P

   Recombinant Factor VIII: Helixate FS

   Human Factor IX: MonoNine

   a) ***COMMITTEE ACTION***—The P&T Committee voted (14 for, 0 opposed, 1 abstained, 0 absent) to recommend the Acting Director, TMA, amend the February 2010 P&T Committee Minutes to reflect the Factor VIII and Factor IX drugs listed, above, have been returned to formulary status on the UF.

   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—Fentanyl Citrate Transmucosal Soluble Film (Onsolis)

Relative Clinical Effectiveness—Fentanyl citrate transmucosal soluble film (Onsolis) is a pure opioid agonist available in a new transmucosal delivery system. It is FDA-approved for the treatment of breakthrough pain in adults with cancer who are opioid tolerant. Onsolis contains the same active drug (fentanyl) via the same route of administration (oral mucosa) as the UF products Actiq (fentanyl transmucosal lozenge; generics) and Fentora (fentanyl transmucosal tablet). It differs from Actiq and Fentora as fentanyl is delivered through a soluble film that adheres to the mucosal membrane and provides protection from the saliva. The film dissolves completely over 15–30 minutes.

There are no direct comparative clinical trials between Onsolis and the other transmucosal fentanyl products. Onsolis is not bioequivalent with other transmucosal fentanyl products. The safety and tolerability profile for Onsolis appears comparable to other transmucosal fentanyl products. The new delivery system offers more efficient absorption with less swallowing of the drug, which could possibly result in less gastrointestinal (GI) adverse effects. Other potential benefits of the new delivery system include reduced ability for diversion and less risk of dental caries.

Onsolis has a restricted distribution risk evaluation and mitigation strategy (REMS) program that requires enrollment by both the physician and patient, limits dispensing to a single retail pharmacy, and provides delivery of the drug via traceable courier. The FDA is requiring, but has not determined an effective date, for similar REMS programs for Actiq and Fentora.

The narcotic analgesic drug class was last reviewed in February 2007. The clinical evaluation for Onsolis included, but was not limited to, the 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, 0 absent) the plausible, yet unproven, benefits of the transmucosal fentanyl buccal film (Onsolis) new delivery system include less GI side effects, less risk of diversion, and less risk of dental caries, compared to other UF transmucosal fentanyl products. The clinical relevance of the proposed advantages is unclear at this time. The FDA-mandated REMS program will ensure use is limited to opioid-tolerant patients.

Relative Cost-Effectiveness—The P&T Committee evaluated the cost of fentanyl citrate transmucosal soluble film (Onsolis) 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 Onsolis is higher than other formulary narcotic analgesics, except the branded drug Actiq.

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstained, 0 absent) that fentanyl citrate transmucosal soluble film (Onsolis) is more costly than generic fentanyl products in the narcotic analgesic drug class. In comparison to generics in this class, the P&T Committee determined that the higher daily cost for Onsolis was offset by its unique delivery system and the strict REMS program, which will limit inappropriate prescribing.

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, 2 opposed, 1 abstained, 0 absent) fentanyl citrate transmucosal soluble film (Onsolis) be designated as 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 fentanyl citrate transmucosal soluble film (Onsolis). Based on the results of the clinical and economic evaluations presented, the P&T Committee voted (14 for, 0 opposed, 1 abstained, 0 absent) fentanyl citrate transmucosal soluble film (Onsolis) would not be added to the BCF.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

B. Triptans—Sumatriptan Needle-Free Injection (Sumavel DosePro)

Relative Clinical Effectiveness—Sumatriptan needle-free injection (Sumavel DosePro) is a new single-use delivery system for administering sumatriptan subcutaneously. Sumatriptan (Imitrex) is available in oral tablets, a nasal spray, and a traditional needle-containing injection device; all are available in generic formulations. The triptans drug class was last reviewed for UF placement in June 2008. Sumatriptan oral tablets and injection (Imitrex STATdose; generics) are currently included on the BCF.

Sumavel DosePro is FDA-approved for treating migraines and cluster headaches. The sumatriptan dose is delivered by a high pressure burst of nitrogen gas, which propels the drug through the subcutaneous space. Pharmacokinetic studies comparing Sumavel DosePro with Imitrex STATdose demonstrated bioequivalence between the two products. Sumavel DosePro obtained FDA approval via section 505(b)(2) of the Federal Food, Drug, and Cosmetic (FDC) Act using data submitted from the original Imitrex STATdose submission. Thus, there are no clinical trials with Sumavel DosePro that measure efficacy for providing pain relief from migraine headaches. Following administration, initially there is a higher incidence of bleeding, swelling, and bruising with Sumavel Dose Pro than with Imitrex STATdose; these adverse effects dissipate, and show no difference in severity with Imitrex STATdose 8 hours after administration. Potential benefits of Sumavel DosePro compared to sumatriptan needle-containing injection include that the device is easy to use, it provides an alternative injection option to patients with severe needle phobia, and it does not require special biohazard disposal (e.g., disposal in household refuse).

The clinical evaluation for Sumavel DosePro 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 (14 for, 0 opposed, 0 abstained, 1 absent) that although sumatriptan needle-free injection (Sumavel DosePro) is easy to use, particularly for patients with dexterity issues, and can be disposed of without special precautions, it does not have a significant, clinically relevant therapeutic advantage in terms of effectiveness, safety, and clinical outcomes compared to the existing UF product, sumatriptan needle-containing injection.

Relative Cost-Effectiveness—The P&T Committee evaluated the cost of sumatriptan needle-free injection (Sumavel DosePro) in relation to the efficacy, safety, tolerability, and clinical outcomes of the other non-oral sumatriptan formulations included in the triptans 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 Sumavel DosePro relative to other non-oral UF sumatriptan agents. Results from the CMA showed the projected weighted average cost per day for Sumavel DosePro is higher than other non-oral sumatriptan formulary agents, with the exception of the Imitrex STATdose proprietary formulation.

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, voted (15 for, 0 opposed, 0 abstained, 0 absent) that sumatriptan needle-free injection (Sumavel DosePro) is more costly compared to current UF agents except the Imitrex STATdose proprietary formulation.

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 (14 for, 0 opposed, 1 abstained, 0 absent) sumatriptan needle-free injection (Sumavel DosePro) be designated nonformulary (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 sumatriptan needle-free injection (Sumavel DosePro) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Sumavel DosePro. (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, 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 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:

IV. UF DRUG CLASS REVIEWS

A. Antilipidemic-1s (LIP-1s)

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the agents in the Antilipidemic-1s (LIP-1s) drug class. This class is currently ranked number one in the Military Health System (MHS), with drug class expenditures exceeding $480 million annually. The class was last reviewed in August 2006. The individual drugs included in the LIP-1s class are listed, below:

Statins: atorvastatin (Lipitor), amlodipine/atorvastatin (Caduet), fluvastatin (Lescol), fluvastatin extended release (ER; Lescol XL), lovastatin (Mevacor, generics), lovastatin ER (Altoprev), pravastatin (Pravachol, generics), rosuvastatin (Crestor), simvastatin (Zocor, generics), and ezetimibe/simvastatin (Vytorin)

Statin combination products and add-on therapies: niacin ER (Niaspan), lovastatin/niacin ER (Advicor), simvastatin/niacin ER (SIMCOR), and ezetimibe (Zetia)

The current BCF agents are pravastatin, simvastatin, niacin ER (Niaspan), and ezetimibe/simvastatin (Vytorin). The NF agents are atorvastatin/amlodipine (Caduet) and rosuvastatin (Crestor). The remaining drugs are classified as UF agents. Generic formulations of simvastatin, pravastatin, and lovastatin are now marketed. Generic formulations of atorvastatin are expected in late 2011.

Relative Clinical Effectiveness Conclusion—The Committee recommended (14 for, 0 opposed, 0 abstained, 1 absent) the following conclusions for the LIP-1s:

1. Across equipotent doses, the statins achieve a similar percentage reduction in low-density lipoprotein (LDL), and a similar percentage increase in high-density lipoprotein (HDL).
2. All statins show a plateau and drop-off in ability to raise HDL at increasing doses.
3. Doubling the dose of a statin provides only an additional 4% to 7% reduction in LDL and 3% to 6 % reduction in non-HDL.
4. There is a strong correlation between the change in LDL and C-reactive protein (CRP). CRP appears to be a strong predictor of coronary heart disease (CHD). It is unclear what emphasis the upcoming National Heart and Lung Blood Institute Adult Treatment Panel (ATP) IV guidelines will place on CRP in managing patients with hypercholesterolemia.
5. A 1:1 log-linear relationship exists between lowering LDL and non-HDL and reduced relative risk of CHD. In one mortality study, non-HDL was a stronger predictor of CHD risk than LDL.
6. With respect to the low-to-moderate intensity statins (statins able to reduce LDL levels by $\leq 45\%$):
   - The results of one meta-analysis show Lipitor, pravastatin, and simvastatin have similar effects in providing long-term cardiovascular (CV) prevention (e.g., reducing all-cause deaths, major coronary events, CV death, and major cerebrovascular events).
   - There are fewer trials published for lovastatin and fluvastatin, but positive outcomes are still shown.
   - Simvastatin at doses ≤ 40 mg will remain the DoD-preferred statin.
7. The high-intensity statins (those statins able to reduce LDL levels by >45%) include Lipitor 40 and 80 mg; Vytorin 10/20, 10/40, and 10/80 mg; Crestor 10, 20, and 40 mg; and simvastatin 80 mg.
8. In trials assessing the primary prevention of CHD, statins do not appear to decrease the risk of all-cause mortality. At a dose of 20 mg, Crestor showed a decreased risk of all-cause mortality in the JUPITER trial. The benefit of Crestor in this trial was limited to patients with CRP> 2 and an additional CHD risk factor besides age. When used in the primary prevention of CHD, statins in general decrease the risk of CV events by 22% to 30%.

9. In trials assessing the secondary prevention of CHD, statins decrease the risk of mortality and the risk of major CV events 21% to 23%. Similar benefits are conferred among patients with or without diabetes. When used in acute coronary syndrome, Lipitor 80 mg decreases the risk of a second event by 16% to 19%. There are no studies with Crestor assessing the secondary prevention of CHD.
10. Vytorin provides added efficacy in terms of LDL lowering, but still lacks clinical outcomes data showing a reduction in CV events. Positive benefits in reducing CV events have been shown with the simvastatin component of Vytorin in The Heart Protection Study and The Scandinavian Simvastatin Survival Study trials.
11. Zetia lowers LDL 15%–20% by a mechanism distinct from that of the statins.
12. Niaspan lowers LDL 5%–15%. However, Niaspan is required in the MHS, as its primary benefit is to raise HDL by 25%.
13. Since the 2006 review, there is no new compelling data for Advicor, SIMCOR, Caduet, Altoprev, or Lescol XL to change the original conclusion that these drugs do not offer additional clinical benefits over the other LIP-1s. These drugs have low utilization in the MHS.
14. With regard to safety, there is no evidence that increases in liver function tests or minor adverse events (gastrointestinal disturbances, headaches, rash, itching) are less likely to occur with one statin versus another; these adverse effects are dose-related.
15. Concerns of proteinuria remain with Crestor 40 mg, but the clinical significance of this effect is unknown.
16. The risk of statin-related myotoxicity increases with increasing dosages. There is no evidence that one statin is less likely to cause myotoxicity than another. The FDA recently updated the labeling for simvastatin 80 mg, warning of the risk of myotoxicity. The overall incidence of rhabdomyolysis is rare with all statins.
17. There is no conclusive data yet to suggest that statin therapy is associated with cognitive decline, behavioral defects, or cancer. However, there is evidence to suggest an increased risk of new onset diabetes with statin therapy (JUPITER trial and Lancet 2010 meta-analysis). The clinical implications of this finding are still unclear.

18. Fluvastatin, pitavastatin (a new statin not yet marketed), pravastatin, and Crestor do not interact with CYP 3A4 and have more favorable drug-drug interaction profiles than the other statins. Pravastatin is renally metabolized and bypasses the CYP 450 system entirely.
19. The Pharmacy Outcomes Research Team (PORT) analyzed LIP-1s utilization in the MHS during a 7-month period between August 1, 2009, and March 31, 2010. Overall, approximately 1.4 million DoD beneficiaries receive lipid-lowering therapies and about 1.2 million DoD beneficiaries receive statins. The percentage of the study group classified as new statin users was 7%. Women comprised 51% of the entire study group; the mean patient age was 42.4 years (standard deviation 11.8 years).

    The majority of use is statin monotherapy (882,000 patients). The most common add-on therapy is ezetimibe (194,000), followed by fibrates (123,000) and niacin (57,000). Zetia is frequently prescribed as Vytorin (73%); only 27% of the study group received Zetia with a statin other than simvastatin. Most niacin is given separately (74%), with only 6,819 patients receiving SIMCOR or Advicor.

    About 29% of all patients receiving statin monotherapy or a statin and Zetia are receiving high-intensity statins (statins able to reduce LDL levels by >45%); 17% of this group is receiving a high-intensity statin alone; 11% are receiving a high-intensity statin plus Zetia. The most common triple therapy is a statin and Zetia and niacin (12,000). Overall, about 73,000 patients receive some combination targeting LDL and HDL/triglycerides.
20. To meet the clinical needs of the majority of MHS patients, the UF must include the low-to-moderate intensity statins simvastatin and pravastatin, and at least one high-intensity statin.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the LIP-ls in relation to the efficacy, safety, tolerability, and clinical outcomes of the other agents in the 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).

Statins: A series of cost-effectiveness analyses (CEAs) and budget impact analysis (BIAs) were used to determine the relative cost-effectiveness of agents in the class.

Four separate cost-effectiveness models were constructed in the analyses of low-to-moderate statins (statins able to reduce LDL levels by ≤ 45%) and high-intensity statins (statins able to reduce LDL levels by >45%). Analyses were based on direct and indirect comparisons of relevant trial data.

1. The Annual Cost per 1% LDL Decrease Model compared the cost-effectiveness of the high % LDL-lowering agents based on annual cost per 1% LDL reduction using a decision analytical model.
2. The Annual Cost per Patient Treated to Goal Model compared the cost-effectiveness of these agents based on annual cost per patient successfully treated to ATP III National Cholesterol Education Program goal using a decision analytical model.
3. The Annual Cost per 1% Non-HDL Decrease Model compared the cost-effectiveness of the high % non-HDL lowering agents based on annual cost per 1% non-HDL reduction using a decision analytical model.
4. The Annual Cost per 1% HDL-increase Model compared the cost-effectiveness of the high % HDL-increasing agents based on annual cost per 1% HDL increase using a decision analytical model.

Statin combination products and add-on therapies: CMA and BIA were used to evaluate the cost-effectiveness of the statin combination products and add-on therapies.

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

Statins (13 for, 0 opposed, 1 abstained, 1 absent)**:**

1. For the low-to-moderate % LDL-lowering agents (≤ 45% LDL reduction) evaluated: simvastatin (10, 20, and 40 mg), Lipitor 10 and 20 mg, and all strengths of pravastatin, the cost-effectiveness of the agents in this class were evaluated using each of the decision analytic models described, above. In pharmacoeconomic terms, simvastatin was considered to be dominant at all equipotent strengths, in terms of cost per LDL reduction, cost per LDL goal attainment, cost per non-HDL reduction, and cost per HDL increase. CEA results showed simvastatin was located along the cost efficiency frontier and considered to be the optimal agent.

Note: Based on low utilization and conclusions presented at the August 2006 P&T Committee Meeting, the following agents were not evaluated in the model(s): simvastatin 5 mg, Crestor 5 mg, ezetimibe/simvastatin (Vytorin) 10/10 mg, fluvastatin IR, fluvastatin ER, lovastatin IR, and lovastatin ER were not included in the CEA).

2. For the high-intensity % LDL-lowering agents (> 45% LDL reduction) evaluated: Lipitor 40 and 80 mg, Crestor 10, 20, and 40 mg, simvastatin/ezetimibe (Vytorin) 10/20, 10/40, 10/80 mg, and simvastatin 80 mg, the cost-effectiveness of the agents in this class were evaluated using each of the decision analytic models described, above. In pharmacoeconomic terms, the results of the first three cost-effectiveness analyses showed Lipitor 40 and 80 mg to be the overall most cost-effective high-intensity agent(s), in terms of cost per % LDL reduction, cost per % LDL goal attainment, and cost per % non-HDL reduction. Crestor 40 mg was more effective but considerably more costly compared to Lipitor at equipotent doses, but not more effective nor less costly than the equipotent dosage of ezetimibe/simvastatin (Vytorin) 10/80 mg. CEA determined Vytorin was not dominant in cost per outcome compared to Lipitor. From a price per % LDL-reduction perspective, Lipitor (all strengths) was more cost-effective than Vytorin. CEA results showed Lipitor 40 and 80mg was located along the cost efficiency frontier and considered to be the optimal agent(s).

3. BIA was used to assess the potential impact of cost scenarios where selected LIP-1s were designated formulary or nonformulary on the UF. Cost scenarios evaluating the impact of designating agents on the BCF were also considered. Results from the BIA for LIP-1s revealed that the scenarios placing Lipitor at all strengths on the BCF and as the step-preferred product in front of a step-therapy requirement and placing all generic agents in front of a step-therapy requirement were the most cost-effective scenarios.

4. The results of the BIA showed that Lipitor was less costly than the other brand agents Crestor and Vytorin in all scenarios evaluated. All scenarios placing Lipitor in the step-preferred position were less costly than all nonstep-scenarios and all other scenarios involving multiple step-preferred branded agents.

Statin combination products and add-on therapies (14 for, 0 opposed, 0 abstained, 1 absent):

1. The CMA results revealed that SIMCOR was the most cost-effective add-on product, based on an analysis of the cost per day of therapy. Cost per day of therapy was calculated using cost per tablet adjusted by daily average consumption (DACON) rates for SIMCOR, Niaspan, Advicor, and Zetia.
2. BIA was used to assess the potential impact of cost scenarios where selected statin combination products and add-on agents were designated formulary or nonformulary on the UF. Scenarios evaluating the impact of designating agents on the BCF were also considered. Results from the BIA revealed the most cost-effective scenario overall to add Niaspan on the BCF and UF, add Zetia on the UF, and designate SIMCOR and Advicor NF. However, designating SIMCOR NF may result in increased usage of Niaspan and increase overall costs. Sensitivity analyses show no individual scenario was dominant after considering the margin for error present in all cost projections. Therefore, the cost avoidance of the aforementioned most cost-effective scenario was within the margin of error.

a) ***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 the following:

(1) Ezetimibe/simvastatin (Vytorin), Atorvastatin (Lipitor), simvastatin (Zocor, generics), fluvastatin (Lescol), fluvastatin ER (Lescol XL), lovastatin (Mevacor, generics), lovastatin ER (Altoprev) and pravastatin (Pravachol, generics) remain classified as formulary on the UF; and that atorvastatin/amlodipine (Caduet) and rosuvastatin (Crestor) be designated formulary agents on the UF, with prior authorization (PA) for the LIP-1s drug class requiring a trial of atorvastatin (Lipitor) and the generic formulations of simvastatin or pravastatin for new patients (12 for, 0 opposed, 2 abstained, 1 absent);

(2) Ezetimibe (Zetia), niacin ER (Niaspan), lovastatin/niacin ER (Advicor), and simvastatin/niacin ER (SIMCOR) remain designated as UF; (13 for, 0 opposed, 1 abstained, 1 absent);

(3) As a result of the above recommendations, there are no LIP-1s designated as nonformulary on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

b) ***COMMI TTEE ACTION: PA CRITERIA***—The Committee recommended (13 for, 1 opposed, 1 abstained, 0 absent) the following PA criteria should apply to the LIP-1s other than generics and Lipitor. Coverage would be approved if the patient met any of the following criteria:

(1) Automated PA criteria:

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

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

(a) The patient has tried the preferred agent and was unable to tolerate treatment due to adverse effects.

(b) The patient is taking a concurrent drug that is metabolized by CYP3A4.

(c) The patient requires ≥55% LDL lowering.

(d) The patient requires primary prevention with rosuvastatin (Crestor) and is not able to take atorvastatin (Lipitor).

Acting Director, TMA, Decision: ☑ *Approved* ☐ *Disapproved*

Approved, but modified as follows:

c) ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (13 for, 1 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

d) ***COMMI TTEE 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, recommended:

(1) Simvastatin (Zocor, generics) and pravastatin (Pravachol, generics) remain BCF; atorvastatin (Lipitor) be added to the BCF; and, ezetimibe/simvastatin (Vytorin) be removed from the BCF (11 for, 0 opposed, 2 abstained, 2 absent);

(2) Niacin ER (Niaspan) remain BCF (13 for, 0 opposed, 1 abstained, 1 absent).

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

B. Alpha Blockers for Benign Prostatic Hyperplasia (BPH)

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the alpha blockers used for BPH currently marketed in the United States. The class is comprised of three non-uroselective agents: terazosin (Hytrin, generics), doxazosin immediate release (IR; Cardura; generics), and doxazosin ER (Cardura XL); and three uroselective agents: alfuzosin (Uroxatral), tamsulosin (Flomax) and silodosin (Rapaflo). Generic formulations of tamsulosin were launched in March 2010. The BPH alpha blocker drug class was first reviewed in August 2005 and reviewed again in November 2007. The newest agent, Rapaflo, was reviewed in August 2009. Current annual expenditures for the BPH alpha blockers are $52 million.

There is an existing automated PA process for the uroselective alpha blockers, which requires a trial of Uroxatral as initial therapy. All the alpha blockers are FDA-approved for treating BPH. The clinical evaluation for the BPH alpha blockers included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions regarding the BPH alpha blockers:

1. There are limited head-to-head trials comparing the BPH alpha blockers; the available placebo-controlled trials and meta-analyses were reviewed. Although all the alpha blockers are superior to placebo, variability in study design and demographics preclude the ability to designate one agent as clinically superior.
2. Based on randomized placebo-controlled trials, terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin produce clinically significant and comparable symptom improvements when compared to placebo.
3. Uroselective agents are well tolerated, with a few differences in safety considerations.
4. Uroselective agents appear to be better tolerated than non-uroselective agents, as measured by withdrawals due to adverse events and discontinuation of therapy.
5. Non-uroselective alpha blockers exhibit a higher rate of vasodilatory adverse effects relative to uroselective alpha blockers
6. All agents have similar warnings regarding intraoperative floppy iris syndrome.
7. The PORT analyzed the rejected claims attributable to the existing automated PA process (step-therapy edit) for the BPH alpha blockers from April 16, 2008, to December 31, 2009.
    a) Over the study period, 154,691 patients received uroselective alpha blockers for BPH in the retail or mail points of service; 43% of the patients encountered the step-therapy edit reject. Step therapy was highly effective at causing switches to preferred products; 81% of the patients who received a selective alpha blocker received the preferred product, alfuzosin, within 90 days. However, a substantial percentage of patients did not receive an alpha blocker within 90 days; 30% of patients did not receive a selective alpha blocker and 26% did not receive any alpha blocker (selective or non-selective).
    b) About 7% of the patients affected by the step therapy edit were female. Results for the women were similar to the overall results: 81% of women receiving a selective alpha blocker were switched to alfuzosin. However, the majority of women (64%) encountering the reject did not receive a selective alpha blocker within 90 days.
    c) When the alpha blocker step-therapy results were compared to previous analyses of UF drugs with step edits, similar results were noted. The percentages for those patients who did not receive a prescription after the step-edit reject were 35% in the newer sedative hypnotics class, and 31%

in the proton pump inhibitor class, versus 26%–30% in the alpha blocker class.

8. A review of the clinical literature since the previous UF reviews did not add substantial new information or support changes in clinical practice.
9. Terazosin, doxazosin, and doxazosin ER have a low degree of therapeutic interchangeability with alfuzosin, tamsulosin, and silodosin in terms of safety and tolerability, due to the higher incidence of discontinuation rates and vasodilatory effects seen with the non-uroselective alpha blockers.
10. Alfuzosin, tamsulosin, and silodosin have a high degree of therapeutic interchangeability; any of these drugs could be expected to meet the needs of the majority of MHS BPH patients requiring an uroselective agent.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the alpha blockers used for BPH in relation to the efficacy, safety, tolerability, and clinical outcomes of the other agents in the 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 and BIA were used to evaluate the cost-effectiveness of the BPH alpha blockers. Currently, there is a national shortage of doxazosin, resulting in a higher price for some dosage strengths.

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (14 for, 0 opposed, 0 abstained, 1 absent) the following:

1. CMA results for the non-uroselective agents revealed that generic terazosin and generic doxazosin IR were the most cost-effective agents based on the weighted average cost per day of therapy.

2. CMA results for the uroselective agents revealed that generic tamsulosin was the most cost-effective agent and Rapaflo (silodosin) was the least cost-effective agent based on the weighted average cost per day of therapy.

3. BIA results revealed the scenario that placed generic tamsulosin alone in front of a step on the UF and the scenario that included generic tamsulosin and Uroxatral (alfuzosin) on the UF in front of a step were the most cost effective.

a) ***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 to recommend (11 for, 3 opposed, 1 abstained, 0 absent) that:

(1) tamsulosin (generic Flomax) and alfuzosin (Uroxatral) be designated as the uroselective UF alpha blockers; terazosin (Hytrin, generics) and doxazosin IR (Cardura) be maintained as the non-uroselective UF alpha blockers;

(2) silodosin (Rapaflo) remain classified as NF with a PA requiring a trial of alfuzosin or generic tamsulosin for new patients; and

(3) doxazosin ER (Cardura XL) be classified as the NF non-uroselective alpha blocker for BPH.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

b) ***COMMI TTEE ACTION: PA CRITERIA***—The automated PA (step therapy) currently in effect requires alfuzosin (Uroxatral) before other NF alpha blockers for BPH, unless there is therapeutic failure, intolerance, or hypersensitivity. The automated PA criteria will now include generic tamsulosin as a preferred BPH alpha blocker, along with alfuzosin (Uroxatral). The P&T Committee voted (13 for, 0 opposed, 2 abstained, 0 absent) to recommend the PA criteria outlined, below, should apply to silodosin (Rapaflo); there is no change to the criteria for silodosin previously in effect. Coverage would be approved if the patient met any of the following criteria:

(1) Automated PA criteria:

(a) The patient has received a prescription for either silodosin (Rapaflo), tamsulosin (generic Flomax), or alfuzosin (Uroxatral) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

(2) PA criteria if automated criteria are not met:

(a) The patient has tried alfuzosin (Uroxatral) or tamsulosin and had an inadequate response or was unable to tolerate treatment due to adverse effects.

(b) Treatment with alfuzosin (Uroxatral) or tamsulosin is contraindicated.

(c) The patient requires an alpha blocker that can be crushed and sprinkled on food.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

c) ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluation of the alpha blockers for BPH, and the conditions for establishing MN for a NF medication, the P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) MN criteria for the uroselective alpha blocker silodosin (Rapaflo), and recommended (14 for, 0 opposed, 1 abstained, 0 absent) MN criteria for the non-uroselective alpha blocker doxazosin ER (Cardura XL). (See Appendix B for full MN criteria.)

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

d) ***COMMI TTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (14 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) ***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, recommended (13 for, 1 opposed, 1 abstained, 0 absent) to retain alfuzosin (Uroxatral) and terazosin (Hytrin) on the BCF, and add tamsulosin (generic Flomax) to the BCF.

Acting Director, TMA, Decision: ☐ Approved ☐ Disapproved

Approved, but modified as follows:

V. UTILIZATION MANAGEMENT

A. PA Requirement for Quinine—Quinine sulfate has been used off-label for years to treat nocturnal leg cramps. The only quinine product approved by the FDA (marketed under the trade name Qualaquin) is only approved for treating malaria; however, the FDA recognizes that the majority of its use is for leg cramps.

In the MHS, between April 1, 2009, and March 31, 2010, over 10,300 patients were prescribed quinine, with over 70% of the prescriptions dispensed from the retail network. The majority of patients receiving quinine sulfate prescriptions are older than 45 years. The current MHS usage is 80% lower than that reported in a DoD P&T Committee analysis from 2004. Results from an analysis of MHS quinine prescriptions during fiscal year 2009 found that out of 11,341 patients, 24% had one or more ICD-9 codes associated with leg cramps and 0.1% had ICD-9 codes associated with malaria; 76% of patients did not have ICD-9 codes for either malaria or leg cramps.

Meta-analyses and professional guidelines conclude that quinine is likely effective in reducing the frequency of muscle cramps, but the magnitude of benefit is small. No drug is currently FDA-approved for leg cramps, and there are no clearly effective pharmacological or nonpharmacological alternatives. A 2006 post-marketing FDA

surveillance study reported that since 1969 there have been 665 reports of adverse events involving quinine sulfate, including 93 deaths. Serious adverse events reported with quinine sulfate include thrombocytopenia, hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura (HUS-TTP), chronic renal impairment associated with HUS-TTP, hypersensitivity reactions, and QT prolongation. The product labeling for Qualaquin was updated in 2009 to state that the risk associated with quinine sulfate when used for nocturnal leg cramps outweighs any potential benefit.

1. ***COMMITTEE ACTION: PA***—Due to continued safety concerns and FDA advisories recommending against use of quinine sulfate for leg cramps, the P&T Committee recommended (13 for, 1 opposed, 1 abstained, 0 absent) a PA be required for quinine sulfate (Qualaquin) that limits use to the FDA-approved indication of malaria. The PA would apply to both existing and new users of quinine sulfate.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

2. ***COMMITTEE ACTION: PA IMPLEMENTATION***—The P&T Committee voted (14 for, 0 opposed, 1 abstained, 0 absent) to recommend the quinine sulfate PA should have 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 the MTFs, no later than a 60-day implementation date. The implementation period will begin immediately following the approval by the Director, TMA.

   Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

   Approved, but modified as follows:

VI. BASIC CORE FORMULARY ISSUES

A. Fluticasone proprionate nasal spray (Flonase, generics)—BCF Deletion

The Nasal Allergy Drugs, which include the nasal corticosteroids, were last reviewed in November 2008. Generic fluticasone propionate nasal spray (Flonase) was selected as the BCF nasal corticosteroid. Supplies of both generic and branded fluticasone propionate nasal spray are limited, due to manufacturing plant closures by the FDA and exit of the proprietary manufacturer from the market. The result is an increase in price from the two remaining generic manufacturers. It is unknown when additional supplies will be available. Due to the aforementioned developments, the P&T Committee recommended deleting fluticasone propionate nasal spray from the BCF. Fluticasone propionate nasal spray will remain on the UF. MTFs are encouraged to provide an alternative nasal corticosteroid in the interim, to meet local needs.

1. ***COMMITTEE ACTION: BCF DELETION***—The Committee voted (13 for, 1 opposed, 1 abstained, 0 absent) to remove fluticasone propionate nasal spray (Flonase, generics) from the BCF immediately upon signing of the May 2010 DoD P&T Committee minutes; it will remain formulary on the UF.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

B. Department of Veterans Affairs (VA)/DoD Joint Contracting Initiatives—Non-Basal Insulins BCF Addition

The P&T Committee was briefed regarding the VA National Acquisition Center contract for the non-basal insulin, including insulin aspart (Novolog) and 70% insulin aspart protamine suspension/30% insulin aspart (Novolog Mix 70/30). The insulin aspart (Novolog) vials are currently on the BCF. As part of the new contract, the insulin aspart pen injection devices (Novolog FlexPen) and insulin aspart PenFill cartridges (Novolog PenFill) are now cost-effective and have a similar price/mL as the vials. Likewise the 70% insulin aspart protamine suspension/30% insulin aspart pen injection device (Novolog Mix 70/30 FlexPen) is now similarly priced to the vials.

1. ***COMMITTEE ACTION: BCF ADDITION***—The Committee voted (14 for, 0 opposed, 1 abstained, 0 absent) to recommend adding the insulin aspart pen injection device (Novolog FlexPen), the insulin aspart PenFill cartridges (Novolog PenFill), and the 70% insulin aspart protamine suspension/30% insulin

aspart pen injection device (Novolog Mix 70/30 FlexPen) to the BCF, immediately upon signing of the May 2010 DoD P&T Committee minutes.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

VII. ITEMS FOR INFORMATION

A. **Pharmacy Outcomes Research Team (PORT)**—The PORT briefed the P&T Committee on their completed, ongoing and future research projects.

VIII. 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 have been established on a DoD Retail Refund Pricing Agreement; these drugs are now compliant with Fiscal Year 2008 National Defense Authorization Act, Section 703. By law, these drugs were designated NF on the UF and subject to pre-authorization prior to use in the retail point of service (POS) and MN in MTFs. These drugs are now eligible to return to their previous formulary status without a pre-authorization requirement. Drugs with 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.

A. ***COMMITTEE ACTION: DRUGS RETURNED TO UF STATUS***—The P&T Committee recommended by consensus the drugs listed in Appendix C return to formulary status on the UF. See Appendix C for the full list of affected medications.

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

B. ***COMMITTEE ACTION: DRUGS MAINTAINING NF STATUS BUT NOT SUBJECT TO PREAUTHORIZATION***—The P&T Committee recommended by consensus the following drugs maintain NF status and not be subject to PA:

Daytrana, Kapidex, Saizen, Azor, Welchol, Cardene SR, and Vyvanse

Acting Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

VIII. CLASS OVERVIEWS

The Antidiabetic Drug Class overview was presented to the P&T Committee. The Antidiabetic Drug Class is comprised of the sulfonylureas, sulfonylurea combinations, alpha glycoside agonists, amylin analogs, biguanides, meglitinides, thiazolidinediones, glucose-like-peptide 1 agents, and the dipeptidyl peptidase-4 (DPP-4) inhibitors. 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 this class will be presented at an upcoming meeting.

IX. ADJOURNMENT

The meeting adjourned at 1700 hours on May 12, 2010, and at 1100 hours on May 13, 2009. The next meeting will be in August 2010.

Appendix A—Attendance

Appendix B—Table of Medical Necessity Criteria

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.

Dr. Charles L. Rice
Acting Director

23 July 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)
Lt Col Thom Bacon, BSC *for 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 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
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 Michele Hupp, MSC	Defense Medical Standardization Board
Guests	
Lt Col Kirk Stocker	AFMOA
Capt Julie Meek	Air Force Pharmacy Resident
Dr. Barbara Vize	United States Public Health Service/ Indian Health Service
Dr. David Trang	University of Incarnate Word Pharmacy School
Dr. Bernadette Heron	VA PBM
Dr. Annabel Schumaker	Lackland AFB

Appendix A—Attendance (continued)

Others Present	
COL Cynthia Clagett	DoD Pharmacoeconomic Center
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

Appendix B—Table of Medical Necessity Criteria

Drug / Drug Class	Medical Necessity Criteria
Silodosin (Rapaflo) **Alpha Blockers for BPH**	• Use of the formulary agent is contraindicated. • 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. • There is no alternative formulary agent available, and the patient requires a drug that can be crushed or sprinkled on food.
Doxazosin ER (Cardura XL) **Alpha Blockers for BPH**	• The patient has experienced or is likely to experience significant adverse effects from formulary alternatives.
Sumatriptan needle-free injection (Sumavel) **Triptans**	• No alternative formulary agent available for patients with needle phobia or those with dexterity issues who cannot manipulate the sumatriptan injection (Imitrex STATdose, generics).

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

Product Name	Subclass	Manufacturer
DEPAKENE	Anticonvulsants	ABBOTT LABS
OMNICEF	3rd gen cephalosporins	ABBOTT LABS
PCE	Macrolide	ABBOTT LABS
DIPENTUM	Medications for inflammatory bowel disease	ALAVEN PHARMA
KADIAN	Higher potency single analgesic agents	ALPHARMA BPD
ALLEGRA	2nd gen antihistamines & combos	AVENTIS PHARM
CYTOXAN	Alkylating agents	BMS ONCO/IMMUN
CATAPRES	Sympatholytics	BOEHRINGER ING.
EVOXAC	Parasympathetic agents	DAIICHI SANKYO
FLOXIN	Otic medications, anti-infective	DAIICHI SANKYO
BANZEL	Anticonvulsants/antimania medications	EISAI INC.
FRAGMIN	Anticoagulants	EISAI INC.
SALAGEN	Parasympathetic agents	EISAI INC.
ZONEGRAN	Anticonvulsants	EISAI INC.
CETROTIDE	LHRH (GNRH) antagonist, pituitary suppressant age	EMD SERONO, INC
LUVERIS	Luteinizing hormones	EMD SERONO, INC
SEROSTIM	Growth hormone	EMD SERONO, INC
ZORBTIVE	Growth hormone	EMD SERONO, INC
BRAVELLE	FSH/LH fertility agents	FERRING PH INC
ENDOMETRIN	Pregnancy facilitating/maintaining agent	FERRING PH INC
REPRONEX	FSH/LH fertility agents	FERRING PH INC
LAMICTAL ODT	Anticonvulsants/antimania medications	GLAXOSMITHKLINE
LAMICTAL ODT (BLUE)	Anticonvulsants/antimania medications	GLAXOSMITHKLINE
LAMICTAL ODT (GREEN)	Anticonvulsants/antimania medications	GLAXOSMITHKLINE
LAMICTAL ODT (ORANGE	Anticonvulsants/antimania medications	GLAXOSMITHKLINE
LAMICTAL XR	Anticonvulsants/antimania medications	GLAXOSMITHKLINE
DERMA-SMOOTHE-FS	Topical corticosteroids	HILL DERM
PERANEX HC	Topical corticosteroids/immune modulators	KENWOOD LAB
FLEXERIL	Skeletal muscle relaxants	McNEIL CONS
UROCIT-K	Urinary agent	MISSION
LITHOSTAT	Ammonia inhibitors	MISSION PHARM
TINDAMAX	Antiprotozoal	MISSION PHARM
LINDANE	Misc topical anti-infectives	MORTON GROVE PH
ERGOLOID MESYLATE	Misc cardiovascular medications	MUTUAL PHARM CO
KERAFOAM	Keratolytics	ONSET THERAPEUT
OPTASE	Misc topical agents	ONSET THERAPEUT
SALKERA	Keratolytics	ONSET THERAPEUT
PROCRIT	RBC stimulants	ORTHO BIOTECH
METANX	Vitamin B preparations	PAN AMERICAN
DILANTIN	Anticonvulsants/antimania medications	PFIZER US PHARM
OGEN	Estrogens & estrogen/androgen combos	PHARMACIA/UPJOHN
TENEX	Sympatholytics	PROMIUS PHARMA
MS CONTIN	Higher potency single analgesic agents	PURDUE PHARMA L
DORAL	Sedative/hypnotics II	QUESTCOR
RIOMET	Biguanides	RANBAXY BRAND D
ANAPROX	NSAIDs	ROCHE LABS
ANAPROX DS	NSAIDs	ROCHE LABS

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

Product Name	Subclass	Manufacturer
KLONOPIN	Anticonvulsants	ROCHE LABS
KYTRIL	5HT3 antiemetics	ROCHE LABS
VALIUM	Anxiolytics	ROCHE LABS
VESANOID	Misc antineoplastics	ROCHE LABS
VIMPAT	Anticonvulsants/antimania medications	SCHWARZ PHARMA
AGRYLIN	Platelet reducing agents	SHIRE US INC.
CARBATROL	Anticonvulsants	SHIRE US INC.
FOSRENOL	Phosphate binders	SHIRE US INC.
LIALDA	Medications for inflammatory bowel disease	SHIRE US INC.
PENTASA	Medications for inflammatory bowel disease	SHIRE US INC.
PROAMATINE	Adrenergic vasopressors	SHIRE US INC.
NEOBENZ MICRO	Keratolytics	SKINMEDICA
ELDEPRYL	Parkinson's medications	SOMERSET PHARM
LOCOID	Topical corticosteroids	TRIAX PHARMACEU
MINOCIN	tetracyclines	TRIAX PHARMACEU
SULFAMYLON	Topical sulfonamides	UDL
ANDROID	Androgens/anabolic steroids	VALEANT
OXSORALEN	Hyperpigmentation agents	VALEANT
TESTRED	Androgens/anabolic steroids	VALEANT
QUIXIN	Ophthalmic antibiotics, quinolones	VISTAKON PHARMA
MUSE	Prostaglandins for ED	VIVUS
FIORICET	Analgesic combos	WATSON PHARMA
MYAMBUTOL	Antitubercular medications	X-GEN PHARMACEU

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
May 2010	Antilipidemic -1s	~~UF~~ Review	▪ Atorvastatin (Lipitor) ▪ Pravastatin(Pravachol, generics) ▪ Simvastatin (Zocor, generics)	▪ Atorvastatin / amlodipine (Caduet) ▪ Ezetimibe (Zetia) ▪ Ezetimibe / simvastatin (Vytorin) ▪ Fluvastatin IR (Lescol) ▪ Fluvastatin ER (Lescol XL) ▪ Lovastatin IR (Mevacor; generics) ▪ Lovastatin ER (Altoprev) ▪ Lovastatin / niacin ER (Advicor) ▪ Niacin IR ▪ Niacin ER (Niaspan) ▪ Rosuvastatin (Crestor) ▪ Simvastatin / niacin ER (Simcor)	▪ Not applicable (no drug designated non-formulary)	Pending 60 days	Step therapy (Automated PA)	August 2006	Step therapy (automated PA) with generics, or atorvastatin as the preferred agents. (note: step therapy does not apply to ezetimibe or niacin)
May 2010	Alpha Blockers for BPH	UF Review	▪ Alfuzosin (Uroxatral) ▪ Tamsulosin (Flomax, generics) ▪ Terazosin (Hytrin; generics)	▪ Doxazosin IR (Cardura; generics)	▪ Silodosin (Rapaflo) ▪ Doxazosin ER (Cardura XL)	Pending 60 days	Step therapy (Automated PA)	August 2009 (silodosin); Nov 2007; Aug 2005	Step therapy (automated PA) with tamsulosin or alfuzosin as the preferred agents. (note: step therapy does not apply to terazosin, doxazosin, or doxazosin ER)
May 2010	Triptans	New Drug Sumatriptan needle-free injection (Sumavel DosePro)	▪ Rizatriptan (Maxalt; Maxalt MLT) ▪ Sumatriptan- oral and one injectable formulation when multi-source generics are available	▪ Eletriptan (Relpax) ▪ Zolmitriptan (Zomig) ▪ Sumatriptan/naproxen (Treximet)	▪ **Sumatriptan needle-free injection (Sumavel DosePro** ▪ Almotriptan (Axert) ▪ Frovatriptan (Frova) ▪ Naratriptan (Amerge)	Sumavel DosePro: Pending 60 days	-	August 2008	-

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 Fentanyl Citrate Buccal Soluble Film (Onsolis)	• 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	• **Fentanyl buccal soluble film (Onsolis)** • Fentanyl transdermal system (Duragesic, generics); transmucosal tablet (Fentora); & transmucosal lozenge (Actiq; generics) • Codeine • Hydromorphone (Dilaudid) • Levorphanol • Meperidine • Methadone • Morphine products (other than BCF selections), Kadian and Avinza (ER products) • Morphine sulfate ER / naltrexone (Embeda) Feb 2010 • Opium tincture • Opium/belladonna alkaloids(suppositories) • Oxycodone IR • Oxycodone ER(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 • Codeine	• Tramadol ER (Ultram ER) Feb 07 • Tramadol ER (Ryzolt) Nov 09 • Tapendatol (Nucynta) Nov 09	Not applicable	-	Feb 2010 Feb 2007 Nov 2009	• Fentanyl Buccal Soluble Film (Onsolis) to remain UF

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
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 (continued)**	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Original Review and Updates	Comments
Feb 2010 (cont)				• **Fentanyl transdermal system** • **Fentanyl transmucosal tablet** • **Fentanyl transmucosal lozenge** • **Fentanyl buccal soluble film** • **Hydromorphone** • **Levorphanol** • **Meperidine** • **Methadone** • **Morphine sulfate ER 24hr** • **Morphine sulfate / naltrexone hydrochloride ER** • **Opium tincture** • **Opium / belladonna alkaloids (suppositories)** • **Oxycodone ER** • **Oxycodone IR** • **Oxymorphone** • **Oxycodone / ASA** • **Oxycodone / APAP** • **Buprenorphine injection** • **Butorphanol** • **Pentazocine / naloxone** • **Propoxyphene** • **Nalbuphine** • **Codeine / APAP** • **Codeine / ASA** • **Codeine / ASA / Carisoprodol** • **Codeine / caffeine / butalbital / APAP or ASA** • **Dihydrocodeine / Caffeine / ASA or APAP** • **Hydrocodone / APAP** • **Pentazocine / APAP** • **Propoxyphene / APAP** • **Propoxyphene / ASA / caffeine** **Tramadol / APAP**				

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
May 2010	Nasal Allergy Drugs	BCF Removal Fluticasone propionate nasal spray (Flonase; generics)	▪ Azelastine (Astelin)	▪ **Fluticasone propionate (generic Flonase)** ▪ **Flunisolide (Nasalide, generics)** ▪ **Ipratropium (Atrovent, generics)** ▪ **Mometasone (Nasonex)**	▪ Azelastine with sucralose (Astepro) ▪ olopatadine (Patanase) ▪ ciclesonide (Omnaris) ▪ fluticasone furoate (Veramyst) ▪ beclomethasone (Beconase AQ) ▪ budesonide (Rhinocort Aqua) ▪ triamcinolone (Nasacort AQ	Pending Upon signing of minutes	-	Nov 05 & Aug 07 for Veramyst) Nov 08 May 08 (Astepro)	-
May 2010	Non-Basal Insulins	BCF Addition	▪ Novolog pens and cartridges ▪ Novolog Mix pens and cartridges	▪ **Not applicable**	▪ Not applicable	Pending upon signing of minutes	-	-	-Joint National Contract with the DoD/VA -Novolog & Novolog Mix vials remain BCF

* New Drug—refers to a new FDA-approved drug in a class previously reviewed for Uniform Formulary (UF) status

APAP: acetaminophen

BPH: benign prostatic hyperplasia

ER: extended release

IR: immediate release

Appendix E—Table of Abbreviations

BAP	Beneficiary Advisory Panel
BCF	Basic Core Formulary
BIA	budget impact analysis
BPH	Benign prostatic hyperplasia
CEA	Cost-effectiveness analysis
CFR	Code of Federal Regulations
CHD	coronary heart disease
CMA	cost minimization analysis
CRP	C-reactive protein
CV	cardiovascular
DM	diabetes mellitus
DoD	Department of Defense
ECF	Extended Core Formulary
ER	extended release
ESI	Express Scripts, Inc
FCP	Federal Ceiling Price
FDA	Food and Drug Administration
FSS	Federal Supply Schedule Price
FY	fiscal year
HA	Health Affairs
HDL	high density lipoprotein cholesterol
HUS-TTP	hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura
IR	immediate release
LDL	low density lipoprotein cholesterol
LIP-1	Antilipidemic-1s drug class
MARR	Mandatory Agreement for Retail Refunds
MHS	Military Health System
MN	medical necessity
MTF	Military Treatment Facility
NDAA	National Defense Authorization Act
OMB	Office of Management and Budget
P&T	Pharmacy and Therapeutics
PA	prior authorization
PEC	Pharmacoeconomic Center
PORT	Pharmaceutical Outcomes Research Team
POS	point of service
PPI	Proton pump inhibitor drug class
QL	quantity limit
REMS	Risk evaluation and mitigation strategy
SED-1	Sedative hypnotic-1 drug class
TG	Triglyceride
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

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