

**DEPARTMENT OF DEFENSE  
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS  
February 2012**

**I. CONVENING**

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on February 16 and 17, 2012, 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 November Minutes**—Jonathon Woodson M.D., Director, approved the minutes for the November 2011 DoD P&T Committee meeting on February 7, 2012.
2. **Correction of August 2011 Minutes—BCF Clarification for Non-steroidal Anti-inflammatory Drugs:** The August 2011 P&T Committee minutes were clarified to state the BCF listing is naproxen 125 mg/5 mL suspension—not ibuprofen suspension—for the oral non-steroidal anti-inflammatory drugs.

**III. REQUIREMENTS**

All clinical and cost evaluations for new drugs and full drug class reviews included, but were not limited to, the requirements stated in 32 Code of Federal Regulations (CFR) 199.21(e)(1).

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

**A. Ophthalmic-1 Class—Alcaftadine Ophthalmic Solution 0.25% (Lastacft)**

*Relative Clinical Effectiveness*—Alcaftadine (Lastacft) is a dual action ophthalmic antihistamine/mast cell stabilizer. It is dosed once daily to prevent symptoms associated with allergic conjunctivitis (AC). The Ophthalmic-1 Class was evaluated for Uniform Formulary (UF) placement in February 2010. The current Basic Core Formulary (BCF) product is olopatadine 0.1% (Patanol); there are no nonformulary (NF) Ophthalmic-1 drugs.

There are no head-to-head trials with alcaftadine and the other dual action ophthalmic antihistamines. Alcaftadine was superior to placebo in preventing ocular itching

associated with AC, but was not superior in relieving conjunctival redness. Alcaftadine's safety profile appears similar to the other ophthalmic antihistamines.

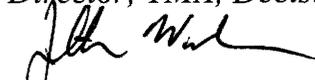
*Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 2 absent) there is no evidence to suggest alcaftadine ophthalmic solution has a compelling clinical advantage over the other dual action agents for AC on the UF.

*Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion*—Cost minimization analysis (CMA) was performed. The weighted average cost per day at all three points of service (POS) was evaluated for alcaftadine ophthalmic solution in relation to other currently available Ophthalmic-1 agents. 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 alcaftadine ophthalmic solution was cost-effective when compared to other 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 (15 for, 0 opposed, 1 abstained, 2 absent) alcaftadine ophthalmic 0.25% solution (Lastacast) remain designated with formulary status on the UF.

Director, TMA, Decision:

Approved  Disapproved



Approved, but modified as follows:

## **B. Narcotic Analgesics—Tapentadol Extended Release Tablets (Nucynta ER)**

Tapentadol extended release (Nucynta ER) is an opioid analgesic with dual modes of action; it is a mu receptor agonist with norepinephrine reuptake inhibition properties. Tapentadol ER is a Schedule II narcotic, and is classified as a high potency analgesic in the Narcotic Analgesics Drug Class. The class was last reviewed for UF placement in February 2007. Tapentadol immediate release (IR) (Nucynta) was reviewed in November 2009 and is currently NF. Tapentadol ER is indicated for moderate to severe pain when continuous, around-the-clock opioid analgesia is needed chronically. In two trials, tapentadol ER demonstrated greater reductions in pain scores compared to placebo, and produced similar reductions in pain scores as oxycodone ER (Oxycontin).

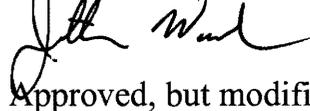
The safety profile of tapentadol ER is typical of the other high potency long-acting opioids. The adrenergic properties of the drug create additional safety concerns with respect to serotonin syndrome and interactions with monoamine oxidase inhibitors. When indirectly compared to oxycodone ER in clinical trials, the frequency of gastrointestinal (GI) adverse events (constipation, nausea, and vomiting) was observed less frequently in the Nucynta ER treatment groups. However, there were more central nervous system (CNS) disorders seen in the Nucynta ER groups.

*Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) that tapentadol extended release (Nucynta ER) offers another long-acting, high-potency narcotic analgesic treatment option that may have less GI adverse events but more CNS adverse events than oxycodone ER. There is no evidence that pain control with tapentadol ER is superior to oxycodone ER.

*Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion*—CMA was performed. Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) that tapentadol ER (Nucynta ER) was more costly on an average weighted cost per day of therapy basis than several other comparators in the high potency narcotic analgesics currently on the UF, including generic morphine sulfate IR and fentanyl patches. Tapentadol ER was less costly than morphine sulfate ER (Avinza and Kadian), oxymorphone ER (Opana ER), oxycodone ER (OxyContin), and hydromorphone ER (Exalgo).

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 (9 for, 8 opposed, 1 abstained, 0 absent) tapentadol extended release (Nucynta ER) remain formulary on the UF. UF status was designated due to the potential for decreased GI intolerance as compared to oxycodone ER, despite the concerns of potential undesirable drug interactions due to norepinephrine reuptake inhibition properties.

Director, TMA, Decision:



Approved, but modified as follows:

Approved  Disapproved

## V. UF DRUG CLASS REVIEWS

### A. Antiplatelet Agents

*Background Relative Clinical Effectiveness*—The P&T Committee evaluated the relative clinical effectiveness of the antiplatelet drugs, which are used for treating acute coronary syndromes, stroke, and peripheral artery disease. The Antiplatelet Drug Class is comprised of the following: clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta), ticlopidine (Ticlid, generics), aspirin/dipyridamole ER (Aggrenox), dipyridamole (Persantine, generics), cilostazol (Pletal, generics), and pentoxifylline (Trental, generics). Aspirin is available over-the-counter and is not part of the TRICARE® benefit.

Clopidogrel was designated with BCF status on the UF in 2002, prior to implementation of the UF Rule. Generic formulations of clopidogrel are expected in May 2012. Military Health System (MHS) expenditures for antiplatelet agents exceed \$260 million annually.

*Relative Clinical Effectiveness Conclusion*—The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 1 absent) to accept the following clinical effectiveness conclusions:

1. With regard to efficacy, the following conclusions were made:
  - Acute coronary syndrome (ACS):
    - Several large clinical trials have shown the effectiveness of clopidogrel in decreasing the incidence of major cardiovascular (CV) events in patients with ACS.
    - Prasugrel and ticagrelor have a faster onset of action and exhibit more complete platelet inhibition, compared to clopidogrel.
    - Guidelines from professional cardiology groups recommend clopidogrel, prasugrel, or ticagrelor as first-line options for treating ACS patients requiring percutaneous coronary intervention (PCI).
    - Prasugrel and ticagrelor are approved solely for ACS; however, prasugrel is limited to patients whose coronary anatomy is known and suitable for PCI.
    - In the TRITON-TIMI 38 trial, prasugrel was more effective than clopidogrel in reducing the composite endpoint of cardiovascular death, non-fatal myocardial infarction (MI), and stroke in ACS patients undergoing PCI. There was no significant difference between prasugrel and clopidogrel for the single endpoint of CV death.

- In the TRITON-TIMI 38 trial, a subgroup analysis showed prasugrel was superior to clopidogrel in patients who are diabetic, those with prior stent thrombosis, and those younger than 65 years.
- In the PLATO trial, ticagrelor was more effective than clopidogrel in reducing the composite endpoint of CV death, non-fatal MI, and stroke in ACS. Ticagrelor was more effective than clopidogrel in reducing the single endpoints of CV death and non-fatal MI, although the trial was not designed to assess differences in mortality.
- In the PLATO trial, a subgroup analysis of the 1,413 U.S. patients found no significant difference between ticagrelor and clopidogrel for major coronary events. This was attributed to the higher aspirin dose utilized in North America versus the rest of the world. Ticagrelor should only be used with aspirin doses lower than 100 mg.
- Definitive statements about comparative clinical effectiveness between prasugrel and ticagrelor are difficult to make because there are no head-to-head studies.
- Stroke
  - A systematic review from the Oregon Drug Effectiveness Review Project (DERP) concluded there was no significant difference between aspirin/dipyridamole ER and clopidogrel for all-cause mortality, CV mortality, and recurrent stroke, in patients with ischemic stroke, based on the PROFESS trial.
  - The DERP review concluded there was no significant difference between ticlopidine and clopidogrel on outcomes of all-cause mortality, CV death, or cerebral infarction in stroke patients.
- Peripheral artery disease (PAD)
  - Cilostazol is the recommended first-line agent to improve walking distance in patients with PAD, while pentoxifylline is the second-line alternative, based on professional guidelines.
  - Clopidogrel and aspirin are recommended to reduce the risk of MI, stroke or vascular death in patients with symptomatic PAD.
- 2. With regards to safety/tolerability, the following conclusions were made:
  - In the TRITON-TIMI 38 trial, prasugrel had a significantly higher rate of bleeding, including non-coronary artery bypass grafting (CABG) related bleeding and fatal bleeding, compared to clopidogrel.

Additional risk factors that increase the bleeding risk with prasugrel include low weight (<60 kg), age greater than 75 years, and prior history of stroke and transient ischemic attack (TIA).

- In the PLATO trial, ticagrelor had a similar rate of major and fatal bleeding compared to clopidogrel; however, the rate of non-CABG-related major bleeding was significantly higher with ticagrelor than clopidogrel. Ticagrelor was associated with a higher rate of non-hemorrhagic adverse events (AEs), including dyspnea, and increases in serum creatinine and uric acid levels.
- Unlike clopidogrel and ticagrelor, prasugrel is contraindicated in patients with previous stroke or TIA.
- Ticlopidine's therapeutic use is greatly limited by its AE profile, including risk of neutropenia and aplastic anemia.
- In stroke patients, clopidogrel had a lower rate of major bleeding and withdrawal due to AEs, compared with aspirin/dipyridamole ER.

### 3. With regards to other factors

- Prasugrel and ticagrelor are less susceptible to genetic variation and drug-drug interactions with proton pump inhibitors (PPIs), compared to clopidogrel.
- The Pharmacy Outcomes Research Team (PORT) conducted an analysis to define a typical MHS Aggrenox user. A total of 13,341 users with an average age of 76 years were identified. Over 82% of patients had received Aggrenox in the last 180 days, with a new user rate of 13%–18%, suggesting that patients had been on Aggrenox for extended periods.

*Relative Cost-Effectiveness*—The P&T Committee evaluated the relative cost-effectiveness of the antiplatelet agents for secondary prevention in ACS, for secondary prevention in stroke, and for PAD. CMAs were performed for the antiplatelet drugs used for stroke and PAD (aspirin/dipyridamole ER, ticlopidine, cilostazol, dipyridamole, and pentoxifylline). Cost-effectiveness analyses (CEAs) and CMAs were used to analyze antiplatelet agents for ACS (clopidogrel, prasugrel, and ticagrelor), as efficacy differences between the agents were noted in the clinical review.

- CMA and BIA were used to assess the potential impact of cost scenarios where selected antiplatelet agents were designated with formulary or NF status on the UF. The impact of generic clopidogrel availability was modeled in the BIA scenarios.

- For the antiplatelet drugs prescribed following ACS, CEAs and CMAs were used to assess the potential impact of the occurrence rates of CV and bleeding events, based on differences highlighted in the clinical review.
- Two separate cost-effectiveness models were constructed in the analyses of antiplatelet agents for ACS secondary prevention: prasugrel (Effient) versus clopidogrel and ticagrelor (Brilinta) versus clopidogrel. Analysis was based on direct comparisons of relevant trial data. The models compared the annual cost per CV event avoided (the composite of nonfatal MI, nonfatal stroke, and death from CV cause).

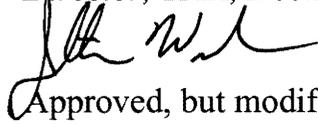
*Relative Cost-Effectiveness Conclusion*—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 against, 0 abstained, 2 absent) the following:

- **Antiplatelet agents for ACS**—CEA results showed that prasugrel (Effient) and ticagrelor (Brilinta) provide reasonable clinical benefit for the increase in treatment cost, as shown by their incremental cost-effectiveness ratios (ICERs) of \$28,083 and \$58,358 per cardiovascular event avoided, respectively.
  - **Antiplatelet agents for stroke**—CMA results showed that aspirin/dipyridamole ER (Aggrenox) was the least cost-effective agent, based on analysis of the average weighted price per day of therapy at all three POS.
  - **Antiplatelet agents for PAD**—CMA results showed that pentoxifylline and cilostazol are similarly cost-effective therapy options.
  - **All antiplatelet agents**—BIA results showed the scenario where all current BCF agents were retained on the BCF, all current UF agents were retained on the UF, and aspirin/dipyridamole ER (Aggrenox) and ticagrelor (Brilinta) were designated NF resulted in the lowest projected cost compared to current MHS expenditures.
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, 3 opposed, 0 abstained, 1 absent) clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta), ticlopidine (Ticlid, generics), aspirin/dipyridamole ER (Aggrenox), dipyridamole (Persantine, generics), cilostazol (Pletal, generics) and pentoxifylline (Trental, generics) remain formulary on the UF. Although the cost-effectiveness review showed aspirin/dipyridamole ER was the least cost-

effective drug for stroke, the P&T Committee recommended that it remain formulary on the UF due to the low new user rate and the advanced age of the patient population. Ticagrelor was also recommended to remain formulary on the UF due its ICER, compared to clopidogrel.

Director, TMA, Decision:

Approved  Disapproved

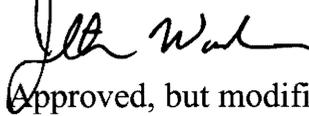


Approved, but modified as follows:

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, 0 abstained, 1 absent) clopidogrel (Plavix) maintain BCF status on the UF.

Director, TMA, Decision:

Approved  Disapproved



Approved, but modified as follows:

## B. Dipeptidyl Peptidase-4 (DPP-4) Inhibitors

The P&T Committee evaluated the relative clinical effectiveness of the DPP-4 inhibitors, which include:

- sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/simvastatin (Juvilynx);
- saxagliptin (Onglyza), saxagliptin/metformin ER (Kombiglyze XR);
- linagliptin (Tradjenta).

Two new products, sitagliptin/metformin ER (Janumet XR) and linagliptin/metformin (Jentadueto) will be reviewed at an upcoming meeting. The DPP-4 inhibitors were previously reviewed in November 2010 as a subclass of the Non-insulin Diabetes Drug Class. Prior Authorization (PA) criteria and step therapy require a trial of metformin or sulfonylurea (SU) prior to using a DPP-4 inhibitor.

MHS expenditures exceed \$119 million annually for DPP-4 inhibitors. In terms of overall utilization at all POS, sitagliptin and sitagliptin/metformin are the most utilized agents and are currently designated with BCF status on the UF.

*Relative Clinical Effectiveness Conclusion*—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions for the DPP-4 inhibitors:

1. Clinical practice guidelines, including the DoD/Veterans Affairs guidelines for diabetes mellitus, do not currently recommend DPP-4 inhibitors for a specific place in therapy but list the class as alternative agents. Metformin remains the recommended first line agent for most patients who do not have a contraindication for metformin therapy.
2. There are no completed long-term studies assessing CV outcomes with sitagliptin, saxagliptin, and linagliptin, although three studies are under way, with results expected in 2014–2018.
3. One head-to-head trial did not show clinically relevant differences in efficacy or safety between sitagliptin and saxagliptin.
4. Sitagliptin, saxagliptin, and linagliptin show similar effects of lowering hemoglobin A1c when used as monotherapy, ranging from 0.4% to 0.9%. When a DPP-4 inhibitor is combined with metformin, the mean decrease in A1c from baseline ranges from 0.4% to 2.5%; when combined with a thiazolidinedione (TZD), the mean decrease in A1c ranges from 0.7% to 1.06%; and when combined with a SU, the mean decrease in A1c ranges from 0.5% to 0.6%.
5. DPP-4 inhibitors are weight neutral, lipid neutral, and have minimal impact on blood pressure.
6. Linagliptin has not been directly compared with saxagliptin or sitagliptin in a clinical trial. A meta-analysis showed the A1c-lowering effect of linagliptin plus metformin was non-inferior to sitagliptin plus metformin. Linagliptin is the only DPP-4 inhibitor that does not require dose adjustments due to renal or hepatic impairment.
7. Juvisync is a fixed-dose combination product containing sitagliptin with the cholesterol-lowering drug simvastatin. There are no clinical trials evaluating Juvisync; it obtained FDA approval based on bioequivalence with the individual components. Juvisync may provide a dosing convenience in patients who require both sitagliptin and a statin.
8. In terms of commonly reported adverse events, there are no clinically relevant differences between sitagliptin, saxagliptin, and linagliptin. Drug interaction profiles are also similar between agents. Pancreatitis has been reported with both sitagliptin and saxagliptin. Acute renal failure has been reported with sitagliptin.

9. There is a high degree of therapeutic interchangeability between sitagliptin, saxagliptin, and linagliptin.
10. The PORT conducted an analysis of the changes in DPP-4 inhibitor utilization following the November 2010 P&T Committee Meeting. At that meeting, sitagliptin and sitagliptin/metformin were designated BCF and step therapy (automated PA) was implemented, requiring a trial of metformin or a SU prior to use of a DPP-4 inhibitor. An increase in DPP-4 utilization has been noted at the MTF and Mail Order POS. Utilization increase at the Mail Order POS may also be due to the change in co-pay structure implemented in October 2011. There has also been a concurrent decline in TZD utilization, which is likely due to safety concerns.
11. The PORT also examined the effects of step therapy at the three POS.
  - **MTFs**—Out of 48,097 patients receiving their first DPP-4 prescription in the period from December 2010 to November 2011, 32% were new users of DPP-4 inhibitors; of these new users, 19%–21% had no evidence of prior use of metformin or SU.
  - **Retail and Mail Order**—In the 8-month evaluation period, 848 DPP-4 inhibitor prescriptions were rejected due to no evidence of prior metformin or SU use. However, 67% of these rejected prescriptions did show that a DPP-4 inhibitor prescription was received within 240 days of the reject, and 52% showed a later prescription for metformin or SU. There was no evidence of a prescription fill for any oral non-insulin diabetes drug in 12% of the rejected claims (“no fill” rate).

*Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion*—CMAs and budget impact analyses (BIA) were used to evaluate the relative cost-effectiveness of the DPP-4 inhibitors. Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

- BIA was used to assess the potential impact of cost scenarios where selected DPP-4 inhibitors were designated with formulary, BCF, or NF status on the UF. The analysis included an evaluation of the potential impact of cost scenarios where DPP-4 inhibitors were designated with preferred product status (step therapy) on the UF; i.e., a trial of a preferred DPP-4 inhibitor would be required before using other DPP-4 inhibitors on the UF.
- BIA results showed the scenario where sitagliptin (Januvia), sitagliptin/metformin (Janumet), and sitagliptin/simvastatin (Juvivync) are step-preferred on the UF, linagliptin (Tradjenta) is non-preferred on the UF, and saxagliptin

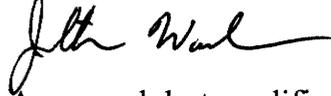
(Onglyza) and saxagliptin/metformin (Kombiglyze XR) are non-preferred and NF was determined to be the most cost-effective.

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 (16 for, 1 opposed, 1 abstained, 0 absent):
  - sitagliptin (Januvia), sitagliptin/metformin (Janumet), and sitagliptin/simvastatin (Juvissync) be designated step-preferred and formulary on the UF;
  - linagliptin (Tradjenta) be designated non-preferred and formulary on the UF;
  - saxagliptin (Onglyza) and saxagliptin/metformin ER (Kombiglyze XR) be designated non-preferred and NF.

This recommendation implements step therapy, which requires a trial of Januvia, Janumet, or Juvissync (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors would require a trial of metformin or sulfonylurea 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 (17 for, 0 opposed, 1 abstained, 0 absent) sitagliptin (Januvia) and sitagliptin/metformin (Janumet) maintain BCF status on the UF.

Director, TMA, Decision:

Approved  Disapproved

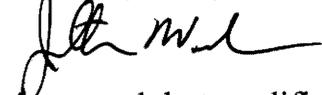


Approved, but modified as follows:

3. **COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA**—Based on the clinical evaluations for saxagliptin (Onglyza) and saxagliptin/metformin ER (Kombiglyze XR) and the conditions for establishing MN for NF medications, the P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) MN criteria for saxagliptin (Onglyza) and saxagliptin/metformin ER (Kombiglyze XR). (See Appendix C for full MN criteria.)

Director, TMA, Decision:

Approved  Disapproved



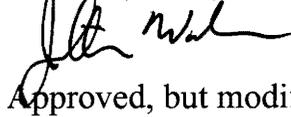
Approved, but modified as follows:

4. **COMMITTEE ACTION: PA CRITERIA**—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 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, Juvisync, Onglyza, Kombiglyze XR, or Tradjenta) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.
  - b) Manual PA criteria for Januvia, Janumet, Juvisync, Onglyza, Kombiglyze XR, or Tradjenta, 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.
- c) In addition to the above criteria regarding metformin and SU, the following PA criteria would apply specifically to saxagliptin (Onglyza), saxagliptin/metformin ER (Kombiglyze XR), and linagliptin (Tradjenta):
- (1) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with saxagliptin- or linagliptin-containing products.
  - (2) The patient has had an inadequate response to a sitagliptin-containing product.
  - (3) The patient has a contraindication to sitagliptin.

Director, TMA, Decision:

Approved  Disapproved



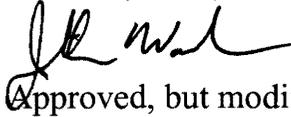
Approved, but modified as follows:

**5. COMMITTEE ACTION: UF AND 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 P&T Committee's recommendation, the effective date is July 11, 2012.

Director, TMA, Decision:

Approved  Disapproved



Approved, but modified as follows:

**C. Attention Deficit Hyperactivity Disorder (ADHD)/Wakefulness-Promoting Agents**

*Relative Clinical Effectiveness*—The P&T Committee evaluated the relative clinical effectiveness of the ADHD and Wakefulness-Promoting Agents Class, which was previously reviewed in November 2006. The drugs in this class are comprised of the following three subclasses: 1) ADHD stimulants, 2) ADHD non-stimulants, and 3) wakefulness-promoting agents.

The ADHD stimulants include lisdexamphetamine (Vyvanse), and long- and short-acting formulations of methylphenidate, amphetamine, and mixed amphetamine salt products. The full list of the drugs in the subclass and the classification of long- and short-acting stimulants are found in Appendix D. Since the November 2006 review, dexamethylphenidate IR (Focalin), mixed amphetamine salts ER and IR (Adderall XR; Adderall), and methylphenidate long-acting (LA) (Ritalin LA) are now available in generic formulations. There is one authorized generic for methylphenidate osmotic-controlled release oral delivery system (OROS), which is produced by the manufacturer of Concerta.

The ADHD non-stimulants subclass is comprised of atomoxetine (Strattera), clonidine ER (Kapvay), and guanfacine ER (Intuniv). The wakefulness-promoting subclass includes modafinil (Provigil), armodafinil (Nuvigil), and sodium oxybate (Xyrem). Generic formulations of modafinil are expected in the 2nd quarter of 2012. Prior Authorization is currently required for modafinil and armodafinil.

The current BCF agents include mixed amphetamine salts ER (Adderall XR, generics), methylphenidate IR (Ritalin, generic) and methylphenidate OROS (Concerta). The current NF products include dexamethylphenidate ER (Focalin XR), dexamethylphenidate IR (Focalin), lisdexamfetamine (Vyvanse), and methylphenidate transdermal system (Daytrana).

#### *Relative Clinical Effectiveness Conclusion*

1. The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 1 absent) on the following conclusions regarding the ADHD stimulants and non-stimulants:
  - a) Methylphenidate IR is more effective than placebo in improving ADHD symptoms in preschool-aged children (4–5 years of age) who do not respond to parental behavior training.
  - b) Based on a DERP systematic review, the following conclusions apply in children and adolescents aged 6–17 years:
    - There are no clinically relevant differences between the IR stimulant formulations.
    - There are no clinically relevant differences between IR stimulant formulations when compared to sustained release (SR) stimulants (Ritalin SR, Metadate CD).
    - There is conflicting evidence when methylphenidate IR is compared with methylphenidate OROS (Concerta). Two double-blinded studies showed no difference in efficacy, while two open-label studies favored methylphenidate OROS.

- There are no clinically relevant differences when SR stimulant formulations are compared to other SR formulations. Minor differences include that methylphenidate CD (Metadate CD) and dexamethylphenidate ER (Focalin XR) show greater response in the morning, while methylphenidate OROS (Concerta) shows greater response in the evening.
  - Lisdexamphetamine (Vyvanse) treatment resulted in similar scores on ADHD rating scales when compared to mixed amphetamine salts ER (Adderall XR).
  - Transdermal methylphenidate (Daytrana) produced similar scores on investigator, teacher, and parent rating scales when compared to methylphenidate OROS (Concerta) over a 7-week period.
- c) In adults (18 years of age and older), there are no clinically relevant differences in efficacy when switching to methylphenidate OROS (Concerta) versus continuing with methylphenidate IR.
  - d) With regards to safety, package labeling for all stimulants contains a black box warning for potential abuse and dependency.
  - e) Use of mixed amphetamine salts (Adderall IR, generic) is associated with a higher incidence of weight loss and insomnia than methylphenidate IR.
  - f) One large randomized controlled trial, the Multimodal Therapy Study of ADHD, reported stimulants caused a decrease in growth velocity in children at 36 months.
  - g) Stimulants do not significantly increase the risk of serious cardiovascular events in children, adolescents, or adults (up to age 64), based on two large cohort studies.
  - h) The stimulants with the lowest potential for abuse/diversion are Vyvanse, Daytrana, and Concerta. In adolescents, American Academy of Pediatrics guidelines recommend prescribing non-stimulants or stimulants with the lowest potential for abuse/diversion, compared to the other stimulant products.
  - i) For patients with swallowing difficulties, Vyvanse is dissolvable in water. Ritalin LA, Metadate CD, Adderall XR, and Focalin XR are formulated in capsules that can be opened and sprinkled on food.
  - j) The PORT analyzed ADHD prescription use in the MHS for the first 4 months of the school year.
    - (1) Use of any ADHD medication is highest among 6–12 year olds (33%) and 13–17 year olds (20%), and declines with age. Use of a

specific long-acting stimulants varies by age group, with Concerta predominating in patients younger than 18, and Adderall XR or its generic predominating in patients older than 18.

(2) Overall, 62% of usage is for a long-acting stimulant alone without another ADHD drug. About 14% of ADHD prescriptions were for a long-acting stimulant with a short-acting stimulant, which varied from 9% with Vyvanse, 11% with Concerta, and up to 27% with Ritalin LA.

2. The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 1 absent) on the following conclusions regarding the ADHD non-stimulants:
  - a) The DERP systematic review concluded atomoxetine (Strattera) is associated with efficacy outcomes similar to methylphenidate IR. Methylphenidate OROS (Concerta) and mixed amphetamine salts ER (Adderall XR, generic) are superior to atomoxetine in terms of response rates.
  - b) There are no head-to-head trials comparing clonidine ER (Kapvay) or guanfacine ER (Intuniv) with other ADHD drugs. Placebo-controlled studies with clonidine ER showed modest benefit when used as add-on or monotherapy. Placebo-controlled studies with guanfacine ER (Intuniv) showed modest benefit up to 8 hours after dosing.
  - c) With regards to safety, the package labeling for atomoxetine (Strattera) contains a black box warning for suicidal ideation. Atomoxetine has a higher incidence of vomiting, nausea, and somnolence compared to stimulants.
  - d) Clonidine ER (Kapvay) and guanfacine ER (Intuniv) are associated most commonly with somnolence and fatigue, although there are no comparative data with other ADHD drugs.
  
3. The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 1 absent) on the following conclusions regarding the wakefulness-promoting drugs:
  - a) A large percentage (estimated 90%) of modafinil (Provigil) and armodafinil (Nuvigil) MHS prescriptions are for non-FDA approved indications.
  - b) There is one head-to-head trial comparing modafinil 200 mg with armodafinil 150 mg in patients with excessive sleepiness due to shift work sleep disorder. There was no significant difference between the two drugs in terms of percentage of responders at 12 weeks.

- c) There are no head-to-head trials comparing modafinil with armodafinil in patients with narcolepsy or obstructive sleep apnea.
- d) The manufacturer of armodafinil (Nuvigil) submitted data to the FDA requesting approval for patients with jet lag, but the application was denied.
- e) The manufacturer of sodium oxybate (Xyrem) sought FDA approval for use in fibromyalgia, but was denied due to abuse potential and safety concerns.
- f) With regards to safety and tolerability, there are no clinically relevant differences in the safety profiles between modafinil and armodafinil.
- g) Sodium oxybate (Xyrem) has a black box warning for abuse/misuse/diversion potential. A restricted distribution program limits dispensing to one centralized pharmacy.
- h) The PORT analyzed usage of modafinil (Provigil) and armodafinil (Nuvigil) in the MHS. For the patients who received armodafinil, 32% were new users; of these new users, only 6% of patients had a previous prescription for modafinil in the previous 180 days, suggesting that the majority of new armodafinil users do not first receive a trial of modafinil.

*Relative Cost-Effectiveness*—The P&T Committee evaluated the relative cost-effectiveness of ADHD long-acting stimulants, short-acting stimulants, and non-stimulants, and the wakefulness-promoting agents. CMAs were performed to compare average daily cost of therapy for all branded and generic drugs within each of the respective subclasses. BIAs of varying formulary scenarios where various agents moved between BCF, UF, and NF status were performed for the long-acting stimulants, the non-stimulants, and the wakefulness-promoting drugs.

- *ADHD*—BIA was used to evaluate the long-acting stimulants, with corresponding sensitivity analyses. For relative comparison with the long-acting stimulants, a composite average daily cost for the short-acting stimulants was also calculated.
- *Wakefulness-promoting agents*—CMA and BIAs were used to evaluate the drugs in this subclass, with corresponding sensitivity analyses. BIAs also considered the potential impact of cost scenarios where current armodafinil (Nuvigil) users were grandfathered (and prior authorization would only apply to new users) versus a no-grandfathering scenario with prior authorization applicable to all users. Sodium oxybate (Xyrem) was not included in the CMA or BIAs due to restricted distribution from one pharmacy. Generic pricing estimates for

modafinil (Provigil) were used in the cost analyses based on its anticipated generic availability.

*Relative Cost-Effectiveness Conclusion*—Based on the results of the economic analysis and other clinical and cost considerations, the P&T Committee concluded the following for the ADHD and wakefulness-promoting agents:

1. The P&T Committee agreed (17 for, 0 opposed, 1 abstained, 0 absent) on the following conclusions regarding the long-acting stimulants: CMA results showed the following ranking, from least costly to most costly: mixed amphetamine salts ER < Ritalin LA < Vyvanse < Focalin XR < Concerta < Daytrana. BIAs results showed that scenarios where the current branded NF long-acting stimulants remained NF generated greatest cost avoidance.
2. The P&T Committee agreed (17 for, 0 opposed, 1 abstained, 0 absent) on the following conclusions regarding the short-acting stimulants: CMA results showed the following ranking, from least costly to most costly: methylphenidate IR (Ritalin generic) < dextroamphetamine tablets (Dexedrine generic) < mixed amphetamine salts (Adderall generic) < dexmethylphenidate (Focalin generic) < methylphenidate SR (Ritalin SR generic) < Metadate CD < Methylin chewable tablet < dextroamphetamine spansules (Dexedrine generic) < Procentra liquid < Desoxyn. Composite costs results showed the short-acting stimulants were more cost-effective than the long-acting stimulants.
3. The P&T Committee agreed (18 for, 0 opposed, 0 abstained, 0 absent) on the following: for the non-stimulants, Strattera was most cost-effective, followed by Intuniv; Kapvay was least cost-effective. BIAs results showed minimal differences in cost-avoidance between branded NF and UF non-stimulants.
4. The P&T Committee agreed (18 for, 0 opposed, 0 abstained, 0 absent) on the following: for the wakefulness-promoting agents, CMA showed the estimated generic modafinil was most cost-effective, followed by Provigil; Nuvigil was least cost-effective. BIAs results showed that scenarios where Nuvigil changes to NF status and all current and new users of Nuvigil undergo the PA process (e.g., not grandfathered) generated greatest cost-avoidance; this scenario also included maintaining the existing PA for Provigil.

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 the following:

<p><i>Stimulants:</i>            dextroamphetamine (Dexedrine, Dextrostat, Procentra solution, generics)            methamphetamine HCl (Desoxyn, generic)            methylphenidate CD (Metadate CD)            methylphenidate IR (Ritalin, generic)            methylphenidate LA (Ritalin LA, generic)            methylphenidate ER (Metadate ER, Methylin ER, generics)            methylphenidate chewable tablets, solution (Methylin, generic)            methylphenidate OROS (Concerta)            methylphenidate SR (Ritalin SR, generic)            mixed amphetamine salts IR (Adderall, generic)            mixed amphetamine salts ER (Adderall XR, generic)</p>	15	1	1	1
<p><i>Non-Stimulants*:</i>            atomoxetine (Strattera)            clonidine ER (Kapvay)            guanfacine ER (Intuniv)</p>	16	0	1	1
<p><i>Wakefulness-Promoting Agents:</i>            modafinil (Provigil)            sodium oxybate (Xyrem)</p>	16	0	1	1

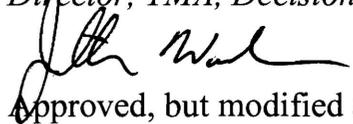
\* Clonidine IR tablets and transdermal system (Catapres, Catapres patch, generic) and guanfacine IR (Tenex, generics) are designated UF in the Miscellaneous Anti-hypertensive Agents Drug Class.

<b>Stimulants:</b>				
desmethylphenidate ER (Focalin XR)	15	1	1	1
lisdexamphetamine (Vyvanse)				
methylphenidate transdermal system (Daytrana)				
<b>Non-Stimulants:</b>				
None designated NF	16	0	1	1
<b>Wakefulness-Promoting Agents:</b>				
armodafinil (Nuvigil)	16	0	1	1

\* Clonidine IR tablets and transdermal system (Catapres, Catapres patch, generic) and guanfacine IR (Tenex, generics) are designated UF in the Miscellaneous Anti-hypertensive Agents Drug Class.

<b>Stimulants:</b>				
dexmethylphenidate IR (Focalin, generic)	15	1	1	1

Director, TMA, Decision:  Approved  Disapproved



Approved, but modified as follows:

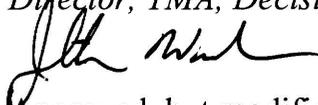
- COMMITTEE ACTION: BCF RECOMMENDATION**—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended:

<i>Stimulants:</i> mixed amphetamine salts ER (Adderall XR, generic) methylphenidate IR (Ritalin, generic) methylphenidate LA (Ritalin LA, generic)† methylphenidate OROS (Concerta)	14	2	1	1
<i>Non-stimulants*:</i> None designated BCF				
<i>Wakefulness-Promoting:</i> None designated BCF				

† Ritalin LA was added to the BCF, to have the most cost-effective long-acting methylphenidate formulation available at all MTFs. Concerta was maintained on the BCF, due to the large numbers of pediatric patients currently stabilized on the drug. Ritalin LA is encouraged to be considered in new patients requiring a long-acting methylphenidate formulation.

\* Clonidine IR tablets (Catapres, generic) are designated BCF in the Miscellaneous Anti-hypertensive Agents Drug Class.

Director, TMA, Decision:             Approved    Disapproved



Approved, but modified as follows:

- 3. COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA**—Based on the clinical evaluations for the ADHD stimulants [dexamethylphenidate ER (Focalin XR), lisdexamphetamine (Vyvanse) and methylphenidate transdermal system (Daytrana)], the wakefulness-promoting agents [armodafinil (Nuvigil)], and the conditions for establishing MN for NF medications, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for armodafinil (Nuvigil) and maintaining the current MN criteria for Focalin XR, Vyvanse, and Daytrana. (See Appendix C for full MN criteria.)

Director, TMA, Decision:             Approved    Disapproved

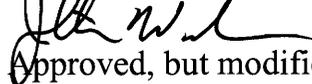


Approved, but modified as follows:

4. **COMMITTEE ACTION: PA CRITERIA**— The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) PA criteria should apply to modafinil (Provigil), armodafinil (Nuvigil), and sodium oxybate (Xyrem). The current PA criteria for modafinil were recommended to be continued without modification. The P&T Committee recommended maintaining the current PA criteria for Nuvigil, with one modification; jet lag would be added to the list of uses not provided. Additionally, the recommendation was that all current and new users of Nuvigil must undergo the PA process. The P&T Committee recommended PA criteria for sodium oxybate, which would be provided only for the current FDA-approved indications. Prior authorization is not intended to apply to modafinil or armodafinil use in active duty operational/readiness situations based on established protocols; MTFs should make necessary allowances for such use. (See Appendix B for full PA criteria).

Director, TMA, Decision:

Approved  Disapproved



Approved, but modified as follows:

5. **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 P&T Committee's recommendation, the effective date is July 11, 2012.

Director, TMA, Decision:

Approved  Disapproved



Approved, but modified as follows:

## VI. UTILIZATION MANAGEMENT

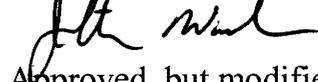
- A. **Crizotinib (Xalkori)—PA:** Crizotinib (Xalkori) is an oral anaplastic lymphoma kinase (ALK) inhibitor indicated for the treatment of patients with ALK-positive non-small cell lung cancer (NSCLC) as detected by a FDA-approved diagnostic test. The FDA has approved a new molecular diagnostic test (Vysis ALK FISH Probe test) designed to

identify ALK-positive NSCLC patients for treatment with Xalkori.

1. **COMMITTEE ACTION: PA CRITERIA**—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to Xalkori capsules, consistent with the FDA-approved product labeling:
  - a) Coverage would be approved for the treatment of patients with documented diagnosis of ALK-positive NSCLC, detected by a FDA-approved test such as Vysis ALK FISH Probe test.

Director, TMA, Decision:

Approved  Disapproved



Approved, but modified as follows: The approved PA limits coverage of the drug to its labeled use. TMA will expedite review of the required test to determine its coverage under 32 CFR 199.4(g)(15). Providers and beneficiaries will be advised to retain receipts for the test for submission for reimbursement following the coverage determination.

**B. Crizotinib (Xalkori)—Quantity Limits (QLs):** QLs and/or days supply limits currently apply to several oral chemotherapy agents. Xalkori is only available at the retail point of service through five specialty pharmacies (Curascript, Acredo, Walgreen's, CVS Caremark, and US Bioservices).

1. **COMMITTEE ACTION: QLs**—The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 1 absent) QLs/days supply limits, restricting the maximum allowable quantity to a 30-day supply at the retail point of service. This is consistent with supply limits for other oral chemotherapy agents.

Director, TMA, Decision:

Approved  Disapproved



Approved, but modified as follows:

**C. Vermurafenib (Zelboraf)—PA:** Vermurafenib (Zelboraf) is an oral kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF<sup>v600E</sup> mutation. Zelboraf is not recommended for use in wild-type BRAF melanoma. The FDA also approved a new molecular diagnostic test (Cobas 4800) designed to detect the BRAF<sup>v600E</sup> mutation and identify patients likely to respond to Zelboraf therapy.

1. **COMMITTEE ACTION: PA**—The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 1 absent) the following PA criteria should apply to Zelboraf tablets, consistent with the FDA-approved product labeling.
  - a) Coverage will be approved for the treatment of patients with documented diagnosis of unresectable or metastatic melanoma with BRAF<sup>v600E</sup> mutation, detected by a FDA-approved test such as Cobas 4800.
  - b) Coverage will not be approved for patients with wild-type BRAF melanoma.

Director, TMA, Decision:

Approved  Disapproved

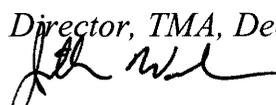
 Approved, but modified as follows: The approved PA limits coverage of the drug to its labeled use. TMA will expedite review of the required test to determine its coverage under 32 CFR 199.4(g)(15). Providers and beneficiaries will be advised to retain receipts for the test for submission for reimbursement following the coverage determination.

**D. Vermurafenib (Zelboraf)—QLs:** QLs and/or days supply limits currently apply to several oral chemotherapy agents.

1. **COMMITTEE ACTION: QLs**—The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 1 absent) QLs/days supply limits, restricting the maximum allowable quantity to a 30-day supply at the retail point of service and a 45-day supply at Mail Order. This is consistent with supply limits for other oral chemotherapy agents.

Director, TMA, Decision:

Approved  Disapproved

 Approved, but modified as follows:

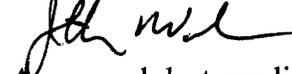
**E. Ivacaftor (Kalydeco)—PA:** Ivacaftor (Kalydeco) is a new oral agent that targets a specific subgroup of patients with Cystic Fibrosis (CF). It is a potentiator of the cystic fibrosis transmembrane conductance regulator (CFTR). Kalydeco is indicated for the treatment of CF in patients aged 6 years of age and older who have a G551D mutation in the CFTR gene. This rare mutation occurs in about 4% of CF patients. In patients for whom the genotype is unknown, a FDA-approved test should be used to detect the presence of the G551D mutation. Kalydeco is not effective in patients with CF who are homozygous for the F508del mutation in the CFTR gene, which occurs in about 90% of

CF patients. There are several FDA-approved in-vitro molecular diagnostic tests designed to simultaneously detect and identify mutations in the CFTR gene.

1. **COMMITTEE ACTION: PA**—The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 1 absent) the following PA criteria should apply to Kalydeco tablets, consistent with the FDA-approved product labeling:
  - a) Coverage will be approved for the treatment of CF patients aged 6 years and older who have a G551D mutation in the CFTR gene, detected by a FDA-approved test.
  - b) Coverage will not be approved for patients who are homozygous for the F508del mutation in the CFTR gene.

Director, TMA, Decision:

Approved  Disapproved



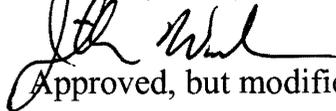
Approved, but modified as follows: The approved PA limits coverage of the drug to its labeled use. TMA will expedite review of the required test to determine its coverage under 32 CFR 199.4(g)(15). Providers and beneficiaries will be advised to retain receipts for the test for submission for reimbursement following the coverage determination.

**F. Ivacaftor (Kalydeco)—QL:** Quantity limits/days supply limits were recommended for Kalydeco.

1. **COMMITTEE ACTION: QL**—The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 1 absent) QLs/days supply limits, restricting the maximum allowable quantity to a 30-day supply at the retail point of service and a 45-day supply at Mail Order.

Director, TMA, Decision:

Approved  Disapproved



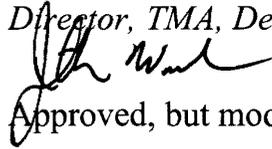
Approved, but modified as follows:

**G. COMMITTEE ACTION: PA IMPLEMENTATION PERIOD FOR XALKORI, ZELBORAF, AND KALYDECO**—The P&T Committee recommended (16 for, 0

opposed, 1 abstain, 1 absent) an effective date of the first Wednesday after a 30-day implementation period in all points of service. The effective date is July 11, 2012.

Director, TMA, Decision:

Approved  Disapproved



Approved, but modified as follows:

## VII. SECTION 703

**A. Section 703**—The P&T Committee reviewed a list of products—Alocril, Avage, Azelex, Betagan, Blephamide, Elestat, Elimate, FML, FML Forte, FML S.O.P., Ocuflen, Ocuflux, Poly-Pred, Poly-Trim, Pred Mild, Pred-G, and Transderm-Scop—to determine MN and PA criteria. These products were identified as not fulfilling refund requirements as required in section 703 of the 2008 National Defense Authorization Act (NDAA). The listed medications were designated NF on the UF at previous P&T Committee meetings.

1. **COMMITTEE ACTION: PA CRITERIA**—The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following should apply to the listed drugs. Coverage at retail network pharmacies would be approved if the patient met all the following criteria:

a) Manual PA criteria:

(1) Use of formulary agent is contraindicated.

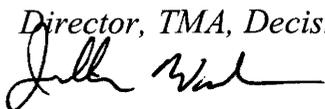
(2) Obtaining the product from home delivery would be detrimental to the patient.

(3) For branded products with AB generic availability, use of the generic product would be detrimental to the patient.

The PA criteria listed above do not apply to any point of service other than retail network pharmacies.

Director, TMA, Decision:

Approved  Disapproved



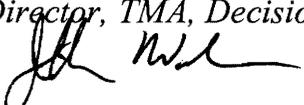
Approved, but modified as follows:

2. **COMMITTEE ACTION: MN CRITERIA**—The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following should apply to the listed drugs:

a) Use of formulary agent is contraindicated.

Director, TMA, Decision:

Approved  Disapproved

  
Approved, but modified as follows:

## VIII. ITEMS FOR INFORMATION

A. The PORT provided the P&T Committee with an update and review of findings on various topics:

- *Comparative costs across pharmacy POS*—Based on an analysis of all non-specialty maintenance medications filled at all three pharmacy POS, the mean cost for a 90-day supply appears to be about 19% lower at MTFs or mail order compared to retail for 4QFY11, adjusting for FY12 co-pay changes. The difference was driven by brand-only medications, which were about 27% lower at MTFs or mail compared to retail; generically available medications were either similar across POS or slightly higher at MTFs/mail order compared to mail order (+2%). This represents a narrowing of the gap between POS; a similar analysis for 4QFY10 showed costs at MTFs/mail order to be about 25% lower overall versus retail, with brand-only and generic medications running about 30% and 15% lower, respectively. Cost differences between MTFs and mail order remained minimal.
- Effective October 1, 2011, co-pays changed from \$3 to \$0 for Tier 1 medications at mail order; \$3 to \$5 for Tier 1 medications at retail; \$9 to \$12 for Tier 2 medications at retail [remaining at \$9 in mail order]; and \$22 to \$25 for Tier 3 medications at both mail order and retail. The PORT reported an increase in mail order utilization during the first four months following the change, most prominently for generic but also occurring for branded medications. The trend continued across all POS towards increased generic use, consistent with recent generic availability for several widely-used medications.

- The PORT also provided a list of the top 100 outpatient medications by DoD expenditures for 1QFY12, which represent about 64% of costs across all POS. Of these, 76 are in classes already reviewed by the P&T Committee at least once. The data facilitated a discussion of potential future drug class reviews.
- The PORT also reported preliminary results from a study of the effect of co-pay differences on medication adherence among DoD beneficiaries, performed in conjunction with the MHS Scientific Advisory Panel. Final results are expected shortly.

## **IX. CLASS OVERVIEWS**

Two drug class overviews were presented to the P&T Committee. The Newer Insomnia Agents Drug Class was last reviewed in February 2007. The Smoking Cessation Drug Class has not previously been reviewed by the P&T Committee. The DoD is currently reviewing a proposed rule to establish a TRICARE smoking cessation program; see Section 713 of the Duncan Hunter NDAA for Fiscal Year 2009. The P&T Committee is responsible for identifying and evaluating pharmaceutical products available through this program, consistent with 32 CFR 199.21(e)(1). The clinical and economic analyses of these classes will be presented at an upcoming meeting.

## **X. ADJOURNMENT**

The meeting adjourned at 1100 hours on February 17, 2012. The next meeting will be in May 2012.

**Appendix A—Attendance: February 2012 P&T Committee Meeting**

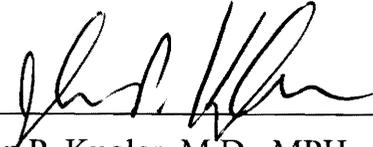
**Appendix B—Prior Authorization Criteria for the Wakefulness-Promoting Drug Class**

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

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

**Appendix E—Table of Abbreviations**

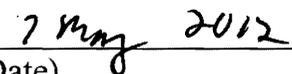
**SUBMITTED BY:**

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

**DECISION ON RECOMMENDATIONS**

Director, TMA, decisions are as annotated above.

  
\_\_\_\_\_  
Jonathan Woodson, M.D.  
Director

  
\_\_\_\_\_  
(Date)

**Appendix A—Attendance: February 2012 P&T Committee Meeting**

<b>Voting Members Present</b>	
John Kugler, COL (Ret.), MC, USA	DoD P&T Committee Chair
CDR Joe Lawrence, 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 Deborah Thompson	Coast Guard, Pharmacy Officer
CDR Traci Hindman, MSC for CAPT Edward Norton, MSC	Navy, Pharmacy Officer (Pharmacy Consultant BUMED)
Col Lowell Sensintaffer, MC	Air Force, Physician at Large
CAPT David Tanen, MC	Navy, Physician at Large
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
COL Doreen Lounsbery, MC	Army, Internal Medicine Physician
COL Ted Cieslak, MC	Army, Physician at Large
LTC Bruce Lovins, MC	Army, Family Practice Physician
CDR Eileen Hoke, MC	Navy, Pediatrics
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Major Jeremy King, MC	Air Force, OB/GYN Physician
Dr. Miguel Montalvo	TRICARE® Regional Office-South Chief of Clinical Operations Division and Medical Director
Mr. Joe Canzolino	U.S. Department of Veterans Affairs
<b>Nonvoting Members Present</b>	
Mr. David Hurt	Associate General Counsel, TMA
CDR Jay Peloquin	Defense Logistics Agency Troop Support
<b>Guests</b>	
Capt Nita Sood via DCO	Pharmacy Operations Directorate
LCDR Charles McKee	Indian Health Service

**Appendix A—Attendance: February 2012 P&T Committee Meeting (continued)**

<b>Guests</b>	
LCDR David Sohl	University of Texas Masters Student
Ms Melanie Richardson via DCO	Pharmacy Operations Directorate
<b>Others Present</b>	
Lt Col Rey Morales, MC	DoD Pharmacoeconomic Center
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
MAJ Misty Cowan, MC	DoD Pharmacoeconomic Center
Lt Col Cynthia Lee, BSC	DoD Pharmacoeconomic Center
LCDR Ola Ojo, MSC	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
Maj David Folmar, BSC	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Angela Allerman	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe	DoD Pharmacoeconomic Center
Dr. Eugene Moore	DoD Pharmacoeconomic Center
Dr. Amy Lugo	DoD Pharmacoeconomic Center
Dr. Libby Hearin	DoD Pharmacoeconomic Center
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Dr. Stephen Yarger	DoD Pharmacy Outcomes Research Team contractor
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor
Dr. Bradley Clarkson	Pharmacy Resident
Capt Danial Oh via DCO	San Antonio Major Medical Command Pharmacy Resident

**Appendix B—Prior Authorization Criteria for the Wakefulness-Promoting Drug Class**

	<b>Modafinil (Provigil)</b>	<b>Armodafinil (Nuvigil)</b>	<b>Sodium Oxybate (Xyrem)</b>
Prior Authorization	<p>Coverage provided for the treatment of:</p> <ul style="list-style-type: none"> <li>▪ Excessive daytime sleepiness associated with narcolepsy, as diagnosed by polysomnogram or MSLT objective testing</li> <li>▪ Excessive daytime sleepiness associated with OSAHS, only after adequate titration of CPAP treatment</li> <li>▪ Excessive sleepiness associated with SWSD, only in patients who work night shifts</li> <li>▪ Excessive fatigue associated with multiple sclerosis, only after secondary causes of fatigue have been addressed</li> <li>▪ Excessive fatigue associated with myotonic dystrophy</li> <li>▪ Depression, only after primary therapy has failed and if the use of other stimulant augmentation is contraindicated</li> <li>▪ Idiopathic hypersomnia diagnosed by a sleep specialist</li> <li>▪ Fatigue associated with traumatic brain injury</li> </ul> <p>Coverage NOT provided for the treatment of other conditions not listed above, including the following:</p> <ul style="list-style-type: none"> <li>▪ Chronic fatigue syndrome</li> <li>▪ Stroke rehabilitation</li> <li>▪ Appetite suppression</li> <li>▪ Parkinson's disease</li> </ul>	<p>Coverage provided for the treatment of:</p> <ul style="list-style-type: none"> <li>▪ Excessive daytime sleepiness associated with narcolepsy, as diagnosed by polysomnogram or MSLT objective testing</li> <li>▪ Excessive daytime sleepiness associated with OSAHS, only after adequate titration of CPAP treatment</li> <li>▪ Excessive sleepiness associated with SWSD, only in patients who work night shifts</li> </ul> <p>Coverage NOT provided for the treatment of other conditions not listed above, including the following:</p> <ul style="list-style-type: none"> <li>▪ Jet lag</li> <li>▪ Excessive fatigue associated with multiple sclerosis</li> <li>▪ Excessive fatigue associated with myotonic dystrophy</li> <li>▪ Depression</li> <li>▪ Idiopathic hypersomnia</li> <li>▪ Fatigue associated with traumatic brain injury</li> <li>▪ Chronic fatigue syndrome</li> <li>▪ Stroke rehabilitation</li> <li>▪ Appetite suppression</li> <li>▪ Parkinson's disease</li> </ul>	<p>Coverage provided for the treatment of:</p> <ul style="list-style-type: none"> <li>▪ Treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy, diagnosed by polysomnogram and MSLT</li> <li>▪ Excessive sleepiness associated with narcolepsy without cataplexy, if the patient has previously tried modafinil (Provigil)</li> </ul> <p>Coverage NOT provided for the treatment of other conditions not listed above or any non-FDA approved use, including the following:</p> <ul style="list-style-type: none"> <li>▪ Fibromyalgia</li> <li>▪ Insomnia</li> <li>▪ Excessive sleepiness not associated with narcolapsy</li> </ul>

CPAP: continuous positive airway pressure  
MSLT: mean sleep latency time

OSAHS: obstructive sleep apnea/hypopnea syndrome  
SWSD: shift work sleep disorder

## Appendix C—Table of Medical Necessity Criteria

Drug / Drug Class	Medical Necessity Criteria
<p>Saxagliptin (Onglyza) Saxagliptin/Metformin ER (Kombiglyze XR)</p> <p><b>Non-insulin Diabetes Drugs: DPP-4 Inhibitors</b></p>	<ul style="list-style-type: none"> <li>• Use of formulary DPP-4 agents contraindicated</li> <li>• The patient has experienced or is likely to experience significant adverse effects from formulary DPP-4 inhibitors</li> </ul>
<p>Dexmethylphenidate ER (Focalin XR) Lisdexamphetamine (Vyvanse) Methylphenidate transdermal (Daytrana)</p> <p><b>ADHD/Wakefulness-Promoting Drugs: Stimulants Subclass</b></p>	<p>No change from previous MN criteria</p> <ul style="list-style-type: none"> <li>• Use of formulary ADHD stimulants is contraindicated</li> <li>• The patient has experienced significant adverse effects from formulary ADHD stimulants</li> <li>• Use of the formulary stimulants has resulted in therapeutic failure</li> <li>• For Daytrana: No alternative formulary agent available—the patient is unable to take oral medications</li> </ul>
<p>Armodafinil (Nuvigil)</p> <p><b>ADHD/Wakefulness-Promoting Drugs: Wakefulness-Promoting Subclass</b></p>	<ul style="list-style-type: none"> <li>• Use of modafinil (Provigil) is contraindicated</li> </ul>

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

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 2012	<b>Antiplatelet Agents</b>	UF Class Review	<ul style="list-style-type: none"> <li>▪ Clopidogrel (Plavix)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Prasugrel (Effient)</li> <li>▪ Ticagrelor (Brilinta)</li> <li>▪ Aspirin/dipyridamole ER (Aggrenox)</li> <li>▪ Ticlopidine (Ticlid, generics)</li> <li>▪ Cilostazol (Pletal, generics)</li> <li>▪ Dipyridamole (Persantine, generics)</li> <li>▪ Pentoxifylline (Trental, generics)</li> </ul>	<ul style="list-style-type: none"> <li>▪ - Not applicable (no drug designated nonformulary)</li> </ul>	Pending signing of minutes/ 60 days	Not applicable	<ul style="list-style-type: none"> <li>▪ Clopidogrel remains BCF</li> </ul>
Feb 2012	<b>Non-Insulin Diabetes Drugs DPP-4 Inhibitors</b>	UF Class Review	<ul style="list-style-type: none"> <li>▪ Sitagliptin (Januvia)</li> <li>▪ Sitagliptin/Metformin (Janumet)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Sitagliptin/Simvastatin (Juvisync)</li> <li>▪ Linagliptin (Tradjenta)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Saxagliptin (Onglyza)</li> <li>▪ Saxagliptin/Metformin ER (Kombiglyze XR)</li> </ul>	Pending 60 days	Step therapy required – see comments	<ul style="list-style-type: none"> <li>▪ Must try metformin and sulfonylurea 1st before any DPP-4 drug</li> <li>▪ Must try sitagliptin-containing product 1st before Onglyza, Kombiglyze XR, and Tradjenta</li> </ul>
Feb 2012	<b>ADHD / Wakefulness-Promoting Drugs Wakefulness-Promoting Drugs</b>	UF Class Review	<ul style="list-style-type: none"> <li>▪ Not applicable</li> </ul>	<ul style="list-style-type: none"> <li>▪ Modafinil (Provigil)</li> <li>▪ Sodium oxybate (Xyrem) – restricted distribution</li> </ul>	<ul style="list-style-type: none"> <li>▪ Armodafinil (Nuvigil)</li> </ul>	Pending 60 days	PA required – see comments	<ul style="list-style-type: none"> <li>▪ All current and new users of Nuvigil must go through PA process</li> </ul>

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 2012	<p align="center"><b>ADHD / Wakefulness-Promoting Drugs</b></p> <p align="center"><b>ADHD Stimulants</b></p>	UF Class Review	<p><b>Long-acting stimulants</b></p> <ul style="list-style-type: none"> <li>▪ Mixed amphetamine salts ER (Adderall XR generics)</li> <li>▪ Methylphenidate LA (Ritalin LA, generic)</li> <li>▪ Methylphenidate OROS (Concerta)</li> </ul> <p><b>Short-acting stimulants</b></p> <ul style="list-style-type: none"> <li>▪ Methylphenidate IR (Ritalin, generic)</li> </ul>	<p><b>Short-acting stimulants</b></p> <ul style="list-style-type: none"> <li>▪ Mixed amphetamine salts IR (Adderall, generic)</li> <li>▪ Dexmethylphenidate IR (Focalin, generic)</li> <li>▪ Dextroamphetamine (Dexedrine, Dextrostat, Procentra solution)</li> <li>▪ Methylphenidate CD (Metadate CD)</li> <li>▪ Methylphenidate ER (Metadate ER, Methylin ER, generic)</li> <li>▪ Methylphenidate chewable tablets, solution (Methylin, generic)</li> <li>▪ Methylphenidate SR (Ritalin SR, generic)</li> <li>▪ Methamphetamine HCl (Desoxyn)</li> </ul>	<p><b>Long-acting stimulants</b></p> <ul style="list-style-type: none"> <li>▪ Dexmethylphenidate ER (Focalin XR)</li> <li>▪ Lisdexamphetamine (Vyvanse)</li> <li>▪ Methylphenidate transdermal system (Daytrana)</li> </ul>	Pending 60 days	Not applicable	<ul style="list-style-type: none"> <li>▪ Ritalin LA now BCF</li> </ul>
Feb 2012	<p align="center"><b>ADHD / Wakefulness-Promoting Drugs</b></p> <p align="center"><b>ADHD Non-Stimulants</b></p>	UF Class Review	<ul style="list-style-type: none"> <li>▪ Not applicable</li> </ul>	<ul style="list-style-type: none"> <li>▪ Atomoxetine (Strattera)</li> <li>▪ Clonidine ER (Kapvay)</li> <li>▪ Guanfacine ER (Intuniv)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Not applicable (no nonformulary drugs)</li> </ul>	Pending 60 days	Not applicable	<ul style="list-style-type: none"> <li>▪ Clonidine IR tabs are BCF</li> <li>▪ Clonidine Patches and guanfacine IR (Tenex, generic are UF) in Misc Anti-hypertensive Drug Class</li> </ul>

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 2012	Ophthalmic-1	New Drug Review	Antihistamine/Mast Cell Stabilizers <ul style="list-style-type: none"> <li>▪ Olopatadine 0.1% (Patanol) (Aug 2010)</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Alcafatinde 0.25% (Lastacraft) (Feb 2012)</b></li> </ul> August 2010 Dual Action Antihistamine/ Mast Cell Stabilizers <ul style="list-style-type: none"> <li>▪ Bepotastine (Bepreve)</li> <li>▪ Olopatadine 0.2% (Pataday)</li> <li>▪ Azelastine (Optivar, generics)</li> <li>▪ Epinastine (Elestat)</li> </ul> Antihistamines <ul style="list-style-type: none"> <li>▪ Emedastine (Emadine)</li> </ul> Mast Cell Stabilizers <ul style="list-style-type: none"> <li>▪ Pemirolast (Alamast)</li> <li>▪ Nedocromil (Alocril)</li> <li>▪ Cromolyn (Crolom/Opticrom, generic)</li> <li>▪ Lodoxamide (Alomide)</li> </ul> NSAIDs <ul style="list-style-type: none"> <li>▪ Ketorolac 0.4% (Acular LS, generic)</li> <li>▪ Ketorolac 0.45% (Acuvail)</li> <li>▪ Ketorolac 0.5% (Acular, generic)</li> <li>▪ Bromfenac (Xibrom)</li> <li>▪ Bromfenac 0.9% (Bromday)</li> <li>▪ Diclofenac (Voltaren, generic)</li> <li>▪ Flurbiprofen (Ocufen, generics)</li> <li>▪ Nepafenac (Nevanac)</li> </ul>	August 2010 <ul style="list-style-type: none"> <li>▪ Not applicable (no drug designated nonformulary)</li> </ul>	Pending signing of minutes/ 60 days	Not applicable	<ul style="list-style-type: none"> <li>▪ Ketotifen (Zaditor, generics) is available OTC</li> </ul>

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 2012	<p align="center"><b>Narcotic Analgesics</b></p> <p align="center"><b>Subclass: High potency single analgesic agents</b></p>	New Drug Review	<p align="center">High potency single analgesic agents</p> <ul style="list-style-type: none"> <li>▪ Morphine sulfate 12 hours ER (MS Contin, generics)</li> <li>▪ Morphine sulfate IR</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Tapentadol extended release (Nucynta ER) (Feb 2012)</b></li> </ul> <p>Previous Decisions</p> <ul style="list-style-type: none"> <li>▪ Hydromorphone ER (Exalgo)</li> <li>▪ Fentanyl buccal soluble film (Onsolis)</li> <li>▪ Fentanyl transdermal system, transmucosal tablet (Fentora); &amp; transmucosal lozenge</li> <li>▪ Hydromorphone (Dilaudid)</li> <li>▪ Levorphanol</li> <li>▪ Meperidine</li> <li>▪ Methadone</li> <li>▪ Morphine products (other than BCF), Kadian and Avinza (ER products)</li> <li>▪ Morphine sulfate ER / naltrexone (Embeda)</li> <li>▪ Opium tincture</li> <li>▪ Opium/belladonna alkaloids(suppositories)</li> <li>▪ Oxycodone IR</li> <li>▪ Oxycodone ER (Oxycontin)</li> <li>▪ Oxymorphone (Opana)</li> <li>▪ Oxymorphone ER (Opana ER)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Tapentadol immediate release (Nucynta) (Nov 2009)</li> </ul>	Pending signing of minutes/ 60 days	Not applicable	—

CD: controlled delivery  
DPP-4: dipeptidyl peptidase-4  
ER: extended release  
LA: long-acting  
SR: sustained release  
OROS: osmotic-controlled release oral delivery system (OROS)

\* TRICARE Formulary Search tool: [http://www.pec.ha.osd.mil/formulary\\_search.php](http://www.pec.ha.osd.mil/formulary_search.php)

## Appendix E—Table of Abbreviations

AC	allergic conjunctivitis
ACS	acute coronary syndrome
AEs	adverse events
ADHD	Attention Deficit Hyperactivity Disorder
ALK	anaplastic lymphoma kinase
BCF	Basic Core Formulary
BIA	budget impact analysis
CABG	coronary artery bypass grafting
CD	controlled delivery
CEA	cost-effectiveness analysis
CF	cystic fibrosis
CFR	Code of Federal Regulations
CFTR	cystic fibrosis transmembrane conductance regulator
CMA	cost minimization analysis
CNS	central nervous system
CV	cardiovascular
DM	diabetes mellitus
DoD	Department of Defense
DERP	Oregon Drug Effectiveness Review Project
DPP-4	dipeptidyl peptidase-4
ER	extended release
FDA	U.S. Food and Drug Administration
GI	gastrointestinal
ICERs	incremental cost-effectiveness ratios
IR	immediate release
LA	long-acting
MHS	Military Health System
MI	myocardial infarction
MN	medical necessity
MTF	Military Treatment Facility
NF	nonformulary
NSCLC	non-small cell lung cancer
OROS	osmotic-controlled release oral delivery system
P&T	Pharmacy and Therapeutics
PA	prior authorization
PAD	peripheral artery disease
PCI	percutaneous coronary intervention
PEC	Pharmacoeconomic Center
PPIs	proton pump inhibitors
PORT	Pharmacy Outcomes Research Team
POS	points of service
QLs	quantity limits
SR	sustained release
SU	sulfonylurea
TZD	thiazolidinedione
TIA	transient ischemic attack
UF	Uniform Formulary
VA	U.S. Department of Veterans Affairs