DECISION PAPER

DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

November 2012

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

A. High Potency Narcotic Analgesics—Oxycodone Immediate Release (IR) (Oxecta)*Relative Clinical Effectiveness Conclusion*—The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Oxecta is the first abuse deterrent IR oxycodone formulation marketed. There is no evidence to suggest oxycodone IR (Oxecta) has a compelling clinical advantage over the other high potency narcotic analgesics included on the Uniform Formulary (UF).

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that oxycodone IR (Oxecta) was not cost-effective when compared to other high potency narcotic analgesics included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) oxycodone IR (Oxecta) be designated nonformulary (NF) due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA***
The P&T Committee recommended (15 for, 1 opposed, 1 abstained, 0 absent) MN criteria for Oxecta: there are no formulary alternatives and the patient requires a tamper resistant formulation of oxycodone IR.

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 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 (POS), and TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is April 17, 2013.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

II. UNIFORM FORMULARY DRUG CLASS REVIEWS

A. Non-Insulin Diabetes Drugs—Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)

Relative Clinical Effectiveness Conclusion—Step therapy implemented in April 2011 requires that new GLP1RA users try metformin or sulfonylurea first, and that new GLP1RA users try exenatide twice daily (BID) (Byetta) before TRICARE® will cover the other agents in this drug subclass. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Exenatide BID injection (Byetta), liraglutide once daily injection (Victoza), and exenatide once weekly injection (Bydureon) all decrease hemoglobin A1c ~ 1%–2% from baseline when used as monotherapy or in combination with other oral agents.
- When compared head-to-head, overall there are no clinically relevant differences between the three GLP1RAs with regard to effect on glycemic control.
- Bydureon offers additional patient convenience given its once weekly dosing regimen and does not require titration compared to Byetta, but is not available in a pre-filled syringe.
- There are no studies evaluating adherence with the three GLP1RAs.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that exenatide BID (Byetta) was the most cost-effective GLP1RA, based on the weighted average cost per day of treatment across all three POS, followed by exenatide once weekly (Bydureon) and liraglutide (Victoza). Results from the cost minimization and budget impact analyses showed scenarios where exenatide BID (Byetta), exenatide once weekly (Bydureon) and liraglutide (Victoza) are all designated UF presented a cost avoidance projection comparable to the current UF scenario where all GLP1RAs are UF. Data was not available to assess the potential pharmacoeconomic impact of longer-acting GLP1RA formulations on medication adherence and health-related outcomes in this cost-effectiveness evaluation.

1. ***COMMITTEE ACTION: UF/BASIC CORE FORMULARY (BCF) RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following:

- Designating exenatide BID (Byetta), liraglutide once daily (Victoza), and exenatide once weekly (Bydureon) as formulary on the UF;
- Excluding Byetta, Victoza, and Bydureon GLP1RAs from the BCF; and,
- Removing the current requirement for a trial of Byetta prior to the other GLP1RAs (removing the subclass step therapy requirement). As a result, there would no longer be a preferred GLP1RA product.

2. ***COMMITTEE ACTION: PRIOR AUTHORIZATION (PA) RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining the current PA requiring a trial of metformin or a sulfonylurea prior to the use of exenatide BID (Byetta), liraglutide once daily (Victoza), or exenatide once weekly (Bydureon). A trial of metformin or a sulfonylurea would not be required for patients with an adverse event, contraindication to, or inadequate response with metformin or sulfonylurea. Use of a GLP1RA product is approved only for patients with type 2 diabetes mellitus. Automated PA criteria (step-therapy) and manual PA criteria remain the same as recommended at the November 2010 P&T Committee meeting, and implemented in April 2011. (See Appendix C for full criteria.)

3. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 30-day implementation period in all POS. Based on the P&T Committee's recommendation, the effective date is March 20, 2013.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

B. Overactive Bladder Drugs (OABs)

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Review of the clinical literature for efficacy, safety, and tolerability data since the last P&T Committee review in 2008 did not add substantial new information.
- Persistence rates within the Military Health System (MHS) remain low at 12% for all the OAB drugs. As needed use of the OAB drugs is 26% in the MHS.

- There are no studies evaluating clinical outcomes, such as reduced fall risk or delayed nursing home placement with the OAB drugs.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 against, 0 abstained, 0 absent) that for preferred formulary placement status, oxybutynin IR (Ditropan, generics) was the least costly agent based on the weighted average cost per day of treatment across all three POS, followed by oxybutynin ER (Ditropan XL, generics), tolterodine ER (Detrol LA), solifenacin (Vesicare), oxybutynin 10% gel (Gelnique), fesoterodine (Toviaz), oxybutynin transdermal delivery system (Oxytrol), trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), darifenacin (Enablex), and tolterodine IR (Detrol, generics).

Results from the cost minimization analysis (CMA) and budget impact analysis (BIA) showed that among available formulary options examined, the scenario where oxybutynin IR, oxybutynin ER, and Detrol LA were designated as step-preferred, with step therapy applied to all current and new users of non-preferred OAB products, was most cost-effective.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following:
    - UF and step-preferred ("in front of the step"): tolterodine extended release (ER) (Detrol LA), oxybutynin IR (Ditropan, generics), and oxybutynin ER (Ditropan XL, generics). Prior authorization would require that all patients try Detrol LA, oxybutynin IR, or oxybutynin ER before TRICARE will cover the other agents in this drug class.
    - UF and non step-preferred ("behind the step"): trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), tolterodine IR (Detrol, generics) and solifenacin (Vesicare)
        - When the generics to Sanctura, Sanctura XR, and Detrol become cost-effective relative to the step-preferred agents, the generics will become step-preferred without further action by the P&T Committee, Beneficiary Advisory Panel, or Director, TMA. A generic agent is cost-effective relative to step-preferred agents when the generic agent's total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the step-preferred agent.
    - NF and non step-preferred: darifenacin (Enablex), fesoterodine (Toviaz), oxybutynin transdermal delivery system (Oxytrol), and oxybutynin 10% gel (Gelnique).

- Step therapy would apply to all users (current and new) of the OAB drugs.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining Detrol LA and oxybutynin ER on the BCF.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) PA criteria for all current and new users of the OAB drugs, requiring a trial of Detrol LA, oxybutynin IR, or oxybutynin ER prior to the use of the other OAB drugs. A trial of the step-preferred OAB drugs would not be required in patients with an adverse event, inadequate response, or contraindication to Detrol LA, oxybutynin ER, or oxybutynin IR. (See Appendix C for full criteria.)

4. ***COMMITTEE ACTION: MN CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Enablex, Toviaz, Oxytrol, and Gelnique 10%. (See Appendix B for full MN criteria.)

5. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is May 15, 2013.

Addendum to the UF recommendation: During a post meeting bid review, it was determined that after-step bids should not be accepted and modeled due to verbiage in the bid solicitation. As a result of this determination, the cost analysis was recalculated. This new cost model was presented to the DoD P&T committee via electronic means. An electronic vote was taken to determine a) whether to accept the new cost review, maintain the current scenario and maintain current UF recommendations, or b) withdraw the UF recommendation, rebid the class and present results at the Feb 2013 meeting.

6. ***COMMITTEE ACTION: ADDENDUM TO UF RECOMMENDATION***
The P&T Committee recommended (9 for, 5 opposed, 0 abstained, 3 absent) to approve the current scenario, which maintains the UF recommendation, step therapy requirements for all new and current users of OAB drugs, and PA criteria.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

C. Gastrointestinal-2 Oral Antibiotic Drugs (GI-2)

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- For hepatic encephalopathy (HE), rifaximin is superior to lactulose in improving symptoms. While rifaximin is approved for monotherapy, it is commonly used in combination with lactulose, and is better tolerated than lactulose.
- For *Clostridium difficile* infection (CDI):
  - Metronidazole is equally effective as vancomycin in treating mild to moderate CDI, but for severe CDI vancomycin results in higher clinical cure rates.
  - Fidaxomicin and vancomycin provide similar clinical cure rates for CDI; however, fidaxomicin decreases recurrence and increases global cure rates to a greater extent than vancomycin.
  - Comparative efficacy for nitazoxanide and rifaximin for CDI cannot be assessed, given the small numbers of trials.
- For travelers' diarrhea (TD), practice guidelines and a systematic review recommend fluoroquinolones (e.g., levofloxacin, ciprofloxacin) as first line treatment. Rifaximin is FDA-approved for TD but is limited to TD caused by noninvasive strains of *Escherichia coli*.
- Rifaximin is not FDA-approved for irritable bowel syndrome (IBS), and there is insufficient evidence to support its use for IBS. Other non-supportable uses of rifaximin include inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non FDA-approved indication.

Relative Cost-Effectiveness Conclusion—Pharmacoeconomic analyses, including CMA, were performed for the GI-2 Drug Class. Cost analyses were based on the disease states discussed in the clinical section. Comparative costs for agents from other drug classes were considered (e.g., lactulose, fluoroquinolones), due to the conclusions from the clinical effectiveness review. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following: for HE, lactulose was the least costly agent, followed by lactulose in combination with neomycin, and then rifaximin (Xifaxan). For CDI, metronidazole was the least costly agent, followed by vancomycin, with

fidaxomicin (Dificid) as the most costly agent. For TD, ciprofloxacin was the least costly agent followed by rifaximin (Xifaxan) and nitazoxanide (Alinia).

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (14 for, 2 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the MHS.
    - UF: metronidazole, vancomycin, neomycin, rifaximin (Xifaxan), nitazoxanide (Alinia), and fidaxomicin (Dificid)
    - Fidaxomicin (Dificid) is available solely in the retail network. Availability of Dificid from mail order is not recommended due to the time constraints for treating acute *C. difficile* infection. Additionally, due to noncompliance with the Trade Agreements Act, Dificid is excluded from mail order and military treatment facilities (MTFs). Efforts to allow availability of Dificid at the MTFs are ongoing at this time.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining metronidazole 250 mg and 500 mg tablets on the BCF.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (15 for, 1 opposed, 1 abstained, 0 absent) PA criteria for rifaximin (Xifaxan) 200 mg for TD. Automated PA criteria would require use of a fluoroquinolone prior to use of rifaximin 200 mg for travelers' diarrhea, unless the patient is under age 18, has a documented allergy to a fluoroquinolone, or is returning from an area with high fluoroquinolone resistance. The P&T Committee also recommended (14 for, 2 opposed, 1 abstained, 0 absent) PA criteria for rifaximin (Xifaxan) 550 mg for hepatic encephalopathy, consistent with the FDA-approved labeling. Other uses of rifaximin are not covered, including *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, and rosacea. (See Appendix C for full criteria.)

4. ***COMMITTEE ACTION: QUANTITY LIMITS (QLs)***—The P&T Committee recommended (15 for, 1 opposed, 1 abstained, 0 absent) QLs for the following GI-2 drugs:
    - Fidaxomicin (Dificid): 20 tablets with no refill in all POS, consistent with the product labeling
    - Rifaximin (Xifaxan) 200 mg: For travelers' diarrhea, if prior authorization is approved, a 3-day supply (9 tablets) in all three POS is

recommended, consistent with the product labeling. For hepatic encephalopathy, if prior authorization is approved, overrides will be allowed.

5. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS. Based in the P&T Committee's recommendation, the effective date is May 15, 2013.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

D. Hepatitis C Drugs*Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Triple therapy with a direct acting antiviral agent (boceprevir or telaprevir), PEG-interferon, and ribavirin increases sustained viral response (SVR) rates to a greater extent than dual therapy with PEG-interferon and ribavirin (PR).
- There is insufficient evidence to conclude whether boceprevir (Victrelis) or telaprevir (Incivek) is superior to the other, due to the lack of direct comparative trials. Telaprevir offers patient convenience due to its shorter treatment course than boceprevir (12 weeks versus 44 weeks), but this has not resulted in higher SVR rates.
- There is insufficient evidence to support a preference of Pegasys over PEG-Intron, but there do not appear to be clinically relevant differences in efficacy.
- Response-guided therapy for clinically appropriate patient populations maintains high levels of efficacy while shortening drug exposure times and treatment course duration.
- Compared with PR dual therapy, boceprevir triple therapy increases the risk for anemia and telaprevir triple therapy increases the risk for anemia and rash.

Relative Cost-Effectiveness Conclusion—CMA results of the direct acting antiviral agents (DAAs) showed response-guided therapy could be less costly with boceprevir than with telaprevir, based on current dosing recommendations. However, when each

agent was taken over its full treatment duration, telaprevir was less costly than boceprevir. The cost-effectiveness analysis concluded that combination use of DAAs plus PEG-interferon alfa and ribavirin was a cost-effective option for the treatment of chronic hepatitis C. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that the most cost-effective scenario placed ribavirin (generics), PEG-interferon alfa-2a (Pegasys), interferon alfa-2b (Intron A), PEG-interferon alfa-2b (PEG-Intron), boceprevir (Victrelis), and telaprevir (Incivek) as formulary on the UF, and ribavirin (Ribapak) and interferon alfacon-1 (Infergen) as NF on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following:
    - UF status for boceprevir (Victrelis), telaprevir (Incivek), PEG-interferon alfa-2a (Pegasys), PEG-interferon alfa-2b (PEG-Intron), interferon alfa-2b (Intron A), and ribavirin (except for the Ribapak formulation); and,
    - NF status for interferon alfacon-1 (Infergen) and the ribavirin Ribapak formulation, due to the lack of compelling clinical advantages and cost disadvantages when compared to the UF products.

2. ***COMMITTEE ACTION: EXTENDED CORE FORMULARY (ECF) RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) designating telaprevir (Incivek), PEG-interferon alfa-2a (Pegasys), and ribavirin 200 mg capsules (generics) as ECF products, based on clinical and cost-effectiveness.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for boceprevir (Victrelis) and telaprevir (Incivek), consistent with the FDA-approved labeling. Prior authorization will expire after 12 weeks for telaprevir and 44 weeks for boceprevir. (See Appendix C for full criteria.)

4. ***COMMITTEE ACTION: QLs***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following QLs:
    - For boceprevir and telaprevir: a 28-day supply per prescription at all three POS, with no multiple fills for multiple co-pays; and,
    - For all the interferon and ribavirin products: a 90-day supply in MTFs and Mail Order, and a 30-day supply in the retail network.

5. ***COMMITTEE ACTION: MN CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for

interferon alfacon-1 (Infergen) and Ribapak. (See Appendix B for full MN criteria.)

6. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is April 17, 2013.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

III. RE-EVALUATION OF NF AGENTS

On an ongoing basis, the DoD Pharmacoeconomic Center monitors changes in the clinical information, current costs, and utilization trends to determine whether the UF status of agents designated as NF needs to be readdressed. The P&T Committee's process for the re-evaluation of NF agents established at the May 2007 meeting was approved by the Director, TMA on June 24, 2007, and is outlined in Appendix E.

The P&T Committee reevaluated the UF status of Lexapro (escitalopram) and pantoprazole (Protonix) in light of recent price reductions in the generic formulations across all three POS.

1. ***COMMITTEE ACTION: ESCITALOPRAM UF RECOMMENDATION AND IMPLEMENTATION***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) reclassification of escitalopram (Lexapro, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

2. ***COMMITTEE ACTION: PANTOPRAZOLE UF RECOMMENDATION AND IMPLEMENTATION***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) reclassification of pantoprazole (Protonix, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

Director, TMA, Decision: ☒ Approved □ Disapproved

Approved, but modified as follows:

IV. UTILIZATION MANAGEMENT

A. PAs

1. **Phosphodiesterase-5 (PDE-5) Inhibitors**—The PA criteria for the PDE-5 Inhibitor Drug Class was reviewed. Prior authorization allows use of a PDE-5 inhibitor following prostatectomy for preservation/restoration of erectile function for one year. There is no published evidence suggesting benefit if the PDE-5 inhibitor is initiated beyond one year after surgery. Recommendations were to clarify the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed.

   The additional recommendations were:

   - For Cialis: that existing criteria that apply to patients with benign prostatic hyperplasia (BPH) also apply to patients with BPH and erectile dysfunction (ED); and,
   - For sildenafil used for primary pulmonary hypertension (PPH): that the sildenafil dosage formulation specifically state 20 mg tablets to discourage use of sildenafil 20 mg tablets for ED.

   a) ***COMMITTEE ACTION: PDE-5 INHIBITOR PA CRITERIA***
   The P&T Committee recommended (14 for, 1 opposed, 2 abstained, 0 absent) PA criteria for the PDE-5 inhibitors (1) clarifying the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed; (2) for Cialis, that the existing criteria also apply to patients with BPH and ED; and, (3) for sildenafil for PPH, that the sildenafil dosage formulation will specifically state 20 mg tablets. (See Appendix C for full criteria.)

2. **Testosterone Replacement Therapy (TRT)**—PA criteria for the TRT Drug Class were developed at the August 2012 meeting and signed by the Director, TMA on November 8, 2012. The P&T Committee reviewed the PA criteria for use of TRT in women, which was based on level A evidence from the American College of Obstetrics and Gynecology, as outlined in a 2011 Clinical Bulletin. The Clinical Bulletin specifically mentions that

there is little evidence to support long-term TRT use (longer than 6 months) in women.

a) ***COMMITTEE ACTION: TRT USE IN WOMEN PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the PA criteria for use of TRT in women to limit use to six months. (See Appendix C for full criteria.)

3. **Injectable Gonadotropins**—PA criteria currently apply to the injectable gonadotropins (fertility agents). Injectable gonadotropins are not covered under the TRICARE pharmacy benefit if they are being used in conjunction with a noncoital reproductive technology. In 2010, the Assistant Secretary of Defense for Health Affairs (ASD(HA)) authorized in vitro fertilization services for the benefit of severely or seriously ill/injured active duty service members. Implementation guidance for these services was developed in an April 2012 ASD(HA) policy.

a) ***COMMITTEE ACTION: INJECTABLE GONADOTROPINS PA CRITERIA***—The P&T Committee recommended (15 for, 0 opposed, 2 abstained, 0 absent) revising the PA criteria for the injectable gonadotropins (fertility agents), to allow for use in conjunction with a noncoital reproductive technology, as outlined in the ASD(HA) April 2012 "Policy for Assisted Reproductive Services for the Benefit of Seriously or Severely Ill/Injured (Category II or III) Active Duty Service Members." A Signed Authorization Memorandum from TMA must be included with the prescription. (See Appendix C for full criteria.)

4. **Adalimumab (Humira)**—The FDA recently approved a new indication for Humira, the designated ECF agent in the targeted immunomodulatory biologics (TIBs) Drug Class. Humira is now indicated for the treatment of moderately to severely active ulcerative colitis following inadequate response to immunosuppressants such as corticosteroids, azathioprine, and 6-mercaptopurine.

a) ***COMMITTEE ACTION: ADALIMUMAB (HUMIRA) PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the existing PA criteria for Humira to incorporate the new indication for ulcerative colitis, consistent with the FDA-approved product labeling. (See Appendix C for full criteria.)

5. **Enzalutamide (Xtandi) and Abiratone (Zytiga)**—Two new drugs for metastatic castration-resistant prostate cancer were recently approved. Xtandi and Zytiga are costly agents with specific FDA-indications, requiring use of prior docetaxel-containing regimens.

    a) ***COMMITTEE ACTION: ENZALUTAMIDE (XTANDI) AND ABIRATONE (ZYTIGA) PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for enzalutamide (Xtandi), and abiratone (Zytiga), consistent with the FDA-approved product labeling. (See Appendix C for full criteria.)

B. QLs

1. **Ipratropium/albuterol (Combivent Respimat)**—Ipratropium/albuterol (Combivent Respimat) oral inhaler is a non chlorofluorocarbon-containing reformulation of ipratropium and albuterol. The current chlorofluorocarbon (CFC) formulation, Combivent, will be phased out and replaced by Combivent Respimat. Combivent supplies are to be exhausted by December 31, 2013. The entire chronic obstructive pulmonary disease drug class will be reviewed formally for UF placement, including the BCF, at an upcoming meeting. Quantity limits currently apply to all oral inhalers.

    a) ***COMMITTEE ACTION: IPRATROPIUM/ALBUTEROL (COMBIVENT RESPIMAT) QL***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) QLs for Combivent Respimat, restricting the maximum allowable quantity at the retail point of service to 2 inhalers in 30 days and 5 inhalers in 90 days at Mail Order and MTFs, consistent with recommended dosing. (See Appendix D.)

2. **Azelastine/fluticasone propionate (Dymista), adalimumab (Humira), enzalutamide (Xtandi), and abiratone (Zytiga)**—The P&T Committee evaluated QLs for several other drugs, including azelastine/fluticasone propionate nasal inhaler (Dymista) (Nasal Allergy Drug Class), Humira for the new indication ulcerative colitis (TIBs Drug Class), and Xtandi and Zytiga (oral chemotherapy drugs for prostate cancer).

    a) ***COMMITTEE ACTION: DYMISTA, HUMIRA, XTANDI, AND ZYTIGA QL***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) QLs for Dymista, Humira for ulcerative colitis, Xtandi, and Zytiga, as outlined in Appendix D, consistent with FDA-approved product labeling.

Director, TMA, Decision: ☒ Approved □ Disapproved

Approved, but modified as follows:

V. SECTION 703

A. Section 703—The P&T Committee reviewed Kaon (branded potassium gluconate) and Pamine (branded methscopolamine) to determine MN and pre-authorization criteria. These two products were identified as not fulfilling refund requirements required in section 703 of the 2008 National Defense Authorization Act. These drugs were designated NF on the UF at previous P&T Committee meetings.

1. ***COMMITTEE ACTION: PRE-AUTHORIZATION CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following should apply to Kaon and Pamine. Coverage at retail network pharmacies would be approved if the patient met all of the following criteria:

   a) Manual Pre-Authorization Criteria:

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

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

   b) Implementation will occur upon signing of the minutes.

   The pre-authorization 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:

VI. OVERVIEWS

Two drug class overviews were presented to the P&T Committee, the oral anticoagulants (vitamin K antagonists, direct thrombin inhibitors, Factor Xa inhibitors), and the drugs for chronic obstructive pulmonary disease (COPD). Neither drug class has previously been reviewed for UF status. The clinical and economic analyses of these classes will be presented at an upcoming meeting.

VII. ITEMS FOR INFORMATION

A. Joint Forces Pharmacy Seminar (JFPS) Presentation—The P&T Committee was briefed on spends and trends in MHS drug utilization, which was presented at the JFPS in October.

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

Feb 13, 2013
Date

DEPARTMENT OF DEFENSE

PHARMACY AND THERAPEUTICS COMMITTEE MINUTES AND RECOMMENDATIONS

November 2012

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on November 14 and 15, 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 August Minutes**—Jonathon Woodson M.D., Director, approved the minutes for the August 2012 DoD P&T Committee meeting on November 8, 2012.
2. **Correction to the May 2012 Minutes**—The May minutes were corrected to state the quantity limits for the smoking cessation products, nicotine gum and nicotine lozenge, are limited to 600 pieces per 60-day claim, rounded to the nearest multiple of the package size (e.g., boxes of 75 or 100). The QL recommendations are contingent on publication of the Final Rule.

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 199.21(e)(1). All Uniform Formulary (UF) and Basic Core Formulary (BCF) recommendations considered the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors. Medical necessity (MN) criteria were based on the clinical and cost evaluations, and the conditions for establishing MN for a nonformulary (NF) medication.

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

A. High Potency Narcotic Analgesics—Oxycodone Immediate Release (IR) (Oxecta)

Relative Clinical Effectiveness—Oxecta is a formulation of oxycodone IR that is tamper resistant but not tamper proof. FDA approval was based on demonstrated bioequivalence to the Roxycodone proprietary formulation of oxycodone IR. One small

"drug liking" study showed a reduced "liking" for Oxecta versus Roxycodone, but the widespread clinical applicability of these results is unknown.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Oxecta is the first abuse deterrent IR oxycodone formulation marketed. There is no evidence to suggest oxycodone IR (Oxecta) has a compelling clinical advantage over the other high potency narcotic analgesics included on the UF.

Relative Cost-Effectiveness Analysis and Conclusion—A pharmacoeconomic analysis was performed. The weighted average cost per tablet at all three points of service (POS) was evaluated for oxycodone IR (Oxecta) in relation to the other drugs in the high potency narcotic subclass. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Oxecta was not cost-effective when compared to other high potency narcotics included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) oxycodone IR (Oxecta) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: MN CRITERIA***—The P&T Committee recommended (15 for, 1 opposed, 1 abstained, 0 absent) MN criteria for Oxecta. (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 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 (POS), and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is April 17, 2013.

V. UF DRUG CLASS REVIEWS

A. Non-Insulin Diabetes Drugs—Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)

Background and Relative Clinical Effectiveness—The GLP1RAs are a subclass of the Non-Insulin Diabetes Drug Class, which is comprised of exenatide twice daily (BID) injection (Byetta), liraglutide once daily injection (Victoza), and exenatide once weekly injection (Bydureon). Bydureon is the newest entrant to the class.

The GLP1RA class was previously reviewed for UF placement in November 2010.

Step therapy implemented in April 2011 requires a trial of metformin or a sulfonylurea prior to use of a GLP1RA. An additional step therapy/prior authorization (PA) requirement has been in effect for the GLP1RAs subclass since April 2011, requiring that new GLP1RA users try exenatide BID (Byetta) before TRICARE® will cover the other agents in this drug subclass. The Pharmacy Outcomes Research Team (PORT) provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

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

- Metformin is the most cost-effective agent and remains the first line treatment in all patients with type 2 diabetes mellitus, unless contraindications exist, due to positive outcomes data from the United Kingdom Prospective Diabetes Study.
- When used as monotherapy or in combination with other oral agents, GLP1RAs decrease hemoglobin A1c approximately 1%–2% from baseline. When compared head-to-head, overall there are no clinically relevant differences between the three GLP1RAs with regard to effect on glycemic control.
- Bydureon and Victoza have a greater effect than Byetta on fasting blood glucose due to a longer duration of action. Byetta has a greater effect on post-prandial glucose than the other two GLP1RAs.
- Gastrointestinal issues are the most common adverse effect with the GLP1RAs. Bydureon has a lower incidence of nausea (14.4%) compared to Victoza (20.7%) or Byetta (34.7%). Injection site reactions are more common with Bydureon (17.1%) than Byetta (12.7%), insulin glargine (1.8%), or placebo (6.4%–13%).
- Bydureon offers additional patient convenience given its once weekly dosing regimen and does not require titration compared to Byetta, but is not available in a pre-filled syringe.
- There are no studies evaluating adherence with the three GLP1RAs.
- There are no published trials that assess long-term outcomes; however, the LEADER and EXSCEL studies evaluating long-term cardiovascular safety are currently ongoing.

Relative Cost-Effectiveness Analysis and Conclusion—Pharmacoeconomic analyses were performed for the GLP1RA subclass, including cost minimization analysis (CMA) and budget impact analysis (BIA). For the BIAs, several of the model's key

assumptions were varied, with corresponding sensitivity analyses conducted. Methods used for CMA and BIAs were based on current step therapy requiring a trial of metformin or a sulfonylurea prior to a patient receiving a GLP1RA.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that exenatide BID (Byetta) was the most cost-effective GLP1RA, based on the weighted average cost per day of treatment across all three POS, followed by exenatide once weekly (Bydureon) and liraglutide (Victoza) (ranked in order from most to least cost-effective). Results from the CMA and BIA showed scenarios where exenatide BID (Byetta), exenatide once weekly (Bydureon), and liraglutide (Victoza) are all designated UF presented a cost avoidance projection comparable (i.e., within a margin of error) to the current UF scenario where all GLP1RAs are UF. Data was not available to assess the potential pharmacoeconomic impact of longer-acting GLP1RA formulations on medication adherence and health-related outcomes in this cost-effectiveness evaluation.

1. ***COMMITTEE ACTION: UF/BCF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following:

    - Designating exenatide BID (Byetta), liraglutide once daily (Victoza), and exenatide once weekly (Bydureon) as formulary on the UF;
    - Excluding Byetta, Victoza, and Bydureon GLP1RAs from the BCF; and,
    - Removing the current requirement for a trial of Byetta prior to the other GLP1RAs (removing the subclass step therapy requirement). As a result, there would no longer be a preferred GLP1RA product.

2. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining the current PA requiring a trial of metformin or a sulfonylurea prior to the use of exenatide BID (Byetta), liraglutide once daily (Victoza), or exenatide once weekly (Bydureon). A trial of metformin or a sulfonylurea would not be required for patients with an adverse event, contraindication to, or inadequate response with metformin or sulfonylurea. Use of a GLP1RA product is approved only for patients with type 2 diabetes mellitus. Automated PA criteria (step-therapy) and manual PA criteria remain the same as recommended at the November 2010 P&T Committee meeting, and implemented in April 2011. (See Appendix C for full criteria.)

3. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 30-day

implementation period in all POS. Based on the P&T Committee's recommendation, the effective date is March 20, 2013.

B. Overactive Bladder Drugs (OABs)

Background and Relative Clinical Effectiveness—The Overactive Bladder (OAB) Drug Class is comprised of darifenacin (Enablex), fesoterodine (Toviaz), oxybutynin IR (Ditropan, generics), oxybutynin extended release (ER) (Ditropan XL, generics), oxybutynin transdermal delivery system (TDS) (Oxytrol), oxybutynin 10% gel (Gelnique), solifenacin (Vesicare), tolterodine IR (Detrol, generics), tolterodine ER (Detrol LA), trospium IR (Sanctura, generics), and trospium ER (Sanctura XR, generics). Generic formulations of Detrol IR, Sanctura IR and Sanctura XR recently entered the market. The OAB drug class has been previously reviewed for UF placement in August 2008, and May and November 2009.

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

- Review of the clinical literature for efficacy, safety, and tolerability data since the last P&T Committee review in 2008 did not add substantial new information.
- The OAB agents are statistically superior to placebo, but the placebo response rates are high for the class, ranging from 30% to 50%.
- There is insufficient evidence to suggest whether one OAB drug is superior to another. Small studies of low quality evidence reported fesoterodine (Toviaz) was statistically superior to tolterodine, and solifenacin (Vesicare) was statistically superior to tolterodine, but the clinical effect is small, relating to a reduction in urge episodes/incontinent episodes of approximately one episode/day.
- No OAB agent has a superior safety profile. Oxybutynin TDS (Oxytrol) causes less dry mouth than tolterodine ER, but has higher withdrawal rates. There is scant safety data for the oxybutynin 10% gel (Gelnique) formulation, but the effects are likely to be similar to oxybutynin TDS with regards to dry mouth.
- Overall, adverse drug effects are lower with the ER formulations than IR formulations. The newer agents do not have significantly lower incidence of dry mouth or constipation than the older OAB drugs.
- Persistence rates within the MHS remain low at 12% for all the OAB drugs. As needed use of the OAB drugs is 26% in the MHS.
- There are no studies evaluating clinical outcomes, such as reduced fall risk or delayed nursing home placement with the OAB drugs.
- There is a high degree of therapeutic interchangeability within the class.

Relative Cost-Effectiveness Analysis and Conclusion—Pharmacoeconomic analyses were performed for the OABs, including CMA and BIA. For the BIAs, several of the model's key assumptions were varied, with corresponding sensitivity analyses conducted. The P&T Committee concluded (17 for, 0 against, 0 abstained, 0 absent) that for preferred formulary placement status, oxybutynin IR (Ditropan, generics) was the least costly agent based on the weighted average cost per day of treatment across all three POS, followed by oxybutynin ER (Ditropan XL, generics), tolterodine ER (Detrol LA), solifenacin (Vesicare), oxybutynin 10% gel (Gelnique), fesoterodine (Toviaz), oxybutynin TDS (Oxytrol), trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), darifenacin (Enablex), and tolterodine IR (Detrol, generics).

BIA results were presented to the P&T Committee and indicated that step therapy scenarios were more cost-effective compared to the current baseline (non step therapy). The MHS projected budgetary impact varied depending on which medication was selected for step-preferred status. CMA and BIA results showed that among available formulary options examined, the scenario where oxybutynin IR, oxybutynin ER, and Detrol LA were designated as step-preferred, with step therapy applied to all current and new users of non-preferred OAB products, was most cost-effective.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following:

    - UF and step-preferred ("in front of the step"): tolterodine ER (Detrol LA), oxybutynin IR (Ditropan, generics), and oxybutynin ER (Ditropan XL, generics). Prior authorization would require that all patients try Detrol LA, oxybutynin IR, or oxybutynin ER before TRICARE will cover the other agents in this drug class.
    - UF and non step-preferred ("behind the step"): trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), tolterodine IR (Detrol, generics) and solifenacin (Vesicare)
        - When the generics to Sanctura, Sanctura XR, and Detrol become cost-effective relative to the step-preferred agents, the generics will become step-preferred without further action by the P&T Committee, Beneficiary Advisory Panel, or Director, TMA. A generic agent is cost-effective relative to step-preferred agents when the generic agent's total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the step-preferred agent.
    - NF and non step-preferred: darifenacin (Enablex), fesoterodine (Toviaz), oxybutynin TDS (Oxytrol), and oxybutynin 10% gel (Gelnique).

- Step therapy would apply to all users (current and new) of the OAB drugs.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining Detrol LA and oxybutynin ER on the BCF.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) PA criteria for all current and new users of the OAB drugs, requiring a trial of Detrol LA, oxybutynin IR, or oxybutynin ER prior to the use of the other OAB drugs. (See Appendix C for full criteria.)

4. ***COMMITTEE ACTION: MN CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Enablex, Toviaz, Oxytrol, and Gelnique 10%. (See Appendix B for full MN criteria.)

5. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is May 15, 2013.

   Addendum to the UF recommendation: During a post meeting bid review, it was determined that after-step bids should not be accepted and modeled due to verbiage in the bid solicitation. As a result of this determination, the cost analysis was recalculated. This new cost model was presented to the DoD P&T committee via electronic means. An electronic vote was taken to determine a) whether to accept the new cost review, maintain the current scenario and maintain current UF recommendations, or b) withdraw the UF recommendation, rebid the class and present results at the Feb 2013 meeting.

6. ***COMMITTEE ACTION: ADDENDUM TO UF RECOMMENDATION***
   The P&T Committee recommended (9 for, 5 opposed, 0 abstained, 3 absent) to approve the current scenario, which maintains the UF recommendation, step therapy requirements for all new and current users of OAB drugs, and PA criteria.

C. Gastrointestinal-2 Oral Antibiotic Drugs (GI-2)

Background and Relative Clinical Effectiveness—The Gastrointestinal-2 Oral Antibiotics (GI-2) Drug Class includes metronidazole (Flagyl, generics), vancomycin (Vancocin, generics), rifaximin (Xifaxan), fidaxomicin (Dificid), nitazoxanide (Alinia) and neomycin (Neo-Fradin, generics). This review focused on clinical effectiveness with regard to hepatic encephalopathy, *Clostridium difficile* infection, travelers' diarrhea, and non FDA-approved (off-label) uses. The class has not been previously reviewed for UF placement. The PORT provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following concerning the GI-2 Drug Class:

- **Hepatic Encephalopathy (HE)**
  - Practice guidelines recommend lactulose as first line therapy for treatment of HE.
  - A Cochrane analysis found antibiotics, including rifaximin, were superior to lactulose in improving HE symptoms.
  - While rifaximin is approved for monotherapy, it is commonly used in combination with lactulose, and is better tolerated than lactulose.
- ***Clostridium difficile* Infection (CDI)**
  - Metronidazole is equally effective as vancomycin in treating mild to moderate CDI, but for severe CDI vancomycin results in higher clinical cure rates.
  - Fidaxomicin and vancomycin provide similar clinical cure rates for CDI; however, fidaxomicin decreases recurrence and increases global cure rates to a greater extent than vancomycin.
  - Comparative efficacy for nitazoxanide and rifaximin for CDI cannot be assessed, given the small numbers of trials.
- **Travelers' Diarrhea (TD)**
  - Practice guidelines recommend fluoroquinolones (e.g., levofloxacin, ciprofloxacin) as first line treatment for TD, unless contraindications exist.
  - A systematic review found ciprofloxacin more effective than rifaximin for prevention of TD.
  - Rifaximin's labeled indication is limited to treatment of TD caused by noninvasive strains of *Escherichia coli*. It is not effective for TD caused by Campylobacter, Shigella, and Salmonella species.
- **Off-label Uses**

- Rifaximin has been evaluated for irritable bowel syndrome (IBS) but is not approved by the FDA for IBS. In two studies, rifaximin showed modest (9%–12%) improvements in response rates compared to placebo; however, there was a significant placebo effect.
- Unanswered questions regarding use of rifaximin for IBS include the durability of response, efficacy for retreatment, prevention of recurrence, *C. difficile* emergence, bacterial resistance, and long-term side effects.
- Nonsupportable uses for rifaximin include CDI, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non FDA-approved indication.

Relative Cost-Effectiveness Analysis and Conclusion—Pharmacoeconomic analyses, including CMA, were performed for the GI-2 Drug Class. Cost analyses were based on the disease states discussed in the clinical section. Comparative costs for agents from other drug classes were considered (e.g., lactulose, fluoroquinolones), due to the conclusions from the clinical effectiveness review. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following: for HE, lactulose was the least costly agent, followed by lactulose in combination with neomycin, and then rifaximin (Xifaxan). For CDI, metronidazole was the least costly agent, followed by vancomycin, with fidaxomicin (Dificid) as the most costly agent. For TD, ciprofloxacin was the least costly agent followed by rifaximin (Xifaxan) and nitazoxanide (Alinia).

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (14 for, 2 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the MHS.
    - UF: metronidazole, vancomycin, neomycin, rifaximin (Xifaxan), nitazoxanide (Alinia), and fidaxomicin (Dificid)
    - Fidaxomicin (Dificid) is available solely in the retail network. Availability of Dificid from mail order is not recommended due to the time constraints for treating acute *C. difficile* infection. Additionally, due to noncompliance with the Trade Agreements Act, Dificid is excluded from mail order and military treatment facilities (MTFs). Efforts to allow availability of Dificid at the MTFs is ongoing at this time.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining metronidazole 250 mg and 500 mg tablets on the BCF.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (15 for, 1 opposed, 1 abstained, 0 absent) PA criteria for rifaximin (Xifaxan) 200 mg for TD. Automated PA criteria would require use of a fluoroquinolone prior to use of rifaximin 200 mg for travelers' diarrhea, unless the patient is under age 18, has a documented allergy to a fluoroquinolone, or is returning from an area with high fluoroquinolone resistance. The P&T Committee also recommended (14 for, 2 opposed, 1 abstained, 0 absent) PA criteria for rifaximin (Xifaxan) 550 mg for hepatic encephalopathy, consistent with the FDA-approved labeling. Other uses of rifaximin are not covered, including *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, and rosacea. (See Appendix C for full criteria.)

4. ***COMMITTEE ACTION: QUANTITY LIMITS (QLs)***—The P&T Committee recommended (15 for, 1 opposed, 1 abstained, 0 absent) QLs for the following GI-2 drugs:

    - Fidaxomicin (Dificid): 20 tablets with no refill in all POS, consistent with the product labeling
    - Rifaximin (Xifaxan) 200 mg: For travelers' diarrhea, if prior authorization is approved, a 3-day supply (9 tablets) in all three POS is recommended, consistent with the product labeling. For hepatic encephalopathy, if prior authorization is approved, overrides will be allowed.

5. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS. Based in the P&T Committee's recommendation, the effective date is May 15, 2013.

D. Hepatitis C Drugs

Background and Relative Clinical Effectiveness—The Hepatitis C Drug Class includes the direct acting antiviral agents (DAAs) boceprevir (Victrelis) and telaprevir (Incivek); the interferon products PEG-interferon alfa-2a (Pegasys), PEG-interferon alfa-2b (PEG-Intron), and interferon alfacon-1(Infergen); and, various ribavirin products, including generics. Interferon alfa-2b (Intron A) is no longer used for treating hepatitis C virus infection and will not be discussed further. The PORT provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

Relative Clinical Effectiveness Conclusion—The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 0 absent) on the following:

- Triple therapy with a direct acting antiviral agent (boceprevir or telaprevir), PEG-interferon, and ribavirin increases sustained viral response (SVR) rates to a greater extent than dual therapy with PEG-interferon and ribavirin (PR).
- There is insufficient evidence to conclude whether boceprevir (Victrelis) or telaprevir (Incivek) is superior to the other, due to the lack of direct comparative trials. Telaprevir offers patient convenience due to its shorter treatment course than boceprevir (12 weeks versus 44 weeks), but this has not resulted in higher SVR rates.
- There is insufficient evidence to support a preference of Pegasys over PEG-Intron, but there do not appear to be clinically relevant differences in efficacy.
- Interferon alfacon-1 (Infergen) has poor efficacy and is not included in current clinical practice guidelines. It no longer holds a niche in the treatment of prior null responders.
- Ribavirin is ineffective as monotherapy, but is critical to prevent relapse of hepatitis C virus infection.
- Compared with PR dual therapy, boceprevir triple therapy increases the risk for anemia and telaprevir triple therapy increases the risk for anemia and rash.
- Response-guided therapy for clinically appropriate patient populations maintains high levels of efficacy while shortening drug exposure times and treatment course duration.
- Overall drug discontinuations due to adverse events ranged from 8%–14% with telaprevir triple therapy versus 3% with PR dual therapy, and was 13% with boceprevir triple therapy versus 12% with PR dual therapy.
- With boceprevir, unique adverse events include dysgeusia, neutropenia, and psychiatric events, compared to anorectal adverse events (hemorrhoids, burning, itching) with telaprevir.

Relative Cost-Effectiveness Analysis and Conclusion—CMA was performed to compare each regimen for hepatitis C treatment (ribavirin, PEG-interferons, and DAAs). A cost-effectiveness analysis (CEA) was also performed comparing triple therapy (DAAs, PEG-interferon, and ribavirin) with dual therapy (PEG-interferon alfa and ribavirin). Additionally, a BIA was performed to compare competing formulary scenarios.

CMA results for the evaluated agents showed most dosage forms of ribavirin were generic and cost-effective. However, Ribapak was deemed not cost-effective compared with other ribavirin dosage forms. Both PEG-interferon alfa products (Pegasys and

PEG-Intron) had comparable costs. Interferon alfacon-1 (Infergen) was identified as not cost-effective when compared with the PEG-interferon agents. CMA results for the DAAs showed response-guided therapy could be less costly with boceprevir than with telaprevir, based on current dosing recommendations. However, when each agent was taken over its full treatment duration, telaprevir was less costly than boceprevir.

While insufficient evidence existed to establish a meaningful clinical difference in efficacy between the DAAs, the clinical effectiveness evaluation demonstrated that DAAs plus PEG-interferon alfa and ribavirin were more effective in combination than PEG-interferon alfa and ribavirin alone in inducing a SVR. The CEA concluded that combination use of DAAs plus PEG-interferon alfa and ribavirin was a cost-effective option for the treatment of genotype 1 chronic hepatitis C in adults with compensated liver disease who were previously untreated or for whom previous treatment had failed.

The BIA results suggested that designating ribavirin (Ribapak) and interferon alfacon-1 (Infergen) as NF on the UF was the most favorable scenario for the MHS.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that the most cost-effective scenario placed ribavirin (generics), PEG-interferon alfa-2a (Pegasys), interferon alfa-2b (Intron A), PEG-interferon alfa-2b (Peg-Intron), boceprevir (Victrelis), and telaprevir (Incivek) as formulary on the UF, and ribavirin (Ribapak) and interferon alfacon-1 (Infergen) as NF on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following:
    - UF status for boceprevir (Victrelis), telaprevir (Incivek), PEG-interferon alfa-2a (Pegasys), PEG-interferon alfa-2b (PEG Intron), interferon alfa-2b (Intron A), and ribavirin (except for the Ribapak formulation); and,
    - NF status for interferon alfacon-1 (Infergen) and the ribavirin Ribapak formulation, due to the lack of compelling clinical advantages and cost disadvantages when compared to the UF products.

2. ***COMMITTEE ACTION: EXTENDED CORE FORMULARY (ECF) RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) designating telaprevir (Incivek), PEG-interferon alfa-2a (Pegasys), and ribavirin 200 mg capsules (generics) as ECF products, based on clinical and cost-effectiveness.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for boceprevir (Victrelis) and telaprevir (Incivek), consistent with the FDA-approved labeling. Prior

authorization will expire after 12 weeks for telaprevir and 44 weeks for boceprevir. (See Appendix C for full criteria.)

4. ***COMMITTEE ACTION: QUANTITY LIMITS (QLs)***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following QLs:

   - For boceprevir and telaprevir: a 28-day supply per prescription at all three POS, with no multiple fills for multiple co-pays; and,
   - For all the interferon and ribavirin products: a 90-day supply in MTFs and Mail Order, and a 30-day supply in the retail network.

5. ***COMMITTEE ACTION: MN CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for interferon alfacon-1 (Infergen) and Ribapak. (See Appendix B for full MN criteria.)

6. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is April, 17, 2013.

VI. RE-EVALUATION OF NF AGENTS

On an ongoing basis, the DoD PEC monitors changes in the clinical information, current costs, and utilization trends to determine whether the UF status of agents designated as NF needs to be readdressed. The P&T Committee's process for the re-evaluation of NF agents established at the May 2007 meeting was approved by the Director, TMA on June 24, 2007, and is outlined in Appendix E.

The P&T Committee reevaluated the UF status of Lexapro (escitalopram) and pantoprazole (Protonix) in light of recent price reductions in the generic formulations across all three POS.

1. ***COMMITTEE ACTION: ESCITALOPRAM UF RECOMMENDATION AND IMPLEMENTATION***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) reclassification of escitalopram (Lexapro, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

2. ***COMMITTEE ACTION: PANTOPRAZOLE UF RECOMMENDATION AND IMPLEMENTATION***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) reclassification of pantoprazole (Protonix, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

VII. UTILIZATION MANAGEMENT

A. PAs

1. **Phosphodiesterase-5 (PDE-5) Inhibitors**—The PA criteria for the PDE-5 Inhibitor Drug Class was reviewed. Prior authorization allows use of a PDE-5 inhibitor following prostatectomy for preservation/restoration of erectile function for one year. There is no published evidence suggesting benefit if the PDE-5 inhibitor is initiated beyond one year after surgery. Recommendations were to clarify the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed.

   The additional recommendations were:

   - For Cialis: that existing criteria that apply to patients with benign prostatic hyperplasia (BPH) also apply to patients with BPH and erectile dysfunction (ED); and,
   - For sildenafil used for primary pulmonary hypertension (PPH): that the sildenafil dosage formulation specifically state 20 mg tablets to discourage use of sildenafil 20 mg tablets for ED.

   a) ***COMMITTEE ACTION: PDE-5 INHIBITOR PA CRITERIA***
   The P&T Committee recommended (14 for, 1 opposed, 2 abstained, 0 absent) PA criteria for the PDE-5 inhibitors (1) clarifying the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed; (2) for Cialis, that the existing criteria also apply to patients with BPH and ED; and, (3) for sildenafil for PPH, that the sildenafil dosage formulation will specifically state 20 mg tablets. (See Appendix C for full criteria.)

2. **Testosterone Replacement Therapy (TRT)**—PA criteria for the TRT Drug Class were developed at the August 2012 meeting and signed by the Director, TMA on November 8, 2012. The P&T Committee reviewed the PA criteria for use of TRT in women, which was based on level A evidence from the American College of Obstetrics and Gynecology, as outlined in a

2011 Clinical Bulletin. The Clinical Bulletin specifically mentions that there is little evidence to support long-term TRT use (longer than 6 months) in women.

a) ***COMMITTEE ACTION: TRT USE IN WOMEN PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the PA criteria for use of TRT in women to limit use to six months. (See Appendix C for full criteria.)

3. **Injectable Gonadotropins**—PA criteria currently apply to the injectable gonadotropins (fertility agents). Injectable gonadotropins are not covered under the TRICARE pharmacy benefit if they are being used in conjunction with a noncoital reproductive technology. In 2010, the Assistant Secretary of Defense for Health Affairs (ASD(HA)) authorized in vitro fertilization services for the benefit of severely or seriously ill/injured active duty service members. Implementation guidance for these services was developed in an April 2012 ASD(HA) policy.

   a) ***COMMITTEE ACTION: INJECTABLE GONADOTROPINS PA CRITERIA***—The P&T Committee recommended (15 for, 0 opposed, 2 abstained, 0 absent) revising the PA criteria for the injectable gonadotropins (fertility agents), to allow for use in conjunction with a noncoital reproductive technology, as outlined in the ASD(HA) April 2012 "Policy for Assisted Reproductive Services for the Benefit of Seriously or Severely Ill/Injured (Category II or III) Active Duty Service Members." A Signed Authorization Memorandum from TMA must be included with the prescription. (See Appendix C for full criteria.)

4. **Adalimumab (Humira)**—The FDA recently approved a new indication for Humira, the designated ECF agent in the targeted immunomodulatory biologics (TIBs) Drug Class. Humira is now indicated for the treatment of moderately to severely active ulcerative colitis following inadequate response to immunosuppressants such as corticosteroids, azathioprine, and 6-mercaptopurine.

   a) ***COMMITTEE ACTION: ADALIMUMAB (HUMIRA) PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the existing PA criteria for Humira to

incorporate the new indication for ulcerative colitis, consistent with the FDA-approved product labeling. (See Appendix C for full criteria.)

5. **Enzalutamide (Xtandi) and Abiratone (Zytiga)**—Two new drugs for metastatic castration-resistant prostate cancer were recently approved. Xtandi and Zytiga are costly agents with specific FDA-indications, requiring use of prior docetaxel-containing regimens.

    a) ***COMMITTEE ACTION: ENZALUTAMIDE (XTANDI) AND ABIRATONE (ZYTIGA) PA CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for enzalutamide (Xtandi), and abiratone (Zytiga), consistent with the FDA-approved product labeling. (See Appendix C for full criteria.)

B. QLs

1. **Ipratropium/albuterol (Combivent Respimat)**—Ipratropium/albuterol (Combivent Respimat) oral inhaler is a non chlorofluorocarbon-containing reformulation of ipratropium and albuterol. The current chlorofluorocarbon (CFC) formulation, Combivent, will be phased out and replaced by Combivent Respimat. Combivent supplies are to be exhausted by December 31, 2013. The entire chronic obstructive pulmonary disease drug class will be reviewed formally for UF placement, including the BCF, at an upcoming meeting. Quantity limits currently apply to all oral inhalers.

    a) ***COMMITTEE ACTION: IPRATROPIUM/ALBUTEROL (COMBIVENT RESPIMAT) QL***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) QLs for Combivent Respimat, restricting the maximum allowable quantity at the retail point of service to 2 inhalers in 30 days and 5 inhalers in 90 days at Mail Order and MTFs, consistent with recommended dosing. (See Appendix D.)

2. **Azelastine/fluticasone propionate (Dymista), adalimumab (Humira), enzalutamide (Xtandi), and abiratone (Zytiga)**—The P&T Committee evaluated QLs for several other drugs, including azelastine/fluticasone propionate nasal inhaler (Dymista) (Nasal Allergy Drug Class), Humira for the new indication ulcerative colitis (TIBs Drug Class), and Xtandi and Zytiga (oral chemotherapy drugs for prostate cancer).

    a) ***COMMITTEE ACTION: DYMISTA, HUMIRA, XTANDI, AND ZYTIGA QL***—The P&T Committee recommended (16 for, 0 opposed, 1

abstained, 0 absent) QLs for Dymista, Humira for ulcerative colitis, Xtandi, and Zytiga, as outlined in Appendix D, consistent with FDA-approved product labeling.

VIII. SECTION 703

A. Section 703—The P&T Committee reviewed Kaon (branded potassium gluconate) and Pamine (branded methscopolamine) to determine MN and pre-authorization criteria. These two products were identified as not fulfilling refund requirements required in section 703 of the 2008 National Defense Authorization Act. These drugs were designated NF on the UF at previous P&T Committee meetings.

1. ***COMMITTEE ACTION: PRE-AUTHORIZATION CRITERIA***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following should apply to Kaon and Pamine. Coverage at retail network pharmacies would be approved if the patient met all of the following criteria:

   a) Manual Pre-Authorization Criteria:

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

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

   b) Implementation will occur upon signing of the minutes.

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

VIII. OVERVIEWS

Two drug class overviews were presented to the P&T Committee, the oral anticoagulants (vitamin K antagonists, direct thrombin inhibitors, Factor Xa inhibitors), and the drugs for chronic obstructive pulmonary disease (COPD). Neither drug class has previously been reviewed for UF status. The clinical and economic analyses of these classes will be presented at an upcoming meeting.

IX. ITEMS FOR INFORMATION

A. Joint Forces Pharmacy Seminar (JFPS) Presentation—The P&T Committee was briefed on spends and trends in MHS drug utilization, which was presented at the JFPS in October.

VIII. ADJOURNMENT

The meeting adjourned at 1130 hours on November 15, 2012. The next meeting will be in February 2013.

Appendix A—Attendance: November 2012 P&T Committee Meeting

Appendix B—Table of Medical Necessity Criteria

Appendix C—Table of Prior Authorization Criteria

Appendix D—Table of Quantity Limits

Appendix E—Criteria for Re-evaluation of Nonformulary Drugs for Uniform Formulary Status

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

Appendix G—Table of Abbreviations

Appendix A—Attendance: November 2012 P&T Committee Meeting

Voting Members Present	
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 Octavio C. Mont, MS for COL John Spain, MS	Army, Pharmacy Officer
Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CDR Aaron Middlekauf for CAPT Deborah Thompson, USCG	Coast Guard, Pharmacy Officer
CAPT Edward Norton, MSC	Navy, Pharmacy Officer (Pharmacy Consultant BUMED)
Col Lowell Sensintaffer, MC	Air Force, Physician at Large
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
COL Doreen Lounsbery, MC	Army, Internal Medicine Physician
CAPT David Tanen, MC	Navy, Physician at Large
COL Bruce Lovins, MC	Army, Family Practice Physician
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Maj Jeremy King, MC	Air Force, OB/GYN Physician
CDR Eileen Hoke, MC	Navy, Pediatrics
Dr. Miguel Montalvo	TRICARE Regional Office-South Chief of Clinical Operations Division and Medical Director
Mr. Joe Canzolino	U.S. Department of Veterans Affairs
Nonvoting Members Present	
Mr. David Hurt	Associate General Counsel, TMA
Maj Dan Castiglia, USAF	Defense Logistics Agency Troop Support

Appendix A—Attendance (continued)

Guests	
Mr. Bill Davies via DCO	TRICARE Management Activity, Pharmaceutical Operations Directorate
CDR Matthew Baker, USPHS	Indian Health Service
Adela Lucero	The MITRE Corporation
Isaac Armstrong	The MITRE Corporation
Lionel Levine	The MITRE Corporation
Others Present	
LTC Chris Conrad, MS	DoD Pharmacoeconomic Center
LCDR Marisol Martinez, USPHS	DoD Pharmacoeconomic Center
LCDR Joshua Devine, USPHS	DoD Pharmacoeconomic Center
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
Lt Col Melinda Henne, MC	DoD Pharmacoeconomic Center
LCDR Ola Ojo, MSC	DoD Pharmacoeconomic Center
LCDR Linh Quach, MSC	DoD Pharmacoeconomic Center
Maj David Folmar, BSC	DoD Pharmacoeconomic Center
MAJ Misty Cowan, MC	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Angela Allerman	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Amy Lugo	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe via DCO	DoD Pharmacoeconomic Center
Dr. Eugene Moore	DoD Pharmacoeconomic Center
Dr. Jeremy Briggs	DoD Pharmacoeconomic Center
Dr. Dean Valibhai	DoD Pharmacoeconomic Center
Dr. Brian Beck	DoD Pharmacoeconomic Center
LT Kendra Jenkins, USPHS	Pharmacy Resident
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Mr. Kirk Stocker	DoD Pharmacy Outcomes Research Team contractor

Appendix B—Table of Medical Necessity Criteria

Drug / Drug Class	Medical Necessity Criteria
• Oxycodone IR (Oxecta) **High Potency Narcotic Analgesics**	• No formulary alternative: the patient requires a tamper resistant formulation of oxycodone IR
• Darifenacin (Enablex) • Fesoterodine (Toviaz) **Overactive Bladder (OAB) Drugs**	• Patient has experienced significant adverse effects from ALL of the formulary OAB medications (Detrol, oxybutynin IR/ER, Detrol IR, Sanctura IR/XR) that are not expected to occur with Enablex or Toviaz.
• Oxybutynin transdermal delivery system (Oxytrol) • Oxybutynin 10% gel (Gelnique) **Overactive Bladder (OAB) Drugs**	• Use of formulary agents is contraindicated. • Patient has experienced significant adverse effects from ALL of the formulary OAB medications that are not expected to occur with Oxytrol or Gelnique 10% (e.g., patient has experienced central nervous system adverse effects with the OAB drugs, but is expected to tolerate Oxytrol or Gelnique 10%). • There is no formulary alternative (e.g., patient requires an OAB drug and is unable to take oral medications).
• Interferon alfacon-1 (Infergen) **Hepatitis C Drugs**	• Use of ALL formulary PEG-interferon alfa-2 products is contraindicated (e.g., due to hypersensitivity), and treatment with Interferon alfacon-1 is not contraindicated. • The formulary agents have resulted in therapeutic failure.
• Ribavirin (Ribapak) **Hepatitis C Drugs**	• Use of ALL formulary ribavirin products is contraindicated (e.g., due to hypersensitivity), and treatment with Ribapak is not contraindicated.

Appendix C—Table of Prior Authorization (PA) Criteria

Drug / Drug Class	Prior Authorization Criteria
• exenatide twice daily (Byetta) • exenatide once weekly (Bydureon) • liraglutide once daily (Victoza) **Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)**	New GLP1RA users are required to try metformin or a sulfonylurea (SU) before receiving Byetta, Bydureon, or Victoza. Automated PA criteria: The patient has received a prescription for metformin or SU at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND Manual PA criteria, if automated criteria are not met: Byetta, Bydureon, or Victoza is approved (e.g., trial of metformin or SU is NOT required) if: 1) The patient has a confirmed diagnosis of Type 2 Diabetes Mellitus 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. 5) The patient has had an inadequate response to metformin and a SU.
• boceprevir (Victrelis) • telaprevir (Incivek) **Hepatitis C Drugs**	New users of boceprevir or telaprevir are required to undergo the PA process. Manual PA Criteria: • Age ≥ 18 • Has laboratory evidence of chronic hepatitis C—a quantified viral load (above undetectable) • Has laboratory evidence of genotype-1 hepatitis C infection • Is not co-infected with the human immunodeficiency virus (HIV) or Hepatitis B virus • Boceprevir or telaprevir will be co-administered with both a PEG-interferon alfa-2a or PEG-interferon alfa-2b product AND ribavirin • The patient has not previously used boceprevir or telaprevir. • For boceprevir, the patient will begin with a 4-week lead-in of both a PEG-Interferon alfa-2a or PEG-interferon alfa-2b product and ribavirin. Prior authorization will expire after 12 weeks for telaprevir and 44 weeks for boceprevir.

Appendix C—Table of PA Criteria (continued)

Drug / Drug Class	Prior Authorization Criteria
• tolterodine IR (Detrol, generics) • trospium IR (Sanctura, generics) • trospium ER (Sanctura XR, generics) • darifenacin (Enablex) • fesoterodine (Toviaz) • oxybutynin transdermal delivery system (Oxytrol) • oxybutynin 10% gel (Gelnique) • solifenacin (Vesicare) **Overactive Bladder (OAB) Drugs**	All new and current OAB drug users are required to try Detrol LA, oxybutynin ER, or oxybutynin IR before receiving Enablex, Toviaz, Detrol, Sanctura, Sanctura XR, Oxytrol, Gelnique 10%, or Vesicare. Automated PA criteria: The patient has received a prescription for Detrol LA, oxybutynin IR or oxybutynin ER at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND Manual PA criteria, if automated criteria are not met (e.g., a trial of Detrol LA, oxybutynin IR, or oxybutynin ER is not required) if: 1) The patient has experienced any of the following issues while receiving Detrol LA, oxybutynin IR, or oxybutynin ER, which is not expected to occur with Detrol IR, Sanctura, Sanctura XR, Vesicare, Enablex, Toviaz, Oxytrol, or Gelnique 10%: – inadequate response; – intolerable adverse effects (e.g., the patient requires Sanctura due to intolerable dry mouth with Detrol LA); or, – contraindication. Coverage is only approved for the following FDA-approved indications: 1) The patient has a confirmed diagnosis of OAB with symptoms of urge incontinence, urgency, and urinary frequency (for all 11 OAB drugs). 2) The patient is older than 6 years with symptoms of detrusor overactivity associated with a neurological condition (e.g., spina bifida), for oxybutynin ER. Other uses, including stress incontinence, will not be approved.

Appendix C—Table of PA Criteria (continued)

Drug / Drug Class	Prior Authorization Criteria
• Rifaximin (Xifaxan) 200 mg **Gastrointestinal-2 Oral Antibiotics (GI-2)**	New users of Xifaxan 200 mg for travelers' diarrhea are required to undergo the PA process. Automated PA Criteria: The patient has received a prescription for a fluoroquinolone at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 60 days, AND Manual PA Criteria: • 200 mg tablets are approved for the following: – Documented use in travelers' diarrhea caused by noninvasive strains of *Escherichia coli* – Patient is between 12 and 18 years of age – Documented trial of a fluoroquinolone for patients > 18 years of age – Documented contraindication or allergy to fluoroquinolone antibiotics in last 60 days – Returning from area with high fluoroquinolone resistance – 200 mg tablets are being used to treat hepatic encephalopathy • 200 mg tablets are not approved for the following: – Diarrhea complicated by fever or bloody stool – Treatment of dysentery – Diarrhea associated with use of antibiotics – Diarrhea caused by bacteria other than *E. coli* – *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved use If prior authorization is approved for travelers' diarrhea, the quantity is limited to a 3-day supply (200mg TID = 9 tablets) at all 3 points of service.
• Rifaximin (Xifaxan) 550 mg **Gastrointestinal-2 Oral Antibiotics (GI-2)**	New users of Xifaxan 550 mg for hepatic encephalopathy are required to undergo the PA process. Manual PA Criteria: • 550 mg tablets are approved for the following: – Documented use in hepatic encephalopathy • 550 mg tablets are not approved for the following: – Travelers' diarrhea, *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved use Prior authorization will expire after 365 days.

Appendix C—Table of PA Criteria (continued)

Drug / Drug Class	Prior Authorization Criteria
• sildenaril (Viagra) • tadalafil (Cialis) • vardenaril (Levitra; Staxyn) **Phosphodiesterase-5 (PDE-5) Inhibitors**	**Post-Prostatectomy:** Coverage IS provided for: • Sildenafil (Viagra), vardenafil (Levitra), or tadalafil (Cialis) for preservation and/or restoration of erectile function post-prostatectomy **Prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed.** ***(recommended at Nov 2012 meeting)*** **BPH or BPH with ED:** Coverage IS provided for: • Tadalafil 5 mg (Cialis 5mg) for patients with benign prostatic hyperplasia (BPH) or **BPH with erectile dysfunction (ED)** meeting prior authorization criteria requiring use of an alpha blocker, unless there is a contraindication, inadequate response, or intolerable adverse effects with the alpha blocker. ***(recommended at Nov 2012 meeting)*** **Primary Pulmonary Hypertension:** Coverage IS provided for: • Sildenafil **20 mg** (Revatio) or tadalafil (Adcirca) for any patient with primary pulmonary hypertension ***(recommended at Nov 2012 meeting)***
• transdermal 2% gel pump (Fortesta) • transdermal solution (Axiron) • transdermal patch (Androderm) • transdermal 1.62% gel pump (Androgel 1.62%) • transdermal 1% gel pump and gel packets (Androgel 1%) • transdermal gel tubes (Testim) • testosterone buccal tablets (Striant) **Testosterone Replacement Therapy (TRT)**	PA criteria required for all topical/buccal TRT products • Men: diagnosis of hypogonadism evidenced by 2 or more AM testosterone levels in presence of symptoms • Children – under age of 17 – not approved – appeal only • Women: – Treatment of hypoactive sexual desire in menopausal women (natural or surgical) – Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone) – **Treatment limited to 6 months** ***(recommended at Nov 2012 meeting)*** – TRT not approved for osteoporosis or urinary incontinence – Coverage for women upon appeal
• Enzalutamide (Xtandi) **Oral Chemotherapy Drugs for Prostate Cancer**	Coverage approved for treatment of patients: ▪ With a documented diagnosis of metastatic castration-resistant prostate cancer, AND ▪ Previous treatment with docetaxel
• Abiratone (Zytiga) **Oral Chemotherapy Drugs for Prostate Cancer**	Coverage approved for treatment of patients: ▪ With a documented diagnosis of metastatic castration-resistant prostate cancer, AND ▪ Prior chemotherapy with docetaxel, AND ▪ Patient is receiving concomitant therapy with prednisone

Appendix C—Table of PA Criteria (continued)

Drug / Drug Class	Prior Authorization Criteria
• follitropin alfa (Gonal-F) • follitropin beta (Follistim, Follistim AQ) • menotropins (Humegon, Pergonal, Repronex) • urofollitropin (Fertinex, Bravelle) **Injectable Gonadotropins (Fertility Agents)**	These drugs are not covered under the TRICARE pharmacy benefit if they are being prescribed for use in conjunction with a noncoital reproductive technology, including but not limited to artificial insemination, in vitro fertilization, or gamete intrafallopian transfer The TRICARE family planning benefit outlined in the Code of Federal Regulations does not include services and supplies related to noncoital reproductive technologies. • **Coverage for fertility drugs is allowed for use in conjunction with a noncoital reproductive technology, as outlined in the April 2012 ASD (Health Affairs) "Policy for Assisted Reproductive Services for the Benefit of Seriously or Severally Ill/Injured (Category II or III) Active Duty Service Members." A Signed Authorization Memorandum from TMA must be included with the prescription *(recommended at Nov 2012 meeting).***
• Adalimumab (Humira) **Targeted Immunomodulatory Biologics (TIBs)**	Coverage approved for patients ≥ 18 years with: ▪ Moderate to severely active rheumatoid arthritis and psoriasis, active psoriatic arthritis, and active ankylosing spondylitis ▪ Moderate to severely active polyarticular juvenile idiopathic arthritis (pediatric patients: 4 to 17 years of age) ▪ Moderate to severely active Crohn's disease following an inadequate response to conventional therapy, loss of response to infliximab or an inability to tolerate infliximab ▪ **Moderately to severely active ulcerative colitis following inadequate response to immunosuppressants (e.g., corticosteroids, azathioprine and 6-mercaptopurine) *(recommended at Nov 2012 meeting)*** Coverage NOT approved for: ▪ Concomitant use with other TIBs (anakinra, abatacept, certolizumab pegol, etanercept, infliximab, and golimumab)

Appendix D—Table of Quantity Limits

Drug / Drug Class	Quantity Limits
• fidaxomicin (Dificid) **Gastrointestinal-2 Oral Antibiotics (GI-2)**	• Retail, Mail Order, and MTF: 20 tablets with no refills
• rifaximin (Xifaxan) 200 mg tablets **Gastrointestinal-2 Oral Antibiotics (GI-2)**	If Prior Authorization is approved: • Retail, Mail Order and MTF: 3-day supply (9 tablets) for travelers' diarrhea; overrides allowed for hepatic encephalopathy
• boceprevir (Victrelis) • telaprevir (Incivek) **Hepatitis C Agents**	• Retail, Mail Order, and MTF: 28-day supply, with no multiple fills for multiple co-pays
• ribavirin (all products, including generics, Copegus, Rebetol, Ribasphere, Ribapak) • Interferon alfa-2b (Intron A) • Interferon alfacon-1 (Infergen) • PEG-interferon alfa-2a (Pegasys) • PEG-interferon alfa-2b (PEG-Intron) **Hepatitis C Agents**	• Retail Network: 30-day supply • Mail Order and MTF: 90-day supply
• ipratropium/albuterol oral inhaler (Combivent Respimat) **Chronic Obstructive Pulmonary Disease (COPD) Drugs**	• Retail: 2 inhalers/30 days • Mail Order and MTF: 5 inhalers/90 days
• azelastine/fluticasone propionate nasal inhaler (Dymista) **Nasal Allergy Drugs**	• Retail: 1 inhalers/30 days • Mail Order and MTF: 3 inhalers/90 days
• adalimumab (Humira) **Targeted Immunomodulatory Biologics (TIBs)**	Ulcerative Colitis • Initiation of therapy: o Retail, Mail Order, and MTF: 6 syringes • Maximum quantity dispensed at any one time: o Retail: 4-week supply (2 packs of 2 syringes) o Mail order and MTF: 6-week supply (3 packs of 2 syringes)
• enzalutamide (Xtandi) **Oral Chemotherapy Drugs for Prostate Cancer**	• Retail: 30-day supply (120 capsules) • Mail Order and MTF: 45-day supply (180 capsules)
• abiratone (Zytiga) **Oral Chemotherapy Drugs for Prostate Cancer**	• Retail: 30-day supply (120 tablets) • Mail Order and MTF: 45-day supply (180 tablets)

Appendix E—Criteria for Re-evaluation of Nonformulary Drugs for Uniform Formulary Status

The P&T Committee's process for the re-evaluation of nonformulary (NF) agents established at the May 2007 meeting was approved by the Director, TMA on June 24, 2007, according to the criteria below:

1) The NF agent becomes generically available and
   a) The generic product is "A-rated" as therapeutically equivalent to the brand name product according to the FDA's classification system.
   b) The generic market supply is stable and sufficient to meet the DoD Military Health System supply demands.
2) The NF agent is cost-effective relative to similar agents on the Uniform Formulary (UF). A NF agent becomes cost-effective when:
   a) The NF agent's total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the UF class to which they were compared.
   b) The NF agent's total weighted average cost based on an alternate measure used during the previous review is less than or equal to that for the UF class to which they were compared. For example, antibiotics may be compared on the cost per course of therapy used to treat a particular condition.

Appendix F—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
Nov 2012	**Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)**	UF Class Review	None	▪ exenatide BID injection (Byetta) ▪ exenatide once weekly injection (Bydureon) ▪ liraglutide once daily injection (Victoza)	N/A	Pending signing of the minutes/ 30 days	PA apply	▪ Current requirement for trial of metformin or a sulfonylurea prior to a GLP1RA still applies. ▪ Byetta is no longer the preferred GLP1RA (the previous step therapy requiring use of Byetta prior to another GLP1RA has been removed).
Nov 2012	**Overactive Bladder Drugs (OABs)**	UF Class Review	▪ Tolterodine ER (Detrol LA)* ▪ Oxybutynin ER (Ditropan XL, generics)* *step-preferred	▪ oxybutynin IR (Ditropan, generics)* ▪ solifenacin (Vesicare) ▪ trospium IR (Sanctura, generics) ▪ trospium ER (Sanctura ER, generics) ▪ tolterodine IR (Detrol IR, generics) *step-preferred	▪ fesoterodine (Toviaz) ▪ darifenacin (Enablex) ▪ oxybutynin transdermal delivery system (Oxytrol) ▪ oxybutynin 10% gel (Gelnique)	Pending signing of the minutes/ 90 days	Step therapy (Automated PA); requires trial of Detrol LA, oxybutynin IR, or oxybutynin ER (step-preferred drugs) prior to another OAB drug.	▪ When generic formulations of trospium IR (Sanctura), trospium ER (Sanctura ER), and tolterodine IR (Detrol) become cost-effective relative to the step-preferred drugs, they will become step-preferred.

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 2012	**Gastrointestinal-2 Oral Antibiotics (GI-2s)**	UF Class Review	▪ metronidazole 250 mg & 500 mg tabs (Flagyl, generics)	▪ fidaxomicin (Dificid)* ▪ metronidazole 375 mg, 750 mg ER tabs (Flagyl, Flagyl ER, generics) ▪ neomycin (Neo-Fradin, generics) ▪ nitazoxanide (Alinia) ▪ rifaximin (Xifaxan) ▪ vancomycin 125 mg, 250 mg oral tabs (Vancocin, generics) *Dificid not available at Mail or MTFs	N/A	Pending signing of the minutes/ 90 days	▪ PA recommendation for rifaximin, limiting use to hepatic encephalopathy (365 days) & traveler's diarrhea (3 days) (See Appendix C) ▪ QLs recommendation for fidaxomicin and rifaximin	▪ QLs for fidaxomicin #20 tabs with no refill ▪ QLs for rifaximin 200 mg #9 tabs with no refills ▪ fidaxomicin (Dificid) not available at Mail Order or MTFs
Nov 2012	**Hepatitis C Drugs**	UF Class Review	Extended Core Formulary (ECF)*: ▪ telaprevir (Incivek) ▪ PEG-interferon alfa-2a (Pegasys) ▪ ribavirin 200 mg capsules (generics); excludes Ribapak formulation	▪ boceprevir (Victrelis) ▪ interferon alfa-2b (Intron A) ▪ PEG-interferon alfa-2b (PEG-Intron) ▪ ribavirin (Copegus, Rebetol, Ribasphere)	▪ interferon alfacon-1 (Infergen) ▪ ribavirin Ribapak formulation	Pending signing of the minutes/60 days	▪ PA recommendation for boceprevir and telaprevir (See Appendix C) ▪ QL recommendation for boceprevir, telaprevir, interferon products, and ribavirin	▪ QLs for boceprevir & telaprevir: 28-day supply at all 3 POS; no multiple fills for multiple co-pays ▪ QL recommendation for interferon products and ribavirin: 90-day supply in MTFs and Mail Order; 30-day supply at retail

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 2012	**Narcotic Analgesics** **Subclass: High potency Single Analgesic Agents**	New Drugs in Already Reviewed Class	High potency single analgesic agents ▪ Morphine sulfate 12 hours ER (MS Contin, generics) ▪ Morphine sulfate IR	Previous Decisions ▪ Hydromorphone ER (Exalgo) ▪ Fentanyl buccal soluble film (Onsolis) ▪ Fentanyl transdermal system, transmucosal tablet (Fentora); and, transmucosal lozenge ▪ 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) ▪ Oxymorphone ER (Opana ER) ▪ Tapentadol extended release (Nucynta ER) (Feb 2012)	**oxycodone IR (Oxecta)** Tapentadol immediate release (Nucynta) (Nov 2009)	Pending signing of the minutes/ 60 days	-	-

* **Extended Core Formulary (ECF):** includes medications in therapeutic classes that are used to support more specialized scopes of practice than those on the BCF. MTFs may choose whether or not to include an ECF therapeutic class on formulary, based on the clinical needs of its patients. However, if an MTF chooses to have an ECF therapeutic class on formulary, it must have all ECF medications in that class on formulary.

TRICARE Formulary Search tool: http://www.pec.ha.osd.mil/formulary_search.php

Appendix G—Table of Abbreviations

ASD(HA)	Assistant Secretary of Defense for Health Affairs
BCF	Basic Core Formulary
BIA	budget impact analysis
BID	twice daily
BPH	benign prostatic hyperplasia
CEA	cost-effectiveness analysis
CFC	chlorofluorocarbon
CDI	*Clostridium difficile* infection
CMA	cost minimization analysis
COPD	chronic obstructive pulmonary disease
DAAs	direct acting antiviral agent
DoD	Department of Defense
E. coli	*Escherichia coli*
ECF	Extended Core Formulary
ED	erectile dysfunction
ER	extended release
FDA	U.S. Food and Drug Administration
GI-2	Gastrointestinal-2 Oral Antibiotics Drug Class
GLP1RAs	glucagon-like peptide-1 receptor agonists
HE	hepatic encephalopathy
IBS	irritable bowel syndrome
IR	immediate release
MHS	Military Health System
MN	medical necessity
MTF	Military Treatment Facility
NF	nonformulary
OAB	Overactive Bladder Drug Class
P&T	Pharmacy and Therapeutics
PA	prior authorization
PDE-5	phosphodiesterase-5
PEC	Pharmacoeconomic Center
PORT	Pharmacy Outcomes Research Team
POS	points of service
PPH	primary pulmonary hypertension
PR	PEG-interferon with ribavirin
QLs	quantity limits
SVR	sustained viral response
TIBs	targeted immunomodulatory biologics
TD	travelers' diarrhea
TDS	transdermal delivery system
TRTs	transdermal and buccal testosterone replacement therapies
UF	Uniform Formulary

DECISION PAPER

DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

August 2012

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

A. Targeted Immunomodulatory Biologics (TIBs)—Abatacept Subcutaneous (SC) Injection (Orencia SC)

Relative Clinical Effectiveness Conclusion—The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that although abatacept SC (Orencia SC) provides an alternative to the tumor necrosis factor (TNF) alpha inhibitors used for treatment of rheumatoid arthritis and offers patient convenience over the abatacept intravenous formulation, there is currently insufficient data to conclude that Orencia SC offers improved efficacy, safety, or tolerability compared to the TNF alpha inhibitors in the TIBs class.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that abatacept SC (Orencia SC) was not cost-effective when compared to other TIBs included on the Uniform Formulary (UF).

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) abatacept SC (Orencia SC) be designated nonformulary (NF) due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA***
Based on the clinical evaluations for abatacept SC (Orencia SC) and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for abatacept SC (Orencia SC). (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 9, 2013.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

B. Glaucoma Drugs: Prostaglandin Analogs—Tafluprost Ophthalmic Solution (Zioptan)

Relative Clinical Effectiveness Conclusion—The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 0 absent) that tafluprost (Zioptan) offers no compelling clinical advantages over the other prostaglandins available on the UF.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that tafluprost (Zioptan) was not cost-effective when compared to the other ophthalmic prostaglandins currently included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) tafluprost (Zioptan) be designated NF because it has no compelling clinical advantages over the other ophthalmic prostaglandin analogues and is not cost-effective compared to latanoprost, the most utilized drug in the Military Health System (MHS).

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for tafluprost (Zioptan) and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for tafluprost (Zioptan). (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 9, 2013.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

C. Oral Non-steroidal Anti-inflammatory Drugs (NSAIDs)—Ibuprofen/Famotidine (Duexis)

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) ibuprofen/famotidine (Duexis) offers no distinct clinical advantages to the combination NSAID/gastroprotective agents already on the UF.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that ibuprofen/famotidine (Duexis) was not cost-effective when compared to other oral NSAIDs agents included on the UF; it was also more costly than the individual components, ibuprofen and famotidine.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) ibuprofen/famotidine (Duexis) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for ibuprofen/famotidine (Duexis) and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for ibuprofen/famotidine (Duexis). (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 9, 2013

Director, TMA, Decision: ☒Approved ☐ Disapproved

Approved, but modified as follows:

D. Oral NSAIDs—Ketorolac Nasal Spray (Sprix)

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) there is no evidence to suggest ketorolac nasal spray

(Sprix) has a compelling clinical advantage over the other oral NSAIDs already on the Basic Core Formulary (BCF) and UF.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that ketorolac nasal spray (Sprix) was more costly, based on an average weighted cost per day of therapy at all three points of service (POS), than the other oral NSAIDs and low-potency narcotic analgesics currently on the BCF and UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee, recommended (16 for, 0 opposed, 1 abstained, 0 absent) ketorolac nasal spray (Sprix) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for ketorolac nasal spray (Sprix) and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for ketorolac nasal spray (Sprix). (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: QUANTITY LIMITS***—The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 0 absent) restricting the maximum allowable quantity to 5 nasal spray bottles/30 days in the mail order pharmacy and retail network, which is consistent with the recommended dosing from the package labeling.

4. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 9, 2013.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

E. Non-Insulin Diabetes Drugs: Dipeptidyl Dipeptidase-4 (DPP-4) Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/ Metformin (Jentadueto)

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) there is no evidence to suggest either sitagliptin/ metformin ER (Janumet XR) or linagliptin/metformin (Jentadueto) have a compelling clinical advantage over the other DPP-4 inhibitor/metformin fixed-dose combinations included on the UF.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that Janumet XR and Jentadueto were cost-effective when compared to other DPP-4 inhibitors included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee, recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following:

    - sitagliptin/metformin ER (Janumet XR) be designated step-preferred and formulary on the UF; and
    - linagliptin/metformin (Jentadueto) be designated non-preferred and formulary on the UF.
    - This recommendation includes step therapy, which requires a trial of sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/ simvastatin (Juvisync), or sitagliptin/metformin ER (Janumet XR) (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors also requires a trial of metformin or sulfonylurea for new patients.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee, recommended (14 for, 1 opposed, 1 abstained, 1 absent) sitagliptin/metformin ER (Janumet XR) be designated with BCF status.

3. ***COMMITTEE ACTION: PRIOR AUTHORIZATION (PA) CRITERIA***
The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 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 filled a prescription for metformin or a sulfonylurea at any MHS pharmacy POS [Military Treatment Facilities (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, Janumet XR, Tradjenta, Jentadueto, Onglyza, or Kombiglyze XR) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

The fixed-dose combination product Janumet XR or Jentadueto is approved (eg, a trial of sulfonylurea is not required if):

(1) The patient has had an inadequate response to metformin or sulfonylurea.

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

(3) The patient has a contraindication to a sulfonylurea.

c) In addition to the above criteria regarding metformin and sulfonylurea, the following PA criteria would apply specifically to linagliptin/metformin metformin (Jentadueto):

(1) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with linagliptin-containing products.

(2) The patient has had an inadequate response to a sitagliptin-containing product.

(3) The patient has a contraindication to sitagliptin.

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENATION PERIOD***
The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS. Based on the P&T Committee's recommendation, the effective date is January 9, 2013.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

II. UNIFORM FORMULARY DRUG CLASS REVIEWS

A. Anticoagulants—Heparin and Related Products

Relative Clinical Effectiveness Conclusion—The P&T Committee agreed (15 for, 0 opposed, 0 abstained, 2 absent) on the following clinical effectiveness conclusions:

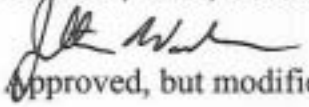
- Enoxaparin (Lovenox, generic) has the widest clinical utility of the subclass, due to its long history of use and largest number of FDA-approved indications.
- Fondaparinux (Arixtra, generic) has fewer FDA-approved indications than enoxaparin. It has a therapeutic niche for patients with a history of heparin-induced thrombocytopenia (HIT).
- The major limitation with dalteparin (Fragmin) is the lack of an FDA-approved indication for treating deep venous thrombosis and pulmonary embolism. The package insert also cautions against use in patients with a history of HIT.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that generic enoxaparin was the most cost-effective agent based on a weighted average cost per unit across all three POS, followed by branded dalteparin (Fragmin), and generic fondaparinux. Budget impact analysis (BIA) results showed that scenarios where generic enoxaparin is included on the BCF and dalteparin (Fragmin) and generic fondaparinux are included on the UF generated the greatest cost-avoidance projection.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee, recommended (15 for, 0 opposed, 1 abstained, 1 absent) enoxaparin, dalteparin (Fragmin), and fondaparinux remain designated as formulary on the UF.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) generic enoxaparin be designated with BCF status, based on clinical and cost effectivness. The BCF recommendation will be implemented upon signing of the minutes.

Director, TMA, Decision: ☒ Approved ☐ Disapproved



Approved, but modified as follows:

B. Androgens Anabolic Steroids—Transdermal and Buccal Testosterone Replacement Therapies (TRTs)

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) the following concerning the TRT agents:

- Although high-quality comparative data is lacking, there appear to be no clinically relevant differences in efficacy between products.
- Transdermal and buccal testosterone replacement products effectively raise testosterone levels in hypogonadal men to the normal range when used in accordance with product labeling.
- Skin-to-skin transfer of transdermal testosterone to women and children should be minimized due to risk of virilization or premature onset of puberty. Testosterone buccal tablets (Striant) carry the lowest risk while the topically applied products carry the highest risk.
- Transdermal and buccal TRTs have a low overall incidence of systemic adverse events, which are not considered to differ clinically across products.
- The most frequent adverse events are dermal application site reactions for the transdermal products and oral application site reactions for buccal tablets; most are mild or transient in nature.

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that transdermal 2% gel pump (Fortesta) was the least costly agent, followed by transdermal solution (Axiron), transdermal patch (Androderm), transdermal 1.62% gel pump (Androgel 1.62%), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal gel tubes (Testim), and testosterone buccal tablets (Striant).

BIA results showed the scenario where transdermal 2% gel (Fortesta) is step-preferred on the UF, all other TRTs are designated non-preferred on the UF or NF, and step therapy is applied to all current and new users of TRTs, was determined to be the most cost-effective scenario.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (13 for, 3 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the MHS:
    - testosterone transdermal 2% gel pump (Fortesta) be designated step-preferred and formulary on the UF;
    - testosterone transdermal patch (Androderm), testosterone transdermal gel tubes (Testim), and testosterone buccal tablets (Striant) be designated non-preferred and formulary on the UF; and
    - testosterone transdermal 1% gel pump and gel packets (Androgel 1%), testosterone transdermal 1.62% gel pump (Androgel 1.62%), and

testosterone transdermal solution (Axiron) be designated non-preferred and NF on the UF.

- This recommendation includes step therapy, which requires a trial of testosterone transdermal 2% gel pump (Fortesta) prior to using other transdermal and buccal TRTs.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) testosterone transdermal 2% gel pump (Fortesta) be designated BCF.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (12 for, 0 opposed, 1 abstained, 4 absent) that the following manual PA criteria should apply to all current and new users of the testosterone replacement therapies. Coverage would be approved if the patient met any of the following criteria:

   a) Manual PA criteria for all transdermal and buccal testosterone replacement products:

      - Patient is male and has a diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism.
      - Patient is a female and receiving testosterone for the following uses:
        - Treatment of hypoactive sexual desire in menopausal women (whether natural or surgical); or
        - Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone).
        - Note that coverage of transdermal or buccal testosterone replacement therapies is not approved for osteoporosis or urinary incontinence.
        - Note that coverage for use in women will be by appeal only.
      - Note that use in adolescents under the age of 17 is not approved and will be by appeal only.

   b) In addition to the above criteria, the following PA criteria would apply specifically to transdermal gel tubes (Testim), transdermal patch (Androderm), buccal tablets (Striant), transdermal 1% gel pump and gel

packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), and transdermal solution (Axiron):

- The patient requires a testosterone replacement therapy that has a low risk of skin-to-skin transfer between family members (for Striant and Androderm only).
- The patient has tried transdermal 2% gel pump (Fortesta) for a minimum of 90 days AND failed to achieve total testosterone levels above 400ng/dL (lab must be drawn 2 hours after Fortesta application) AND denied improvement in symptoms.
- The patient has a contraindication or relative contraindication to Fortesta (e.g., hypersensitivity to a component [including alcohol]; concomitant disulfiram use) that does not apply to Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.
- The patient has experienced a clinically significant skin reaction to Fortesta that is not expected to occur with Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

4. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for transdermal 1.62% gel pump (Androgel 1.62%), transdermal 1% gel pump and gel packets (Androgel 1%), the transdermal solution (Axiron), and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Androgel 1.62%, Androgel 1%, and Axiron. (See Appendix B for full MN criteria.)

5. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is February 6, 2013.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

III. SECTION 703

A. Section 703—The P&T Committee reviewed a list of products—Amicar (branded aminocaproic acid), Kineret (anakinra), Phoslo (branded calcium acetate), Rheumatrex (branded methotrexate), Oxadrin (branded oxandrolone), Denavir (penciclovir), and Transderm-Scop (scopolamine patch)—to determine MN and pre-authorization criteria. These products were identified as not fulfilling refund requirements as required in section 703 of the 2008 National Defense Authorization Act. These drugs were made NF on the UF at previous P&T Committee meetings.

1. ***COMMITTEE ACTION: PRE-AUTHORIZATION CRITERIA***—The P&T Committee recommended (12 for, 0 opposed, 1 abstained, 4 absent) the following should apply to the drugs listed above. Coverage at retail network pharmacies would be approved if the patient met all the following criteria:

    a) Manual Pre-Authorization Criteria:

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

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

The Pre-Authorization 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:

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

NOV 8 2012

Date

DEPARTMENT OF DEFENSE

PHARMACY AND THERAPEUTICS COMMITTEE MINUTES AND RECOMMENDATIONS

August 2012

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on August 15 and 16, 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 May Minutes**—Jonathon Woodson M.D., Director, approved the minutes for the May 2012 DoD P&T Committee meeting on August 8, 2012.
2. **Clarification to the February 2012 Minutes**—The February minutes were clarified to state, for the Sedative Hypnotics-1 class, zolpidem IR is the sole Basic Core Formulary (BCF) drug.

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 199.21(e)(1). All Uniform Formulary (UF) and BCF recommendations considered the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors. Medical necessity (MN) criteria were based on the clinical and cost evaluations, and the conditions for establishing MN for a nonformulary (NF) medication.

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

A. Targeted Immunomodulatory Biologics (TIBs)—Abatacept Subcutaneous Injection (Orencia SC)

Relative Clinical Effectiveness—Abatacept (Orencia) inhibits the activation of T-cells and is approved for treating moderate to severe active rheumatoid arthritis (RA) in adults. It was first marketed in 2005 as an intravenous (IV) infusion, which is only available through the TRICARE medical benefit. A new subcutaneous (SC) abatacept

formulation intended for self-injection is now available. FDA-approval of abatacept SC was based on its demonstrated non-inferiority to abatacept IV. Prior authorization criteria and quantity limits apply to the TIBs and were placed on abatacept SC in November 2011, which are consistent with the FDA-approved package labeling.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that although abatacept SC (Orencia SC) provides an alternative to the tumor necrosis factor (TNF) alpha inhibitors used for treatment of RA and offers patient convenience over the abatacept IV formulation, there is currently insufficient data to conclude that Orencia SC offers improved efficacy, safety, or tolerability compared to the TNF alpha inhibitors in the TIBs class.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—A pharmacoeconomic analysis was performed. The weighted average cost per month at all three points of service (POS) was evaluated for abatacept SC (Orencia SC) in relation to the other drugs in the TIBs class indicated for treatment of RA. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Orencia SC was not cost-effective when compared to other TIBs included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) abatacept SC (Orencia SC) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for abatacept SC (Orencia SC) and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for abatacept SC (Orencia SC). (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 9, 2013.

B. Glaucoma Drugs: Prostaglandin Analogs—Tafluprost Ophthalmic Solution (Zioptan)

Relative Clinical Effectiveness—Tafluprost ophthalmic solution (Zioptan) is a preservative-free prostaglandin analog indicated for the reduction of elevated intraocular pressure (IOP) in patients with glaucoma or ocular hypertension. In one head-to-head comparison, tafluprost proved inferior to latanoprost in lowering IOP, failing to meet the pre-specified margin for non-inferiority. Whether preservative-free tafluprost is associated with decreased adverse events compared to preservative-containing tafluprost remains to be determined.

Relative Clinical Effectiveness Conclusion—The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 0 absent) that tafluprost (Zioptan) offers no compelling clinical advantages over the other prostaglandins available on the UF.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—A pharmacoeconomic analysis was performed. The weighted average cost per day at all three POS was evaluated for tafluprost (Zioptan) in relation to the other ophthalmic prostaglandin analogues. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Zioptan was not cost-effective when compared to the other ophthalmic prostaglandins currently included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) tafluprost (Zioptan) be designated NF because it has no compelling clinical advantages over the other ophthalmic prostaglandin analogues and is not cost-effective compared to latanoprost, the most utilized drug in the Military Health System (MHS).

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for tafluprost (Zioptan) and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for tafluprost (Zioptan). (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 9,

2013.

C. Oral Non-steroidal Anti-inflammatory Drugs (NSAIDs)—Ibuprofen/Famotidine (Duexis)

Relative Clinical Effectiveness—Ibuprofen/famotidine (Duexis) is the first fixed-dose combination of a non-selective NSAID with an H2 antagonist. Ibuprofen and famotidine are currently on the BCF and UF, respectively, and are available over-the-counter. Other combination NSAID/gastroprotective agents on the UF include esomeprazole/enteric-coated naproxen (Vimovo), diclofenac/misoprostol (Arthrotec), and the COX-2 inhibitor celecoxib (Celebrex). No studies with Duexis have evaluated clinically important upper GI events (bleeding, perforation, obstruction). Although the fixed-dose combination of famotidine and ibuprofen offers the convenience of a gastroprotective agent with an NSAID, the three-times daily dosing regimen may affect patient compliance. Systematic reviews and national professional guidelines state a preference for NSAID with proton pump inhibitor or NSAID with misoprostol versus an NSAID with H2 antagonist for reducing GI ulcers.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) ibuprofen/famotidine (Duexis) offers no distinct clinical advantages to the combination NSAID/gastroprotective agents already on the UF.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—A pharmacoeconomic analysis was performed. The weighted average cost per day at all three POS was evaluated for ibuprofen/famotidine (Duexis) in relation to the other oral gastroprotective NSAIDs. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Duexis was not cost-effective when compared to other oral NSAIDs agents included on the UF; it was also more costly than the individual components, ibuprofen and famotidine.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) ibuprofen/famotidine (Duexis) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for ibuprofen/famotidine (Duexis) and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for ibuprofen/famotidine (Duexis). (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 9, 2013.

D. Oral NSAIDs—Ketorolac Nasal Spray (Sprix)

Relative Clinical Effectiveness—Ketorolac nasal spray (Sprix) is the first NSAID administered by the intranasal route. There is no direct comparative data with ketorolac nasal spray or other oral NSAIDs or low potency narcotic analgesics. The studies used to obtain FDA-approval were conducted using a placebo control in the in-patient setting where concomitant morphine or rescue analgesia was administered. Reduced morphine requirements were seen at 24 hours in some studies with Sprix—whether these results are clinically relevant is difficult to determine. Opioid-sparing drugs on the UF include other NSAIDs and tramadol. Sprix is limited by a five-day duration of use, and warnings not seen with other NSAIDs, including contraindications for use in patients with a history of GI bleeding or renal dysfunction.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) there is no evidence to suggest ketorolac nasal spray (Sprix) has a compelling clinical advantage over the other oral NSAIDs already on the BCF and UF.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—A pharmacoeconomic analysis was performed. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that ketorolac nasal spray (Sprix) was more costly, based on an average weighted cost per day of therapy at all three POS, than the other oral NSAIDs and low-potency narcotic analgesics currently on the BCF and UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee, recommended (16 for, 0 opposed, 1 abstained, 0 absent) ketorolac nasal spray (Sprix) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for ketorolac nasal spray (Sprix) and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained,

0 absent) MN criteria for ketorolac nasal spray (Sprix). (See Appendix B for full MN criteria.)

3. ***COMMITTEE ACTION: QUANTITY LIMITS***—The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 0 absent) restricting the maximum allowable quantity to 5 nasal spray bottles/30 days in the mail order pharmacy and retail network, which is consistent with the recommended dosing from the package labeling.

4. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD*** The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 9, 2013.

E. Non-Insulin Diabetes Drugs: Dipeptidyl Dipeptidase-4 (DPP-4) Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)

Relative Clinical Effectiveness—Janumet XR and Jentadueto are fixed-dose combination products containing metformin in either an extended release (ER) formulation with sitagliptin (Janumet XR) or an immediate release (IR) formulation with linagliptin (Jentadueto). Sitagliptin is also available in a fixed-dose combination product with metformin IR (Janumet).

Both Janumet XR and Jentadueto were approved via the FDA 505(b)(2) process, requiring only proof of bioequivalence to their respective individual components. There are no efficacy studies with either agent. The combination of sitagliptin with metformin IR reduces hemoglobin A1c by 0.51% to 0.67%, while the combination of linagliptin with metformin IR decreases A1c by 0.4% to 0.5%. No studies evaluating clinical outcomes (e.g., cardiovascular death, myocardial infarction, and stroke) are available for the DPP-4 inhibitors, but trials are underway.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) there is no evidence to suggest either sitagliptin/ metformin ER (Janumet XR) or linagliptin/metformin (Jentadueto) have a compelling clinical advantage over the other DPP-4 inhibitor/metformin fixed-dose combinations included on the UF.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—A pharmacoeconomic analysis was performed. The weighted average cost per day at all three POS was evaluated for sitagliptin/metformin ER (Janumet XR) and linagliptin/ metformin (Jentadueto) in relation to the other drugs in the DPP-4 inhibitors subclass. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that Janumet XR and Jentadueto were cost-effective when compared to other DPP-4 inhibitors included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee, recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following:

    - sitagliptin/metformin ER (Janumet XR) be designated step-preferred and formulary on the UF; and
    - linagliptin/metformin (Jentadueto) be designated non-preferred and formulary on the UF.
    - This recommendation includes step therapy, which requires a trial of sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/ simvastatin (Juvisync), or sitagliptin/metformin ER (Janumet XR) (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors also requires a trial of metformin or sulfonylurea for new patients.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee, recommended (14 for, 1 opposed, 1 abstained, 1 absent) sitagliptin/metformin ER (Janumet XR) be designated with BCF status, as sitagliptin-containing products have the majority of the current DPP-4 inhibitor utilization and are the most cost-effective agents.

3. ***COMMITTEE ACTION: PRIOR AUTHORIZATION (PA) CRITERIA***
   Existing automated prior authorization (step therapy) requires a trial of metformin or a sulfonylurea prior to use of a DPP-4 inhibitor. Additionally, sitagliptin-containing products (Januvia, Janumet, Janumet XR, and Juvisync) are the preferred agents in the DPP-4 inhibitors subclass. New users must try a preferred product before trying linagliptin or saxagliptin-containing products.

   The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 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 filled a prescription for metformin or a sulfonylurea at any MHS pharmacy POS [Military Treatment Facilities (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, Janumet XR, Tradjenta, Jentadueto, Onglyza, or Kombiglyze XR) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

The fixed-dose combination product Janumet XR or Jentadueto is approved (eg, a trial of sulfonylurea is not required if):

(1) The patient has had an inadequate response to metformin or sulfonylurea.

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

(3) The patient has a contraindication to a sulfonylurea.

c) In addition to the above criteria regarding metformin and sulfonylurea, the following PA criteria would apply specifically to linagliptin/metformin metformin (Jentadueto):

(1) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with linagliptin-containing products.

(2) The patient has had an inadequate response to a sitagliptin-containing product.

(3) The patient has a contraindication to sitagliptin.

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENATION PERIOD***
The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS. Based on the P&T Committee's recommendation, the effective date is January 9, 2013.

V. UF DRUG CLASS REVIEWS

A. Anticoagulants—Heparin and Related Products

Background and Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the Heparin and Related Products subclass of the anticoagulants. (The newer oral anticoagulants, including the Factor Xa inhibitors and direct thrombin inhibitors will be discussed at a later date.) The drugs in this subclass include unfractionated heparin, which is available in many generic formulations and will not be discussed further, enoxaparin (Lovenox), dalteparin (Fragmin), and fondaparinux (Arixtra). Two products, tinzaparin (Innohep) and ardeparin (Normiflow), were voluntarily discontinued by their manufacturers due to nonsafety reasons. The subclass has not previously been reviewed for UF placement. Generic biologic formulations of enoxaparin and fondaparinux are available; both are FDA AP-rated (therapeutically equivalent parenteral products) to Lovenox and Arixtra, respectively.

Relative Clinical Effectiveness Conclusion—The P&T Committee agreed (15 for, 0 opposed, 0 abstained, 2 absent) on the following clinical effectiveness conclusions:

- Enoxaparin has the widest clinical utility of the subclass, due to its long history of use, largest number of FDA-approved indications, availability in several dosage strengths, and recommendations by the American College of Chest Physicians for use in special populations (pregnancy, pediatrics). The package labeling cautions against use in patients with a history of heparin-induced thrombocytopenia (HIT).
- Fondaparinux has fewer FDA-approved indications than enoxaparin. It has a therapeutic niche for patients with a history of HIT. The risk of bleeding is increased in patients with low body weight (<50 kg), the elderly, and in patients with decreased renal function.
- The major limitation with dalteparin is the lack of an FDA-approved indication for treating deep venous thrombosis and pulmonary embolism. The package insert also cautions against use in patients with a history of HIT.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—Cost minimization (CMA) and budget impact analyses (BIA) were used to evaluate the drugs in this subclass, with corresponding sensitivity analyses. Due to recent availability of generic fondaparinux (Arixtra), an estimated generic drug price was used in the cost analyses. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that generic enoxaparin was the most cost-effective agent based on a weighted average cost per unit across all three POS, followed by branded dalteparin (Fragmin), and generic fondaparinux (ranked in order from most cost-effective to least cost-effective). BIA results showed that, among currently available formulary options, scenarios where generic enoxaparin is included on the BCF and dalteparin (Fragmin) and generic fondaparinux are included on the UF generated the greatest cost-avoidance projection.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee, recommended (15 for, 0 opposed, 1 abstained, 1 absent) enoxaparin, dalteparin (Fragmin), and fondaparinux remain designated as formulary on the UF.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) generic enoxaparin be designated with BCF status, based on clinical and cost effectivness. This clarifies the previous BCF listing for the low-molecular weight heparins stating that MTFs could choose between dalteparin (Fragmin), enoxaparin, or tinzaparin (Innohep). The BCF recommendation will be implemented upon signing of the minutes.

B. Androgens Anabolic Steroids—Transdermal and Buccal Testosterone Replacement Therapies

Background and Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the transdermal and buccal testosterone replacement therapies (TRTs), which are used for treating adult male hypogonadism. The TRT class is comprised of the following formulations of topical or buccal testosterone: transdermal patch (Androderm), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), transdermal solution (Axiron), transdermal 2% gel pump (Fortesta), buccal tablets (Striant), and transdermal gel tubes (Testim).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) the following concerning the TRT agents:

- Although high-quality comparative data is lacking, there appear to be no clinically relevant differences in efficacy between products.
- Transdermal and buccal testosterone replacement products effectively raise testosterone levels in hypogonadal men to the normal range when used in accordance with product labeling.
- Skin-to-skin transfer of transdermal testosterone to women and children should be minimized due to risk of virilization or premature onset of puberty. Testosterone buccal tablets (Striant) carry the lowest risk while the topically applied products carry the highest risk.
- Transdermal and buccal TRTs have a low overall incidence of systemic adverse events, which are not considered to differ clinically across products.

- The most frequent adverse events are dermal application site reactions for the transdermal products and oral application site reactions for buccal tablets; most are mild or transient in nature.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion
Pharmacoeconomic analyses were performed for the topical and buccal testosterone class, including CMA and BIA. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that transdermal 2% gel pump (Fortesta) was the least costly agent, followed by transdermal solution (Axiron), transdermal patch (Androderm), transdermal 1.62% gel pump (Androgel 1.62%), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal gel tubes (Testim), and testosterone buccal tablets (Striant).

The analyses also evaluated the potential budgetary impact of cost scenarios where selected TRTs were designated with preferred product status (step therapy) on the UF; i.e., a trial of a preferred TRT would be required before using other TRTs. BIA results showed scenarios implementing step therapy were more cost-effective than scenarios without step therapy. The scenario where transdermal 2% gel (Fortesta) is step-preferred on the UF, all other TRTs are designated non-preferred on the UF or NF, and step therapy is applied to all current and new users of TRTs, was determined to be the most cost-effective scenario.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (13 for, 3 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the MHS:
    - testosterone transdermal 2% gel pump (Fortesta) be designated step-preferred and formulary on the UF;
    - testosterone transdermal patch (Androderm), testosterone transdermal gel tubes (Testim), and testosterone buccal tablets (Striant) be designated non-preferred and formulary on the UF; and
    - testosterone transdermal 1% gel pump and gel packets (Androgel 1%), testosterone transdermal 1.62% gel pump (Androgel 1.62%), and testosterone transdermal solution (Axiron) be designated non-preferred and NF on the UF.
    - This recommendation includes step therapy, which requires a trial of testosterone transdermal 2% gel pump (Fortesta) prior to using other transdermal and buccal TRTs.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) testosterone transdermal 2% gel pump (Fortesta) be designated BCF.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (12 for, 0 opposed, 1 abstained, 4 absent) that the following manual PA criteria should apply to all current and new users of the testosterone replacement therapies. Coverage would be approved if the patient met any of the following criteria:

    a) Manual PA criteria for all transdermal and buccal testosterone replacement products:

        - Patient is male and has a diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism;
        - Patient is a female and receiving testosterone for the following uses:
            - Treatment of hypoactive sexual desire in menopausal women (whether natural or surgical); or
            - Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone).
            - Note that coverage of transdermal or buccal testosterone replacement therapies is not approved for osteoporosis or urinary incontinence.
            - Note that coverage for use in women will be by appeal only.
        - Note that use in adolescents under the age of 17 is not approved and will be by appeal only.

    b) In addition to the above criteria, the following PA criteria would apply specifically to transdermal gel tubes (Testim), transdermal patch (Androderm), buccal tablets (Striant), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), and transdermal solution (Axiron):

        - The patient requires a testosterone replacement therapy that has a low risk of skin-to-skin transfer between family members (for Striant and Androderm only).

- The patient has tried transdermal 2% gel pump (Fortesta) for a minimum of 90 days AND failed to achieve total testosterone levels above 400ng/dL (lab must be drawn 2 hours after Fortesta application) AND denied improvement in symptoms.
- The patient has a contraindication or relative contraindication to Fortesta (e.g., hypersensitivity to a component [including alcohol]; concomitant disulfiram use) that does not apply to Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.
- The patient has experienced a clinically significant skin reaction to Fortesta that is not expected to occur with Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

4. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluations for transdermal 1.62% gel pump (Androgel 1.62%), transdermal 1% gel pump and gel packets (Androgel 1%), the transdermal solution (Axiron), and the conditions for establishing MN for NF medications, the P&T Cominittee recommended (16 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Androgel 1.62%, Androgel 1%, and Axiron. (See Appendix B for full MN criteria.)

5. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***
The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is February 6, 2013.

VI. SECTION 703

A. Section 703—The P&T Committee reviewed a list of products—Amicar (branded aminocaproic acid), Kineret (anakinra), Phoslo (branded calcium acetate), Rheumatrex (branded methotrexate), Oxadrin (branded oxandrolone), Denavir (penciclovir), and Transderm-Scop (scopolamine patch)—to determine MN and pre-authorization criteria. These products were identified as not fulfilling refund requirements as required in section 703 of the 2008 National Defense Authorization Act. These drugs were made NF on the UF at previous P&T Committee meetings.

1. ***COMMITTEE ACTION: PRE-AUTHORIZATION CRITERIA***—The P&T Committee recommended (12 for, 0 opposed, 1 abstained, 4 absent) the following should apply to the drugs listed above. Coverage at retail network pharmacies would be approved if the patient met all the following criteria:

a) Manual Pre-Authorization Criteria:

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

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

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

VII. ITEMS FOR INFORMATION

A. Pharmacy Outcomes Research Team (PORT)—The PORT updated the P&T Committee on their various activities and research initiatives, and presented data on utilization patterns and effects of formulary changes in four drug classes:

- Antiplatelet agents—This class was reviewed in February 2012, with clopidogrel (Plavix) remaining on the BCF. A key element of the cost-effectiveness evaluation was the anticipated generic availability of clopidogrel. As of July 2012, generic clopidogrel accounted for more than 98% of all use in the retail network, accompanied by an approximately 72% decrease in the average cost per unit compared to April 2012. At least one clopidogrel generic formulation is available to MTFs under a Federal Supply Schedule contract. The P&T Committee acknowledged that MTFs may encounter delayed availability of clopidogrel generics through their prime vendors, but encouraged perseverance, given the volume of use and the potential for cost avoidance.
- Antilipidemics-1—An automated step therapy program/PA was implemented in October 2010, requiring use of the preferred statin agents (atorvastatin, lovastatin, pravastatin, simvastatin) prior to treatment with non-preferred agents (e.g., rosuvastatin, ezetimibe/simvastatin, etc). The P&T Committee noted that step therapy is working, as evidenced by a gradual decline in the use of non-preferred agents (particularly the lower dosage strengths) in the retail and mail POS, and the low percentage (<3%) of rejected claims under the step therapy program relative to total claims (paid claims plus rejected claims).
- Leukotriene Antagonists—A PA requirement for montelukast (Singulair) was implemented in March 2012. The PA allows for the treatment of asthma, but limits use for treatment of allergic rhinitis, unless the patient has failed or experienced an adverse event with nasal corticosteroids. The P&T Committee noted an overall decline in Singulair use, particularly in the retail and mail order POS. Additionally, there was no spike in usage in April 2012, which historically was noticeable and attributed to seasonal usage of Singulair, likely for allergic rhinitis. No information was available at the time of the meeting

concerning impact of the very recent generic approval of montelukast in August 2012.

- Phosphodiesterase-5 inhibitors for Erectile Dysfunction—In November 2011, sildenafil (Viagra) replaced vardenafil (Levitra) on the BCF (effective February 2012) and as the preferred agent under the existing step therapy/PA program (effective April 2012). MTFs are rapidly switching from Levitra to Viagra. It is too early to determine the full effect on relative market share of these agents at retail and mail.

B. TRICARE Formulary Search Tool—Information regarding updates to the TRICARE Formulary Search Tool was provided to the P&T Committee and is available at *http://pec.ha.osd.mil/formulary_search.php*.

VIII. ADJOURNMENT

The meeting adjourned at 1100 hours on August 16, 2012. The next meeting will be in November 2012.

Appendix A—Attendance: August 2012 P&T Committee Meeting

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

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

Appendix D—Table of Abbreviations

Appendix A—Attendance: August 2012 P&T Committee Meeting

Voting Members Present	
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, MS	Army, Pharmacy Officer
Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CAPT Deborah Thompson, USCG, via DCO	Coast Guard, Pharmacy Officer
CAPT Edward Norton, MSC	Navy, Pharmacy Officer (Pharmacy Consultant BUMED)
Col Lowell Sensintaffer, MC	Air Force, Physician at Large
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
COL Doreen Lounsbery, MC	Army, Internal Medicine Physician
LTC Amy Young, MC for COL Ted Cieslak, MC	Army, Physician at Large
COL Michael Wynn, MC for LTC Bruce Lovins, MC	Army, Family Practice Physician
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Major Jeremy King, MC	Air Force, OB/GYN Physician
CDR Eileen Hoke, MC	Navy, Pediatrics
Dr. Miguel Montalvo	TRICARE Regional Office-South Chief of Clinical Operations Division and Medical Director
Mr. Joe Canzolino	U.S. Department of Veterans Affairs
Nonvoting Members Present	
Mr. David Hurt	Associate General Counsel, TMA
COL Todd Williams, MS	Defense Medical Materiel Program Office
CDR Jay Peoloquin, MSC	Defense Logistics Agency Troop Support

Appendix A—Attendance (continued)

Guests	
Mr. Bill Davies via DCO	TRICARE Management Activity, Pharmaceutical Operations Directorate
CDR Matthew Baker, USPHS	Indian Health Service
Others Present	
LTC Chris Conrad, MS	DoD Pharmacoeconomic Center
Lt Col Melinda Henne, MC	DoD Pharmacoeconomic Center
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
LCDR Ola Ojo, MSC	DoD Pharmacoeconomic Center
LCDR Marisol Martinez, USPHS	DoD Pharmacoeconomic Center
LCDR Joshua Devine, USPHS	DoD Pharmacoeconomic Center
Maj David Folmar, BSC	DoD Pharmacoeconomic Center
LCDR Linh Quach, MSC	DoD Pharmacoeconomic Center
Dr. Angela Allerman	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe	DoD Pharmacoeconomic Center
Dr. Eugune Moore	DoD Pharmacoeconomic Center
Dr. Jeremy Briggs	DoD Pharmacoeconomic Center
Dr. Dean Valibhai	DoD Pharmacoeconomic Center
Dr. Brian Beck	DoD Pharmacoeconomic Center
Dr. Amy Lugo via DCO	DoD Pharmacoeconomic Center
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor

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

Drug / Drug Class	Medical Necessity Criteria
• Testosterone transdermal solution pump; 30 mg/actuation; (Axiron) • Testosterone 1%; 25 mg/2.5 gm, 50 mg/5 gm transdermal gel packets, and 12.5 mg /actuation gel pump (Androgel 1%) • Testosterone 1.62% transdermal gel pump; 20.25 mg/actuation (Androgel 1.62%) **Testosterone Replacement Therapies**	• Use of ALL formulary testosterone replacement products is contraindicated (e.g., due to hypersensitivity), and treatment with Axiron, Androgel 1%, or Androgel 1.62% is not contraindicated. • Patient has experienced or is likely to experience significant adverse effects from the formulary agents. • The formulary agents have resulted in therapeutic failure.
• Ibuprofen/famotidine (Duexis) **Non-steroidal Anti-Inflammatory Drugs (NSAIDS)**	• Use of formulary agents is contraindicated.
• Ketorolac nasal spray (Sprix) **Non-steroidal Anti-Inflammatory Drugs (NSAIDS)**	• Use of formulary agents is contraindicated. • The patient requires a nasal NSAID formulation and cannot take NSAIDs via any other route.
• Tafluprost ophthalmic solution (Zioptan) **Ophthalmic Prostaglandins**	• The use of formulary alternatives is contraindicated. • The patient has experienced or is likely to experience significant adverse effects from the formulary agents.
• Abatacept SQ (Orencia) **Targeted Immunomodulatory Biologics (TIBs)**	• The use of formulary alternatives is contraindicated. • The patient has experienced or is likely to experience significant adverse effects from the formulary agents. • The formulary agents have resulted or are likely to result in therapeutic failure. • The patient previously responded to a non-formulary agent, and changing to a formulary agent would incur unacceptable risk. • The patient is currently receiving abatacept IV and is switching to abatacept SQ.

Appendix C—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
Aug 2012	**Testosterone Replacement Therapies** **Topical and Buccal products subclass**	UF Review	• testosterone transdermal 2% gel pump; 10 mg/actuation (Fortesta)	• testosterone 50 mg/5 gm transdermal gel tubes (Testim) • testosterone 2 mg/24 hr, 4 mg/24 hr transdermal patches (Androderm) • testosterone 30 mg buccal tablets (Striant)	• testosterone transdermal solution pump; 30 mg/actuation; (Axiron) • testosterone 1%; 25 mg/2.5 gm, 50 mg/ 5 gm transdermal gel packets, and 12.5 mg/ actuation gel pump (Androgel 1%) • testosterone 1.62% transdermal gel pump; 20.25 mg/actuation (Androgel 1.62%)	Pending signing of minutes/ 90 days	PA required; see Comments	• All current and new users of topical and buccal testosterone replacement products must go through the PA process to ensure diagnosis of hypogonadism • Fortesta 2% gel pump is the preferred product; all users of topical and buccal testosterone replacement products must have trial of Fortesta 2% gel prior to other products
Aug 2012	**Anticoagulants** **Heparin and related products subclass**	UF Review	• enoxaparin (generic)	• dalteparin (Fragmin) • fondaparinux (generic)	• Not applicable (no products designated as nonformulary)	Pending signing of minutes	-	• enoxaparin generic designated 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 2012	**Non-Steroidal Anti-inflammatory Drugs** Previous review: Aug 2011	New Drugs in Already Reviewed Classes Ibuprofen/ famotidine (Duexis) Ketorolac nasal spray (Sprix)	• ibuprofen 400 mg, 600 mg & 800 mg (generic) • indomethacin 25 mg & 50 mg (generic) • meloxicam 7.5 mg & 15 mg (generic) • naproxen 250 mg & 500 mg & 125 mg/5 mL susp (generic)	• celecoxib (Celebrex) • diclofenac/misoprostol (Arthrotec) • diclofenac potassium tablets (Cataflam generic) • diclofenac sodium tablets (Voltaren generic) • diflunisal • etodolac • fenoprofen • flurbiprofen • ketoprofen • ketorolac • meclofenamate • nabumetone • naproxen sodium 275 mg & 550 mg (Anaprox, generic) • oxaprozin • piroxicam • sulindac • tolmetin • naproxen/esomeprazole (Vimovo)	*August 2012* • **ibuprofen/famotidine (Duexis)** • **ketorolac nasal spray (Sprix)** *August 2011* • diclofenac potassium liquid-filled capsules (Zipsor) 25 mg • diclofenac potassium powder packets 50 mg (Cambia) • naproxen sodium ER (Naprelan CR, generic) 375 mg, 500 mg, & 750 mg ER tabs, dosing card • mefenamic acid (Ponstel, generic) 250 mg	Pending signing of minutes/ 60 days	Quantity Limits for ketorolac nasal spray (Sprix): 5 bottles for 30-day supply in both the Retail Network and Mail Order Pharmacy	• ibuprofen/ famotidine (Duexis) designated nonformulary • ketoralac nasal spray (Sprix) designated nonformulary
Aug 2012	**Glaucoma Agents** **Ophthalmic Prostaglandin Subclass** Previous review: Aug 2011	New Drug in Already Reviewed Class Tafluprost (Zioptan)	• latanoprost (generic)	• bimatoprost (Lumigan)	*August 2012* • **tafluprost (Zioptan)** *February 2007* • travoprost (Travatan Z)	Pending signing of minutes/ 60 days	-	• tafluprost (Zioptan) designated nonformulary
Aug 2012	**Non-Insulin Diabetes Drugs** **DPP-4 Inhibitors Subclass** Previous reviews: Feb 2012 and Nov 2012	New Drug in Already Reviewed Class sitagliptin/ metformin ER (Janumet XR) linagliptin/ metformin IR (Jentadueto)	*August 2012* • **sitagliptin/ metformin ER (Janumet XR)** *Feb 2012* • sitagliptin (Januvia) • sitagliptin/metformin (Janumet)	*August 2012* • **linagliptin/metformin IR (Jentadueto)** *February 2012* • sitagliptin/Simvastatin (Juvisync) • linagliptin (Tradjenta)	*February 2012* • saxagliptin (Onglyza) • saxagliptin/metformin ER (Kombiglyze XR)	Pending signing of minutes/ 60 days	Step therapy required – see comments	• Must try metformin and sulfonylurea 1st before any DPP-4 drug • Must try sitagliptin-containing product 1st before Tradjenta, Jentadueto, Onglyza, or Kombiglyze XR

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 2012	**Targeted Immuno-modulatory Biologics** Previous review: Nov 2007	New Drug in Already Reviewed Class abatacept SQ (Orencia SC)	• adalimumab SQ (Humira)	• alefacept (Amevive)	*August 2012* • **abatacept SQ (Orencia)** *Nov 2007 and Aug 2009* • etanercept (Enbrel) (etanercept) • anakinra (Kineret) • certolizumab (Cimzia) • golimumab (Simponi)	60 days	• PA limiting use to FDA-approved indications was approved in Nov 2011 • QLs approved in Nov 2011 • Retail: 4 syringes/28 days • Mail Order: 8 syringes/56 days	• abatacept SQ (Orencia) designated nonformulary • adalimumab (Humira) is the formulary alternative for treating rheumatoid arthritis

* TRICARE Formulary Search tool: http://www.pec.ha.osd.mil/formulary_search.php

Appendix D—Table of Abbreviations

BCF	Basic Core Formulary
BIA	budget impact analysis
C.F.R.	Code of Federal Regulations
CMA	cost minimization analysis
DoD	Department of Defense
DPP-4	dipeptidyl dipeptidase-4
ECF	Extended Core Formulary
ER	extended release
FDA	U.S. Food and Drug Administration
FR	Federal Register
GI	gastrointestinal
HIT	heparin-induced thrombocytopenia
IOP	intraocular pressure
IR	immediate release
IV	intravenous
MHS	Military Health System
MN	medical necessity
MTF	Military Treatment Facility
NDAA	National Defense Authorization Act
NF	nonformulary
NSAIDs	non-steroidal anti-inflammatory drugs
P&T	Pharmacy and Therapeutics
PA	prior authorization
PEC	Pharmacoeconomic Center
PORT	Pharmacy Outcomes Research Team
POS	points of service
QLs	quantity limits
RA	rheumatoid arthritis
SC	subcutaneous
TIBs	targeted immunomodulatory biologics
TNF	tumor necrosis factor
TRTs	transdermal and buccal testosterone replacement therapies
UF	Uniform Formulary
U.S.C.	United States Code
VA	U.S. Department of Veterans Affairs

DECISION PAPER

DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

May 2012

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

A. Gabapentin enacarbil (Horizant) and gabapentin (Gralise)

Relative clinical effectiveness conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 0 absent) the following: gabapentin enacarbil (Horizant) and gabapentin (Gralise) are once-daily formulations of gabapentin (Neurontin, generics). There is no evidence to suggest either drug has a compelling clinical advantage over the other drugs for non-opioid pain syndromes included on the Uniform Formulary (UF).

Relative cost- effectiveness conclusion (15 for, 0 opposed, 0 abstained, 0 absent) Gabapentin enacarbil (Horizant) and gabapentin (Gralise) were not cost-effective when compared to other non-opioid pain syndrome agents included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee, recommended (14 for, 0 opposed, 1 abstained, 0 absent) gabapentin enacarbil (Horizant) and gabapentin (Gralise) be designated nonformulary (NF) due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: PRIOR AUTHORIZATION (PA) CRITERIA***
Existing step therapy/PA requires a trial of generic gabapentin prior to pregabalin (Lyrica) in new users. The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) that both gabapentin enacarbil (Horizant) and gabapentin (Gralise) be designated non-step-preferred, requiring a trial of generic gabapentin in new users. Coverage would be approved if the patient met any of the following step therapy/PA criteria:

   a) Automated PA criteria: The patient has filled a prescription for gabapentin at any Military Health System (MHS) pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

   b) Manual PA criteria: The patient has a contraindication to or experienced adverse events with gabapentin or the formulary non-opioid pain syndrome agents which is not expected to occur with Horizant or Gralise.

3. ***COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following MN criteria for Horizant and Gralise: the patient has a contraindication to or has experienced an adverse effect from gabapentin or the formulary non-opioid pain syndrome agents.

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 30-day implementation period in all points of service (POS), and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is September 19, 2012.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

II. UNIFORM FORMULARY DRUG CLASS REVIEWS

Relative clinical effectiveness conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 0 absent) the newer sedative hypnotic agents all improve sleep latency (onset) compared to placebo. Sleep maintenance is improved with zolpidem IR (Ambien, generic), zolpidem CR (Ambien CR, generic), eszopiclone (Lunesta), and doxepin (Silenor). Based on an indirect comparison, there do not appear to be clinically relevant differences between zolpidem CR and Lunesta in terms of objective sleep measures.

Relative cost effectiveness conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 0 absent) zolpidem IR was the least costly agent, followed by zaleplon, zolpidem CR, eszopiclone (Lunesta), doxepin (Silenor), zolpidem SL (Edluar), and ramelteon (Rozerem). BIA results showed minimal differences between scenarios, but the projected budgetary impact in the MHS did vary depending on market movement of zolpidem CR when designated step-preferred versus non-step-preferred, rate of price decline of generic zolpidem CR, and market migration of generic drugs versus branded products

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (12 for, 1 opposed, 2 abstained, 0 absent) the following scenario for the UF, which includes a drug for sleep onset (zolpidem IR), a drug for sleep maintenance (zolpidem CR and Lunesta), and a non-controlled drug (Silenor), and is the most cost-effective option for the MHS:

- zolpidem IR and zaleplon be designated formulary on the UF and step-preferred. This recommendation incorporates step therapy, which requires a trial of zolpidem IR or zaleplon (step-preferred drugs) in new users before use of another newer sedative hypnotic drug;
- zolpidem CR, doxepin (Silenor), and eszopiclone (Lunesta) be designated formulary on the UF and non-step-preferred;
- ramelteon (Rozerem) and zolpidem SL (Edluar) remain NF and non-step-preferred (behind the step);
- zolpidem oral spray (Zolpimist) is not covered by a written agreement by the manufacturer to honor the pricing standards required by 10 United States Code 1074g(f). Pursuant to 32 Code of Federal Regulations (C.F.R.) 199.21(q)(2)(A), Zolpimist is designated NF.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) zolpidem IR maintain BCF status on the UF.

3. ***COMMITTEE ACTION: PA CRITERIA***—Existing step therapy/PA requires a trial of generic zolpidem IR prior to the other newer sedative hypnotics in new users. The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to the newer sedative hypnotics drug class. Coverage would be approved if the patient met any of the following criteria:
   a) Automated PA criteria: The patient has filled a prescription for zolpidem IR or zaleplon at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.
   b) Manual PA criteria: The patient has an inadequate response to, been unable to tolerate due to adverse effects, or has a contraindication to zolpidem IR or zaleplon.

4. ***COMMITTEE ACTION: MN CRITERIA***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) retaining the current MN criteria for zolpidem SL (Edluar) and ramelteon (Rozerem): the patient has had an inadequate response to, been unable to tolerate due to adverse effects, or has contraindications to zolpidem IR or zaleplon, or there is no alternative formulary agent.

5. ***COMMITTEE ACTION: PRE-AUTHORIZATION AND MN CRITERIA FOR ZOLPIDEM ORAL SPRAY (ZOLPIMIST)***—Pursuant to 32 Code of Federal Regulations (C.F.R.) 199.21(q)(2)(B), the P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following pre-authorization criteria should apply to availability of Zolpimist through retail network pharmacies. Coverage at retail network pharmacies would be approved if the patient met any of the following criteria:

   a) Manual Pre-Authorization Criteria:

      (1) Use of the formulary agent is contraindicated.

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

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

   (b) Medical Necessity Criteria:

      (1) Use of the formulary agent is contraindicated.

COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS. Based on the P&T Committee's recommendation, the effective date is October 17, 2012.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

All recommended actions pertaining to Zolpimist are to be held in abeyance until verification is received from the Department of Veterans Affairs that Zolpimist is a covered drug under the Veterans Health Care Act.

III. SPECIAL PROGRAMS

A. Smoking Cessation Program

Background Relative Clinical Effectiveness—Drugs for smoking cessation [varenicline (Chantix), bupropion SR 150 mg (Zyban), and nicotine patch, gum, lozenge, nasal spray (Nicotrol NS), and inhaler (Nicotrol)] are currently excluded from the TRICARE® benefit by regulation (32 C.F.R 199.4(g)(65)). The Duncan Hunter National Defense Authorization Act for Fiscal Year 2009 requires the availability, at no cost to the beneficiary, of pharmaceuticals used for smoking cessation to select

beneficiary groups with a limitation on the availability of such pharmaceuticals to the national mail order pharmacy program under the TRICARE program if appropriate. The Proposed Rule, which provides that smoking cessation pharmaceutical agents, including FDA-approved over-the-counter pharmaceutical agents, are available through the TRICARE Mail Order Pharmacy or the MTF, has been published in the Federal Register (76 FR 58199), comments have been received, and the Final Rule is pending publication.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 0 absent) the following: varenicline (Chantix), bupropion SR, and nicotine replacement therapy (NRT) are efficacious versus placebo for improving long-term smoking abstinence. Combination therapy, in particular nicotine patch plus gum, is more efficacious than monotherapy. Varenicline (Chantix) is the most efficacious monotherapy for smoking cessation. Safety concerns exist with varenicline, including adverse neuropsychiatric effects (behavioral changes, agitation, suicide/suicidal ideation, and depression). In patients with pre-existing stable cardiovascular (CV) disease, generally the benefit of abstinence outweighs the increased adverse CV risk with varenicline. Local MTFs remain at liberty to design their own smoking cessation program, defining which elements will be included in that program.

Relative Cost-Effectiveness Analysis and Conclusion—The P&T Committee concluded (15 for, 0 against, 0 abstained, 0 absent) the following:

- Cost-minimization results showed that nicotine patch and gum were the least costly products among the NRTs, and bupropion SR was the least costly non-NRT option.
- Cost-effectiveness analyses results demonstrated that, in adult patients who smoke more than 10 cigarettes a day, combination therapy (nicotine patch plus gum) was the most cost-effective treatment for tobacco dependence offering the greatest improvement in rates of long-term smoking abstinence. Although less cost-effective than combination therapy, varenicline was recognized as a cost-effective option when evaluating abstinence rates with monotherapy.
- Budget impact analysis showed inclusion of all 7 smoking cessation products in the Smoking Cessation Programs was the most favorable scenario for the MHS.

1. ***COMMITTEE ACTION: COVERAGE RECOMMENDATION***—The P&T Committee recommended (13 for, 1 opposed, 1 abstained, 0 absent) varenicline (Chantix), bupropion SR 150 mg, and nicotine (as patch, gum, lozenge, nasal spray, and inhaler) be covered agents in the TRICARE Smoking Cessation Program, contingent on publication of the Final Rule. This coverage recommendation allows for several treatment modalities to

accommodate patient preference and provide optimal access and opportunity for successful abstinence. No smoking cessation drugs were recommended to be excluded from the program.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) bupropion SR 150 mg; nicotine patch 7 mg, 14 mg, and 21 mg; and, nicotine gum 2 mg and 4 mg be designated BCF on the UF, contingent on publication of the Final Rule.

3. ***COMMITTEE ACTION: VARENICLINE PA***—The P&T Committee rejected (6 in favor of prior authorization for varenicline, 8 opposed, 1 abstained, 0 absent) the proposal that PA criteria should apply to varenicline (Chantix). PA criteria for varenicline were proposed for safety concerns, primarily neuropsychiatric AEs. While the P&T Committee recognized the potential for safety concerns with varenicline, they also concluded that a PA was not required to ensure safe prescribing with the medication because the risks with varenicline are understood by prescribing providers and can be successfully managed without PA criteria.

4. ***COMMITTEE ACTION: COVERED BENEFICIARY CRITERIA AND PA FOR A 3rd QUIT ATTEMPT***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following coverage criteria should apply to all seven smoking cessation products [varenicline (Chantix), bupropion SR 150 mg, nicotine gum, patch, lozenge, nasal spray, and inhaler)], consistent with the requirements in the Proposed Rule, and contingent on publication of the Final Rule. Coverage not approved for patients under the age of 18 or for Medicare-eligible beneficiaries. Coverage for a 3rd quit attempt within one year may be pre-approved if the provider has verified that the patient would benefit from a 3rd quit attempt.

5. ***COMMITTEE ACTION: QUANTITY LIMITS (QLs)***—The P&T Committee recommended (14 for, 0 opposed, 1 abstain, 0 absent) QLs/days supply limits, restricting the maximum allowable smoking cessation quantity to a 60-day supply per claim at the TRICARE Mail Order POS, with a maximum 240-day supply per rolling 365-day period. Additionally, nicotine gum and nicotine lozenge would be limited to 300 pieces per 60-day claim, rounded to the nearest multiple of the package size (e.g., boxes of 75 or 100). The QL recommendations are contingent on publication of the Final Rule.

6. ***COMMITTEE ACTION: IMPLEMENTATION PERIOD***

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in the MTF and mail order POS, following publication of the Final Rule.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

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

August 8, 2012
Date

DEPARTMENT OF DEFENSE

PHARMACY AND THERAPEUTICS COMMITTEE MINUTES AND RECOMMENDATIONS

May 2012

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on May 16, 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 February 2012 DoD P&T Committee meeting on May 7, 2012. A 6–12 month follow-up of safety for tapentadol ER (Nucynta ER) was requested by the Director.
2. **Correction of November 2011 Minutes—BCF Clarification for Short-Acting Beta Agonists:** The August 2011 P&T Committee minutes were clarified to state the Basic Core Formulary (BCF) listing for nebulized albuterol is the 0.083% 2.5 mg/3 mL formulation—not the 0.5% 2.5 mg/5mL vial—for the short-acting beta agonists.
3. **Correction of August 2011 Minutes—Prior Authorization (PA) Implementation Date for Singulair:** The PA implementation date for montelukast (Singulair) was changed from February 1, 2012, to March 21, 2012.

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 (C.F.R.) 199.21(e)(1). All Uniform Formulary (UF) and BCF recommendations considered the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors. Medical necessity (MN) criteria were based on the clinical and cost evaluations, and the conditions for establishing MN for a nonformulary (NF) medication.

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

A. Gabapentin enacarbil (Horizant) and gabapentin (Gralise)

Relative Clinical Effectiveness—Gabapentin enacarbil (Horizant) and gabapentin (Gralise) are once-daily formulations of gabapentin (Neurontin, generics). At the time of the May 2012 meeting, Horizant was FDA-approved for treating restless leg syndrome (RLS), but was undergoing FDA review for post-herpetic neuralgia. The Depression/Non-opioid Pain Syndrome Drug Class was reviewed for UF status at the November 2011 DoD P&T Committee meeting. Gabapentin (Neurontin, generics) is currently on the BCF. Step therapy/PA requires a trial of generic gabapentin prior to pregabalin (Lyrica) in new users.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 0 absent) for both Horizant and Gralise, although the two drugs are dosed once daily versus multiple daily dosing required with generic gabapentin, there is no evidence to suggest either drug has a compelling clinical advantage over the other drugs for non-opioid pain syndromes included on the UF. Dosing conversion guidelines between Horizant, Gralise, and generic gabapentin are not available and these agents are not interchangeable due to differing pharmacokinetic properties. Gralise requires a large tablet burden to reach recommended dosing. Both drugs may cause significant somnolence and sedation, and Horizant carries a warning for adversely impairing driving ability.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—A pharmacoeconomic analysis was performed. The weighted average cost per day at all three points of service (POS) was evaluated for gabapentin enacarbil (Horizant) and gabapentin (Gralise) in relation to the other drugs for non-opioid pain syndromes. The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 0 absent) that Horizant and Gralise were not cost-effective when compared to other non-opioid pain syndrome agents included on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee, recommended (14 for, 0 opposed, 1 abstained, 0 absent) gabapentin enacarbil (Horizant) and gabapentin (Gralise) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

2. ***COMMITTEE ACTION: GABAPENTIN ENACARBIL (HORIZANT) AND GABAPENTIN (GRALISE) PA CRITERIA***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) that both gabapentin enacarbil (Horizant) and gabapentin (Gralise) be designated non-step-preferred, requiring a trial of generic gabapentin in new users. Coverage would be approved if the patient met any of the following step therapy/PA criteria:

    a) Automated PA criteria:

(1) The patient has filled a prescription for gabapentin at any Military Health System (MHS) pharmacy POS [Military Treatment Facilities (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 a contraindication to gabapentin or the formulary non-opioid pain syndrome agents, which is not expected to occur with Horizant or Gralise.

(2) The patient has experienced adverse events (AEs) with gabapentin or the formulary non-opioid pain syndrome agents, which is not expected to occur with Horizant or Gralise.

3. ***COMMITTEE ACTION: MN CRITERIA***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following MN criteria for Horizant and Gralise:

a) The patient has a contraindication to gabapentin or the formulary non-opioid pain syndrome agents.

b) The patient has experienced AE with gabapentin or the formulary non-opioid pain syndrome agents.

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***
The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 30-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is September 19, 2012

V. UF DRUG CLASS REVIEWS

A. Newer Sedative Hypnotics Drugs

Background Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the Newer Sedative Hypnotics (SED-1s), which are used for treating insomnia. The SED-1s class is comprised of the following: zolpidem

immediate-release (IR) (Ambien; generics), zolpidem extended-release (CR) (Ambien CR; generics), zolpidem oral spray (Zolpimist), zolpidem sublingual (SL) (Edluar), eszopiclone (Lunesta), zaleplon (Sonata; generics), ramelteon (Rozerem), and doxepin (Silenor).

A step therapy/PA requirement has been in effect for the SED-1s class since August 2007, requiring that new SED-1s users try the preferred agent, zolpidem IR, before TRICARE® will cover the other agents in this drug class.

Zolpidem oral spray (Zolpimist) is not covered by a written agreement by the manufacturer to honor the pricing standards required by 10 United States Code (U.S.C.) 1074g(f).

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

- The SED-1s all improve sleep latency (onset) compared to placebo. Sleep maintenance is improved with zolpidem IR, zolpidem CR, eszopiclone, and doxepin.
- Based on an indirect comparison, there do not appear to be clinically relevant differences between zolpidem CR and eszopiclone in terms of objective sleep measures.
- Doxepin improves insomnia by improving sleep maintenance; no comparative data exists with other drugs in the class.
- Zolpidem oral spray does not have comparative clinical trials with other SED-1s. FDA approval was granted based on the data originally submitted with Ambien. Zolpimist may pose additional risk for abuse given its dosage form.
- A recently published trial (Kripke, 2012) documented an increased risk of death with insomnia drugs. The interpretation of the results is hampered by several limitations in study design. No further recommendations regarding sedative hypnotic drug prescribing can be made at this time.
- The potential for abuse/misuse exists with the newer sedative hypnotics, with the exception of ramelteon and doxepin.
- The Pharmacy Outcomes Research Team (PORT) presented the results of several analyses assessing the outcomes of step therapy over the last four years. There was a decline in the number of step therapy rejections over time and an increase in utilization of the preferred product, zolpidem IR, suggesting that prescribers were aware of the step therapy requirement. The step therapy requirement did not move market share away from the MTFs, as 26% of the zolpidem IR prescriptions originated from civilian providers.

Relative Cost-Effectiveness Analysis and Conclusion—Pharmacoeconomic analyses were performed for the SED-1s class, including cost minimization analysis (CMA) and budget impact analyses (BIA). The P&T Committee concluded (15 for, 0 against, 0 abstained, 0 absent) zolpidem IR was the least costly agent, followed by zaleplon, zolpidem CR, eszopiclone (Lunesta), doxepin (Silenor), zolpidem SL (Edluar), and ramelteon (Rozerem). BIA results showed minimal differences between scenarios, but the projected budgetary impact in the MHS did vary depending on market movement of zolpidem CR when designated step-preferred versus non-step-preferred, rate of price decline of generic zolpidem CR, and market migration of generic drugs versus branded products.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (12 for, 1 opposed, 2 abstained, 0 absent) the following:

    - zolpidem IR and zaleplon be designated formulary on the UF and step-preferred. This recommendation incorporates step therapy, which requires a trial of zolpidem IR or zaleplon (step-preferred drugs) in new users before use of another SED-1s drug;
    - zolpidem CR, doxepin (Silenor), and eszopiclone (Lunesta) be designated formulary on the UF and non-step-preferred;
    - ramelteon (Rozerem) and zolpidem SL (Edluar) remain NF and non-step-preferred (behind the step);
    - zolpidem oral spray (Zolpimist) is not covered by a written agreement by the manufacturer to honor the pricing standards required by 10 United States Code 1074g(f). Pursuant to 32 Code of Federal Regulations (C.F.R.) 199.21(q)(2)(A), Zolpimist is designated NF.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) zolpidem IR maintain BCF status on the UF.

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to the SED-1s class. Coverage would be approved if the patient met any of the following criteria:

    a) Automated PA criteria: The patient has received a prescription for zolpidem IR or zaleplon at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

    b) Manual (paper) PA criteria, if automated criteria are not met: The patient has had an inadequate response to, been unable to tolerate due to adverse

effects, or has contraindications to zolpidem IR or zaleplon (e.g., hypersensitivity, aberrant behaviors, or intolerable rebound insomnia).

4. ***COMMITTEE ACTION: MN CRITERIA***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) retaining the current MN criteria for zolpidem SL (Edluar) and ramelteon (Rozerem):

   a) The patient has had an inadequate response to, been unable to tolerate due to adverse effects, or has contraindications to zolpidem IR or zaleplon (e.g., hypersensitivity, aberrant behaviors, or intolerable rebound insomnia).

   b) There is no alternative formulary agent. For zolpidem SL (Edluar), the patient is unable to swallow or has swallowing difficulties. For ramelteon (Rozerem), patient requires a non-controlled agent due to potential for abuse and cannot take doxepin (Silenor).

5. ***COMMITTEE ACTION: PRE-AUTHORIZATION AND MN CRITERIA FOR ZOLPIDEM ORAL SPRAY (ZOLPIMIST)***—Pursuant to 32 Code of Federal Regulations (C.F.R.) 199.21(q)(2)(B), the P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following pre-authorization criteria should apply to availability of Zolpimist through retail network pharmacies. Coverage at retail network pharmacies would be approved if the patient met any of the following criteria:

   a) Manual Pre-Authorization Criteria:

      (1) Use of the formulary agent is contraindicated.

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

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

   (b) Medical Necessity Criteria:

      (1) Use of the formulary agent is contraindicated.

6. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD*** The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS. Based on the P&T Committee's recommendation, the effective date is October 17, 2012.

VI. SPECIAL PROGRAM REVIEW

A. Smoking Cessation Program

Background Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the FDA-approved agents for smoking cessation. These agents include: varenicline (Chantix), bupropion SR 150 mg (Zyban), and nicotine, provided in five unique routes of administration (patch, gum, lozenge, nasal spray, and inhaler). Nicotine, via the patch, gum, and lozenge are available over-the-counter but are considered for coverage, by prescription, as part of this program.

Presently, the smoking cessation agents are not part of the TRICARE benefit, but are provided locally at most MTFs. The P&T Committee has not previously reviewed the smoking cessation drugs, as they were excluded from the TRICARE benefit by regulation (32 C.F.R. 199.4(g)(65)). The Duncan Hunter National Defense Authorization Act for Fiscal Year 2009 requires the availability, at no cost to the beneficiary, of pharmaceuticals used for smoking cessation to select beneficiary groups with a limitation on the availability of such pharmaceuticals to the national mail order pharmacy program under the TRICARE program if appropriate. The Proposed Rule has been published in the Federal Register (76 FR 58199), comments have been received, and the Final Rule is pending publication.

The Proposed Rule would limit coverage of smoking cessation products to the MTFs and TRICARE Mail Order Pharmacy POS, and to select beneficiary groups. The Proposed Rule allows two quit attempts, defined as 120-day periods, to be available annually to eligible beneficiaries. Medication coverage for a third attempt may be offered with prior authorization.

Relative Clinical Effectiveness Conclusion—The P&T Committee agreed (15 for, 0 opposed, 0 abstained, 0 absent) to accept the following clinical effectiveness conclusions:

- Varenicline (Chantix), bupropion SR, and nicotine replacement therapy (NRT) are efficacious versus placebo for improving long-term smoking abstinence. There is additive efficacy when the smoking cessation drugs are combined with behavioral therapy.
- For combination therapy, nicotine patch plus gum or nasal spray is the most efficacious smoking cessation therapy. Use of the nasal spray is limited by poor tolerability.
- Varenicline (Chantix) is the most efficacious monotherapy for smoking cessation.
- Safety concerns exist for varenicline (Chantix). Although the available data has limitations in study design and shows conflicting results, overall there appears to

be an association between varenicline and adverse neuropsychiatric events to include behavioral changes, agitation, suicide/suicidal ideation, and depression.

- Caution should be exercised if varenicline is prescribed to patients with active psychiatric comorbidities.
- Varenicline has shown efficacy in patients with cardiovascular (CV) disease and chronic obstructive pulmonary disease. There is conflicting data as to whether varenicline is associated with a higher risk of adverse CV events, including non-fatal myocardial infarction, need for coronary revascularization, hospitalization for angina, and peripheral vascular disease. However, the benefits of smoking cessation with varenicline are felt to outweigh the risks in patients with pre-existing, stable CV disease.
- Varenicline is more efficacious in terms of abstinence at 52 weeks than bupropion SR. Bupropion SR is more efficacious than the NRT patch. There is additive efficacy if bupropion SR is added on to NRT (either gum or patch). However, the combination is no better than bupropion monotherapy if the bupropion is initiated first.
- When varenicline is compared to bupropion SR in randomized, controlled trials, the most commonly reported AEs are nausea (29%), insomnia (14%), abnormal dreams (13%), and headache (13%). The most common AEs with bupropion include insomnia (21%), nausea (7%), and dry mouth (10%).
- Bupropion carries a black box warning for changes in behavior, depressed mood, hostility, and suicidal ideation.
- All smoking cessation drugs show poor rates of compliance in both effectiveness and efficacy trials. Patient preference for a particular medication modality will determine compliance. Long-term abstinence may occur in cases of incomplete compliance. The typical long-term abstainer will make four or more serious quit attempts before finding success.
- Local MTFs remain at liberty to design their own smoking cessation program, defining which elements will be included in that program.

Relative Cost-Effectiveness Analysis and Conclusion—CMA and cost-effectiveness analyses (CEAs) were used to compare the different treatment options for smoking cessation, as efficacy and safety differences between the agents were noted in the clinical review. BIA was also performed to compare several program scenarios. The P&T Committee concluded (15 for, 0 against, 0 abstained, 0 absent) the following:

- CMA results showed that nicotine patch and gum were the least costly products among available NRTs, and bupropion SR was the least costly non-NRT option.

- CEA results demonstrated that, in adult patients who smoke more than 10 cigarettes a day, combination therapy (nicotine patch plus gum) was the most cost-effective treatment for tobacco dependence offering the greatest improvement in rates of long-term smoking abstinence. Although less cost-effective than combination therapy, varenicline was recognized as a cost-effective option when evaluating abstinence rates with monotherapy.
- BIA results showed that inclusion of bupropion SR, varenicline, and nicotine (as patch, gum, lozenge, nasal spray, and inhaler) in the TRICARE Smoking Cessation Program was the most favorable scenario for the MHS.

1. ***COMMITTEE ACTION: COVERAGE RECOMMENDATION***—The P&T Committee recommended (13 for, 1 opposed, 1 abstained, 0 absent) varenicline (Chantix), bupropion SR 150 mg, and nicotine (as patch, gum, lozenge, nasal spray, and inhaler) be covered agents in the TRICARE Smoking Cessation Program, contingent on publication of the Final Rule. No smoking cessation drugs were recommended to be excluded from the program.

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) bupropion SR 150 mg; nicotine patch 7 mg, 14 mg, and 21 mg; and, nicotine gum 2 mg and 4 mg be designated BCF on the UF, contingent on publication of the Final Rule.

3. ***COMMITTEE ACTION: VARENICLINE PA***—The P&T Committee rejected (6 in favor of prior authorization for varenicline, 8 opposed, 1 abstained, 0 absent) the proposal that PA criteria should apply to varenicline (Chantix). PA criteria for varenicline were proposed for safety concerns, primarily neuropsychiatric AEs. While the P&T Committee recognized the potential for safety concerns with varenicline, they also concluded that a PA was not required to ensure safe prescribing with the medication because the risks with varenicline are understood by prescribing providers and can be successfully managed without PA criteria.

4. ***COMMITTEE ACTION: COVERED BENEFICIARY CRITERIA AND PA FOR A 3rd QUIT ATTEMPT***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following coverage criteria should apply to all seven smoking cessation products [varenicline (Chantix), buproprion SR 150 mg, nicotine gum, patch, lozenge, nasal spray, and inhaler], consistent with the requirements in the Proposed Rule, and contingent on publication of the Final Rule. Coverage not approved for patients under the age of 18 or for Medicare-eligible beneficiaries. Coverage for a 3rd quit attempt within one year may be

pre-approved if the provider has verified that the patient would benefit from a 3rd quit attempt.

5. ***COMMITTEE ACTION: QUANTITY LIMITS (QLs)***—The P&T Committee recommended (14 for, 0 opposed, 1 abstain, 0 absent) QLs/days supply limits, restricting the maximum allowable smoking cessation quantity to a 60-day supply per claim at the TRICARE Mail Order POS, with a maximum 240-day supply per rolling 365-day period. Additionally, nicotine gum and nicotine lozenge would be limited to 300 pieces per 60-day claim, rounded to the nearest multiple of the package size (e.g., boxes of 75 or 100). The QL recommendations are contingent on publication of the Final Rule.

6. ***COMMITTEE ACTION: IMPLEMENTATION PERIOD***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in the MTF and mail order POS, following publication of the Final Rule.

VII. ITEMS FOR INFORMATION

A. Weight Loss Drugs Update—Currently C.F.R. 199.4 states that weight loss control medications are not a covered TRICARE pharmacy benefit. A brief overview of weight loss medications was provided, due to increasing awareness by the White House of the childhood obesity epidemic and recent actions by the FDA Endocrinologic and Metabolic Drugs Advisory Committee, which recommended three investigational weight loss drugs for approval. The P&T Committee will review the clinical and cost-effectiveness of the weight loss drugs if the regulation changes.

B. Non-approved drugs—The P&T Committee was briefed on the dispensing of non-FDA-approved drugs from the retail POS and the C.F.R. requirements for TRICARE coverage of prescription medications. Recommendations were made to develop an internal process to identify and review nonapproved products, determine the beneficiary impact of excluding these products, and work with the retail network contractor to potentially exclude coverage of these nonapproved products.

C. Compounded Medications under the TRICARE Benefit—The P&T Committee was briefed on compounded medications dispensed from the retail and mail order POS. MHS expenditures for compounded medications are significant and increasing, and compounded medications have a high potential for inappropriate use. Further updates and initiatives in the area of compounded medications will be provided to the P&T Committee.

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

E. **Prescription Omega-3-Acid Esters (Lovaza) PA Update**—An update on the results of the PA for Lovaza was provided. Since implementation of the PA in July 2011, there was an initial steep decline in the numbers of Lovaza prescriptions filled, which has stabilized.

F. **Renin Angiotension Antihypertensive Agents (RAAs) PA Update**—The P&T Committee was briefed on recent developments in the RAAs class. Two products are now available in generic formulations, eprosartan (Teveten) and irbesartan (Avapro). No recommendations were made to change the existing step therapy/PA. The class is slated for re-review following generic availability of additional proprietary products and publication of updated hypertension guidelines from the National Heart Lung and Blood Institute.

VIII. ADJOURNMENT

The meeting adjourned at 1645 hours on May 16, 2012. The next meeting will be in August 2012.

Appendix A—Attendance: May 2012 P&T Committee Meeting

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

Appendix C—Table of Abbreviations

Appendix A—Attendance: May 2012 P&T Committee Meeting

Voting Members Present	
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
LTC Ricardo Nannini, MSC for COL Carole Labadie, MSC	Army, Pharmacy Officer
Col David Bobb, BSC for Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CAPT Deborah Thompson, USCG	Coast Guard, Pharmacy Officer
CAPT Edward Norton, MSC	Navy, Pharmacy Officer (Pharmacy Consultant BUMED)
Col Lowell Sensintaffer, MC	Air Force, 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
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Major Jeremy King, MC	Air Force, OB/GYN Physician
Mr. Joe Canzolino	U.S. Department of Veterans Affairs
Nonvoting Members Present	
Mr. David Hurt	Associate General Counsel, TMA
LCDR Tiffany Scott	Defense Logistics Agency Troop Support
Guests	
Mr. Bill Davies via DCO	TRICARE Management Activity, Pharmaceutical Operations Directorate
Donna Oetama	University of Incarnate Word, Feik School of Pharmacy
Tuyet Pham	University of Incarnate Word, Feik School of Pharmacy
Kathy Uriarte	University of Incarnate Word, Feik School of Pharmacy

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

Guests	
Tina Christi Lopez	University of Incarnate Word, Feik School of Pharmacy
Others Present	
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
MAJ Misty Cowan, MC	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 via DCO	DoD Pharmacoeconomic Center
LCDR Joshua Devine	DoD Pharmacoeconomic Center
Dr. Dean Valibhai	DoD Pharmacoeconomic Center
Dr. Brian Beck	DoD Pharmacoeconomic Center
Dr. Amy Lugo	DoD Pharmacoeconomic Center
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor
Dr. Bradley Clarkson	Pharmacy Resident
Lt Kellye Donovan	Pharmacy Resident

Appendix B—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
May 2012	**Smoking Cessation Program**	Program Review	**Nicotine Products** OTC Nicotine Transdermal System 7-, 14-, 21mg OTC Nicotine gum 2-, 4 mg **Other FDA-approved Products** Bupropion SR 150 mg	**Covered in the Program (not BCF)** Nicotine Nasal Spray (Nicotrol NS) Nicotine Inhalation (Nicotrol) OTC Nicotine Lozenge Varenicline (Chantix)	None	Pending publication of Final Rule Rule	Quantity limits apply to Nicotine gum and lozenge – 300 pieces/60 days	•OTC nicotine replacement products can be covered and included on the BCF, but require a prescription •2 quit attempts/120 days allowed; 3rd quit attempt requires PA
May 2012	**Newer Sedative Hypnotics (SED-1s)**	UF Class Review	Zolpidem IR Zaleplon	Zolpidem ER Eszopiclone (Lunesta) Doxepin (Silenor)	Rozerem (Ramelteon) Zolpidem sublingual (Edluar)	Pending signing of the minutes/ 60 days	Step therapy (Automated PA); requires trial of zolpidem IR or zaleplon before any other SED-1	Zolpimist not covered

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 2012	**Depression and Non-opioid Pain Syndrome Agents/ GABA analog subclass**	New Drugs in Already Reviewed Class	*SSRIs:* citalopram fluoxetine sertraline *SNRIs:* venlafaxine IR venlafaxine ER *SPARIs:* trazodone *NDRIs:* bupropion HCl IR bupropion HCl SR bupropion HCl ER *GABA analogs:* gabapentin *TCAs:* amitriptyline doxepin imipramine HCl nortriptyline	*SSRIs:* fluvoxamine paroxetine HCl IR paroxetine HCl CR paroxetine mesylate *SNRIs:* venlafaxine ER tablets *SARIs:* nefazodone *TCAs:* desipramine imipramine pamoate protriptyline *A2RAs:* mirtazapine tablets mirtazapine ODT	*SSRIs:* escitalopram (Lexapro) fluoxetine (Sarafem) fluoxetine weekly (Prozac Weekly) *SNRIs:* desvenlafaxine (Pristiq) duloxetine (Cymbalta) milnacipran (Savella) *SARIs:* trazodone ER (Oleptro) vilazodone (Viibryd) *NDRIs:* bupropion HBr (Aplenzin) *GABA analogs:* pregabalin (Lyrica) **gabapentin enacarbil (Horizant)** **gabapentin ER (Gralise)**	Pending signing of the minutes/ 60 days	Step therapy (Automated PA)	For step therapy: Horizant and Gralise are NF and non-step-preferred. All new users of are required to try gabapentin first.

* TRICARE Formulary Search tool: http://www.pec.ha.osd.mil/formulary_search.php

Appendix C—Table of Abbreviations

AEs	adverse events
BCF	Basic Core Formulary
BIA	budget impact analysis
CEA	cost-effectiveness analysis
C.F.R.	Code of Federal Regulations
CMA	cost minimization analysis
CR	controlled release
CV	cardiovascular
DoD	Department of Defense
ER	extended release
FDA	U.S. Food and Drug Administration
FR	Federal Register
IR	immediate release
MHS	Military Health System
MN	medical necessity
MTF	Military Treatment Facility
NDAA	National Defense Authorization Act
NF	nonformulary
NRT	nicotine replacement therapy
P&T	Pharmacy and Therapeutics
PA	prior authorization
PEC	Pharmacoeconomic Center
PORT	Pharmacy Outcomes Research Team
POS	points of service
QLs	quantity limits
RAAs	Renin Angiotensin Antihypertensive Drug Class
RLS	restless leg syndrome
SED-1s	Newer Sedative Hypnotic Drug Class
SL	sublingual
UF	Uniform Formulary
U.S.C.	United States Code
VA	U.S. Department of Veterans Affairs

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% (Lastacaft)

Relative Clinical Effectiveness—Alcaftadine (Lastacaft) 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. Alcafatidine 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, 1abstained, 2 absent) alcaftadine ophthalmic 0.25% solution (Lastacaft) 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, 1abstained, 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 ☐ Disapproved

Approved, but modified as follows:

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 (Juvisync);
- 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 saxagliption 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 of 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 (Juvisync) 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 (Juvisync) 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 Juvisync (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, dexmethylphenidate 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 dexmethylphenidate ER (Focalin XR), dexmethylphenidate 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 dexmethylphenidate 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 AHDH 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:

Drugs designated with formulary status on UF	For	Opposed	Abstain	Absent
Stimulants: 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)	15	1	1	1
Non-Stimulants:* atomoxetine (Strattera) clonidine ER (Kapvay) guanfacine ER (Intuniv)	16	0	1	1
Wakefulness-Promoting Agents: modafinil (Provigil) sodium oxybate (Xyrem)	16	0	1	1

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

Drugs designated with NF status on UF:	For	Opposed	Abstain	Absent
Stimulants: desmethylphenidate ER (Focalin XR) lisdexamphetamine (Vyvanse) methylphenidate transdermal system (Daytrana)	15	1	1	1
Non-Stimulants: None designated NF	16	0	1	1
Wakefulness-PromotingAgents: armodafinil (Nuvigil)	16	0	1	1

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

Drugs approved to move from NF status to Formulary status on UF:	For	Opposed	Abstain	Absent
Stimulants: dexmethylphenidate IR (Focalin, generic)	15	1	1	1

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:

Drugs designated with BCF status:	For	Opposed	Abstain	Absent
Stimulants: mixed amphetamine salts ER (Adderall XR, generic) methylphenidate IR (Ritalin, generic) methylphenidate LA (Ritalin LA, generic)† methylphenidate OROS (Concerta) *Non-stimulants*:* None designated BCF *Wakefulness-Promoting:* None designated BCF	14	2	1	1

† 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 (Catapress, generic) are designated BCF in the Miscellaneous Anti-hypertenisve 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 theADHD stimulants [dexmethylphenidate ER (Focalin XR), lisdexamphetamine (Vyvnase) 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 $BRAF^{V600E}$ 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 $BRAF^{V600E}$ 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 $BRAF^{V600E}$ 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, Elimite, FML, FML Forte, FML S.O.P., Ocufen, Ocuflox, 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

7 May 2012
(Date)

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

Voting Members Present	
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
Nonvoting Members Present	
Mr. David Hurt	Associate General Counsel, TMA
CDR Jay Peloquin	Defense Logistics Agency Troop Support
Guests	
Capt Nita Sood via DCO	Pharmacy Operations Directorate
LCDR Charles McKee	Indian Health Service

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

Guests	
LCDR David Sohl	University of Texas Masters Student
Ms Melanie Richardson via DCO	Pharmacy Operations Directorate
Others Present	
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

	Modafinil (Provigil)	Armodafinil (Nuvigil)	Sodium Oxybate (Xyrem)
Prior Authorization	Coverage provided for the treatment of: ▪ Excessive daytime sleepiness associated with narcolepsy, as diagnosed by polysomnogram or MSLT objective testing ▪ Excessive daytime sleepiness associated with OSAHS, only after adequate titration of CPAP treatment ▪ Excessive sleepiness associated with SWSD, only in patients who work night shifts ▪ Excessive fatigue associated with multiple sclerosis, only after secondary causes of fatigue have been addressed ▪ Excessive fatigue associated with myotonic dystrophy ▪ Depression, only after primary therapy has failed and if the use of other stimulant augmentation is contraindicated ▪ Idiopathic hypersomnia diagnosed by a sleep specialist ▪ Fatigue associated with traumatic brain injury Coverage NOT provided for the treatment of other conditions not listed above, including the following: ▪ Chronic fatigue syndrome ▪ Stroke rehabilitation ▪ Appetite suppression ▪ Parkinson's disease	Coverage provided for the treatment of: ▪ Excessive daytime sleepiness associated with narcolepsy, as diagnosed by polysomnogram or MSLT objective testing ▪ Excessive daytime sleepiness associated with OSAHS, only after adequate titration of CPAP treatment ▪ Excessive sleepiness associated with SWSD, only in patients who work night shifts Coverage NOT provided for the treatment of other conditions not listed above, including the following: ▪ Jet lag ▪ Excessive fatigue associated with multiple sclerosis ▪ Excessive fatigue associated with myotonic dystrophy ▪ Depression ▪ Idiopathic hypersomnia ▪ Fatigue associated with traumatic brain injury ▪ Chronic fatigue syndrome ▪ Stroke rehabilitation ▪ Appetite suppression ▪ Parkinson's disease	Coverage provided for the treatment of: ▪ Treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy, diagnosed by polysomnogram and MSLT ▪ Excessive sleepiness associated with narcolepsy without cataplexy, if the patient has previously tried modafinil (Provigil) Coverage NOT provided for the treatment of other conditions not listed above or any non-FDA approved use, including the following: ▪ Fibromyalgia ▪ Insomnia ▪ Excessive sleepiness not associated with narcolapsy

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
Saxagliptin (Onglyza) Saxagliptin/Metformin ER (Kombiglyze XR) **Non-insulin Diabetes Drugs: DPP-4 Inhibitors**	• Use of formulary DPP-4 agents contraindicated • The patient has experienced or is likely to experience significant adverse effects from formulary DPP-4 inhibitors
Dexmethylphenidate ER (Focalin XR) Lisdexamphetamine (Vyvanse) Methylphenidate transdermal (Daytrana) **ADHD/Wakefulness-Promoting Drugs: Stimulants Subclass**	No change from previous MN criteria • Use of formulary ADHD stimulants is contraindicated • The patient has experienced significant adverse effects from formulary ADHD stimulants • Use of the formulary stimulants has resulted in therapeutic failure • For Daytrana: No alternative formulary agent available—the patient is unable to take oral medications
Armodafinil (Nuvigil) **ADHD/Wakefulness-Promoting Drugs: Wakefulness-Promoting Subclass**	• Use of modafinil (Provigil) is contraindicated

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	**Antiplatelet Agents**	UF Class Review	▪ Clopidogrel (Plavix)	▪ Prasugrel (Effient) ▪ Ticagrelor (Brilinta) ▪ Aspirin/dipyridamole ER (Aggrenox) ▪ Ticlopidine (Ticlid, generics) ▪ Cilostazol (Pletal), generics) ▪ Dipyridamole (Persantine, generics) ▪ Pentoxifylline (Trental, generics)	▪ - Not applicable (no drug designated nonformulary)	Pending signing of minutes/ 60 days	Not applicable	▪ Clopidogrel remains BCF
Feb 2012	**Non-Insulin Diabetes Drugs** **DPP-4 Inhibitors**	UF Class Review	▪ Sitagliptin (Januvia) ▪ Sitagliptin/Metformin (Janumet)	▪ Sitagliptin/Simvastatin (Juvisync) ▪ Linagliptin (Tradjenta)	▪ Saxagliptin (Onglyza) ▪ Saxagliptin/Metformin ER (Kombiglyze XR)	Pending 60 days	Step therapy required – see comments	▪ Must try metformin and sulfonylurea 1st before any DPP-4 drug ▪ Must try sitagliptin-containing product 1st before Onglyza, Kombiglyze XR, and Tradjenta
Feb 2012	**ADHD / Wakefulness-Promoting Drugs** **Wakefulness-Promoting Drugs**	UF Class Review	▪ Not applicable	▪ Modafinil (Provigil) ▪ Sodium oxybate (Xyrem) – restricted distribution	▪ Armodafinil (Nuvigil)	Pending 60 days	PA required – see comments	▪ All current and new users of Nuvigil must go through PA process

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	**ADHD / Wakefulness-Promoting Drugs** **ADHD Stimulants**	UF Class Review	**Long-acting stimulants** ▪ Mixed amphetamine salts ER (Adderall XR generics) ▪ Methylphenidate LA (Ritalin LA, generic) ▪ Methylphenidate OROS (Concerta **Short-acting stimulants** ▪ Methylphenidate IR (Ritalin, generic)	**Short-acting stimulants** ▪ Mixed amphetamine salts IR (Adderall, generic) ▪ Dexmethylphenidate IR (Focalin, generic) ▪ Dextroamphetamine (Dexedrine, Dextrostat, Procentra solution) ▪ Methylphenidate CD (Metadate CD) ▪ Methylphenidate ER (Metadate ER, Methylin ER, generic) ▪ Methylphenidate chewable tablets, solution (Methylin, generic) ▪ Methylphenidate SR (Ritalin SR, generic) ▪ Methamphetamine HCl (Desoxyn)	**Long-acting stimulants** ▪ Dexmethylphenidate ER (Focalin XR) ▪ Lisdexamphetamine (Vyvanse) ▪ Methylphenidate transdermal system (Daytrana)	Pending 60 days	Not applicable	▪ Ritalin LA now BCF
Feb 2012	**ADHD / Wakefulness-Promoting Drugs** **ADHD Non-Stimulants**	UF Class Review	▪ Not applicable	▪ Atomoxetine (Strattera) ▪ Clonidine ER (Kapvay) ▪ Guanfacine ER (Intuniv)	▪ Not applicable (no nonformulary drugs)	Pending 60 days	Not applicable	▪ Clonidine IR tabs are BCF ▪ Clonidine Patches and guanfacine IR (Tenex, generic are UF) in Misc Anti-hypertensive Drug 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	Comments
Feb 2012	**Ophthalmic-1**	New Drug Review	Antihistamine/Mast Cell Stabilizers ▪ Olopatadine 0.1% (Patanol) (Aug 2010)	▪ **Alcafatinde 0.25% (Lastacaft) (Feb 2012)** August 2010 Dual Action Antihistamine/ Mast Cell Stabilizers ▪ Bepotastine (Bepreve) ▪ Olopatadine 0.2% (Pataday) ▪ Azelastine (Optivar, generics) ▪ Epinastine (Elestat) Antihistamines ▪ Emedastine (Emadine) Mast Cell Stabilizers ▪ Pemirolast (Alamast) ▪ Nedocromil (Alocril) ▪ Cromolyn (Crolom/Opticrom, generic) ▪ Lodoxamide (Alomide) NSAIDs ▪ Ketorolac 0.4% (Acular LS, generic) ▪ Ketorolac 0.45% (Acuvail) ▪ Ketorolac 0.5% (Acular, generic) ▪ Bromfenac (Xibrom) ▪ Bromfenac 0.9% (Bromday) ▪ Diclofenac (Voltaren, generic) ▪ Flurbiprofen (Ocufen, generics ▪ Nepafenac (Nevanac)	August 2010 ▪ Not applicable (no drug designated nonformulary)	Pending signing of minutes/ 60 days	Not applicable	▪ Ketotifen (Zaditor, generics) is available OTC

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	**Narcotic Analgesics** **Subclass: High potency single analgesic agents**	New Drug Review	High potency single analgesic agents ▪ Morphine sulfate 12 hours ER (MS Contin, generics) ▪ Morphine sulfate IR	▪ **Tapentadol extended release (Nucynta ER) (Feb 2012)** Previous Decisions ▪ Hydromorphone ER (Exalgo) ▪ Fentanyl buccal soluble film (Onsolis) ▪ Fentanyl transdermal system, transmucosal tablet (Fentora); & transmucosal lozenge ▪ 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) ▪ Oxymorphone ER (Opana ER)	▪ Tapentadol immediate release (Nucynta) (Nov 2009)	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

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