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