DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS
August 2010

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on August 11, and 12, 2010, at the DoD Pharmacoeconomic Center (PEC), Fort Sam Houston, Texas.

II. ATTENDANCE

The attendance roster is found in Appendix A.

A. Review Minutes of Last Meetings

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

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

III. UNIFORM FORMULARY (UF) DRUG CLASS REVIEWS

A. Renin Angiotensin Antihypertensive Agents (RAAs)

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

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

The individual RAAs are listed below:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Acting Director, TMA, Decision: ☒ Approved ☐ Disapproved

11/10/10

Approved, but modified as follows:

2. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 2 absent) the following PA criteria should apply to the non-preferred RAAs, aliskiren (Tekturna), aliskiren/HCTZ (Tekturna HCT), aliskiren/valsartan (Valturna), candesartan (Atacand), candesartan/HCTZ (Atacand HCT), eprosartan (Teveten), eprosartan/HCTZ (Teveten HCT), irbesartan (Avapro), irbesartan/HCTZ (Avalide), olmesartan (Benicar), olmesartan/HCTZ (Benicar HCT), and olmesartan/amlodipine (Azor). Coverage would be approved if the patient met any of the following criteria:

   a) Automated PA criteria:

      (1) The patient has received a prescription for losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT) telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), or valsartan/amlodipine/HCTZ (Exforge HCT) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

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

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

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

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

11/10/10

Approved, but modified as follows:

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

Acting Director, TMA, Decision: ☒ Approved □ Disapproved

11/8/10

Approved, but modified as follows

4. ***COMMITTEE ACTION: BCF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended:
    a) losartan, losartan HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), valsartan (Diovan), valsartan/HCTZ (Diovan HCT) be designated with BCF status (15 for, 0 opposed, 1 abstained, 0 absent);
    b) captopril, benazepril/amlodipine (Lotrel generics), lisinopril, lisinopril HCTZ, ramipril remain on the BCF (15 for, 0 opposed, 1 abstained, 0 absent).

Acting Director, TMA, Decision: ☒ Approved □ Disapproved

11/8/10

Approved, but modified as follows:

B. Ophthalmic-1s

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

The individual Ophthalmic-1s are listed below:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Approved, but modified as follows:

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

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

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

Approved, but modified as follows:

IV. UTILIZATION MANAGEMENT—QUANTITY LIMITS (QL)

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

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

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

Approved, but modified as follows:

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

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

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

Approved, but modified as follows:

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

1. ***COMMITTEE ACTION: QL***—The P&T Committee voted (15 for, 0 opposed, 1 abstained, 0 absent) to recommend QLs for certolizumab pegol of 1 kit (6 syringes) with no refills in the mail order pharmacy and 1 kit (6 syringes) with no refills in the retail network, which is consistent with the recommended dosing from the product labeling and avoids breaking apart packages.

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

Approved, but modified as follows:

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

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

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

Approved, but modified as follows:

V. ITEMS FOR INFORMATION

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

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

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

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

VI. CLASS OVERVIEWS

Overviews for two drug classes were presented to the P&T Committee. The inflammatory bowel disease/irritable bowel syndrome drug class is comprised of the 5-aminosalicylates, gastrointestinal steroids, and the 5-HT3 antagonists. The pancreatic enzymes were also reviewed. The P&T Committee provided expert opinion regarding those clinical outcomes considered most important for the PEC to use in completing the clinical effectiveness reviews and developing the appropriate cost-effectiveness models. The clinical and economic analyses of these classes will be presented at an upcoming meeting.

VII. ADJOURNMENT

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

Appendix A—Attendance

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

Appendix C—Table of Abbreviations

SUBMITTED BY:

Actual Signing date was 8 NOV 2010

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

DECISION ON RECOMMENDATIONS

Director, TMA, decisions are as annotated above.

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

11/18/2010
(Date)

Appendix A—Attendance

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

Appendix A—Attendance (continued)

Others Present	
COL Cynthia Clagett	DoD Pharmacoeconomic Center
Lt Col Rey Morales	DoD Pharmacoeconomic Center
Lt Col Cynthia Lee, BSC	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
LCDR Ola Ojo	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Eugene Moore	DoD Pharmacoeconomic Center
Dr. Angela Allerman	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe	DoD Pharmacoeconomic Center
Dr. Jeremy Briggs	DoD Pharmacoeconomic Center
Dr. Brian Beck	DoD Pharmacoeconomic Center
Dr. Amy Lugo	DoD Pharmacoeconomic Center
Dr. Dean Valibhai	DoD Pharmacy Operations Center contractor
Mr. Stephen Yarger	DoD Pharmacy Outcomes Research Team contractor
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor

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

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

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

Date	DoD PEC Drug Class	Type of Action*	BCF/ECF Medications MTFs must have BCF meds on formulary	UF Medications MTFs may have on formulary	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Comments
May 2010	Alpha Blockers for BPH	UF Review	▪ Alfuzosin (Uroxatral) ▪ Tamsulosin (Flomax, generics) ▪ Terazosin (Hytrin; generics)	▪ Doxazosin IR (Cardura; generics)	▪ Silodosin (Rapaflo) ▪ Doxazosin ER (Cardura XL)	Pending 60 days	Step therapy (Automated PA)	Step therapy (automated PA) with tamsulosin (Flomax, generics) or alfuzosin as the preferred agents (note: step- therapy does not apply to terazosin, doxazosin, or doxazosin ER)

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

Appendix C—Table of Abbreviations

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