DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS
November 2011

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on November 9, 2011, 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**—Jonathan Woodson M.D., Director, approved the minutes for the August 2011 DoD P&T Committee meeting on October 27, 2011.
2. **Correction of May 2011 Minutes—BCF Clarification for Risperidone:** The May 2011 P&T Committee minutes were clarified to state the BCF listing for risperidone is for the oral tablets, and does not include the orally disintegrating tablets (ODT). Risperidone orally disintegrating tablets are included on the Uniform Formulary (UF).

B. Follow-up to September Beneficiary Advisory Panel Meeting

1. A letter from a beneficiary regarding PDE-5 inhibitors was read publicly at the meeting and acknowledged by the P&T Committee.

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).

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

A. Osteoporosis Drugs—Risedronate Delayed Release (Atelvia)

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of a newly approved bisphosphonate, risedronate delayed release (DR) tablets (Atelvia). It is only approved for the treatment of postmenopausal osteoporosis. Risedronate is also available in an immediate release (IR) formulation, under the trade name Actonel, which has other FDA indications in addition to postmenopausal osteoporosis. Generic formulations of risedronate IR are expected in 2012. The

osteoporosis drug class, which includes the bisphosphonates, was reviewed for UF placement in June 2008.

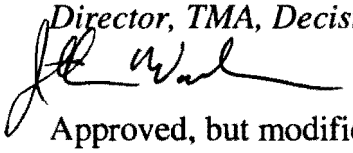
Atelvia was developed to allow coadministration with food, and it is administered immediately after breakfast. Other oral bisphosphonates (alendronate, ibandronate, risedronate IR) require administration with water 30–60 minutes in the morning prior to breakfast. Clinical trials with Atelvia have only evaluated changes in bone mineral density; there are no studies assessing Atelvia's affect on outcomes of fracture prevention.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) risedronate DR (Atelvia) offers some convenience to the patients in terms of administration schedule, but there are no studies assessing patient compliance, and it has limited clinical trial data and safety information compared to risedronate IR (Actonel). Alternative treatments are available for patients who cannot comply with the administration schedule of the other oral bisphosphonates.

Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion—Cost-minimization analysis (CMA) was performed. Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) Atelvia was more costly when compared to other bisphosphonates on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors the P&T Committee, based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) risedronate DR (Atelvia) be designated nonformulary (NF) .

Director, TMA, Decision: ☒Approved ☐ Disapproved



Approved, but modified as follows:

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

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: MN IMPLEMENTATION PERIOD***—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service. Based on the P&T Committee's recommendation, the effective date is April 18, 2012.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

V. UF DRUG CLASS REVIEWS

A. Depression and Non-Opioid Pain Syndrome Agents

Background Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the Depression and Non-Opioid Pain Syndrome Drug Class. The class is comprised of the former UF Antidepressants-1 (AD-1s) Drug Class [selective serotonin reuptake inhibitors (SSRIs), selective serotonin/norepinephrine reuptake inhibitors (SNRIs), serotonin antagonist reuptake inhibitors (SARIs), norepinephrine/dopamine reuptake inhibitors (NDRIs), alpha-2 receptor antagonists (A2RAs), serotonin partial agonist/reuptake inhibitors (SPARIs)]; the gamma-aminobutyric acid (GABA) analogs; and the tricyclic antidepressants (TCAs). Military Health System (MHS) expenditures for the Depression and Non-Opioid Pain Syndrome Drug Class exceed $490 million annually.

The class as a whole has not been previously reviewed; however, the AD-1s were reviewed in November 2005, and the GABA analogs were reviewed in February 2006. The drugs in this class are:

- SSRIs: citalopram, escitalopram (Lexapro), fluoxetine, fluoxetine 90 mg weekly regimen (Prozac Weekly), fluoxetine in special packaging (Sarafem), fluvoxamine, paroxetine hydrochloride (HCl) IR, paroxetine HCl controlled release (CR), paroxetine mesylate (Pexeva), sertraline

- SNRIs: duloxetine (Cymbalta), desvenlafaxine (Pristiq), milnacipran (Savella), venlafaxine IR, venlafaxine extended release (ER) capsules, venlafaxine ER tablets
- SARIs: nefazodone, trazodone IR, trazodone ER (Oleptro)
- NDRIs: bupropion HCl IR, bupropion HCl SR, bupropion ER, bupropion hydrobromide (HBr) (Aplenzin)
- A2RAs: mirtazapine tablets, mirtazapine ODT
- SPARIs: vilazodone (Viibryd)
- GABAs: gabapentin, pregabalin (Lyrica)
- TCAs: amitriptyline, desipramine, doxepin, imipramine HCl, imipramine pamoate, nortriptyline, protriptyline

The two newest entrants to the class are trazodone ER (Oleptro) and vilazodone (Viibryd). Two new gabapentin formulations have been approved by the FDA, gabapentin ER (Gralise) and gabapentin encarbil ER (Horizant), but will be reviewed at an upcoming DoD P&T Committee meeting.

For the clinical and cost effectiveness reviews, the Depression and Non-Opioid Pain Syndrome drugs were also evaluated in relation to the skeletal muscle relaxant cyclobenzaprine, and the monoamine oxidase inhibitors (MAOIs), when appropriate.

In order to support the clinical and cost-effectiveness evaluations in this complex class, the Pharmacy Outcomes Research Team (PORT) analyzed prior use of agents in this class among DoD beneficiaries initiating treatment with desvenlafaxine, duloxetine, milnacipran, or pregabalin between April 1, 2011, and June 30, 2011. A total of 135,402 new users (defined as no use of the index medication during the prior 180 days) of one of these four agents were included in the analysis.

The four study medications (desvenlafaxine, duloxetine, milnacipran, pregabalin) were chosen for analysis based on both clinical and economic considerations: all four are widely used or have potential for wide use, have alternatives that offer equal or greater clinical value, and offer the potential for minimizing costs with neutral or beneficial effects on patient outcomes. The analysis was undertaken to estimate new user rates, understand prescribing patterns, and to assess the number of beneficiaries likely to be affected by step therapy programs involving these agents.

Drugs in the class were divided into three groups (with some overlap) for purposes of the analysis:

- Group A (the four study medications): desvenlafaxine, duloxetine, milnacipran, pregabalin;
- Group B (medications used for depression): SSRIS, SNRIs (except milnacipran), TCAs, mirtazapine, bupropion, SARIs, MAOIs; and

- Group C (medications used for non-opioid pain syndromes): SNRIs including milnacipran, TCAs, cyclobenzaprine, GABA analogs (gabapentin and pregabalin).

For purposes of estimating the potential impact of step therapy programs for each of these agents, the "step-preferred" agents (medications that must be tried prior to receiving the study medication) were defined based on clinical considerations, available alternatives, and patterns of prior use.

- Desvenlafaxine is the active metabolite of venlafaxine. For the majority of patients, it offers no clinical advantage compared to the parent compound. Of 15,009 patients for whom desvenlafaxine was the index medication, only about 20% (3,057 patients) were new users; of these, 10% (299 patients) had received a previous prescription for venlafaxine. Looking back 2 years, desvenlafaxine was the first SNRI (venlafaxine, desvenlafaxine, or duloxetine) in 73% of patients, and the first medication for depression (Group B) medication in 25%. About ~11,000 new users annually could be affected by a requirement to try venlafaxine before desvenlafaxine.

- Duloxetine is an SNRI used both for depression and non-opioid pain syndromes, including fibromyalgia. Due to the complexity of depression and non-opioid pain treatment pathways and technical considerations of the step therapy look-back period, a conservative approach was taken with regard to step therapy requirements: the only patients affected are those for whom duloxetine is the first Group B or Group C medication prescribed in the last 180 days. Of 67,375 patients with duloxetine as their index medication, about 18% were new users. Of these, 64% had either a Group B or C medication. This leaves 36% of all new duloxetine users who would potentially be affected by a step therapy program that requires trial of any other Group B or C medication prior to receiving duloxetine.

- Milnacipran is an SNRI; however, in the United States it is indicated only for fibromyalgia. Accordingly, milnacipran was compared to the Group C medications, which includes other medications used for fibromyalgia. Of the 4,536 patients with milnacipran as their index medication, 26% were new users (no milnacipran in the last 180 days). Of these, 58% had a Group C medication in the last 180 days, leaving 42% of new milnacipran users who would potentially be affected by a step therapy program that requires a trial of any other Group C medication prior to receiving milnacipran.

- Pregabalin is a GABA analog similar to gabapentin, which is generically available. Both are used for neuropathic pain syndromes; there is little

clinical evidence to support a substantial difference in efficacy or safety between the two. Of 48,482 patients with pregabalin as their index medication, about 23% were new users (no pregabalin in the last 180 days). Of these, only 24% had a gabapentin Rx in the last 180 days, leaving 76% of new pregabalin users who would potentially be affected by a step therapy program that requires a trial of gabapentin prior to receiving pregabalin.

Relative Clinical Effectiveness Conclusion

1. The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 1 absent) upon the following conclusions regarding drugs used for depression, anxiety and other disorders (SSRIs, SNRIs, SARIs, NDRIs, A2RAs, SPARIs):
    - There are no compelling differences in efficacy to clearly differentiate one agent over the others.
    - High nonresponder rates in major depressive disorder (MDD) and anxiety disorders for each of the agents necessitate including a variety of agents on the UF.
    - Fluoxetine, and possibly escitalopram, are the only agents found to have a favorable risk to benefit profile in the treatment of MDD in children and adolescents.
    - Trials with duloxetine show no differences in efficacy with the comparator agents (fluoxetine, paroxetine, and venlafaxine), despite maximal doses of duloxetine and submaximal doses of the comparators.
    - Vilazodone is efficacious versus placebo for the treatment of MDD. Its unique mix of receptors may be beneficial to some patients. There are no head-to-head trials comparing vilazodone efficacy to other antidepressant agents and long-term data is limited.
    - Trazodone ER is efficacious versus placebo for the treatment of MDD. The effect appears to be heavily influenced by its sedating properties.
    - Mirtazapine consistently demonstrates the most rapid onset of action.
    - Beyond the FDA-indications, there is insufficient evidence to draw conclusions regarding the comparative efficacy of the antidepressants with respect to generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, or post-traumatic stress disorder.

- There is a high degree of therapeutic interchangeability for the majority of the antidepressants, when used for MDD.
- Discontinuation rates due to adverse events (AEs) are similar between agents.
- There is wide variation in the specific AE profiles of the antidepressant agents, which is due to their differences in receptor binding properties.
- Factors including activation/sedation properties, weight changes, sexual dysfunction, drug interactions (most commonly based on protein-binding, cytochrome P-450 CYP isoenzyme induction/inhibition), or therapeutic duplication may guide treatment decisions in individual patients.
- Rare serious AEs for mirtazapine, nefazodone, and trazodone typically limit these drugs to second-line status.
- Minor differences in other factors including different salt forms (HCl versus HBr), delivery mechanisms (IR versus ER), or active metabolites of the parent compound (desvenlafaxine versus venlafaxine) may reduce the number of drugs with the same active ingredient that are required for inclusion on the UF.

2. The P&T Committee agreed (18 for, 0 opposed, 0 abstained, 0 absent) upon the following conclusions regarding drugs used for non-opioid pain syndromes.
    - No published, direct head-to-head studies are available that compare duloxetine, milnacipran, and pregabalin for the treatment of diabetic peripheral neuropathy (DPN), fibromyalgia (FM), or post-herpetic neuralgia (PHN). Meta-analyses and systematic reviews are the primary sources for data analysis among agents.
    - Definitive statements about comparative clinical effectiveness between duloxetine and pregabalin are difficult to make given the lack of head-to-head studies.
    - The TCAs (particularly amitriptyline) and cyclobenzaprine have substantial data supporting their use, at low doses, in several pain syndromes, and are supported as first-line therapy by many clinical practice guidelines.
    - *Fibromyalgia:*
        - A meta-analysis published in JAMA 2009 concluded the following:

        - There is strong evidence for the efficacy of antidepressants (TCAs, SNRIs, SSRIs, MAOIs) in the treatment of FM.
        - Antidepressants were shown to decrease pain, sleep disturbance, and depressed mood and improve HRQoL. The effect sizes were smaller for SNRIs, SSRIs, and MAOIs than for TCAs. There is strong evidence against a favorable effect of antidepressants on improving fatigue.
    - A systematic review from the Oregon Drug Effectiveness Review Project (DERP) showed the following:
        - Paroxetine IR was superior to the TCA amitriptyline in decreasing pain and sleep disturbance in one head-to-head study.
        - Amitriptyline was similar to duloxetine, milnacipran, and pregabalin on outcomes of relieving pain and fatigue. There was insufficient data on other outcomes (changes in patient rating scales) to compare the drugs.
        - Milnacipran was inferior to duloxetine on outcomes of pain, depressed mood, and health-related quality of life (HRQoL), and inferior to both duloxetine and pregabalin on improving sleep disturbance.
        - Duloxetine was not effective in reducing pain in male, nonwhite, and older patients.
    - In a meta-analysis by Straube and colleagues, 24% of FM patients taking pregabalin at higher doses (450mg–600mg) obtained at least 50% pain relief based on the patient global impression of change rating scale. The pregabalin dose-response relationship for efficacy in FM was not as striking as that seen in other conditions.
- *Post-Herpetic Neuralgia*: According to the PLoS Medicine systematic review (2005), there is evidence of analgesic efficacy (number needed to treat < 5.0) in PHN for TCAs, opioids, gabapentin, tramadol, and pregabalin.
- *Chronic Low Back Pain* (CLBP):
    - Duloxetine has received an indication for chronic musculoskeletal pain based on studies in CLBP and osteoarthritis of the knee. Duloxetine should not be used first line for CLBP. Acetaminophen, NSAIDs, and a trial of a

TCA should be used prior to use of duloxetine for this indication.

- In the clinical trials used to obtain FDA approval for CLBP, half of the patients treated with duloxetine achieved at least a 30% improvement in pain, which is statistically significant but not clinically significant. There is a significant placebo response (~ 40%) compared to duloxetine when used for CLBP.
- Treating 5–8 patients with duloxetine resulted in modest improvement in pain (a minimally perceptible difference) in one patient treated for 13 weeks.

- *Phantom Limb Pain*
  - Only limited information is available. Current VA/DoD guidelines recommend pregabalin, gabapentin, antidepressants (e.g., SSRIs, or TCAs).
  - Two small trials (<45 patients) reported in the DERP review showed a moderate benefit with gabapentin compared to placebo.
  - There is no published data with pregabalin and a clinical trial with duloxetine was terminated early.
- Safety and Tolerability
  - Duloxetine: An additional safety warning exists regarding use in patients with hepatic impairment. Withdrawals due to AEs occurred more often with duloxetine (15%) than placebo (8%). Duloxetine is more likely to cause nausea, somnolence, constipation, and decreased appetite versus placebo.
  - Pregabalin is similar to gabapentin in AEs, although more peripheral edema and weight gain are likely with pregabalin compared to gabapentin. Pregabalin causes more dizziness and somnolence compared to placebo.
  - For both duloxetine and pregabalin, more patients with neuropathic pain discontinue taking the active drug compared with placebo.
  - Titration and tapering is required with all of the agents.
- Other factors that differentiate the drugs: Duloxetine is dosed once daily and its patent is expected to expire December 2013; pregabalin is dosed three times daily and is a controlled medication. All agents

must be dosed based on either renal or hepatic concerns. Most pharmacy benefit managers have some form of restriction in place for duloxetine, milnacipran and pregabalin.

3. The P&T Committee agreed (18 for, 0 opposed, 0 abstained, 0 absent) upon the following conclusions regarding the TCAs:
    - *Depression*
        - In the primary care setting, based on one meta-analysis (McGillivray), there was a trend in favor of TCAs over SSRIs, although the p-value was not significant in terms of the weighted mean difference in depression scores. There was no significant difference between TCAs and SSRIs in terms of improvement in the Clinical Global Impression (CGI) scale.
        - Another meta-analysis (Arroll) showed that there were no apparent differences between SSRIs and TCAs in terms of an indirect comparison of the CGI, as the relative risks versus placebo were similar (1.37 with SSRIs versus 1.26 with TCAs) and the confidence intervals overlapped.
        - Use of TCAs for depression has largely been replaced by the SSRIs and SNRIs due to safety issues.
    - *DPN*: One meta-analysis (Wong) showed TCAs were significantly more effective than placebo in terms of the odds ratio for 50% decrease in pain over 3–6 weeks.
    - *Fibromyalgia*: The JAMA meta-analysis showed TCAs have large effect sizes for reducing pain, fatigue, and sleep disturbances compared to SSRIs, SNRIs, and MAOIs. There were no significant differences when amitriptyline was compared with cyclobenzaprine and nortriptyline in the DERP review.
    - *PHN*: TCAs are significantly more effective than placebo.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the depression and non-opioid pain syndrome agents. Based on the clinical findings regarding efficacy, safety, tolerability, other factors, and clinical outcomes with these agents, CMAs were performed to compare individual agents as well as combinations of these agents primarily used in the treatment of depression, non-opioid pain syndromes, or both. Budget impact analyses (BIAs) were also performed to compare competing formulary scenarios in the evaluation of the cost-effectiveness of the various groupings of these agents. Various scenarios incorporating step therapy were also evaluated, based on clinical

considerations, available alternatives, and patterns of prior use derived from the PORT analysis outlined above.

Depression Analysis: One analysis evaluated the drugs for depression, including the SSRIs, NDRIs, and the SARIs. The cost of these agents was compared across therapeutic classes in a CMA. The A2RAs, SPARIs, and TCAs were also included in this CMA.

Depression Analysis—desvenlafaxine (Pristiq) versus venlafaxine: The SNRIs (desvenlafaxine and venlafaxine) were also modeled individually in a CMA and BIA to evaluate use of step therapy, where a trial of venlafaxine would be required for new users of desvenlafaxine.

Non-Opioid Pain Syndromes Analysis—pregabalin (Lyrica) versus gabapentin: This analysis included the GABA analogs, pregabalin, and gabapentin. The cost-effectiveness of pregabalin (Lyrica) versus gabapentin was determined in a CMA and BIA to evaluate use of step therapy, where a trial of gabapentin would be required for new users of pregabalin.

Depression and Non-Opioid Pain Syndromes Analysis—duloxetine (Cymbalta) and milnacipran (Savella): CMA and BIA were used to evaluate the cost-effectiveness of duloxetine and milnacipran. The combined depression and non-opioid pain syndromes analyses were grouped into the same categories outlined in the PORT analysis. The depression analysis group ("Group B drugs") included the SSRIs, SNRIs (except milnacipran), TCAs, mirtazapine, bupropion, SARIs, and MAOIs. The non-opioid pain syndrome analysis group ("Group C drugs") included the SNRIs (with milnacipran), TCAs, cyclobenzaprine, and GABA analogs (gabapentin and pregabalin). The final analysis compared the depression and non-opioid pain syndrome drugs together. Costs for each of the subgroups, along with the individual weighted average costs for duloxetine and milnacipran, were used in the CMAs and BIAs to evaluate various step therapy scenarios for the drugs of interest: duloxetine (Cymbalta) versus the depression and non-opioid pain syndrome drugs, and milnacipran (Savella) versus the non-opioid pain syndrome drugs.

Relative Cost-Effectiveness Conclusion—Based on the results of the economic analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 against, 0 abstained, 0 absent) the following for the depression and/or non-opioid pain syndrome agents:

Depression Analysis: CMA results for the depression drugs [SSRIs, SARIs, NDRIs, A2RAs, SPARIs, TCAs, and MAOIs, (not including the SNRIs)], showed the following ranking, from least costly to most costly: SARIs (predominantly generic trazodone) <TCAs < A2RAs < SSRIs (using current prices for escitalopram) < NDRIs < MAOIs < SPARIs. When looking specifically at new entrants to the class, trazodone ER (Oleptro) and vilazodone (Viibryd) were less cost-effective than other antidepressants.

The same is true of bupropion HBr (Aplenzin). Several current NF antidepressants are now available or are expected to become available in cost-effective generic formulations, including escitalopram (Lexapro), fluoxetine in special packaging (Sarafem), fluoxetine weekly (Prozac weekly), and paroxetine CR (Paxil CR).

Desvenlafaxine (Pristiq) versus venlafaxine: CMA results for desvenlafaxine and venlafaxine versus the other depression drugs showed SARIs, TCAs, A2RAs, SSRIs, and NDRIs to be less costly than the SNRIs. Among the SNRIs, venlafaxine was more cost-effective than desvenlafaxine, based on cost per day of treatment. BIA was used to assess the potential impact of cost scenarios where selected agents 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 was venlafaxine IR/ER as step-preferred on the UF/BCF, with desvenlafaxine (Pristiq) designated NF and non-step-preferred; a trial of venlafaxine IR/ER would be required for new users of desvenlafaxine. Cost-effective generic formulations of venlafaxine ER capsules are now available.

Non-Opioid Pain Syndromes Analysis and pregabalin (Lyrica) versus gabapentin: CMA results specifically focusing on pregabalin (Lyrica) versus gabapentin for non-opioid pain syndromes showed that TCAs and cyclobenzaprine, which are predominantly generic were less costly than the GABA analogs. Among the GABA analogs, gabapentin was more cost-effective than pregabalin (Lyrica), based on the cost per day of treatment between these two agents. BIA was used to assess the potential impact of cost scenarios where selected agents 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 was gabapentin as step-preferred on the UF/BCF, with pregabalin (Lyrica) designated NF and non-step-preferred; a trial of gabapentin would be required for new users of pregabalin.

Depression and Non-Opioid Pain Syndromes Analysis and duloxetine (Cymbalta) and milnacipran (Savella): CMA results specifically focused on duloxetine (Cymbalta) versus all depression and non-opioid pain syndrome drugs (Groups B and C drugs), and milnacipran (Savella) versus all non-opioid pain syndrome drugs (Group C drugs). CMA results showed that generic SSRIs, SNRIs, SARIs, NDRIs, A2RAs, SPARIs, TCAs, MAOIs, GABA analogs and cyclobenzaprine were less costly for the treatment of depression and non-opioid pain syndromes than duloxetine (Cymbalta) or milnacipran (Savella). Milnacipran (Savella) is less costly than duloxetine (Cymbalta), based on the cost per day of treatment; however, clinical evidence and FDA labeling supports the use of duloxetine in a wider range of indications than milnacipran.

BIA was used to assess the potential impact of cost scenarios where selected agents 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 that

maintaining all depression and non-opioid pain syndrome drugs in their current BCF/UF status, maintaining duloxetine and milnacipran both as NF and non-step-preferred, was the most cost-effective scenario. Since indications for use and prior medication history beyond a 180-day lookback window cannot be determined, a trial of any other Group B or C drug was required for new users of duloxetine. Similarly, a trial of any Group C drug was required for milnacipran.

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:

Drugs Reviewed with Formulary Status on UF List	For	Opposed	Abstain	Absent
SSRIs: citalopram fluoxetine fluvoxamine paroxetine HCl IR paroxetine HCl CR paroxetine mesylate sertraline *SNRIs:* venlafaxine IR venlafaxine ER venlafaxine ER tablets *SARIs:* nefazodone trazodone *NDRIs:* bupropion HCl IR bupropion HCl SR bupropion HCl ER *TCAs:* amitriptyline desipramine doxepin imipramine HCl imipramine pamoate nortriptyline protriptyline *A2RAs:* mirtazapine tablets mirtazapine ODT	17	0	1	0
GABA analogs: gabapentin	16	1	1	0

Drugs designated with NF status on UF	For	Opposed	Abstain	Absent
SNRIs: desvenlafaxine (Pristiq)[1] *SARIs:* trazodone ER (Oleptro) *NDRIs:* bupropion HBr (Aplenzin)	17	0	1	0
SNRIs: duloxetine (Cymbalta)[2] milnacipran (Savella)[3] *GABA analogs:* pregabalin (Lyrica)[4] *SPARIs:* vilazodone (Viibryd)	16	1	1	0

Drugs approved to move from NF status to Formulary status on UF once cost-effective generic formulations become available	For	Opposed	Abstain	Absent
escitalopram (Lexapro) fluoxetine in special packaging (Sarafem) fluoxetine weekly (Prozac weekly)	17	0	1	0

[1] Desvenlafaxine (Pristiq) is nonformulary and non-step-preferred. All new users of Pristiq are required to try venlafaxine. *See* Prior Authorization Criteria, below.

[2] Duloxetine (Cymbalta) is nonformulary and non-step-preferred. All new users of Cymbalta are required to try an antidepressant [Group B drug—SSRI, SNRI (except milnacipran), TCA, mirtazapine, bupropion, SARI, or MAOI] or non-opioid pain syndrome agent [Group C drug—SNRI including milnacipran, TCA, cyclobenzaprine, gabapentin or pregabalin]. *See* Prior Authorization Criteria, below.

[3] Milnacipran (Savella) is nonformulary and non-step-preferred. All new users of Savella are required to try a non-opioid pain syndrome agent [Group C drug—SNRI including milnacipran, TCA, cyclobenzaprine, gabapentin or pregabalin]. *See* Prior Authorization Criteria, below.

[4] Pregabalin (Lyrica) is nonformulary and non-step-preferred. All new users of Lyrica are required to try gabapentin. *See* Prior Authorization Criteria, below.

Director, TMA, Decision: ☒ Approved □ Disapproved

Approved, but modified as follows:

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

Drug Class/Drug Name	Role	Approved	Abstain	Absent
SSRIs: citalopram fluoxetine, excluding fluoxetine in special packaging (Sarafem) and fluoxetine weekly (Prozac weekly) sertraline *SNRIs:* venlafaxine IR venlafaxine ER *SPARIs:* trazodone excluding trazodone ER (Oleptro) *NDRIs:* bupropion HCl IR bupropion HCl SR bupropion HCl ER *GABA analogs:* gabapentin *TCAs:* amitriptyline doxepin imipramine HCl nortriptyline	17	0	1	0

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: DESVENLAFAXINE (PRISTIQ) PRIOR AUTHORIZATION (PA) CRITERIA***—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) that desvenlafaxine (Pristiq) be designated step non-preferred, requiring a trial of venlafaxine in new users. Coverage would be approved if the patient met any of the following step therapy/PA criteria:

   a) Automated PA criteria:

      (1) The patient has filled a prescription for any venlafaxine product at any MHS pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

   b) Manual (paper) PA criteria, if automated criteria are not met: PA criteria will be developed from existing MN criteria. The existing MN criteria are as follows:

      (1) The patient requires treatment with an SNRI due to failure of another formulary depression agent or has experienced adverse events from the other formulary antidepressant.

      (2) The patient has a contraindication to venlafaxine or failed therapy with venlafaxine, which is not expected to occur with desvenlafaxine (Pristiq).

      (3) The patient has experienced adverse events with venlafaxine which is not expected to occur with desvenlafaxine (Pristiq).

      (4) The patient has previously responded to desvenlafaxine (Pristiq) and changing to a formulary depression agent would incur unacceptable risk.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows: The existing MN criteria are approved as the manual (paper) PA criteria. The Pharmacoeconomic Center staff may make minor changes, NOT involving changes to the underlying criteria, to prior authorization forms, such as correcting contact information or rewording clinical questions, without further involvement of the DoD P&T Committee and the Beneficiary Advisory Panel and without further approval of the Director, TMA.

4. ***COMMITTEE ACTION: PREGABALIN (LYRICA) PA CRITERIA***—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) that pregabalin (Lyrica) be designated non-step-preferred, requiring a trial of gabapentin in new users. Coverage would be approved if the patient met any of the following step therapy/PA criteria:

   a) Automated PA criteria:

      (1) The patient has filled a prescription for gabapentin at any 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: PA criteria will be developed from existing MN criteria. The existing MN criteria are as follows:

      (1) The patient has failed therapy with gabapentin or the formulary non-opioid pain syndrome agents.

      (2) The patient has a contraindication to gabapentin or the formulary non-opioid pain syndrome agents which is not expected to occur with pregabalin (Lyrica).

      (3) The patient has experienced adverse events with gabapentin or the formulary non-opioid pain syndrome agents, which is not expected to occur with pregabalin (Lyrica).

(4) The patient has previously responded to pregabalin (Lyrica).and changing to a formulary non-opioid pain syndrome agent would incur unacceptable risk.

Director, TMA, Decision: ☒Approved ☐ Disapproved

Approved, but modified as follows: The existing MN criteria are approved as the manual (paper) PA criteria. The Pharmacoeconomic Center staff may make minor changes, NOT involving changes to the underlying criteria, to prior authorization forms, such as correcting contact information or rewording clinical questions, without further involvement of the DoD P&T Committee and the Beneficiary Advisory Panel and without further approval of the Director, TMA.

5. ***COMMITTEE ACTION: DULOXETINE (CYMBALTA) PA CRITERIA***— The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) that duloxetine (Cymbalta) be designated non-step-preferred, requiring a trial of any antidepressant [Group B drug—SSRI, SNRI (except milnacipran), TCA, mirtazapine, bupropion, SARI, or MAOI] or non-opioid pain syndrome agent [Group C drug—SNRI including milnacipran, TCA, cyclobenzaprine, gabapentin or pregabalin] in new users. Coverage would be approved if the patient met any of the following step therapy/PA criteria:

   a) Automated PA criteria:

      (1) The patient has filled a prescription for any antidepressant (Group B) or non-opioid pain medicine (Group C) 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: PA will be developed from existing MN criteria. The existing MN criteria are as follows:

      (1) The patient has failed therapy with failed therapy with the formulary depression/non-opioid pain syndrome agents, which is not expected to occur with duloxetine (Cymbalta).

(2) The patient has a contraindication to the formulary depression/non-opioid pain syndrome agents which is not expected to occur with duloxetine (Cymbalta).

(3) The patient has experienced adverse events with the formulary depression/non-opioid pain syndrome agents, which is not expected to occur with duloxetine (Cymbalta).

(4) The patient has previously responded to duloxetine (Cymbalta).and changing to a formulary depression/non-opioid pain syndrome agent would incur unacceptable risk.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows: The existing MN criteria are approved as the manual (paper) PA criteria. The Pharmacoeconomic Center staff may make minor changes, NOT involving changes to the underlying criteria, to prior authorization forms, such as correcting contact information or rewording clinical questions, without further involvement of the DoD P&T Committee and the Beneficiary Advisory Panel and without further approval of the Director, TMA.

6. ***COMMITTEE ACTION: MILACIPRAN (SAVELLA) PA CRITERIA***—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) that milnacipran (Savella) be designated non-step-preferred requiring a trial of any non-opioid pain syndrome agent [Group C drug—SNRI, including milnacipran, TCA, cyclobenzaprine, gabapentin or pregabalin] in new users. Coverage would be approved if the patient met any of the following criteria:

   a) Automated PA criteria:

      (1) The patient has filled a prescription for any non-opioid pain syndrome agent (Group C) 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: PA criteria will be developed from existing MN criteria. . The existing MN criteria are as follows:

(1) Use of the formulary non-opioid pain syndrome agents is contraindicated.

(2) The patient has experienced adverse effects from the formulary non-opioid pain syndrome agents.

(3) Use of the formulary non-opioid pain syndrome agents has resulted in therapeutic failure.

(4) The patient has previously responded to milnacipran (Savella) and changing to a formulary non-opioid pain syndrome agent would incur unacceptable risk.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows: The existing MN criteria are approved as the manual (paper) PA criteria. The Pharmacoeconomic Center staff may make minor changes, NOT involving changes to the underlying criteria, to prior authorization forms, such as correcting contact information or rewording clinical questions, without further involvement of the DoD P&T Committee and the Beneficiary Advisory Panel and without further approval of the Director, TMA.

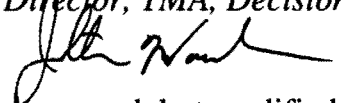
7. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical and cost evaluation of the Depression/Non-Opioid Pain Syndrome agents, and the conditions for establishing MN for a NF medication, the P&T Committee recommended (17 for, 0 opposed, 1 abstained, 1 absent) maintaining the current MN criteria for bupropion HBr (Aplenzin); desvenlafaxine (Pristiq); duloxetine (Cymbalta); milnacipran (Savella); pregabalin (Lyrica); and, until cost-effective generics become available, escitalopram (Lexapro); fluoxetine in special packaging (Sarafem), and fluoxetine weekly (Prozac weekly). The P&T Committee also recommended MN criteria for trazodone ER (Oleptro) and vilazodone (Viibryd). (See Appendix C for full MN criteria.)

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

8. ***COMMITTEE ACTION: UF AND MN IMPLEMENTATION PERIOD***—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is April 18, 2012.

Director, TMA, Decision: ☒ Approved ☐ Disapproved



Approved, but modified as follows:

B. Short-Acting Beta Agonists (SABAs)

Relative Clinical Effectiveness—The P&T Committee evaluated the clinical effectiveness of the inhaled Short-Acting Beta Agonists (SABAs). There are three SABA products marketed in the United States, which are formulated as pressurized metered dose inhalers (MDIs) or solutions for inhalation: albuterol (a racemic mixture), levalbuterol (the (R)-enantiomer form of albuterol), and pirbuterol. The SABA inhaled solutions include albuterol (Accuneb, generics; various concentrations), and levalbuterol (Xopenex).

Hydrofluoroalkane (HFA) replaced chlorofluorocarbon (CFC) as the propellant in albuterol MDIs in December 2008. The SABA MDI formulations include albuterol HFA (Ventolin HFA, Proventil HFA, ProAir), levalbuterol HFA (Xopenex), and pirbuterol (Maxair). Pirbuterol (Maxair) is the sole remaining CFC MDI on the market, and will be discontinued in December 2013. The three albuterol HFA products are not considered therapeutically interchangeable by the FDA.

The SABA drug class was previously reviewed for UF placement in November 2008. In fiscal year 2011, over $43M was spent on the SABAs at all three points of service in the MHS.

Information regarding the safety, effectiveness, and clinical outcomes of the SABAs was considered by the Committee. The clinical effectiveness review for the SABAs was limited to the outpatient setting; emergency department use was evaluated only when pertinent.

Relative Clinical Effectiveness Conclusion—The P&T Committee voted (18 for, 0 against, 0 abstained, 0 absent) to accept the following clinical effectiveness conclusions:

1. In terms of efficacy/clinical effectiveness, there is little evidence to suggest there are clinically relevant differences between the SABAs for their FDA-

approved indications. There is no new significant information to change the clinical effectiveness conclusion from the November 2008 UF review.

- Evidence-based guidelines from the VA/DoD Clinical Practice Group (updated 2009), Global Initiative for Asthma, National Heart, Lung and Blood Institute/National Asthma Education & Prevention Program, and Global Initiative for Chronic Obstructive Lung Disease do not list a preference for one SABA over another for treating asthma, exercise-induced bronchospasm (EIB) or chronic obstructive pulmonary disease (COPD).
- For asthma, all the SABAs are more efficacious than placebo at improving the change in forced expiratory volume in one second $\geq$ 12% from baseline, whether administered via MDI or inhalational solution.
- There are no head-to-head studies comparing albuterol MDI with levalbuterol (Xopenex) MDI in adults or children.
- For adults with asthma, there is little evidence to suggest there are clinically relevant differences between albuterol and levalbuterol when administered via the nebulized route in either the outpatient or emergency department settings—in terms of number of puffs of rescue medication used daily or from hospitalization admission rates.
- For children with asthma, there are conflicting and inconclusive results as to whether there are efficacy differences between albuterol and levalbuterol inhalation solution when administered in the outpatient setting or emergency department.
- EIB—Placebo-controlled trials with albuterol administered via MDI 15 to 30 minutes before exercise reported statistically significant results in terms of preventing exercise-related symptoms compared to placebo. Although levalbuterol MDI (Xopenex) is not currently approved by the FDA for EIB, the results of placebo-controlled phase III trials do not suggest that the effect of levalbuterol at preventing EIB symptoms would differ from albuterol.
- COPD—There is insufficient evidence to compare the SABAs when used in COPD.

2. With regards to safety/tolerability, the following conclusions were made:
   - SABAs are associated with similar systemic adverse effects. A systematic review found no clinically relevant differences in discontinuation rates due to changes in heart rate, blood pressure, palpitations, nervousness, anxiety, tremor, hyperglycemia or hypokalemia between albuterol and levalbuterol inhalation solution.

- In the outpatient setting, in adults and children, the incidence of the withdrawal rates due to AEs and overall AE rates were similar between albuterol and levalbuterol inhaled solutions. However, in children there is insufficient evidence from the outpatient studies to determine whether there are clinically relevant differences in the incidence of tachycardia, as conflicting results were reported.
- There is insufficient data with the SABA MDI formulations to assess safety differences between albuterol and levalbuterol.

3. With regards to differences between the SABAs in terms of other factors, the following conclusions were made:
    - Special populations—The P&T Committee recognized that the FDA-approved pediatric age ranges differ between the products.
    - HFA formulations—There are only minor differences between the HFA formulations of albuterol and levalbuterol, including presence of a dose counter (Ventolin HFA is the only product with a dose counter), requirements for priming, storage conditions, and excipients (Ventolin HFA is the only SABA that does not contain alcohol). However, per FDA ruling, the HFA albuterol agents are not interchangeable.
    - Delivery devices—The Ventolin MDI is not compatible with the Lever Haler spacer, but is compatible with all other spacer devices.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the SABAs Drug Class. Based on the clinical findings regarding efficacy, safety, tolerability, and clinical outcomes with SABAs, cost-minimization analyses (CMAs) were performed to compare the metered-dose inhalers (MDIs) and inhalation solutions. Additionally, a BIA was performed to compare competing formulary scenarios for the MDIs. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA results with the SABAs MDIs showed albuterol HFA (Ventolin HFA, Proventil HFA, ProAir HFA) inhalers are most cost-effective. While levalbuterol (Xopenex) is comparable to albuterol HFA with regards to cost, pirbuterol (Maxair) is not cost-effective relative to the other MDIs in the class. BIA results indicated that pirbuterol (Maxair) MDI designated with NF status on the UF was the most cost-effective scenario for the MHS. When the inhalation solutions were compared, albuterol (generic; 2.5 mg/3mL concentration) was the most cost-effective inhalation solution.

Relative Cost-Effectiveness Conclusion—Based on the results of the economic analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0

opposed, 1 abstained, 0 absent) that the most cost-effective scenario designated albuterol HFA (Ventolin HFA, Proventil HFA, ProAir HFA), levalbuterol HFA (Xopenex HFA), albuterol inhalation solution (Accuneb, generics), and levalbuterol inhalation solution (Xopenex) with formulary status on the UF and pirbuterol CFC (Maxair) inhaler with NF status on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) albuterol HFA (Ventolin HFA, Proventil HFA, ProAir HFA), levalbuterol HFA (Xopenex HFA), albuterol inhlation solution (Accuneb, generics), and levalbuterol inhalation solution (Xopenex) remain formulary on the UF. The P&T Committee recommended that pirbuterol CFC inhaler (Maxair) be designated NF on the UF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

☐ Approved, but modified as follows:

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) albuterol HFA (Ventolin HFA) and albuterol inhalation solution (generic; 2.5mg/0.5mL concentration) be designated with BCF status.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

☐ Approved, but modified as follows:

C. Phosphodiesterase Type-5 (PDE-5) Inhibitors for Erectile Dysfunction (ED)

The P&T Committee evaluated the cost-effectiveness analysis for the PDE-5 inhibitors for ED at an interim telephonic meeting held on December 15, 2011. The attendance roster for the interim meeting is found in Appendix B. Please refer to the August 2011 P&T Committee minutes for the relative clinical effectiveness review and conclusions.

Relative Cost Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the PDE-5 inhibitors sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra, Staxyn) for erectile dysfunction. Based on clinical findings regarding efficacy, safety, tolerability, other relevant factors, and clinical outcomes with these agents, CMAs were performed to compare individual agents. BIAs were also performed to compare competing formulary scenarios.

During this drug class evaluation, the DoD joined the VA in a joint national contracting effort. Sildenafil (Viagra) was selected as the winner of the VA/DoD national contract. To comply with the terms of the joint national contract, all scenarios considered in this review included sildenafil (Viagra) as a UF and BCF agent with all other agents designated NF.

Relative Cost Effectiveness Conclusion—Based on the results of the economic analysis and other clinical and cost considerations, the P&T Committee concluded (11 for, 0 opposed, 0 abstained, 0 absent) the following for the PDE-5 inhibitors:

- CMA results showed that sildenafil (Viagra) was the most cost-effective agent across all three points of service.

- BIA was used to compare the potential impact of discontinuing the current step therapy program (which requires a trial of vardenafil for new users with prescriptions for sildenafil or tadalafil) with scenarios where step therapy was maintained, but sildenafil (Viagra) replaced vardenafil as the step-preferred agent. Additional formulary scenarios evaluating the impact of implementing new retail restrictions were also considered. BIA results showed that, among currently available formulary options, the most cost-effective scenario placed sildenafil (Viagra) on the BCF and as the step-preferred product on the UF, with vardenafil (Levitra, Staxyn) and tadalafil (Cialis) designated NF and non-step preferred. Sensitivity analysis results supported the above conclusion.

- The P&T Committee discussed a potential program designed to strongly encourage the use of mail order instead of retail, for appropriate medications. The P&T Committee concluded that the PDE-5s would be well-suited to such a program clinically and including this drug class in such a program, if it becomes available, would most likely generate additional cost avoidance.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (11 for, 0 opposed, 0 abstained, 0 absent):

a) Sildenafil (Viagra 25 mg, 50 mg, and 100 mg) be designated with formulary status on the UF.

b) Tadalafil (Cialis 2.5 mg, 5 mg, 10 mg, and 20 mg) and vardenafil (Levitra 2.5 mg, 5 mg, 10 mg, and 20 mg; Staxyn 10 mg) be designated NF on the UF, based on cost-effectiveness.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee voted (11 for, 0 opposed, 0 abstained, 0 absent) to recommend that sildenafil (Viagra 25 mg, 50 mg, and 100 mg) tablets be designated with BCF status immediately on signing of the November 2011 P&T Committee minutes by the Director, TMA.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical evaluation of tadalafil (Cialis) and vardenafil (Levitra and Staxyn) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (11 for, 0 opposed, 0 abstained, 0 absent) MN criteria for Cialis, Levitra, and Staxyn. (See Appendix C for full MN criteria.)

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all

points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is April 18, 2012.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

5. ***COMMITTEE ACTION: STEP THERAPYAND PA CRITERIA***—The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 0 absent) that step therapy apply to the PDE-5 inhibitors for the treatment of ED. For all new users of PDE-5 inhibitors, the following criteria apply:

   a) Automated Criteria:
   Coverage approved for treatment of ED if:
      (i) The patient has received a prescription for sildenafil (Viagra), tadalafil (Cialis), or vardenafil (Levitra and Staxyn) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days, AND
      (ii) The patient is a male aged 40 years or older.

   b) Manual Criteria:

   Coverage approved if:

      (i) Patient has tried sildenafil (Viagra) and has had an inadequate response or was unable to tolerate treatment due to adverse effects.

      (ii) Treatment with sildenafil (Viagra) is contraindicated.

      (iii) Patient is less than 40 years of age and is being treated for ED of organic or mixed organic/psychogenic origin. [Must try sildenafil (Viagra) first or indicate inability to due to reasons stated above in b) (i) or b) (ii)].

      (iv) Patient is less than 40 years of age and is being treated for drug-induced ED where the causative drug cannot be altered or discontinued. [Must try sildenafil (Viagra) first or indicate inability to due to reasons stated above in b) (i) or b) (ii)].

Coverage approved for the following non-ED uses requiring daily therapy:

(v) Use of tadalafil (Cialis or Adcirca) for Pulmonary Arterial Hypertension (PAH)

(vi) Use of any PDE-5 inhibitor for preservation/restoration of erectile function after prostatectomy

(vii) Use of any PDE-5 inhibitor for Raynaud's Phenomenon

(viii) Use of Cialis 5 mg for treatment of benign prostatic hyperplasia (BPH)

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

6. ***COMMITTEE ACTION: PA IMPLEMENTATION PLAN***—The P&T Committee voted (11 for, 0 opposed, 0 abstained, 0 absent) to recommend the PA implementation plan be timed to coincide with that established for the UF decision for tadalafil and vardenafil.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

7. ***COMMITTEE ACTION: QUANTITY LIMITS (QLs)***—The P&T Committee considered QLs for the treatment of ED as well as QLs for other indications. Based on the results of the clinical and economic evaluations presented, the P&T Committee recommended (11 for, 0 opposed, 0 abstained, 0 absent) the following QLs:

Treatment of ED:

Mail Order: Collective QL of 18 tablets per 90 days

Retail: Collective QL of 6 tablets per 30 days

Daily therapy for the approved indications (PAH, preservation or restoration of erectile function after prostatectomy, Raynaud's Phenomenon and BPH):

Mail Order: 90-days supply

Retail: 30-days supply

Director, TMA, Decision: ☒Approved ☐ Disapproved

Approved, but modified as follows:

VI. UTILIZATION MANAGEMENT

A. Tadalafil (Cialis)—PA: The PDE-5 inhibitor tadalafil (Cialis) 5 mg received FDA approval in October 2011 for treatment of BPH and ED with BPH. All PDE-5 inhibitors are currently subject to prior authorization, step therapy, quantity limits, and MN criteria. Prior authorization and step therapy also apply to the alpha-1 blockers used for BPH.

The DoD P&T Committee reviewed the clinical efficacy of tadalafil for BPH. Although the efficacy of tadalafil and the alpha-1 blockers for BPH cannot be directly compared, alpha-1 blockers provide relief of BPH urinary symptoms to a greater extent than PDE-5 inhibitors, based on changes from baseline in the International Prostate Symptom Scale reported in clinical trials. The P&T Committee also recommended that trial of a preferred alpha-1 blocker would be required for new users of tadalafil for BPH.

1. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) in addition to the existing PDE-5 inhibitors automated and manual PA criteria, the following PA criteria should also apply to the tadalafil when used for BPH:

a) Manual PA criteria:

(1) Patient is being treated for BPH and the dosing regimen prescribed is tadalafil 5 mg once daily AND

(a) The patient has tried tamsulosin or alfuzosin and had an inadequate response;

OR

(b) The patient has tried tamsulosin or alfuzosin and was unable to tolerate them due to adverse effects;

OR

(c) Treatment with tamsulosin or alfuzosin is contraindicated.

(d) Prior authorization for the BPH indication will expire after 1 year from input date.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: Tadalafil PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) an effective date upon signing of the November 2011 P&T Committee minutes by the Director, TMA.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

B. Tramadol ER (Conzip)—QLs: Conzip is a new tramadol ER formulation. It is FDA-approved for the management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain. QLs are currently in place for other tramadol ER formulations (Ultram ER, Ryzolt, generics), which are consistent with their product labeling.

1. ***COMMITTEE ACTION: QLs***—The P&T Committee recommended (15 for, 0 against, 1 abstain, 2 absent) QLs of 90 capsules /90 days in the mail order pharmacy and 30 capsules/30 days in the retail network, which is consistent with the recommended dosing from the product labeling.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

C. Sunitinib malate (Sutent)—QLs: In May 2011, Sunitinib malate was FDA-approved for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease. The manufacturer's dosing recommendation includes the following regimen: 37.5 mg orally once daily, continuously without a scheduled off-treatment period.

1. ***COMMITTEE ACTION: QLs***—The P&T Committee recommended (15 for, 0 against, 1 abstain, 2 absent) the following QLs for sunitinib malate (Sutent):

Retail:

12.5mg: 120 caps/30 days
25mg: 60 caps/30 days
50mg: 30 caps/30 days

Mail:

12.5mg: 252 caps/84 days
25mg: 120 caps/84 days
50mg: 60 caps/84 days

The above QLs are consistent with the recommended dosing from the product labeling.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

D. Abatacept (Orencia)—PA: A subcutaneous injection of abatacept (Orencia) has been marketed. Orencia will be reviewed as a new FDA-approved drug in the Targeted Immunomodulatory Biologics (TIBs) Drug Class at an upcoming DoD P&T Committee meeting. PA requirements apply to the other TIBs in the UF. The P&T Committee

agreed that the following PA criteria should apply to Orencia, consistent with the FDA-approved labeling and PA requirements for the other TIBs.

1. Coverage would be approved for the treatment of adult patients with moderate to severely active rheumatoid arthritis.
2. Coverage would not be provided for concomitant use with adalimumab (Humira), anakinra (Kineret), certolizumab (Cimzia), etanercept (Enbrel), infliximab (Remicade), golimumab (Simponi), or rituximab (Rituxan).

a) ***COMMITTEE ACTION: PA***—The P&T Committee recommended (15 for, 0 against, 1 abstain, 2 absent) approving the PA criteria outlined above.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

E. Abatacept (Orencia)—QLs: QLs are currently in place for the TIBs, which are consistent with the product labeling.

1. ***COMMITTEE ACTION: QLs***—The P&T Committee recommended (15 for, 0 against, 1 abstain, 2 absent) QLs of 8 syringes/56 days in the mail order pharmacy and 4 syringes/28 days in the retail network, which is consistent with the recommended dosing from the product labeling and avoids wastage.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

VII. ITEMS FOR INFORMATION

A. Antilipidemic-1s (LIP-1s)—Clarification of PA criteria: In May 2010, the P&T Committee recommended step therapy and PA criteria for the LIP-1s Drug Class, and designated generic statins and atorvastatin (Lipitor) as step-preferred drugs within the class. Since implementation, an audit revealed the need to clarify the manual PA

criteria. The P&T Committee recommended clarifications to the manual PA criteria to accurately reflect their intent.

VIII. CLASS OVERVIEWS

Three drug class overviews were presented to the P&T Committee. The Attention Deficit Hyperactivity Disorder and Narcolepsy Drug Class was last reviewed in November 2006. The Dipeptidyl-Peptidase 4 Inhibitors Drug Class was presented in November 2010 as part of the Non-Insulin Diabetes Drug Class. Information regarding antiplatelet drugs was also presented; this drug class has never been 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.

IX. ADJOURNMENT

The meeting adjourned at 1710 hours on November 9, 2011. An interim telephonic follow-on meeting was held on December 15, 2011. The next meeting will be in February 2012.

Appendix A—Attendance: November 2011 P&T Committee Meeting

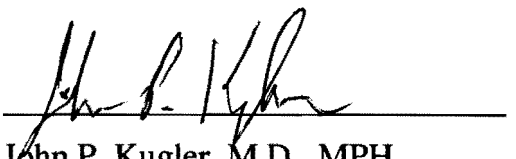
Appendix B—Attendance: December 15, 2011 Interim Meeting

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

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

Appendix E—Table of Abbreviations

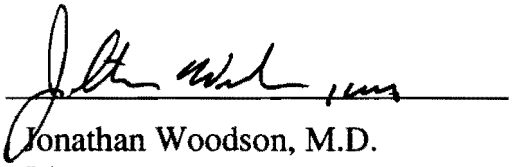
SUBMITTED BY:



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

DECISION ON RECOMMENDATIONS

Director, TMA, decisions are as annotated above.



Jonathan Woodson, M.D.
Director

7 Feb. 2012
(Date)

Appendix A—Attendance: November 2011 P&T Committee Meeting

Voting Members Present	
John Kugler, COL (Ret.), MC, USA	DoD P&T Committee Chair
CDR Joe Lawrence	Director, DoD Pharmacoeconomic Center (Recorder)
Col George Jones, BSC	Deputy Chief, Pharmaceutical Operations Directorate
LTC Ric Nannini for COL Carole Labadie, MSC	Army, Pharmacy Officer
Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CAPT Dennis Alder	Coast Guard, Pharmacy Officer
CAPT Edward Norton	Navy, Pharmacy Officer (Pharmacy Consultant BUMED)
Col Lowell Sensintaffer, MC	Air Force, Physician at Large
CAPT David Tanen, MC	Navy, Physician at Large
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
LTC Jack Lewi for COL Doreen Lounsbery, MC	Army, Internal Medicine Physician
LTC Daniel Hsu for COL Ted Cieslak, MC	Army, Physician at Large
LTC Bruce Lovins, MC	Army, Family Practice Physician
CDR Eileen Hoke, MC	Navy, Pediatrics
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Major Jeremy King, MC	Air Force, OB/GYN Physician
Dr. Miguel Montalvo	TRICARE® Regional Office-South Chief of Clinical Operations Division and Medical Director
Mr. Joe Canzolino	U.S. Department of Veterans Affairs
Nonvoting Members Present	
Mr. David Hurt	Associate General Counsel, TMA
CDR Jay Peloquin	Defense Logistics Agency Troop Support
Guests	
Dr. Warren Lockette	Chief Medical Officer, TRICARE Management Activity

Appendix A—Attendance: November 2011 P&T Committee Meeting (continued)

Guests	
COL Todd Williams	Defense Medical Materiel Program Office
CDR Mike Lee	Indian Health Service
Capt Justin Lusk	AMEDD Center and School
Dr. Vincent Calabrese	Department of Veterans Affairs
Ronda Wenzel	University of Incarnate Word Pharmacy Intern
Ellen Tsay	University of Maryland Pharmacy Intern
Others Present	
Lt Col Rey Morales	DoD Pharmacoeconomic Center
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
MAJ Misty Cowan	DoD Pharmacoeconomic Center
Lt Col Cynthia Lee, BSC	DoD Pharmacoeconomic Center
LCDR Ola Ojo	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
Maj David Folmar	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Angela Allerman	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe	DoD Pharmacoeconomic Center
Dr. Joshua Devine	DoD Pharmacoeconomic Center
Dr. Dean Valibhai	DoD Pharmacoeconomic Center
Dr. Brian Beck	DoD Pharmacoeconomic Center
Dr. Amy Lugo via teleconference	DoD Pharmacoeconomic Center
Dr. Libby Hearin	DoD Pharmacoeconomic Center
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor
Dr. Bradley Clarkson	Pharmacy Resident

Appendix B—Attendance: December 15, 2011 Interim Meeting

Voting Members Present via DCO	
John Kugler, COL (Ret.), MC, USA	DoD P&T Committee Chair
CDR Joe Lawrence	Director, DoD Pharmacoeconomic Center (Recorder)
Col George Jones, BSC	Deputy Chief, Pharmaceutical Operations Directorate
LTC Ric Nannini for COL Carole Labadie, MSC	Army, Pharmacy Officer
Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CAPT Edward Norton	Navy, Pharmacy Officer (Pharmacy Consultant BUMED)
Col Lowell Sensintaffer, MC	Air Force, Physician at Large
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
LTC Bruce Lovins, MC	Army, Family Practice Physician
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Dr. Miguel Montalvo	TRICARE® Regional Office-South Chief of Clinical Operations Division and Medical Director
Nonvoting Members Present via DCO	
Mr. David Hurt	Associate General Counsel, TMA
Others Present	
Lt Col Cynthia Lee, BSC	DoD Pharmacoeconomic Center
LCDR Ola Ojo	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
Maj David Folmar	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Angela Allerman via DCO	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe via DCO	DoD Pharmacoeconomic Center
Dr. Joshua Devine	DoD Pharmacoeconomic Center
Dr. Eugene Moore	DoD Pharmacoeconomic Center
Dr. Stephen Yarger	DoD Pharmacy Outcomes Research Team contractor

Appendix B—Attendance December 15, 2011 Interim Meeting (continued)

Others Present	
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor
Dr. Bradley Clarkson	Pharmacy Resident

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

Drug / Drug Class	Medical Necessity Criteria
Risedronate delayed release (Atelvia) **Osteoporosis Agents**	• Use of risedronate IR, ibandronate oral, and alendronate is contraindicated. • Patient has experienced significant adverse effects from risedronate IR, ibandronate oral, and alendronate.
Trazodone extended release (Oleptro) **Depression / Non-Opioid Pain Syndrome Agents**	• Use of the formulary depression/non-opioid pain syndrome agents is contraindicated.
Vilazodone (Viibryd) **Depression / Non-Opioid Pain Syndrome Agents**	• No alternative formulary agent – patient requires a drug with activity as serotonin-1a partial agonist/reuptake inhibitor and is unable to tolerate buspirone plus a selective serotonin reuptake inhibitor.
Tadalafil (Cialis) **PDE-5 Inhibitors**	• Use of Viagra is contraindicated • Patient has experienced significant adverse effects from Viagra • Viagra has resulted in therapeutic failure
Vardenafil (Levitra, Staxyn) **PDE-5 Inhibitors**	• Use of Viagra is contraindicated • Patient has experienced significant adverse effects from Viagra • Viagra has resulted in therapeutic failure

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

Date	DoD PEC Drug Class	Type of Action*	BCF/ECF Medications MTFs must have BCF meds on formulary	UF Medications MTFs may have on formulary	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Comments
Nov 2011	**Depression and Non-Opioid Pain Syndrome Agents**	UF Class Review	**SSRIs:** citalopram fluoxetine sertraline **SNRIs:** venlafaxine IR venlafaxine ER **SPARIs:** trazodone **NDRIs:** bupropion HCl IR bupropion HCl SR bupropion HCl ER **GABA analogs:** gabapentin **TCAs:** amitriptyline doxepin imipramine HCl nortriptyline	**SSRIs:** citalopram fluoxetine fluvoxamine paroxetine HCl IR paroxetine HCl CR paroxetine mesylate sertraline **SNRIs:** venlafaxine IR venlafaxine ER venlafaxine ER tablets **SARIs:** nefazodone trazodone **NDRIs:** bupropion HCl IR bupropion HCl SR bupropion HCl ER **TCAs:** amitriptyline desipramine doxepin imipramine HCl imipramine pamoate nortriptyline protriptyline **A2RAs:** mirtazapine tablets mirtazapine ODT **GABA analogs:** gabapentin	**SSRIs:** escitalopram (Lexapro) fluoexetine (Sarafem) fluoxetine weekly (Prozac Weekly) **SNRIs:** desvenlafaxine (Pristiq) duloxetine (Cymbalta) milnacipran (Savella) **SARIs:** trazodone ER (Oleptro) **SPARIs:** vilazodone (Viibryd) **NDRIs:** bupropion HBr (Aplenzin) **GABA analogs:** pregabalin (Lyrica)	Pending signing of minutes/ 60 days	Step therapy (Automated PA)	Step therapy will apply for four agents in this class: Pristiq is NF and non step-preferred. All new users of Pristiq are required to try venlafaxine first. Cymbalta is NF and non step-preferred. All new users of Cymbalta are required to try an antidepressant (Group B drug) or non-opioid pain syndrome agent (Group C) first. Savella is NF and non step-preferred. All new users of Savella are required to try a non-opioid pain syndrome agent (Group C) first. Lyrica is NF and non step-preferred. All new users of Lyrica are required to try gabapentin first.

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 2011	**Short Acting Beta Agonists (SABAs)**	UF Class Review	No change from previous review November 2008 • albuterol nebulizing solution (0.083% [2.5 mg/3 mL]) • Ventolin HFA MDI	• albuterol nebulizing solution (0.5% [2.5 mg/0.5 mL] • albuterol nebulizing solution (Accuneb) • Proair HFA • Proventil HFA • Levalbuterol HFA (Xopenex HFA) • Levalbuterol nebulzing solution (Xopenex) • Ventolin HFA MDI	• pirbuterol CFC (Maxair)	Not Applicable	Existing QLs apply	-
Nov 2011	**Phosphodiesterase -5 (PDE-5) Inhibitors for Erectile Dysfunction (ED)**	UF Class Review	• sildenafil (Viagra)	• sildenafil (Viagra)	• tadalafil (Cialis) • vardenafil (Levitra, Staxyn)	Pending signing of minutes/ 60 days	Step therap y (Automated PA) and QLs apply	Viagra is BCF and step-preferred. Cialis and Levitra are NF and non step-preferred
Nov 2011	**Osteoporosis Agents** **Subclass: bisphosphonates**	New Drug in Already Reviewed Class	No change from previous review June 2008 • alendronate • alendronate with Vitamin D • ibandronate	• alendronate • alendronate with Vitamin D • ibandronate • risedronate IR (Actonel) • risedronate IR with calcium (Actonel with Calcium)	• risedronate DR (Atelvia)	Pending signing of minutes/ 60 days	-	-

Group B drugs: SSRIs, SNRIs (except milnacipran), TCAs, mirtazapine, bupropion, SARIs, or MAOIs
Group C drugs: SNRIs including milnacipran, TCAs, cyclobenzaprine, gabapentin or pregabalin

CFC: chlorofluorocarbon
DR: delayed release
ER: extended release
HFA: hydrofluoroalkane
IR: immediate release
QLs: quantity limits

Appendix E—Table of Abbreviations

AEs	adverse events
A2RAs	alpha-2 receptor antagonists
BCF	Basic Core Formulary
BPH	benign prostatic hypertrophy
BIA	budget impact analysis
CFC	chlorofluorocarbon
CFR	Code of Federal Regulations
CLBP	chronic low back pain
CMA	cost minimization analysis
COPD	chronic obstructive pulmonary disease
DoD	Department of Defense
DERP	Oregon Drug Effectiveness Review Project
DPN	diabetic peripheral neuropathy
DR	delayed release
ED	erectile dysfunction
EIB	exercise-induced bronchospasm
ER	extended release
FM	Fibromyalgia
FDA	U.S. Food and Drug Administration
GABA	gamma-aminobutyric acid
CGI	Clinical Global Impression
HFA	Hydrofluoroalkane
HRQoL	health-related quality of life
IR	Immediate release
MDD	major depressive disorder
MHS	Military Health System
MN	medical necessity
MDIs	metered-dose inhalers
MTF	Military Treatment Facility
NF	Nonformulary
NDRIs	norepinephrine/dopamine reuptake inhibitors
NSAIDs	non-steroidal anti-inflammatory drugs
ODT	orally dissolving tablets
P&T	Pharmacy and Therapeutics
PA	prior authorization
PAH	pulmonary artery hypertension
PEC	Pharmacoeconomic Center
PDE-5	phosphodiesterase type-5 inhibitor
PORT	Pharmaceutical Outcomes Research Team
PHN	post-herpetic neuralgia
QLs	quantity limits
SABAs	Short-Acting Beta Agonists
SSRIs	selective serotonin reuptake inhibitors
SNRIs	selective serotonin/norepinephrine reuptake inhibitors
SARIs	serotonin antagonist reuptake inhibitors
SPARIs	serotonin partial agonist/reuptake inhibitors
TIBs	Targeted Immunomodulatory Biologics
UF	Uniform Formulary
VA	U.S. Department of Veterans Affairs

DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS
August 2011

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on August 10 and 11, 2011, at the DoD Pharmacoeconomic Center (PEC), Fort Sam Houston, Texas.

II. ATTENDANCE

The attendance roster is found in Appendix A.

A. Review Minutes of Last Meetings

1. **Approval of May Minutes**—Jonathon Woodson M.D. Director, approved the minutes for the May 2011 DoD P&T Committee meeting on August 5, 2011.
2. **Addendum to the May Minutes**—Jonathon Woodson M.D. ASD(HA) also approved on August 5, 2011 the retail network and mail order pharmacy co-pay changes for tiers 1(generic), 2 (formulary) and 3 (non-formulary) and for retail non-network pharmacies, which are effective October 1, 2011.

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

A. Renin Angiotensin Antihypertensives (RAAs)—Azilsartan (Edarbi)

Relative Clinical Effectiveness—Azilsartan (Edarbi) is a once daily angiotensin receptor blocker (ARB), the eighth ARB to enter the market. It is classified in the RAAs drug class. The class was last reviewed in August 2010. The clinical evaluation for Edarbi included, but was not limited to, the requirements stated in 32 Code of Federal Regulations (CFR) 199.21(e)(1).

Edarbi is indicated for the management of hypertension, alone or in combination with other agents. It has no other FDA-approved indications and there are no clinical outcomes (e.g., reduction in heart failure hospitalization, death, or type 2 diabetic renal disease) studies completed, in-process, or planned. Because of corresponding published reductions in stroke and all-cause mortality, a reduction of either systolic or diastolic blood pressure (BP) of 2 mm Hg or more is considered clinically meaningful for this review.

In seven clinical trials—two published and five unpublished—Edarbi demonstrated efficacy in treating hypertension. In two studies, it demonstrated superiority to valsartan

(Diovan), a step-preferred, basic core formulary (BCF) agent, at a clinically meaningful reduction in systolic BP of 3-5 mm Hg. Additionally, Edarbi showed non-inferiority and statistical superiority (and a potentially clinically meaningful systolic BP reduction of 1-2 mm Hg) to olmesartan (Benicar). In terms of safety, there is no evidence that Edarbi is more or less safe, on average, than any of the seven other ARBs.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (14 for, 0 opposed, 0 abstained, 1 absent) azilsartan (Edarbi) offers a compelling therapeutic advantage over valsartan and possibly olmesartan, but does not have clinical outcomes studies available.

Relative Cost-Effectiveness—Although the clinical review concluded Edarbi produced a clinically relevant reduction in BP compared to other ARBs, cost-minimization analysis (CMA) was used to compare its cost to the other ARBs, consistent with the cost analysis for the ARBs subclass conducted at the August 2010 UF review for the RAAS. CMA was performed to evaluate Edarbi's cost in comparison to other UF RAAs drugs, including generic losartan, telmisartan (Micardis), valsartan (Diovan), irbesartan (Avapro), olmesartan (Benicar), and candesartan (Atacand). Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (14 for, 0 opposed, 0 abstained, 1 absent) that Edarbi was more costly than telmisartan (Micardis), valsartan (Diovan), irbesartan (Avapro), olmesartan (Benicar), and less costly than Atacand (candesartan).

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors the P&T Committee, based upon its collective professional judgment, recommended (13 for, 0 opposed, 1 abstained, 1 absent) azilsartan (Edarbi) remain formulary on the UF.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (13 for, 0 opposed, 1 abstained, 1 absent) azilsartan (Edarbi) be excluded from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: PRIOR AUTHORIZATION (PA) CRITERIA***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) that azilsartan (Edarbi) be designated non-step preferred requiring the following step-therapy/PA criteria. 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 Military Health Service (MHS) pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

      (2) The patient has received a prescription for azilsartan (Edarbi) 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).

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service. Based on the P&T Committee's recommendation, the effective date is January 4, 2012.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows

B. RAAs—Aliskiren/Amlodipine/Hydrochlorothiazide (Amturnide)

Relative Clinical Effectiveness—Amturnide is a once daily triple-fixed dose combination (FDC) antihypertensive product. It contains aliskiren, a direct renin inhibitor (DRI), amlodipine, a dihydropyridine calcium channel blocker (DHP CCB), and hydrochlorothiazide (HCTZ), a thiazide-type diuretic. Amturnide is the third triple-combination antihypertensive to enter the market. It is classified in the RAAs drug class due to the aliskiren (DRI) component. This class was last reviewed in August 2010. The clinical evaluation for Amturnide included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Amturnide is indicated for the management of hypertension as an add-on or switch from two of the components, or as a substitute for all three titrated components, but not for initial therapy. It has no other FDA-approved indications and there are no clinical outcomes studies completed, in-process, or planned. Aliskiren has outcomes studies underway, while amlodipine and HCTZ have well-established published outcomes data.

In three unpublished clinical trials, Amturnide demonstrated efficacy in treating hypertension versus the efficacy demonstrated by dual combinations of the individual component medications. In terms of safety, there is no evidence that Amturnide is more or less safe, on average, than either of the two other triple FDCs,

valsartan/amlodipine/HCTZ (Exforge HCT) and olmesartan/amlodipine/HCTZ (Tribenzor). The combination of these three drug classes (DRI, DHP CCB and thiazide diuretic) has no compelling advantage in terms of efficacy over giving other combinations (e.g., ARB/DHP CCB/HCTZ). In terms of safety, the Amturnide FDC partially offsets the peripheral edema common to CCBs, the hypokalemia common to diuretics, and the hyperkalemia sometimes seen with ARBs.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (14 for, 0 opposed, 0 abstained, 1 absent) that Amturnide does not offer a compelling therapeutic advantage in terms of efficacy or safety over other antihypertensive FDCs currently on the UF.

Relative Cost-Effectiveness—CMA was performed to evaluate the cost of aliskiren/amlodipine/HCTZ (Amturnide) in relation to the other UF RAAs drugs, including the following: aliskiren/HCTZ (Tekturna HCT) plus generic amlodipine, benazepril/amlodipine, telmisartan/amlodipine (Twynsta), olmesartan/HCTZ (Benicar HCT), valsartan/amlodipine (Exforge), valsartan/amlodipine/HCTZ (Exforge HCT), olmesartan/amlodipine (Azor), and olmesartan/amlodipine/HCTZ (Tribenzor). Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (13 for, 0 opposed, 0 abstained, 2 absent) Amturnide was more costly than Exforge (valsartan containing triple FDC), but less costly than Tribenzor (olmesartan containing FDC).

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (12 for, 0 opposed, 1 abstained, 2 absent) aliskiren/amlodipine/HCTZ (Amturnide) remain formulary on the UF, as the FDC of DRI/amlodipine/HCTZ may be necessary for hypertensive patients requiring 3 drugs who do not respond to other triple FDC RAAs.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (12 for, 0 opposed, 1 abstained, 2 absent) aliskiren/amlodipine/HCTZ (Amturnide) be excluded from the BCF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) aliskiren/amlodipine/HCTZ (Amturnide) be designated non-step preferred requiring the following step-therapy/PA criteria. 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.

      (2) The patient has received a prescription for aliskiren/amlodipine/HCTZ (Amturnide) 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).

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service. Based on the P&T Committee's recommendation, the effective date is January 4, 2012.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows

C. Non-Insulin Diabetes Drugs Dopamine Agonist—Bromocriptine Mesylate (Cycloset)

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of a newly approved formulation of bromocriptine, bromocriptine mesylate (Cycloset). The clinical review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

Cycloset is a centrally-acting dopamine agonist (DA) and is the only DA approved for the treatment of diabetes. This agent falls into the new DA subclass of the Non-Insulin Diabetes Drugs, which was reviewed for UF placement in November 2010. The other subclasses include dipeptidyl-peptidase 4 inhibitors (DPP-4s), thiazolidinediones (TZDs), glucagon-like peptide-1 receptor agonists biguanides, sulfonylureas (SUs), meglitinides, and alpha-glucosidase inhibitors. Step therapy (automated PA) applies for the Non-Insulin Diabetes Drug Class, which requires a trial of metformin or a sulfonylurea.

Bromocriptine is an old drug with a new use. It was first approved in 1978 for the treatment of Parkinson's disease and has uses in other endocrine-related disorders such as hyperprolactinemia, acromegaly, and prolactin-secreting adenomas. Bromocriptine should not be used to suppress lactation since an increase in stroke and myocardial infarction were reported in postpartum women. The new bromocriptine Cycloset product is a quick release formulation administered in the morning. Other bromocriptine mesylate formulations are available, including immediate release (IR) 2.5 tablets and scored tablets, and 5 mg IR capsules (Parlodel, generics). Decreased levels of dopamine may contribute to insulin resistance, and increasing dopamine activity in the morning is effective at improving glucose dysregulation. Cycloset is indicated as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes mellitus (T2DM).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 1 absent) the following conclusions for bromocriptine mesylate (Cycloset):

- Uptitration of Cycloset is required to achieve the maximum therapeutic benefit. Patients start with 0.8mg (1 tab) daily and increase by 0.8mg in weekly increments to a maximally tolerated dose of 4.8mg daily. The minimum therapeutic dose is 1.6mg daily.

- When used as monotherapy, Cycloset decreased glycosolated hemoglobin or hemoglobin A1c (HbA1c) 0.1% from baseline compared to placebo. Cycloset decreased HbA1c 0.1-0.4% from baseline when added to a SU and a produced a maximum 0.5% decrease from baseline when combined with both metformin and a SU.

- There are no head-to-head studies to date with other non-insulin diabetes medications and no long-term outcomes studies currently in progress.

- Bromocriptine mesylate is weight neutral; however, as with other medications, more weight gain is likely when administered with a SU or TZD. It may have a beneficial effect on lipid levels and BP.

- Nausea is the primary side effect (~31%) although bromocriptine mesylate is generally well tolerated. The incidence of serious adverse events is similar to placebo.

- There was a statistically significant decrease in major cardiovascular events with Cycloset noted in one 52-week study. However, the clinical relevance of this secondary endpoint is not clear.

- Many potential drug interactions exist with Cycloset, including strong CYP 3A4 inducers or inhibitors; highly protein-bound drugs (e.g. salicylates, sulfonamides, chloramphenicol, probenecid); dopamine receptor antagonists; ergot-related drugs and sympathomimetic drugs.

- According to current T2DM treatment guidelines, the place in therapy for bromocriptine mesylate (Cycloset) remains unknown.

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

Relative Cost-Effectiveness Conclusion—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (13 for, 0 opposed, 0 abstained, 2 absent) Cycloset was more costly when compared to step-preferred UF agents (metformin, SU, DPP-4 inhibitors, TZDs) and generic bromocriptine mesylate IR.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (12 for, 1 opposed, 1 abstained, 1 absent) bromocriptine mesylate (Cycloset) be designated NF and non-step preferred.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA***—Based on the clinical evaluation of bromocriptine mesylate (Cycloset) and the conditions for establishing MN for a NF medication, the P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) MN criteria for bromocriptine mesylate (Cycloset). (See Appendix B for full MN criteria.)

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: PA CRITERIA***—Step therapy applies to this new subclass (dopamine agonists) requiring prior trial of metformin or a sulfonylurea. Bromocriptine mesylate (Cycloset) is recommended to be designated as non-step preferred and NF. The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to bromocriptine mesylate (Cycloset).

   a) Automated PA criteria:

      (1) The patient has received a prescription for metformin or SU at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

      (2) The patient has received a prescription for bromocriptine mesylate (Cycloset) 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 a confirmed diagnosis of T2DM.
      (2) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.
      (3) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.
      (4) The patient has a contraindication or has had inadequate therapy to both metformin and a SU.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this decision. Based on the P&T Committee's recommendation, the effective date is January 4, 2012.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

D. Narcotic Analgesics—Buprenorphine Transdermal System (Butrans)

Relative Clinical Effectiveness—Butrans is a transdermal formulation of buprenorphine, a semi-synthetic opioid with mixed agonist/antagonist activity at opioid receptors. It is a Schedule III drug, classified as a low-potency single analgesic agent in the Narcotic Analgesics Drug Class. The class was last reviewed in February 2007. The clinical evaluation for Butrans included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

There are other formulations of buprenorphine commercially available: parenteral formulations for post-operative pain management and sublingual tablets for the management of opioid-dependence. Butrans is indicated for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock, opioid analgesic for an extended period of time. One transdermal system allows for systemic delivery of buprenorphine, continuously over seven days, which offers a convenient regimen for patients.

In two unpublished clinical trials, Butrans demonstrated efficacy in treating chronic low back pain. There are no direct head-to-head studies comparing it to other long-acting narcotic agents of similar potency marketed in the United States. In terms of safety, there are some additional concerns with Butrans compared to other narcotics, particularly the risk of QTc prolongation at doses greater than 20mcg/hr, which will limit its use in patients with unstable cardiac disease. The major safety issue with Butrans is buprenorphine-induced respiratory depression. This poses a concern for elderly patients or those with impaired pulmonary function since the effects of buprenorphine are not completely reversible with naloxone (an opioid antagonist). Butrans is not intended for patients requiring treatment with high–dose opioids (>80 mg/day of morphine or equivalent), another factor that may limit its use in patients stable on alternative opioid analgesics. Butrans provides an additional treatment option when a long-acting, low-potency analgesic is needed.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 0 absent) that other than the convenience of less frequent dosing, buprenorphine transdermal system (Butrans) offers no other compelling therapeutic advantages over the other low potency narcotic analgesics currently on the UF.

Relative Cost-Effectiveness—The P&T Committee evaluated Butran's cost relative to the other low-potency agents in the Narcotic Analgesics Drug Class. CMA was performed based on clinical findings that efficacy, safety, tolerability, and factors other than patient convenience found among the agents in this class were similar at equipotent doses. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e) (2).

Relative Cost-Effectiveness Conclusion—The P&T Committee, based upon its collective professional judgment, concluded (15 for, 0 opposed, 0 abstained, 0 absent) that buprenorphine transdermal system (Butrans) was more costly, based on an average weighted cost per day of therapy, than other low-potency single analgesic agents currently on the UF. However, Butrans was less costly than the sublingual formulations of buprenorphine already on the UF.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (12 for, 2 opposed, 1 abstained, 0 absent) buprenorphine transdermal system (Butrans) remain formulary on the UF with prior authorization to ensure appropriate use of the drug.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (15 for, 0 opposed, 0 abstained, 0 absent) buprenorphine transdermal system (Butrans) be excluded from the BCF.

Director, TMA, Decision: ☑ Approved □ Disapproved

Approved, but modified as follows:

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

    a) Manual PA criteria:

        (1) Coverage provided for patients ≥18 yrs with moderate-to-severe chronic pain requiring opioid therapy.

            (a) Opioid naïve patients (prior use of <30 mg/day of morphine or equivalent in past 60 days) are limited to Butrans 5 mcg/hr patch.

            (b) Opioid tolerant patients (prior use of 30mg/day to 80 mg/day of morphine or equivalent within past 60 days or Butrans 5 mcg/hr patch) can receive Butrans 10 mcg/hr and 20 mcg/hr patches.

            (c) Maximum dose of Butrans is 20 mcg/hr.

        (2) Coverage NOT provided for treatment of opioid-dependence.

        (3) Coverage NOT provided for patients:

            (a) Requiring >80 mg/day of morphine or equivalent for pain control;

            (b) With significant respiratory depression or severe bronchial asthma;

            (c) With long QT syndrome or family history of long QT syndrome;

            (d) On concurrent Class 1A (procainamide, quinidine) or Class III (dofetilide, amiodarone, sotalol) antiarrythmics.

Director, TMA, Decision: ☑ Approved □ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service. Based on the P&T Committee's recommendation, the effective date is January 4, 2012.

Director, TMA, Decision: ☑ Approved □ Disapproved

Approved, but modified as follows

IV. UF DRUG CLASS REVIEWS

A. Oral Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Background Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the oral NSAIDs. There are 26 drugs in the class, comprised of 19 different chemical entities. Generic formulations are available for 21 drugs and there are 5 branded products: Celebrex, Arthrotec, Vimovo, Zipsor, and Cambia. Celecoxib (Celebrex) is the only cyclooxygenase-2 (COX-2) selective inhibitor available in the United States. Two FDCs of an NSAID with an anti-ulcer drug are available. Arthrotec is a combination of diclofenac and the prostaglandin analog misoprostol. Vimovo is the first FDC of an NSAID and a proton pump inhibitor (PPI) and is comprised of naproxen and esomeprazole. Diclofenac potassium liquid-filled capsules (Zipsor) contains 25 mg of diclofenac potassium, which is the lowest diclofenac dosage strength marketed; it is solely indicated for relief of mild-to-moderate acute pain. Cambia is a formulation of diclofenac potassium in powder packets for suspension.

The partially COX-2-selective NSAIDs include meloxicam, nabumetone, and etodolac. The remaining drugs in the class are the non-COX-2-selective NSAIDs: diclofenac potassium tablets (Cataflam, generics), diclofenac sodium (Voltaren, generics), diflunisal, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid (Ponstel, generics), naproxen (Naprosyn, generics),

naproxen sodium (Anaprox, generics), naproxen sodium extended release (ER) (Naprelan CR, generics), oxaprozin, piroxicam, sulindac, and tolmetin.

The oral NSAIDs have not previously been reviewed; however, prior to implementation of the Uniform Formulary Rule in 2005, the following drugs were added to the BCF: ibuprofen, indomethacin, meloxicam, and naproxen. The clinical review focused on use of the oral NSAIDs for adults with chronic pain due to osteoarthritis, rheumatoid arthritis, soft-tissue pain, back pain, or ankylosing spondylitis. The review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 1absent) the following conclusions for the Oral NSAIDs:

With regards to efficacy,

1. For short-term pain relief (less than 6 months), all of the oral NSAIDs have a similar effect on reducing chronic pain in adults due to osteoarthritis, rheumatoid arthritis, soft-tissue pain, back pain, or ankylosing spondylitis, based on systematic reviews from the Oregon Drug Effectiveness Review Project (DERP), and the Cochrane group.
2. There is no significant difference in efficacy of pain relief with celecoxib (Celebrex) versus the partially COX-2 selective or nonselective NSAIDs, based on results from randomized controlled trials, meta-analyses, and a systematic review from the Agency for Healthcare Research and Quality (AHRQ; Chou 2007).
3. Diclofenac potassium liquid-filled capsules (Zipsor) were superior to placebo for reducing pain following bunionectomy in two trials. There are no head-to-head trials comparing Zipsor to the other NSAIDs.
4. The FDC of naproxen with esomeprazole (Vimovo) was superior to placebo and non-inferior to celecoxib for reducing pain in patients with osteoarthritis of the knee in two trials.

With regard to gastrointestinal (GI) safety,

5. All the NSAIDs increase the risk of serious GI adverse reactions, including bleeding, inflammation, ulceration, and perforation of the stomach or intestines, which can be fatal.
6. Celecoxib showed benefit for short-term (therapy duration less than or equal to 6 months) GI safety versus nonselective NSAIDs based on meta-analyses (DERP and AHRQ) and the SUCCESS trial. However, celecoxib did not show benefit for long-term (therapy duration greater than 6 months) GI safety (CLASS trial; DERP and AHRQ meta-analyses; FDA analysis).
7. In one trial, celecoxib plus aspirin versus naproxen plus the PPI lansoprazole plus aspirin showed no significant difference for development

of endoscopically-confirmed ulcers at 12 weeks (short-term) (Goldstein 2007).

8. Celecoxib versus diclofenac plus the PPI omeprazole showed no significant differences in terms of recurrent ulcer bleeding at 6 months (short-term GI safety) (Chan 2002 New England Journal of Medicine).
9. The GI protective effects of celecoxib therapy alone versus NSAID plus PPI were recently evaluated in the CONDOR study. The results showed short-term GI safety benefit for celecoxib for the composite endpoint of upper and lower GI bleeds when compared to diclofenac plus omeprazole. The results were primarily due to a lower risk of a decrease in hemoglobin (due to presumed occult bleeding of GI origin in the small bowel) in the celecoxib group. (Chan 2010 Lancet)
10. For high-risk patients, taking celecoxib with a PPI may provide increased GI protection versus long-term celecoxib monotherapy. The results of one good-quality trial reported that celecoxib plus omeprazole significantly lowered recurrent GI bleeding in very high-risk GI patients (12-month trial) (Chan 2007 Lancet).
11. For the partially selective NSAIDs, nabumetone showed short-term GI safety benefit compared to nonselective NSAIDs in a single meta-analysis of fair quality (Huang 1999). Etodolac and meloxicam showed no consistent differences in conferring GI safety benefit as compared to nonselective NSAIDs, based on randomized controlled trials and observational studies.
12. For the non-COX-2-selective NSAIDs, clinical trial data suggest that all nonselective NSAIDs are associated with relatively similar risks of serious GI events.
13. Further study is needed to determine the comparative GI safety benefits of concomitant use of an NSAID with various gastroprotective agents (misoprostol, H2 blocker, PPI) in preventing clinical GI events. Misoprostol decreases the risk of clinically relevant GI events, but is associated with a significant increase in nausea, diarrhea, and abdominal pain.
14. In terms of endoscopically visualized gastric ulcers and discontinuation of therapy due to GI adverse events, Vimovo showed short-term GI safety benefit in patients taking low-dose aspirin versus enteric-coated naproxen alone in two trials.
15. There is insufficient data with Zipsor to assess GI risks.

With regard to cardiovascular (CV) safety,

16. NSAIDs may cause an increased risk of serious CV thrombotic events, myocardial infarction (MI), and stroke, which can be fatal.
17. Based on indirect analyses and observational studies, naproxen appears to be risk-neutral with regard to cardiovascular events; however, a black box warning is still present in the package insert for CV events.
18. Celecoxib, partially-selective NSAIDs, and nonselective NSAIDs have an increased risk of CV events, but there are no consistent differences in the incidence of CV events between them (with the exception of naproxen), based on clinical trials, and the DERP and AHRQ analyses.
19. No CV events related to Vimovo and Zipsor were reported in short-term clinical trials, but there is limited data available.

With regard to tolerability,

20. Relative to nonselective NSAIDs, COX-2 selective and partially selective NSAIDs demonstrated improved or similar tolerability profiles. There are no clear differences in tolerability between the nonselective NSAIDs
21. Vimovo showed a significant benefit in tolerability as compared to use of enteric-coated naproxen alone.

With regard to other factors,

22. Two NSAIDs are available over-the-counter without a prescription: ibuprofen and naproxen.
23. Four NSAIDs are formulated as oral suspensions: indomethacin, meloxicam, ibuprofen, and naproxen.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the oral NSAIDs. Based on the clinical findings regarding efficacy, safety, tolerability, and clinical outcomes with NSAIDs, a CMA was performed to compare the non-COX-2 selective/partially-COX-2 selective NSAIDs and NSAID/anti-ulcer FDCs. A cost-effectiveness analysis (CEA) was conducted to compare celecoxib (Celebrex) with the nonselective NSAIDs for treatment of osteoarthritis, and a budget impact analysis (BIA) was performed to compare competing formulary scenarios. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA results for nonselective/partially-selective NSAIDs showed that these products are the most cost-effective option within the oral NSAID class and should be used prior to treatment with NSAID/anti-ulcer FDCs or celecoxib (Celebrex) when clinically appropriate. However, several specific

nonselective/partially-selective NSAIDs were recognized as not being cost-effective relative to the other agents in the class, including naproxen sodium ER (Naprelan CR, generic), diclofenac potassium liquid-filled capsules (Zipsor), diclofenac potassium powder packets (Cambia), and mefenamic acid (Ponstel, generic). The NSAID/anti-ulcer FDCs were comparable on costs with other agents in the oral NSAID class.

Results of the CEA demonstrated that celecoxib was more costly than the nonselective/partially-selective NSAIDs. Published clinical evidence suggested lower risk of GI events with celecoxib compared to nonselective NSAIDs in the short-term (less than or equal to 6 months). However, the cost of preventing an additional ulcer complication with celecoxib was high due to the large difference in cost and small risk reduction in the published clinical data with celecoxib compared to nonselective NSAIDs. Longer-term evidence (greater than 6 months) with celecoxib remains inconclusive with regards to GI risk. Based on these findings, celecoxib should be reserved for patients at high risk for adverse GI events.

The BIA compared several formulary scenarios, including a scenario with an automated PA (step therapy) requiring a trial of generic formulations of partially-selective or nonselective NSAIDs prior to use of celecoxib, and a scenario without an automated PA (no step therapy). The BIA results concluded that the no step-therapy scenario was more cost-effective than the scenario with step therapy for new users of celecoxib.

Relative Cost Effectiveness Conclusion—Based on the results of the economic analysis and other clinical and cost considerations, the P&T Committee concluded (14 for, 0 opposed, 0 abstained, 1 absent) that the most cost-effective scenario designated the following with formulary status on the UF: diclofenac potassium, diclofenac sodium, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, meloxicam, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, sulindac, tolmetin, naproxen/esomeprazole (Vimovo), diclofenac/misoprostol (Arthrotec), and celecoxib (Celebrex).

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 (13 for, 0 opposed, 1 abstained, 1 absent) the following remain formulary on the UF without step therapy: diclofenac potassium, diclofenac sodium, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, meloxicam, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, sulindac, tolmetin, naproxen/esomeprazole (Vimovo),

diclofenac/misoprostol (Arthrotec), and celecoxib (Celebrex). The P&T Committee recommended diclofenac potassium liquid-filled capsules (Zipsor), diclofenac potassium powder packets (Cambia), naproxen sodium ER (Naprelan CR), and mefenamic acid (Ponstel) be designated NF.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

☐ Approved, but modified as follows:

2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (13 for, 0 opposed, 1 abstained, 1 absent), ibuprofen (400 mg, 600 mg, 800 mg tablets and ~~125 mg/5 mL suspension~~), indomethacin (25 mg, 50 mg), meloxicam (7.5 mg, 15 mg) and naproxen (250 mg, 500 mg) remain designated with BCF status.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

☐ Approved, but modified as follows:

3. ***COMMITTEE ACTION: MN CRITERIA***—Based on the clinical and cost evaluation of the oral NSAIDs and the conditions for establishing MN for a NF medication, the P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) MN criteria for diclofenac potassium liquid-filled capsules (Zipsor), diclofenac potassium powder packets (Cambia), naproxen sodium ER (Naprelan CR), and mefenamic acid (Ponstel). Since there are many formulary alternatives available, the MN criteria would require that a formulary alternative be contraindicated. (See Appendix B for full MN criteria.)

Director, TMA, Decision: ☒ Approved ☐ Disapproved

☐ Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (13 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 4, 2012

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

B. Contraceptive Agents

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the drugs in the Contraceptive Agents class. The clinical review for the contraceptive products included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1). The Contraceptives Agents class is comprised of three subclasses: oral contraceptive products (OCPs), miscellaneous contraceptives (transdermal patch, vaginal ring, medroxyprogesterone injections) and emergency contraceptives. The subclasses are outlined in Table 1 on pages 30–33.

The Contraceptive Agents were previously reviewed in May 2006 for UF status. Generic formulations are available for several products (See Table 1). Four new OCPs have recently entered the market: drospirenone 3mg/ethinyl estradiol (EE) 20 mcg/levomefolate Ca 0.451mg (Beyaz), norethindrone acetate 1mg/EE 10mcg/ferrous fumerate 75mg (Lo Loestrin Fe), levonorgesterol 0.1mg/EE 20mcg and levonorgesterol 0.1mg/EE 10mcg for extended use (LoSeasonique), and drospirenone 3mg/EE 30mcg/levomefolate Ca 0.451mg (Safyral). One new emergency contraceptive is also available, ulipristal (Ella).

Several OCPs are available on the UF and BCF, and all the miscellaneous contraceptives are currently designated as UF. For the emergency contraceptives, in November 2009, levonorgestrel 0.75 mg (Next Choice, Plan B generic) was designated as BCF and levonorgestrel 1.5 mg (Plan B One Step) was designated as Uniform formulary.

The Contraceptive Drug Class accounted for $87 million in MHS expenditures in FY 2010. In terms of MHS utilization, drospirenone 3mg/EE 20mcg (Yaz, generics) is the most utilized contraceptive, followed by norgestimate 0.18mg/0.215mg/0.25mg/EE 25mcg (Ortho Tri-Cyclen Lo).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended the following conclusions for the contraceptives:

- **Oral Contraceptives Subclass**—For the OCPs subclass, the P&T Committee, voted (15 for, 0 against, 0 abstained, 0 absent) the following conclusions were made:

  1. The differences among the OCPs include estrogen content, progestogen content, regimen, phasic formulation, and non-contraceptive benefits (e.g., acne, premenstrual dysmorphic disorder). The most commonly utilized OCPs are the low-estrogen products containing 20-30 mcg of EE. OCPs commonly include an estrogen with a progestin (combined OCP).
  2. There are no clinically relevant differences in contraceptive effectiveness among the different OCPs, as they all have Pearl Indices (pregnancies per 100 woman-years of use) ranging from < 1 to <3. Current literature does not provide sufficient evidence that combined OCPs containing ≤ 20 mcg EE differ from those with higher EE dosage in preventing pregnancy. However, combined OCPs with ≤ 20 mcg EE are associated with higher rates of changes in bleeding and amenorrhea.
  3. The continuous and extended cycle products (Lybrel, Seasonale, Seasonique, LoSeasonique), allow for shorter, fewer or no periods. The Cochrane reviewers concluded extended or continuous cycle contraceptives are reasonable options for women without contraindications to therapy. Of note, the same regimen can be reproduced by eliminating the pill-free interval of monophasic combined OCPs for 2-3 cycles.
  4. Most if not all combined contraceptives offer non-contraceptive benefits, including control of heavy menstrual bleeding or irregular cycles, and reduction of acne, dysmenorrhea, endometriosis pain and menstrual migraines, regardless of FDA approval for uses other than pregnancy prevention.
  5. The most commonly reported adverse effects of oral contraceptives include breast tenderness, headache, migraine, nausea, nervousness, vomiting, dizziness, weight gain, fluid retention, tiredness, decline of libido, and increased blood pressure.
  6. The use of combined OCPs confers an increased risk of venous thromboembolism (VTE). Based on epidemiological data, the risk of VTE with drospirenone (found in Yaz, drosperinone 3mg/EE 30mcg [Yasmin], Sayfral and Beyaz) is about 2-3 times higher than levonorgestrel-containing OCPs; this risk appears similar to the risk with the third-generation progestins (e.g., desogestrel). FDA is currently reviewing all available data regarding the increased VTE risk with drospirenone-containing oral contraceptives.

7. Comments regarding the newest OCPs include the following: dienogest 2mg/3mg/estradiol valerate 3mg/2mg/2mg/1mg, (Natazia) has complicated dosing instructions if a dose is missed, and the benefits of a quadraphasic OCP remain to be determined. For Beyaz and Safyral, these two products are similar to Yaz and Yasmin, respectively, with the exception of folate, which is added to decrease the risk of neural tube defects if a pregnancy occurs during therapy. Efficacy for both Beyaz and Sayfral was based on data with the innovator products, and clinical trial data is not available. Lo Loestrin Fe has the lowest dose of EE available in an OCP, and had a Pearl Index of 2.92 in the open-label trial used to gain FDA approval. LoSeasonique is a low-EE dose extended cycle OCP given for 91 days (84 days of estrogen and progesterone and 7 days of low dose estrogen).

- **Miscellaneous Contraceptives Subclass**—For the miscellaneous contraceptives subclass, the P&T Committee, based upon its collective professional judgment voted (15 for, 0 against, 0 abstained, 0 absent)

  1. Contraceptive products offer alternative routes of administration including depot medroxyprogesterone acetate (DMPA) injections, a transdermal patch (Ortho Evra), and a vaginal ring (Nuvaring).
  2. Trials have demonstrated similar contraceptive effectiveness for the patch or vaginal ring as the combined OCs. The injectable DMPA contraceptives are highly effective agents; no pregnancy was reported in the three, year-long trials used to gain FDA approval.
  3. Based on a comparative trial, adverse effects of the transdermal patch appear similar to the combined OCP comparator, with the exception of a higher incidence of site application reactions, breast symptoms (e.g., breast tenderness), and dysmenorrhea. Other concerns with the Ortho Evra patch include adhesion problems and application site reactions. The OrthoEvra patch has a black box warning with respect to greater risk of VTE than oral contraceptives, and higher consistent estrogen blood levels (systemic exposure ~ 60% higher than combined OCs).
  4. The most common adverse effects of the vaginal ring were vaginitis, headache, vaginal secretion, weight gain, and nausea. One concern with Nuvaring is deployment limitations related to storage requirements.
  5. Women receiving injectable DMPA may lose significant bone mineral density, an effect which may not be completely reversible. Injectable DMPA products carry a black box warning regarding this risk. Other concerns with injectable DMPA include progressive (and substantial) weight gain, amenorrhea, irregular menses and unpredictable

spotting/bleeding; and lack of immediate reversibility (10 months to return to baseline fertility)

6. The miscellaneous contraceptives serve a niche role and are appropriate contraceptive options for select patients.

- **Emergency Contraceptives Subclass**—For the miscellaneous contraceptives subclass, the P&T Committee, (14 for, 1 against, 0 abstained, 0 absent)

1. Levonorgestrel (Next Choice, generic Plan B; Plan B One Step) has a 3-day window of effectiveness following unprotected intercourse or contraceptive failure, and is available over-the-counter (OTC) for women older than 17 years. Ulipristal (Ella) is a new prescription emergency contraceptive which is effective for up to 5 days after unprotected intercourse.
2. Levonorgestrel 0.75 mg taken in 2 doses 12 hours apart has an efficacy rate of about 95% if taken within 24 hours of unprotected intercourse. Efficacy decreases over time; the efficacy rate is 86% if taken within 25-48 hours, and 58% if taken within 49 to 72 hours of unprotected intercourse. The single-dose 1.5-mg levonorgestrel regimen is as effective as the two-dose regimen taken 12 hours apart.
3. Ulipristal (Ella) is effective at preventing pregnancy following unprotected intercourse, based on the two pivotal trials. No decrease in efficacy occurred over the 120 hour study period. Two head-to-head comparisons of Ella 30 mg with levonorgestrel 1.5mg, are available. In one study Ella was non-inferior to levonorgestrel at preventing pregnancy (Creinin 2006). The other study demonstrated that Ella prevented more unintended pregnancies than levonorgestrel when administered within 72 and 120 hours after unprotected intercourse (observed pregnancy rate with Ella 1.90, 95% CI 1.13-3.12, versus levonorgestrel 2.50, 95% CI 1.68-3.94; p = 0.037; (Glasier 2010).
4. Ella was well tolerated in the clinical trials and its side effect profile is similar to that of levonorgestrel. The most common adverse effects were headache, abdominal pain, nausea and dysmenorrhea. Long term safety with Ella remains unknown.

Relative Cost-Effectiveness—The P&T Committee evaluated the relative cost-effectiveness of the oral contraceptive products (OCPs), the miscellaneous contraceptives (patch, vaginal ring, medroxyprogesterone injections), and the emergency contraceptives. CMAs and BIAs were performed based on clinical findings that the efficacy, safety, tolerability, and other factors among the OCPs were similar with regard to contraception when used correctly. CMAs were used to analyze the miscellaneous contraceptives. CEAs and CMAs were used to analyze the emergency contraceptives, as efficacy differences between the agents were noted in the clinical

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

- CMA and BIA were used to assess the potential impact of cost scenarios where selected OCPs were designated with formulary or NF status on the UF. Two of the selected products are currently designated with BCF status: Yaz, and Yasmin. Four new agents selected are currently designated with formulary status on the UF: Beyaz, Loestrin Fe, LoSeasonique, and Safyral. Cost scenarios evaluating the impact of designating selected agents on the BCF were also considered.
- CMA alone was performed on the miscellaneous contraceptives (patch, vaginal ring, and medroxyprogesterone intramuscular (IM) and subcutaneous formulations) because there is limited generic competition within the class.
- In the emergency contraceptives subclass, CEA and CMA analyses were used to assess potential impact of pregnancies avoided, based on the clinically reviewed differences between the agents. The relative drug costs of the various treatment regimens were also assessed.

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

- **Oral Contraceptives Subclass**—For the OCPs subclass, the P&T Committee, based upon its collective professional judgment, voted (14 for, 0 against, 0 abstained, 1 absent) as follows: BIA showed the scenario where all current BCF agents were retained on the BCF, all current UF agents that had been previously reviewed were retained on the UF, and all current NF, as well as the four new agents, were designated with NF status resulted in the lowest cost estimate compared to current MHS expenditures.
- **Miscellaneous Contraceptives Subclass**—For the miscellaneous contraceptives subclass, the P&T Committee, based upon its collective professional judgment, voted (15 for, 0 against, 0 abstained, 0 absent) as follows: CMA results showed that the average weighted price per day of therapy at all three points of service for the miscellaneous contraceptives was comparable to formulary agents included in the OCPs subclass.
- **Emergency Contraceptives Subclass**—For the emergency contraceptives subclass, the P&T Committee, based upon its collective professional judgment, voted (15 for, 0 against, 0 abstained, 0 absent) as follows: CEA results for the emergency contraceptive agents showed that at current costs, the incremental cost effectiveness ratio with ulipristal (Ella) was less than the projected annual median cost of a live birth in the United States and treatment with ulipristal is a cost-effective alternative compared to levonorgestrel in the MHS. The CMA

results showed that Next Choice was the most cost-effective agent, followed by Plan B One-Step and Ella.

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

    - **OCPs Subclass**—For the OCPs subclass, the P&T Committee voted (14 for, 0 against, 0 abstained, 1 absent) that the Jolessa branded generic formulation of levonorgestrel 0.15mg/EE 30mcg, extended regimen (Seasonale, generics) be designated formulary on the UF (UF listing only applies to the Jolessa formulation), and to retain the following drugs on the UF: drospirenone 3mg/EE 20mcg, (Yaz, generics), levonorgestrel 0.1mg/EE 20mcg, (Sronyx, generics), norethindrone1mg/EE 20mcg +/- ferrous fumerate, (Loestin 1/20 or Loestrin Fe 1/20 generics), drospirenone 3mg/EE 30mcg (Yasmim, generics), levonorgestrel 0.15mg/EE 30mcg (Levora, generics), norgestrel 0.3mg/EE 30mcg, (Lo/Ovral, generics), desogestrel 0.15mg/EE 30mcg (Desogen, generics), norethindrone 1.5mg/EE 30mcg +/- ferrous fumerate (Loestrin 1.5/30 or Loestrin Fe 1.5/30, generics), norethindrone 1mg/EE 35mcg (Norinyl 1+35, generics), norgestimate 0.25mg/EE 35mg (Mononessa, generics), norethindrone 0.5mg/EE 35mcg (Modicon, generics), ethynodiol diacetate 1mg/EE 35mcg (Zovia 1/35E, generics), Norinyl 1+50 (norethindrone 1mg/mestranol 50mcg, generics), ethynodiol diacetate 1mg/EE 50mg (Zovia 1/50E), norgestrel 0.5mg/EE 50mcg (Ogestrel), 0.5mg/1mg/EE 35mcg (Necon 10/11 norethindrone), desogestrel 0.15mg/EE 20mcg/10mcg (Mircette, generics), norgestimate 0.18mg/0.215mg/0.25mg/EE 25mcg (Ortho-Tri Cyclen Lo), norgestimate 0.18mg/0.215mg/0.25mg/EE 35mcg (Trinessa generics), levonorgestrel 0.05mg/0.075mg/0.125mg/EE 30mcg/40mcg/30mcg (Trivora, generics), norethindrone 0.5mg/1mg/0.5mg/EE 35mcg (Tri-Norinyl, generics), norethindrone 0.5mg/0.75mg/1mg/EE 35mcg (Ortho-Novum 7/7/7, generics), desogestrel 0.1mg/0.125mg/0.15mg/EE 25mcg (Cyclessa, generics), and Nor-Q-D (norethindrone 0.35mg, (Nor-Q-D generics).

      The following OCPs were designated NF or retained NF status on the UF:

        - norethindrone acetate 1mg/EE 10mcg (Lo Loestrin Fe)
        - levonorgestrel 0.1mg/EE 20mcg + 10mcg (LoSeasonique)
        - drospirenone 3mg/EE 20mcg/levomefolate 0.451mg (Beyaz)

- drospirenone/EE 30mcg/levomefolate 0.451mg (Safyral)
- levonorgestrel 90mcg/EE 20mcg, continuous regimen (Lybrel, generic)
- norethindrone acetate 1mg/EE 20mg, extended regimen (Loestrin 24 Fe)
- norethindrone 0.4mg/EE 35mcg (Ovcon-35 generics; also includes Femcon Fe chewable and Zeosa chewable)
- norethindrone 1mg/EE 50mcg (Ovcon-50)
- levonorgestrel 0.15mg/EE 30mcg + 10mcg, extended regimen (Seasonique, generics)
- norethindrone 1mg/EE 20mcg/30mcg/35mcg/ferrous fumerate 75mg (Estrostep Fe, generics)
- dienogest 2mg/3mg/estradiol valerate 3mg/2mg/2mg/1mg, (Natazia)
- levonorgestrel 0.15mg/EE 30mcg, extended regimen (Seasonale, generics, including Introvale and Quasense), with the exception of Jolessa branded generic

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

- **Miscellaneous Contraceptive Subclass**—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) the following drugs remain formulary on the UF: norelgestromin/EE 50 mcg transdermal (Ortho Evra), etonorgestrel/EE vaginal ring (NuvaRing), medroxyprogesterone acetate 150 mg/mL (Depo-Provera IM, generics), and medroxyprogesterone acetate 104 mg/0.65 mL (Depo-SubQ Provera 104). No miscellaneous contraceptive agent was recommended for NF placement.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

- **Emergency Contraceptive Subclass**—The P&T Committee recommended (12 for, 0 opposed, 3 abstained, 0 absent) the following drugs remain formulary on the UF: levonorgestrel 0.75mg (Next Choice; Plan B generic), levonorgestrel 1.5mg (Plan B One Step), and that ulipristal (Ella) be designated formulary on the UF. No emergency contraceptive was recommended for NF placement

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

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

   - **OCPs Subclass**—The P&T Committee recommended (13 for, 1 opposed, 0 abstained, 1 absent) the following drugs remain designated BCF:
     - drospirenone 3mg/EE 20mcg (Yaz, generics)
     - levonorgestrel 0.1mg/EE 20mcg (Sronyx, generics)
     - drosperinone 3mg/EE 30mcg (Yasmin, generics)
     - levonorgestrel 0.15mg/EE 30mcg (Levora, generics)
     - norethindrone 1mg/EE 35mcg (Norinyl 1+35, generics)
     - norgestimate 0.25mg/EE 35mcg (Mononessa, generics)
     - norgestimate 0.18mg/0.215mg/0.25mg/EE 25mcg (Ortho-Tri Cyclen Lo)
     - norgestimate 0.18mg/0.215mg/0.25mg/EE 35mcg (Trinessa, generics)
     - norethindrone 0.35mg (Nor-Q-D, generics).
     - Additionally, levonorgesterol 0.15mg/EE 30 mcg for extended use, the Jolessa branded formulation of Seasonale, was added to the BCF, due to patient compliance and because cost-effective generics are now available at prices comparable to other generic BCF agents.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

- **Miscellaneous Contraceptive Subclass**—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) that none of the miscellaneous contraceptives be designated as BCF.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

- **Emergency Contraceptive Subclass**—The P&T Committee recommended (13 for, 0 opposed, 2 abstained, 0 absent) 0.75 mg levonorgestrel (Next Choice; generic Plan B) remain designated BCF.

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

3. ***COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA***—Based on the clinical evaluation of contraceptive agents, and the conditions for establishing MN for NF medications, the P&T Committee recommended (14 for, 0 against, 0 abstained, 1 absent) MN criteria for the following OCPs: Beyaz, Safyral, Lo Loestrin Fe, and LoSeasonique, and to maintain the existing MN criteria for Seasonale or equivalents (e.g., Quasense, Introvale—excludes Jolessa brand), Loestrin Fe 24 and equivalents, Natazia, Ovcon 50 and equivalents, Lybrel and equivalent, Ovcon 35 and equivalents, including Femcon Fe chewable and Zeosa, Seasonique, and Estrostep Fe and equivalents. (See Appendix B for full MN criteria.)

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

4. ***COMMITTEE ACTION: UF IMPLEMENTATION PERIOD***—The P&T Committee recommended (14 for, 0 against, 0 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision. Based on the P&T Committee's recommendation, the effective date is January 4, 2012.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

5. ***COMMITTEE ACTION: EMERGENCY CONTRACEPTION QUANTITY LIMITS (QLs)***—The P&T Committee recommended (13 for, 0 against, 2 abstained, 0 absent) maintaining the current QLs for all the emergency contraceptives of one fill per prescription with no refills.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

Table 1: Drugs in the Contraceptives Class

	Brand Name	Manufacturer	Equiv	Estrogen (mcg)	Progestogen	Estrogen Activity	Progesterone Activity	Androgen Activity
Monophasic OCPs with 10mcg EE	Lo Loestrin Fe	Warner Chilcott	-	EE 10	1.0 mg norethindrone acetate	Low	High	Medium
Monophasic OCPs with 20mcg EE	Aviane	Duramed	AB1	EE 20	0.1 mg levonorgestrel	Low	Low	Low
	Lutera	Watson						
	Orsythia	Qualitest						
	Lessina	Barr	AB2					
	Sronyx	Watson						
	LoSeasonique	Duramed	-	EE 20+ 10	0.10 mg levonorgestrel	Low	Low	Low
	Lybrel	Wyeth	AB	EE 20	0.9 mg levonorgestrel	Low	Low	Low
	Amethyst	Watson						
	Junel 1/20	Barr	AB	EE 20	1.0 mg norethindrone acetate	Low	High	Medium
	Loestrin 1/20	Teva						
	Microgestin 1/20	Watson						
	Junel Fe 1/20	Barr	AB					
	Gildess Fe 1/20	Qualitest						
	Loestrin Fe 1/20	Teva						
	Microgestin Fe 1/20	Watson						
	Loestrin 24 Fe	Warner Chilcott	-	EE 20	1.0 mg norethindrone acetate	Low	High	Medium
	Beyaz	Bayer	-	EE 20	3 mg drospirenone	Low	Unclear	No
	Yaz	Bayer	AB	EE 20	3 mg drospirenone	Low	Unclear	No
	Gianvi	Teva						
	Loryna	Sandoz						
Monophasic OCPs with 25mcg EE	Generess FE	Watson	-	EE 25	0.8 mg norethindrone acetate	Low		
Monophasic OCPs with 30mcg EE	Altavera	Sandoz	AB	EE 30	0.15 mg levonorgestrel	Low	Medium	Medium/High
	Levora 0.15/30-28	Watson						
	Nordette-28	Duramed						
	Portia-28	Barr						
	Seasonale	Duramed	AB					
	Introvale	Sandoz						
	Quasense	Watson						
	Jolessa	Barr						
	Seasonique	Duramed	AB	EE 30 + 10	0.15 mg levonorgestrel	Low	Medium	Medium
	Amethia	Watson						
	Cryselle	Barr	AB	EE 30	0.3 mg norgestrel	Low	Medium	Medium/High
	Lo/Ovral	Wyeth						
	Low-Ogestrel-28	Watson						

	Apri	Barr	AB	EE 30	0.15 mg desogestrel	Low	High	Low
	Desogen	Organon						
	Emoquette	Qualitest						
	Ortho-Cept	Ortho						
	Reclipsen	Watson						
	Solia	Prasco						
	Junel 1.5/30	Barr	AB	EE 30	1.5 mg norethindrone acetate	Low	High	High
	Loestrin 1.5/30	Duramed						
	Microgestin 1.5/30	Watson						
	Gildess Fe 1.5/30	Qualitest	AB					
	Junel Fe 1.5/30	Barr						
	Loestrin-Fe 1.5/30	Duramed/Barr						
	Microgestin Fe 1.5/30	Watson						
	Yasmin	Berlex	AB	EE 30	3 mg drospirenone	Low	Unclear	No
	Ocella	Barr						
	Syeda	Sandoz						
	Zarah	Watson						
	Safyral	Bayer	-	EE 30	3 mg drospirenone	Low	Unclear	No
Monophasic OCPs with 35mcg EE	Brevicon	Watson	AB	EE 35	0.5 mg norethindrone	Medium	Low	Low
	Modicon	Ortho						
	Necon	Watson						
	Nortrel 0.5/35	Barr						
	Femcon Fe (chewable)	Warner-Chilcott	AB	EE 35	0.4 mg norethindrone	Medium	Low	Low
	Zeosa	Teva						
	Ovcon-35	Warner-Chilcott	AB					
	Balziva	Barr						
	Briellyn	Glenmark						
	Zenchent	Watson						
	Mononessa	Watson	AB	EE 35	0.25 mg norgestimate	Medium	Low	Low
	Ortho-Cyclen	Ortho						
	Previfem	Qualitest						
	Sprintec	Barr						

	Cyclafem 1/35	Qualitest	AB	EE 35	1.0 mg norethindrone	Medium	Medium/High	Medium
	Necon	Watson						
	Norinyl 1+35	Watson						
	Nortrel	Barr						
	Ortho-Novum 1/35	Ortho						
	Kelnor	Barr	AB	EE 35	1.0 mg ethynodiol diacetate	Medium	High	Low
	Zovia 1/35E	Watson						
Monophasic OCPs with 50mcg EE or mestranol	Necon 1/50	Watson	AB	Mes 50	1 mg norethindrone	Medium	Medium	Medium
	Norinyl 1+50	Watson						
	Ovcon-50	Warner Chilcott	-	EE 50	1 mg norethindrone	High	Medium	Medium
	Zovia 1/50E	Watson	-	EE 50	1.0 mg ethynodiol diacetate	High	High	Medium/High
	Ogestrel	Watson	-	EE 50	0.5 mg norgestrel	High	High	High
Biphasic OCPs	Necon 10/11	Watson	-	EE 35	0.5 mg/1.0 mg norethindrone	High	Medium	Low/Medium
	Azurette	Watson	AB	EE 20/10mcg	0.150mg desogestrel	Low	High	Low
	Kariva	Barr						
	Mircette	Duramed/Barr						
Triphasic OCPs	Ortho Tri-Cyclen Lo	Ortho	AB	EE 25	0.18/0.215/0.25 mg norgestimate	Low	Low	Low
	Tri-Lo Sprintec	Barr						
	Ortho Tri-Cyclen	Ortho	AB	EE 35	0.18/0.215/0.25 mg norgestimate	Medium	Low	Low
	Trinessa	Watson						
	Tri-Previfem	Qualitest						
	Tri-Sprintec	Barr						
	Enpresse	Barr	AB	EE 30/40/30	0.05/0.075/0.125 mg levonorgestrel	Medium	Low	Low/Medium
	Levonest	Novast Lab						
	Trivora	Watson						
	Aranelle	Barr	AB	EE 35	0.5/1/0.5 mg norethindrone	Medium	Medium	Low/Medium
	Leena	Watson						
	Tri-Norinyl	Watson						
	Cyclafem 7/7/7	Qualitest	AB	EE 35	0.5/0.75/1 mg norethindrone	Medium	Medium	Low/Medium
	Necon 7/7/7	Watson						
	Nortrel 7/7/7	Barr						
	Ortho-Novum 7/7/7	Ortho						

	Caziant	Watson	AB	EE 25	0.1/0.125/0.15 mg desogestrel	Low	High	Low
	Cesia	Prasco						
	Cyclessa	Organon						
	Velivet	Barr						
	Estrostep Fe	Warner-Chilcott	AB	EE 20/30/35	1.0 mg norethindrone	Low	High	Medium
	Tri-Legest FE	Barr						
	Tilia FE	Watson						
Quadriphasic OCPs	Natazia	Bayer	-	Estradiol valerate 3/2/2/1 mg	2/3 mg dienogest	Low		
Progestogen-Only OCPs	Camila	Barr	AB1	-	0.35 mg norethindrone	-		
	Heather	Glenmark						
	Nora-BE	Watson						
	Nor-QD	Watson						
	Errin	Barr	AB2					
	Micronor	Ortho						
	Norethindrone	Glenmark						
	Jolivette	Watson						
Contraceptive patch	Ortho Evra	Ortho	--	*> 50mcg EE (based on Ortho Evra data; ~60% > exposure than with 35 mcg EE)	0.20 mg norelgestromin			
Contraceptive vaginal ring	Nuvaring	Organon		~ 15 mcg EE	~0.12 mg etonogestrel			
Injectable Contraceptives	Depo-subqProvera104**	Pfizer	-	-	104 mg/0.65mL			
	Depo-provera (syr/vl)	Pfizer	AB	-	150 mg/mL			
	Medroxyprogesterone acetate ((syr/vl)	Greenstone						
	Medroxyprogesterone acetate ((syr/vl))	Teva		-	150 mg/mL			
Emergency Contraceptives	Plan B	Duramed	AB	-	0.75 mg levonorgestrel			
	Next Choice	Watson						
	Plan B One-Step	Teva	-	-	1.5mg levonorgestrel			
	Ella	Watson	-	-	30 mg ulipristal			

C. Phosphodiesterase Type 5 (PDE-5) Inhibitors for Erectile Dysfunction (ED)

Relative Clinical Effectiveness—The P&T Committee evaluated the clinical effectiveness of the PDE-5 Inhibitors for the treatment of ED. The drugs in the class include sildenafil (Viagra), tadalafil (Cialis), vardenafil oral tablets (Levitra), and one new drug—vardenafil orally dissolving tablets (ODT) (Staxyn). The PDE-5s for ED were previously reviewed in August 2009; at that time, vardenafil was designated with BCF status, with an automated PA requiring a trial of vardenafil prior to sildenafil or tadalafil, which were designated NF. Quantity limits are in place for the PDE-5s for ED.

Vardenafil ODT (Staxyn) contains the same chemical ingredient as vardenafil oral tablets (Levitra). It is available in 10 mg ODT tablets, which is the recommended dose for all patients. In contrast, the starting dose for vardenafil oral tablets is 5 mg in patients older than age 65. Pharmacokinetic studies with vardenafil 10 mg ODT show a higher area under the curve compared to vardenafil 10 mg oral tablets. The two placebo-controlled trials used to obtain FDA approval reported superior efficacy with Staxyn in treating ED. Information regarding the safety, effectiveness, and clinical outcomes of the PDE-5s for ED subclass was considered. The clinical review included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 0 absent) the following conclusions for the PDE-5s for ED:

With regards to efficacy,

1. There are no head-to-head comparative trials between the PDE-5 inhibitors assessing efficacy for ED.
2. Based on meta-analyses by AHRQ, Cochrane, and BioMed Central, indirect comparisons suggest that there are similar improvements between vardenafil oral tablets, sildenafil, and tadalafil in the following endpoints: International Index of Erectile Function (IIEF) "EF" domain change, percentage of patients responding "Yes" to Global Assessment question 1 (which asks "Did this treatment improve your erections?"), and percentage of patients reporting improved erections.
3. The improvement in IIEF score with Staxyn appears similar to that seen in the AHRQ review based on indirect comparison.
4. The 2009 PDE-5 UF review reported there was insufficient evidence to conclude that daily therapy for ED was superior to on demand therapy. There is no new evidence to change this conclusion
5. The improvement in IIIEF score with Staxyn appears similar to that seen in the AHRQ review based on indirect comparison.

With regard to safety,

6. There is insufficient evidence to conclude that there are clinically relevant differences in safety between PDE-5 inhibitors for ED.
7. Clinical trials with vardenafil ODT have identified no safety issues that were not previously identified in the studies of the vardenafil film-coated tablets. However, unlike the other PDE-5s, vardenafil ODT is not recommended for use in patients with renal or hepatic impairment.

With regard to other factors,

8. The PDE-5 inhibitors are highly therapeutically interchangeable, when used for treating ED.

Relative Cost-Effectiveness, Relative Cost-Effectiveness Conclusion, UF Recommendation, BCF Recommendation—Due to contract solicitation issues, the cost effectiveness review and P&T Committee conclusions for the PDE-5 inhibitors for ED will be presented at a future meeting.

1. ***COMMITTEE ACTION: QLs***—The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) QLs for Staxyn, consistent with the QLs for the other PDE-5 inhibitors for ED. The collective QL for Staxyn is 16 ODT per 90 days in the Mail Order Pharmacy and the collective QL is 6 ODT per 30 days in the Retail Network.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

V. BCF ISSUES—SIMVASTATIN 80 MG BCF DELETION

In June 2011, the FDA updated the package inserts of products containing simvastatin 80 mg (Zocor, generic; and simvastatin/ezetimibe, Vytorin 80/10) to reflect safety concerns. Based on results of the published SEARCH trial and an internal analysis, the FDA concluded there was a higher risk of myopathy and rhabdomyolysis with simvastatin 80 mg, when compared to simvastatin 20 mg. Accordingly, there are new contraindications with other drugs and warnings limiting use to patients already stabilized on simvastatin 80 mg for longer than 12 months. Currently there over 11,000 MHS patients receiving simvastatin 80 mg. Although there are several limitations to this data, including the fact the FDA did not evaluate patient-level adverse reaction reports, the P&T Committee agreed to remove simvastatin 80 mg from the BCF, and to update the existing automated step therapy criteria for the Antilipidemic-1s.

1. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee voted (12 for, 1 opposed, 1 abstained, 1 absent) to remove the simvastatin 80 mg dosage strength (Zocor; generics) from the BCF.

Director, TMA, Decision: ☒Approved □ Disapproved

Approved, but modified as follows:

VI. UTILIZATION MANAGEMENT

A. Montelukast (Singulair)—PA: PA criteria were proposed for montelukast. National and international treatment guidelines, as well as pertinent published clinical literature, were used to define supportable indications for use of montelukast. Utilization data from the MHS population was presented to the P&T Committee with respect to indications deemed supportable.

1. ***COMMITTEE ACTION: PA CRITERIA***—The P&T Committee recommended (12 for, 1 opposed, 1 abstained, 1 absent) the following PA criteria should apply to montelukast. Montelukast will be approved only for patients under the age of 19 and patients 19 or older who show evidence of use for an FDA-approved and guideline-supported indication. All current and new users of montelukast must meet one of the following criteria to pass through the PA process.

    a) Automated PA criteria:

        (1) Patient is ≤18 years of age.

        (2) Patient has received an inhaled corticosteroid or combination inhaled corticosteroid/inhaled long-acting beta agonist during the previous 180 days at a MTF, retail network pharmacy, or the mail order pharmacy.

    b) Manual PA criteria:

        (1) Coverage approved if:

            (a) The patient/provider documents use of montelukast for seasonal allergic rhinitis (or nasal polyposis) with evidence of a inadequate therapy with a nasal corticosteroid dispensed during the previous 180 days at a MTF, a retail network pharmacy, or the mail order pharmacy; or

(b) The patient/provider documents intolerance (due to experienced adverse events) or contraindication to either inhaled or intranasal corticosteroids.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

2. ***COMMITTEE ACTION: Montelukast PA IMPLEMENTATION PERIOD***— The P&T Committee recommended (12 for, 0 opposed, 2 abstained, 1 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all points of service; and 2) TMA send a letter to beneficiaries affected by this UF decision. The effective date is February 1, 2012.

Director, TMA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

B. Prescription Omega-3 Acid (Lovaza)—PA: Prior authorization for all current and new users of prescription omega-3-acid (Lovaza) was recommended at the February 2011 Committee meeting, limiting Lovaza use to the current FDA-approved indication for patients with triglyceride (TG) levels greater than 500 mg/dL. Since implementation of the PA requirements in July 2011, several questions regarding the PA form have been raised by providers and patients regarding patients with TG levels less than 500 mg/dL. P&T Committee members were briefed on the current status of the Lovaza PA program. Recommendations were made to clarify the decision point for patients with TG < 500mg/dL to more accurately reflect the intent of the P&T Committee.

1. ***COMMITTEE ACTION: LOVAZA PA FORM CLARIFICATION AND IMPLEMENTATION***—The P&T Committee recommended (12 for, 0 against, 1 abstained, 2 absent) updating the Lovaza PA form as noted above. Implementation can occur administratively.

Director, TMA, Decision: ☑ Approved □ Disapproved

Approved, but modified as follows:

VII. ITEMS FOR INFORMATION

A. Pharmacy Outcomes Research Team (PORT): The PORT updated the P&T Committee on prescribing trends and patient outcomes in several drug classes where step therapy (automated PA) had been implemented.

B. Rosiglitazone (Avandia) Risk Evaluation and Mitigation Strategy (REMS)—Rosiglitazone (Avandia) was designated NF at the November 2010 P&T Committee meeting, due to well-established safety concerns and the FDA requirement for a REMS program by the manufacturer. The details of the REMS are now available. Rosiglitazone products will be withdrawn from supply chains beginning October 18, 2011, and patients will not be able to buy their prescriptions in retail pharmacies after November 18, 2011. Further information regarding availability will be provided on the TRICARE Formulary Search Tool.

C. Saxagliptin/Metformin ER (Kombiglyze XR) PA Criteria—The manual PA criteria for Kombiglyze XR were updated to remove the criteria regarding adverse events or history of lactic acidosis with metformin.

D. Disease-Modifying Drugs for Multiple Sclerosis Drug Class—The UF review of the injectable drugs for multiple sclerosis originally scheduled for this meeting was tabled.

VIII. ADJOURNMENT

The meeting adjourned at 1700 hours on August 10, 2011, and at 1130 hours on August 11, 2011. The next meeting will be in November 2011.

Appendix A—Attendance

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

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

Appendix D—Table of Abbreviations

SUBMITTED BY:

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

DECISION ON RECOMMENDATIONS

Director, TMA, decisions are as annotated above.

Jonathan Woodson, M.D.
Director

27 Oct 2011
(Date)

Appendix A—Attendance

Voting Members Present	
John Kugler, COL (Ret.), MC, USA	DoD P&T Committee Chair
CDR Joe Lawrence	Director, DoD Pharmacoeconomic Center (Recorder)
Col George Jones, BSC	Deputy Chief, Pharmaceutical Operations Directorate
COL Pete Bulatao, MSC for COL Carole Labadie, MSC	Army, Pharmacy Officer
Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CAPT Vernon Lew	Coast Guard, Pharmacy Officer
COL Doreen Lounsbery, MC	Army, Internal Medicine Physician
CAPT Edward Norton	Navy, Pharmacy Officer (Pharmacy Consultant BUMED)
COL Ted Cieslak, MC	Army, Physician at Large
Major Jeremy King, MC	Air Force, OB/GYN Physician
LTC Bruce Lovins, MC	Army, Family Practice Physician
CDR Michelle Perello for CAPT Walter Downs, MC	Navy, Internal Medicine Physician
LT Christina Olsen for CDR Eileen Hoke, MC	Navy, Pediatrics
Lt Col Sam Munro, MC	Air Force, Physician at Large
Mr. Joe Canzolino	Department of Veterans Affairs
Nonvoting Members Present	
Mr. David Hurt	Associate General Counsel, TMA
CDR Michele Hupp, MSC	Defense Medical Standardization Board
Maj Achilles Hamilothoris	Defense Logistics Agency Troop Support
Guests	
CDR Joe Bryant	Indian Health Service
Dr. Lisa Longo	VA PBM
ENS Nicole Crosby	DoD Pharmaceutical Operations Directorate
Debra Nguyen	UIW Pharmacy Intern

Appendix A—Attendance (continued)

Others Present	
Lt Col Rey Morales	DoD Pharmacoeconomic Center
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
MAJ Misty Cowan	DoD Pharmacoeconomic Center
Lt Col Cynthia Lee, BSC	DoD Pharmacoeconomic Center
LCDR Ola Ojo	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Eugene Moore	DoD Pharmacoeconomic Center
Dr. Angela Allerman	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe	DoD Pharmacoeconomic Center
Dr. Joshua Devine	DoD Pharmacoeconomic Center
Dr. Brian Beck	DoD Pharmacoeconomic Center
Dr. Amy Lugo	DoD Pharmacoeconomic Center
Dr. Jeremy Briggs	DoD Pharmacoeconomic Center
Dr. Stephen Yarger	DoD Pharmacy Outcomes Research Team contractor
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Dr. Bradley Clarkson	Pharmacy Resident

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

Drug / Drug Class	Medical Necessity Criteria
Drospirenone 3 mg/EE 20 mcg / levomefolate 0.451 mg (Beyaz) **Contraceptives**	• Use of ALL formulary oral contraceptives is contraindicated (e.g., due to hypersensitivity), and treatment with Beyaz is not contraindicated.
Drospirenone 3 mg/EE 30 mcg / levomefolate 0.451 mg (Sayfral) **Contraceptives**	• Use of ALL formulary oral contraceptives is contraindicated (e.g., due to hypersensitivity), and treatment with Sayfral is not contraindicated.
Norethindrone acetate 1mg/EE 10 mcg / ferrous fumarate 75 mg (Lo Loestrin Fe) **Contraceptives**	• Use of ALL formulary oral contraceptives is contraindicated (e.g., due to hypersensitivity), and treatment with Lo Loestrin Fe is not contraindicated.
Levonorgestrel 0.1 mg/EE 20 mcg, EE 10 mcg for extended use (LoSeasonique) **Contraceptives**	• Use of ALL formulary oral contraceptives is contraindicated (e.g., due to hypersensitivity), and treatment with Lo Seasonique is not contraindicated.
Estradiol valerate/dienogest (Natazia) **Contraceptives**	(No change from previous criteria) • Use of formulary agents contraindicated. • No alternative formulary agent available (if other oral contraceptive agents do not provide adequate bleeding and cycle control).
Norethindrone acetate 1mg/EE 20 mcg (Loestrin 24 Fe) **Contraceptives**	(No change from previous criteria) • Use of formulary agents contraindicated.
Levonorgestrel 0.9 mg /EE 20 mcg for extended use (Lybrel and equivalents) **Contraceptives**	No change from previous criteria) • The patient has experienced significant adverse effects from formulary combined Ocs and is expected to tolerate a non-formulary contraceptive agent. • Use of formulary combined Ocs has resulted in therapeutic failure.

Drug / Drug Class	Medical Necessity Criteria
Norethindrone 0.4mg/EE 35 mcg (Ovcon-35 and equivalents; includes Femcon Fe chewable and Zeosa) Norethindrone 1mg/EE 50mcg (Ovcon-50) Levonorgestrel 0.15 mg /EE 30 mcg, EE 10 mcg for extended use (Seasonique) Norethindrone 1 mg/EE 20/30/35 mcg / ferrous fumerate 75mg (Estrostep Fe and equivalents) Levonorgestrel 0.15 mg/EE 30 mcg for extended use (Seasonale and equivalents; with the exception of Jolessa brand) **Contraceptives**	(No change from previous criteria) • Use of formulary agents contraindicated. • The patient has experienced significant adverse effects from formulary combined Ocs and is expected to tolerate a non-formulary contraceptive agent. • Use of formulary combined Ocs has resulted in therapeutic failure.
Bromocriptine mesylate (Cycloset) **Non-Insulin Diabetes Drugs – Dopamine Agonists**	• The use of formulary alternatives is contraindicated. • The patient has experienced significant adverse effects from the formulary alternatives.
Diclofenac potassium liquid filled capsules (Zipsor) Diclofenac potassium powder packets (Cambia) Naproxen sodium ER (Naprelan CR) Mefenamic acid (Ponstel) **Oral Non-steroidal Anti-Inflammatory Drugs (NSAIDs)**	• Use of formulary alternatives is contraindicated.

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

Date	DoD PEC Drug Class	Type of Action*	BCF/ECF Medications MTFs must have BCF meds on formulary	UF Medications MTFs may have on formulary	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Comments
Aug 2011	**Contraceptive Agents** **Oral Contraceptives Subclass**	UF Review	▪ EE 20 mcg; 3 mg drospirenone (Yaz) ▪ EE 20 mcg; 0.1 mg levonorgestrel (Lutera, Sronyx or equiv) ▪ EE 30 mcg; 3 mg drospirenone (Yasmin) ▪ EE 30 mcg; 0.15 mg levonorgestrel (Levora, Nordette or equiv) ▪ EE 30 mcg; 0.15 mg levonorgestrel extended cycle (**Jolessa only**) ▪ EE 35 mcg; 1.0 mg norethindrone (Norinyl 1+35, Ortho Novum 1/35 or equiv) ▪ EE 35 mcg; 0.25 mg norgestimate (Mononessa, Ortho Cyclen or equiv) ▪ EE 25 mcg; 0.18/0.215/0.25 mg norgestimate (Ortho Tri-Cyclen Lo) ▪ EE 35 mcg; 0.18/0.215/0.25 mg norgestimate (Trinessa, Ortho Tri-Cyclen or equiv) ▪ 0.35 mg norethindrone (Nor-QD, Micronor or equiv)	▪ EE 20 mcg; 1.0 mg norethindrone ▪ EE 20 mcg; 1.0 mg norethindrone; ferrous fumarate ▪ EE 30 mcg; 0.3 mg norgestrel ▪ EE 30 mcg; 0.15 mg desogestrel ▪ EE 30 mcg; 1.5 mg norethindrone ▪ EE 30 mcg; 1.5 mg norethindrone; ferrous fumarate ▪ EE 35 mcg; 0.5 mg norethindrone ▪ EE 35 mcg; 1.0 mg ethynodiol diacetate ▪ Mestranol 50 mcg; 1 mg norethindrone ▪ EE 50 mcg; 1 mg ethynodiol diacetate ▪ EE 50 mcg; 0.5 mg norgestrel ▪ EE 35 mcg; 0.5/1.0 mg norethindrone ▪ EE 20/10 mcg; 0.15 mg desogestrel ▪ EE 30/40/30 mcg; 0.05/0.075/0.125 mg levonorgestrel ▪ EE 35 mcg; 0.5/1/0.5 mg norethindrone ▪ EE 35 mcg; 0.5/0.75/1 mg norethindrone ▪ EE 25 mcg; 0.1/0.125/0.15 mg desogestrel	▪ EE 10 mcg; 1.0 mg norethindrone; ferrous fumarate (Lo Loestrin Fe) ▪ EE 20 mcg/norethindrone acetate 1 mg – 24 day regimen (Loestrin 24 Fe) ▪ EE 20 mcg; 3 mg drospirenone; levomefolate calcium 0.451mg (Beyaz) ▪ EE 20 mcg/levonorgestrel 0.9 mg – 28 day continuous regimen (Lybrel or equiv) ▪ EE 20/10 mcg; 0.10 mg levonorgestrel (LoSeasonique or equiv) ▪ EE 30 mcg; 3 mg drospirenone; levomefolate calcium 0.451mg (Safyral) ▪ EE 30 mcg; levonorgestrel 0.15 mg generics (Seasonale or equiv – excludes Jolessa) ▪ EE 35 mcg; 0.4 mg norethindrone (Femcon Fe chew tab, Ovcon 35 or equiv) ▪ EE 50 mcg; 1 mg norethindrone (Ovcon 50) ▪ EE 30/10 mcg; 0.15 mg levonorgestrel (Seasonique or equiv) ▪ EE 20/30/35 mcg; norethindrone 1 mg (Estrostep Fe or equiv) ▪ Estradiol valerate 3/2/2/1 mg; dienogest 2/3 mg (Natazia)	Pending signing of minutes/ 60 days	-	-

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 2011	**Contraceptive Agents** **Miscellaneous Contraceptives and Emergency Contraceptives Subclass**	UF Review	*Miscellaneous Contraceptives* (None) *Emergency Contraceptives* ▪ 0.75 mg levonorgestrel (Next Choice; generic Plan B)	*Miscellaneous Contraceptives* ▪ norelgestromin 0.2 mg transdermal (Ortho-Evra) ▪ etonorgestrel 0.12 mg vaginal ring (Nuvaring) ▪ 104 mg/0.65mL depot medroxyprogesterone acetate injection (Depo-subq Provera 104) ▪ 150 mg/mL depot medroxyprogesterone acetate injection *Emergency Contraceptives* ▪ 1.5 mg levonorgestrel (Plan B One Step) ▪ 30 mg Ulipristal acetate (Ella)	▪ No miscellaneous or emergency contraceptives designated NF	Pending signing of minutes/ 60 days	Emergency Contraceptives: 1 fill per prescription/no refills	-
Aug 2011	**Non-Steroidal Anti-inflammatory Drugs**	UF Review	▪ ibuprofen 400 mg, 600 mg & 800 mg, & ~~125 mg/5 mL susp~~ (generic) ▪ indomethacin 25 mg & 50 mg (generic) ▪ meloxicam 7.5 mg & 15 mg (generic) ▪ naproxen 250 mg & 500 mg (generic)	▪ celecoxib (Celebrex) ▪ diclofenac/misoprostol (Arthrotec) ▪ diclofenac potassium tablets (Cataflam generic) ▪ diclofenac sodium tablets (Voltaren generic) ▪ diflunisal ▪ etodolac ▪ fenoprofen ▪ flurbiprofen ▪ ketoprofen ▪ ketorolac ▪ meclofenamate ▪ nabumetone ▪ naproxen sodium 275 mg & 550 mg (Anaprox, generic) ▪ oxaprozin ▪ piroxicam ▪ sulindac ▪ tolmetin ▪ naproxen/esomeprazole (Vimovo)	▪ diclofenac potassium liquid filled capsules (Zipsor) 25 mg ▪ diclofenac potassium powder packets 50 mg (Cambia) ▪ naproxen sodium ER (Naprelan CR, generic) 375 mg, 500 mg, & 750 mg ER tabs, dosing card ▪ mefenamic acid (Ponstel, generic) 250 mg	Pending signing of minutes/ 60 days	None	-

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 2011	**Renin-Angiotensin Antihypertensive class** **Subclass: ARBs**	New Drugs in Already Reviewed Class Azilsartan (Edarbi) Aliskiren /amlodipine /HCTZ (Amturnide)	No change from previous decision Aug 2010 **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)	*August 2011* • Azilsartan (Edarbi) • Aliskerin/amlodipine/HCTZ (Amturnide) See August 2010 minutes for previous decision	▪ No change from previous decision Aug 2010. Not applicable (no drug designated non-formulary)	Pending signing of minutes/ 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: Azilsartan (Edarbi) and Aliskiren/ /amlodipine/HCTZ (Amturnide) are UF but behind the step
Aug 2011	**Non-Insulin Diabetes Drugs** **Subclass: Dopamine agonists**	New Drug in Already Reviewed Class Bromocriptine mesylate (Cycloset)	No change from previous decision Nov 2010 **Biguanides** ▪ Metformin IR 500, 850, 1000 mg (generics) ▪ Metformin ER 500, 750 mg (generics) **Sulfonylureas** ▪ Glipizide (generics) ▪ Glyburide (generics) ▪ Glyburide micronized (generic)	See November 2010 minutes for other subclasses	*August 2011* ▪ Bromocriptine mesylate (Cycloset) ▪ See November 2010 minutes for other subclasses (no change to previous decision)	Pending signing of minutes/ 60 days	Step therapy (Automated PA)	Step Therapy (automated PA) with metformin and sulfonylureas as step-preferred drugs

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 201	**Narcotic Analgesics** **Subclass: Low potency single analgesic agents**	New Drug in Already Reviewed Class Buprenorphine 47hosphodies (Butrans)	**Low potency single analgesic agents (Nov 2009)** ▪ Tramadol IR	**Low potency single analgesic agents:** *August 2011* • Buprenorphine Transdermal (Butrans) *Feb 2007 & Nov 2009* • Buprenorphine sublingual • Butorphanol intranasal • Pentazocine/naloxone • Nalbuphine • Tramadol (Rybix)	▪ Tramadol ER (Ultram ER, Ryzolt – Nov 2009)	Pending signing of minutes/ 60 days	PA: Manual QL – 4 per month	Manual PA for buprenorphine transdermal system (Butrans) to ensure safe and appropriate use

Appendix D—Table of Abbreviations

AHRQ	Agency for Healthcare Research and Quality
ARB	angiotensin receptor blocker
BCF	Basic Core Formulary
BIA	budget impact analysis
CV	cardiovascular
CEA	cost-effectiveness analysis
CCB	calcium channel blocker
CFR	Code of Federal Regulations
CMA	cost minimization analysis
COX-2	cyclooxygenase-2
DA	dopamine agonist
DERP	Oregon Drug Effectiveness Review Project
DHP	dihydropyridine
DoD	Department of Defense
DPP-4	dipeptidyl-peptidase-4
DRI	direct renin inhibitor
ED	erectile dysfunction
EE	ethinyl estradiol
ER	extended release
FDA	U.S. Food and Drug Administration
FDC	fixed dose combination
GI	gastrointestinal
HbA1C	Hemoglobin A1C
HCTZ	hydrochlorothiazide
IIED	International Index of Erectile Function
IM	intramuscular
MHS	Military Health System
MN	medical necessity
MTF	Military Treatment Facility
NF	nonformulary
NSAIDs	Non-steroidal Anti-inflammatory Drug Class
OCPs	oral contraceptive products
ODT	orally dissolving tablets
P&T	Pharmacy and Therapeutics
PA	prior authorization
PEC	Pharmacoeconomic Center
PDE-5	48hosphodiesterase type-5
PORT	Pharmaceutical Outcomes Research Team
PPI	proton pump inhibitor
QL	quantity limit
RAAs	Renin Angiotensin Antihypertensives
Sus	sulfonylureas
TZDs	thiazolidinediones
T2DM	Type 2 Diabetes Mellitus
UF	Uniform Formulary
VTE	venous thromboembolism