DECISION PAPER

DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

May 2012

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

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

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

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

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

2. ***COMMITTEE ACTION: PRIOR AUTHORIZATION (PA) CRITERIA***
   Existing step therapy/PA requires a trial of generic gabapentin prior to pregabalin (Lyrica) in new users. The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 0 absent) that both gabapentin enacarbil (Horizant) and gabapentin (Gralise) be designated non-step-preferred, requiring a trial of generic gabapentin in new users. Coverage would be approved if the patient met any of the following step therapy/PA criteria:
   a) Automated PA criteria: The patient has filled a prescription for gabapentin at any Military Health System (MHS) pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.
   b) Manual PA criteria: The patient has a contraindication to or experienced adverse events with gabapentin or the formulary non-opioid pain syndrome agents which is not expected to occur with Horizant or Gralise.

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

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

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

II. UNIFORM FORMULARY DRUG CLASS REVIEWS

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

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

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

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

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

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

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

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

   a) Manual Pre-Authorization Criteria:

      (1) Use of the formulary agent is contraindicated.

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

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

   (b) Medical Necessity Criteria:

      (1) Use of the formulary agent is contraindicated.

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

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

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

III. SPECIAL PROGRAMS

A. Smoking Cessation Program

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

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

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

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

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

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

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

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

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

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

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

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

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

Director, TMA, Decision: ☑ Approved ☐ Disapproved

Approved, but modified as follows:

SUBMITTED BY:

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

DECISION ON RECOMMENDATIONS

Director, TMA, decisions are as annotated above.

Jonathan Woodson, M.D.
Director

August 8, 2012
Date

DEPARTMENT OF DEFENSE

PHARMACY AND THERAPEUTICS COMMITTEE MINUTES AND RECOMMENDATIONS

May 2012

I. CONVENING

The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee convened at 0800 hours on May 16, 2012, at the DoD Pharmacoeconomic Center (PEC), Fort Sam Houston, Texas.

II. ATTENDANCE

The attendance roster is found in Appendix A.

A. Review Minutes of Last Meetings

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

III. REQUIREMENTS

All clinical and cost evaluations for new drugs and full drug class reviews included, but were not limited to, the requirements stated in 32 Code of Federal Regulations (C.F.R.) 199.21(e)(1). All Uniform Formulary (UF) and BCF recommendations considered the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors. Medical necessity (MN) criteria were based on the clinical and cost evaluations, and the conditions for establishing MN for a nonformulary (NF) medication.

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

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

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

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

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

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

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

    a) Automated PA criteria:

(1) The patient has filled a prescription for gabapentin at any Military Health System (MHS) pharmacy POS [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

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

(1) The patient has a contraindication to gabapentin or the formulary non-opioid pain syndrome agents, which is not expected to occur with Horizant or Gralise.

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

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

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

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

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

V. UF DRUG CLASS REVIEWS

A. Newer Sedative Hypnotics Drugs

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

   a) Manual Pre-Authorization Criteria:

      (1) Use of the formulary agent is contraindicated.

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

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

   (b) Medical Necessity Criteria:

      (1) Use of the formulary agent is contraindicated.

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

VI. SPECIAL PROGRAM REVIEW

A. Smoking Cessation Program

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

VII. ITEMS FOR INFORMATION

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

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

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

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

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

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

VIII. ADJOURNMENT

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

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

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

Appendix C—Table of Abbreviations

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

Voting Members Present	
John Kugler, COL (Ret.), MC, USA	DoD P&T Committee Chair
CDR Joe Lawrence, MSC	Director, DoD Pharmacoeconomic Center (Recorder)
Col George Jones, BSC	Deputy Chief, Pharmaceutical Operations Directorate
LTC Ricardo Nannini, MSC for COL Carole Labadie, MSC	Army, Pharmacy Officer
Col David Bobb, BSC for Col Mike Spilker, BSC	Air Force, Pharmacy Officer
CAPT Deborah Thompson, USCG	Coast Guard, Pharmacy Officer
CAPT Edward Norton, MSC	Navy, Pharmacy Officer (Pharmacy Consultant BUMED)
Col Lowell Sensintaffer, MC	Air Force, Physician at Large
CAPT Walter Downs, MC	Navy, Internal Medicine Physician
COL Doreen Lounsbery, MC	Army, Internal Medicine Physician
COL Ted Cieslak, MC	Army, Physician at Large
LTC Bruce Lovins, MC	Army, Family Practice Physician
Lt Col William Hannah, MC	Air Force, Internal Medicine Physician
Major Jeremy King, MC	Air Force, OB/GYN Physician
Mr. Joe Canzolino	U.S. Department of Veterans Affairs
Nonvoting Members Present	
Mr. David Hurt	Associate General Counsel, TMA
LCDR Tiffany Scott	Defense Logistics Agency Troop Support
Guests	
Mr. Bill Davies via DCO	TRICARE Management Activity, Pharmaceutical Operations Directorate
Donna Oetama	University of Incarnate Word, Feik School of Pharmacy
Tuyet Pham	University of Incarnate Word, Feik School of Pharmacy
Kathy Uriarte	University of Incarnate Word, Feik School of Pharmacy

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

Guests	
Tina Christi Lopez	University of Incarnate Word, Feik School of Pharmacy
Others Present	
LCDR Bob Selvester, MC	DoD Pharmacoeconomic Center
MAJ Misty Cowan, MC	DoD Pharmacoeconomic Center
LCDR Ola Ojo, MSC	DoD Pharmacoeconomic Center
LCDR Marisol Martinez	DoD Pharmacoeconomic Center
Maj David Folmar, BSC	DoD Pharmacoeconomic Center
Dr. David Meade	DoD Pharmacoeconomic Center
Dr. Shana Trice	DoD Pharmacoeconomic Center
Dr. Angela Allerman	DoD Pharmacoeconomic Center
Dr. Teresa Anekwe via DCO	DoD Pharmacoeconomic Center
LCDR Joshua Devine	DoD Pharmacoeconomic Center
Dr. Dean Valibhai	DoD Pharmacoeconomic Center
Dr. Brian Beck	DoD Pharmacoeconomic Center
Dr. Amy Lugo	DoD Pharmacoeconomic Center
Dr. Esmond Nwokeji	DoD Pharmacy Outcomes Research Team contractor
Ms. Deborah Garcia	DoD Pharmacy Outcomes Research Team contractor
Dr. Bradley Clarkson	Pharmacy Resident
Lt Kellye Donovan	Pharmacy Resident

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

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

Date	DoD PEC Drug Class	Type of Action*	BCF/ECF Medications MTFs must have BCF meds on formulary	UF Medications MTFs may have on formulary	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Comments
May 2012	**Depression and Non-opioid Pain Syndrome Agents/ GABA analog subclass**	New Drugs in Already Reviewed Class	*SSRIs:* citalopram fluoxetine sertraline *SNRIs:* venlafaxine IR venlafaxine ER *SPARIs:* trazodone *NDRIs:* bupropion HCl IR bupropion HCl SR bupropion HCl ER *GABA analogs:* gabapentin *TCAs:* amitriptyline doxepin imipramine HCl nortriptyline	*SSRIs:* fluvoxamine paroxetine HCl IR paroxetine HCl CR paroxetine mesylate *SNRIs:* venlafaxine ER tablets *SARIs:* nefazodone *TCAs:* desipramine imipramine pamoate protriptyline *A2RAs:* mirtazapine tablets mirtazapine ODT	*SSRIs:* escitalopram (Lexapro) fluoxetine (Sarafem) fluoxetine weekly (Prozac Weekly) *SNRIs:* desvenlafaxine (Pristiq) duloxetine (Cymbalta) milnacipran (Savella) *SARIs:* trazodone ER (Oleptro) vilazodone (Viibryd) *NDRIs:* bupropion HBr (Aplenzin) *GABA analogs:* pregabalin (Lyrica) **gabapentin enacarbil (Horizant)** **gabapentin ER (Gralise)**	Pending signing of the minutes/ 60 days	Step therapy (Automated PA)	For step therapy: Horizant and Gralise are NF and non-step-preferred. All new users of are required to try gabapentin first.

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

Appendix C—Table of Abbreviations

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