EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel Comments
25 April 2013

The Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) commented on the recommendations from the DoD Pharmacy and Therapeutics Committee February 2013 Meeting.

UF CLASS REVIEWS: TOPICAL PAIN AGENTS

1. Topical Pain Agents—Panel Vote on UF Recommendation

The P&T Committee recommended: lidocaine 5% patch (Lidoderm) and diclofenac 1% gel (Voltaren) remain designated with formulary status on the UF, and recommended NF status for diclofenac 1.5% solution (Pennsaid drops) and diclofenac 1.3% patch (Flector), based on clinical and cost effectiveness.

2. Topical Pain Agents—Panel Questions and Comments

Dr. Salom asked for an exception to the PA criteria for "occupational or clinical reasons" to the limitation for indicated use to postherpatic neuralgia and asked about the reason for that. Dr. Meade said that was discussed by the Committee and the sometime need to avoid narcotic use explained the decision.

Without further discussion, the Panel voted on the UF Recommendations as follows:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA:

These comments were taken under consideration prior to my final decision.

3. Topical Pain Agents—Panel Vote on PA Criteria

The P&T Committee recommended manual PA criteria apply to all current and new users of lidocaine 5% patch (Lidoderm). Coverage is approved for patients who have a diagnosis of postherpetic neuralgia, other peripheral neuropathic pain, and for patients with non-neuropathic pain where an occupational or clinical reason exists and other analgesics are contraindicated. Coverage is not approved for other uses of Lidoderm.

Without further discussion, the Panel voted on the PA criteria as follows:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA:

☒ *These comments were taken under consideration prior to my final decision.*

4. **Topical Pain Agents—Panel Vote on Implementation Plan**

The P&T Committee recommended (16 for, 1 opposed, 0 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS.

Without further discussion, the Panel voted on the Implementation Plan as follows:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA:

☒ *These comments were taken under consideration prior to my final decision.*

UF CLASS REVIEWS—ORAL ANTICOAGULANT DRUGS

1. **Oral Anticoagulant Drugs—Panel Vote on UF Recommendations**

The P&T Committee recommended warfarin (Coumadin, generic), dabigatran (Pradaxa), and rivaroxaban (Xarelto) remain formulary on the UF.

2. **Oral Anticoagulant Drugs—Panel Questions and Comments**

The BAP had no questions of the presenters concerning this drug class.

Without further discussion, the Panel voted on the UF recommendations as follows:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA:

These comments were taken under consideration prior to my final decision.

RECENTLY APPROVED U.S. FDA AGENTS

1. **Newer Sedative Hypnotic-1 (SED-1s) Agents — Panel Vote on UF Recommendations**

   The P&T Committee recommended zolpidem sublingual low dose (Intermezzo) be designated NF due to the lack of compelling clinical advantages and cost disadvantage compared to UF products.

2. **Newer Sedative Hypnotic-1 (SED-1s) Agents — Panel Questions**

   Dr. Salom asked whether the MHS had the ability to restrict zolpidem prescriptions for women. Dr. Meade answered that that was suggested and said the subject would be addressed later in the presentation on Prior Authorizations.

   Dr. Sampsel said if the Committee had considered asking to have the automated profile program adjusted to allow the differentiation, noting that they have had experience with some of the other agents. Dr. Meade replied that it is a question of "and/or" logic in the programming, which has been difficult to achieve operationally.

   Dr. Salom asked the DFO whether it would be within the purview of the Panel to make a recommendation to the Department of Defense regarding making a change to the automated program. CDR Lawrence stated that it would be appropriate. Dr. Salom indicated he would raise that matter as a separate recommendation, after the scheduled vote.

   Dr. Crum asked about the number of users of agents in this class, noting that the figures supplied and discussed in the presentation was in terms of number of doses.

   Dr. Khurana asked whether it would help to change the PA in regard to immediate-release zolpidem. Dr. Meade answered that most of the drugs on the PA are the lower-use drugs. The vast majority of users of these drugs are not subject to Prior Authorization.

   Without further discussion, the Panel voted on the UF recommendations as follows:

   Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA:

These comments were taken under consideration prior to my final decision.

3. **Newer Sedative Hypnotic-1 (SED-1s) Agents — Panel Vote on PA Recommendations**

Existing automated prior authorization (step therapy) requires a trial of generic zolpidem IR or zaleplon, the step-preferred agents, prior to the other SED-1s in new users. The P&T Committee recommended the following PA criteria should apply to Intermezzo. 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 Military Health System (MHS) pharmacy point of service (POS), military treatment facilities (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 affects, or has a contraindication to zolpidem IR or zaleplon.

Without further discussions, the Panel voted on the PA recommendations as follows:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA:

These comments were taken under consideration prior to my final decision.

4. **Newer Sedative Hypnotic-1 (SED-1s) Agents — Panel Vote on Implementation Plan**

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

Without further discussion, the Panel voted on the Implementation Plan as follows:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA:

These comments were taken under consideration prior to my final decision.

5. Newer Sedative Hypnotic-1 (SED-1s) Agents — Additional BAP Recommendations

Dr. Salom then brought before the Panel the question of whether to recommend that the Department of Defense try to develop a step therapy process in which patients have to try more than one preferred agent before using a Non-Formulary agent. The Panel recognizes that this is operationally difficult to do.

Dr. Crum noted that there would be a lot of paperwork involved and said he would probably not be in favor of the recommendation. Dr. Sampsel said she would like to see it done by using the automated process to look back on more than one agent. Mr. Tackitt asked if it would be mandated that the patient try more than one preferred agent; Dr. Sampsel said she would recommend that because there are lots of formulary options. Mr. Tackitt asked whether that shouldn't be a clinical decision. Dr. Sampsel said she is concerned about working on the operational problem.

The Chair called for a Panel vote on submitting a recommendation that DoD try to develop a step therapy process that would have patients try more than one preferred formulary agent before using a Non-Formulary agent.

Without further discussion the Panel voted on the Additional Recommendation as follows:

Concur: 7 Non-concur: 1 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA:

These comments were taken under consideration prior to my final decision.

UTILIZATION MANAGEMENT—PRIOR AUTHORIZATIONS

1. **Tretinoin Age Limits—Panel Vote**

The P&T Committee recommended removing the age limit for tretinoin products that are not exclusively labeled for cosmetic use at all 3 MHS POS (MTF, Mail Order, and the Retail Network). Tretinoin products/derivatives specifically indicated for cosmetic use as a result of the aging process (e.g., Renova, Refissa, Avage) remain excluded from the Pharmacy benefit.

2. **Tretinoin Age Limits—Panel Questions**

Ms. Buchta asked how MHS will verify that the product is not being used for cosmetic purposes. Dr. Meade replied that they won't be able to.

Other Panel members noted that MHS might be able to tell if the usage increases.

Without further discussion, the Panel voted on the PA as follows:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

There were no further comments from the Panel.

Director, TMA

These comments were taken under consideration prior to my final decision.

Zolpidem Gender-Based Dosing

The P&T Committee discussed whether PA criteria are needed for zolpidem products, given new recommendations from the FDA in January 2013 regarding dosing in women. For women, lower dosing is recommended, as blood levels in some patients may be high enough the morning after use to impair activities that require alertness, including driving. A review of MHS prescriptions in the last six months of 2012 showed significant use of the higher zolpidem dosages in women.

Zolpidem Gender-Based Dosing—Committee Action

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 0 absent) to not institute gender-based dosing PA criteria for zolpidem products, and to instead educate providers of the new recommendations, and notify patients via beneficiary newsletters of the concerns regarding impaired driving and activities requiring mental alertness the morning after use. The P&T Committee recommended re-evaluating this issue in six months to review MHS prescribing trends and whether additional measures are necessary.

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
April 25, 2013
Washington, D.C.

Panel Members Present:

- Ira Salom, Chairperson
- Kathryn Buchta,
- John Crum
- Steven Hein
- Amit Khurana
- Lisa Le Gette
- Elizabeth Sampsel
- Robert Duane Tackitt

Members Not Present:

- Katherine O'Neill-Tracy

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. CDR Joseph Lawrence, USN, the Designated Federal Officer (DFO), called the proceedings to order at 9:00 A.M. CDR Lawrence indicated the Panel has been convened to review and comment on the therapeutic drug class recommendations resulting from the February 13 and 14, 2013 Department of Defense (DoD) Pharmacy and Therapeutic (P&T) Committee meeting held in San Antonio, TX.

Agenda

The agenda for this meeting of the Panel is:

- Welcome and opening remarks
- Public citizen comments
- Review and Panel discussion of P&T Committee recommendations for the following therapeutic drug classes:

  - *Drug Class Reviews:*
    - Pain Agents—Topical Pain Agents
    - Oral Anticoagulants
  - *Designated Newly Approved Drugs:*
    - Newer Sedative Hypnotic—1s (SED-1s)—Zolpidem sublingual low dose tablets (Intermezzo)

- *Utilization Management Issues*
  - Prior Authorization Criteria
    - Tretinoin Age Limits
    - Zolpidem Gender-Based Dosing

Opening Remarks

The DFO indicated that Title 10 United States Code (U.S.C.) section 1074g subsection b requires the Secretary of Defense to establish a DoD Uniform Formulary (UF) of pharmaceutical agents, and establishes the P&T Committee to review the formulary on a periodic basis and make additional recommendations regarding the formulary as the Committee determines necessary and appropriate.

In addition, 10 U.S.C. section 1074g subsection c also requires the Secretary to establish a UF Beneficiary Advisory Panel (BAP) to review and comment on the development of the UF. The Panel includes members that represent non-governmental organizations and associations that represent the views and interests of a large number of eligible covered beneficiaries. Comments of the Panel must be considered by the Director, TRICARE Management Activity (TMA) before establishing the UF or implementing changes to the UF. The Panel's meetings are conducted in accordance with the Federal Advisory Committee Act (FACA).

The duties of the Uniform Formulary Beneficiary Advisory Panel include:

- To review and comment on the recommendations of the P&T Committee concerning the establishment of the UF and subsequent recommended changes. Comments to the Director, TMA, regarding recommended formulary status, pre-authorizations, and the effective dates for changing drugs from "formulary" to "non-formulary" status must be reviewed by the Director, TMA before making a final decision.
- To hold quarterly meetings in an open forum. The Panel may not hold meetings except at the call of or with the advance approval of the DFO in consultation with the Chairperson of the Panel.
- To prepare minutes of the proceedings and prepare comments for the Secretary or his designee regarding the Uniform Formulary or changes to the Formulary. The minutes will be available on the website and comments will be prepared for the Director, TMA.

As guidance to the Panel regarding this meeting, CDR Lawrence said the role of the BAP is to comment on the UF recommendations made by the P&T Committee at their last meeting. While the Department appreciates that the BAP may be interested in the drug classes selected for review, drugs recommended for the basic core formulary (BCF) or specific pricing data, these topics do not fall under the purview of the BAP.

The P&T Committee met for approximately 11 hours conducting its reviews of the drug class recommendations presented today. Since the present meeting is considerably shorter, the Panel will not receive the same extensive information that is presented to the P&T Committee

members. However, the BAP will receive an abbreviated version of each presentation and its discussion. The materials provided to the Panel are available on the TRICARE website.

This meeting is being recorded and detailed minutes of this meeting are being prepared. The BAP minutes, the DoD P&T Committee meeting minutes and the Director's decisions will be available on the TRICARE website in approximately four to six weeks.

The DFO next provided the ground rules for conducting the meeting:

- All discussions take place in the open public forum. There is to be no committee discussion outside the room, during breaks or at lunch.
- Audience participation is limited to private citizens who signed up to address the Panel.
- Members of the Pharmacoeconomic Center (PEC) and the P&T Committee are available to answer questions related to the BAP's deliberations. Should a misstatement be made, these individuals may interrupt to ensure the minutes accurately reflect relevant facts, regulations or policy.

CDR Lawrence then introduced the individual Panel members (see list above) and noted housekeeping considerations.

Private Citizen Comments

The DFO opened the meeting for private citizen comments. There were none.

Chairperson's Opening Remarks

The DFO next turned the meeting over to the new Panel Chair, Dr. Ira Salom, who thanked the prior chair, Ms. Deborah Fryar for her dedicated service and her commitment to the work of the Panel. He then opened the meeting for the first drug class review presentation.

DRUG CLASS REVIEW PRESENTATIONS

(PEC Script)
(Dr. Meade)

I'm Dave Meade, Director of Clinical Operations at the Pharmacoeconomic Center ("PEC" for short). Joining me is Doctor and retired Army Colonel John Kugler, the Chairman of the P & T Committee, who will provide the physician perspective and comment on the recommendations made by the P & T Committee. Joining us from the Tricare Management Activity is Captain Nita Sood, USPHS, Chief of Staff of the Pharmacy Operations Directorate.

The DoD Pharmacoeconomic Center supports the DoD P & T Committee by conducting the relative (relative meaning in comparison to the other agents defined in the same class) clinical-effectiveness analyses and relative cost-effectiveness analyses of the drug classes under review and consideration by the DoD P & T Committee for the Uniform Formulary (UF).

We are here to present an overview of the analyses presented to the P & T Committee. 32 Code of Federal Regulations (CFR) establishes procedures for inclusion of pharmaceutical agents on the Uniform Formulary based upon both relative clinical effectiveness and relative cost effectiveness.

The goal of this presentation is not to provide you with the same in-depth analyses presented to the DoD P & T Committee but a summary of the processes and analyses presented to the DoD P & T Committee. These include:

1) A brief overview of the relative clinical-effectiveness analyses considered by the DoD P & T Committee. All reviews include but are not limited to the sources of information listed in 32 CFR 199.21 (e)(1).
2) A brief general overview of the relative cost-effectiveness analyses. This overview will be general in nature since we are unable to disclose the actual costs used in the economic models. This overview will include the factors used to evaluate the costs of the agents in relation to the safety, effectiveness, and clinical outcomes.

a. The DoD P & T Committee's Uniform Formulary recommendation is based upon its collective professional judgment when considering the analyses from both the relative clinical- and relative cost-effectiveness evaluations. The Committee reviewed three Uniform Formulary Drug Classes (or sub-classes) – Pain Agents—Topical Pain Agents, Pulmonary II Drugs for COPD and Oral Anticoagulants. Additionally, one newly approved drug was reviewed – Zolpidem sublingual low dose tablets (Intermezzo)

3) The DoD P & T Committee's recommendation as to the effective date of the agents being changed from formulary tier to the non-formulary tier of the Uniform Formulary. Based on 32 CFR 199.21 such change will not be longer than 180 days from the final decision date but may be less.

We've given you a handout which includes the Uniform Formulary recommendations for all the drugs discussed today; these are found on pages 2 through 5. There are tables and utilization figures for each of the drug classes. We'll be using trade names as much as possible, so you can refer to your handout throughout the presentation.

I. UF CLASS/SUBCLASS REVIEWS— Topical Pain Agents

Topical Pain Agents—Relative Clinical Effectiveness

(PEC Script)

(Dr. Meade)

Drugs in the Topical Pain sub-class are listed on page 2. The Topical pain class was never been previously reviewed. Figure 1 of the handout on page 2 shows the utilization of the agents.

The Pharmacy Outcomes Research Team (PORT) provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Lidocaine 5% patch (Lidoderm) is effective for the management of its orphan indication, postherpetic neuralgia (PHN) or nerve pain due to damage caused by the varicella zoster virus. There is insufficient evidence supporting use of Lidoderm for other nerve pain syndromes caused by diabetes, HIV virus or complex regional pain syndrome; however, several professional guidelines support its use. There is a lack of data regarding use of Lidoderm for other off-label conditions, including widespread or deep pain conditions such as fibromyalgia or chronic pain associated with osteoarthritis.
- A review of MHS prescribing trends showed a high discontinuation rate for Lidoderm, with a similar prevalence between unique user new starts and discontinuations.
- A Pharmacy Outcomes Research Team (PORT) analysis showed that Lidoderm is commonly prescribed in the MHS for off-label, non-supportable uses (e.g., musculoskeletal pain) that are not associated with neuropathic pain.
- There are no head-to-head trials comparing the topical diclofenac products (Voltaren gel, Pennsaid drops, and Flector patch) in terms of efficacy or safety. However, indirect evidence suggests the agents are highly interchangeable with regard to efficacy. Limited evidence suggests the agents are as effective as oral diclofenac.
- The incidence of gastrointestinal (GI) adverse events is lower with the topical diclofenac products compared to oral nonsteroidal anti-inflammatory drugs (NSAIDs), offering a potential advantage for patients with a history of GI bleeding or peptic ulcers.

Topical Pain Agents—Relative Cost Effectiveness

(Dr. Meade)

Relative Cost-Effectiveness Conclusion—Pharmacoeconomic analyses were performed for the topical pain agent subclass, including cost minimization analysis (CMA) and budget impact analysis (BIA). For the BIAs, several of the model's key assumptions were varied, with corresponding sensitivity analyses conducted.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that among topical diclofenac products, diclofenac gel (Voltaren) was the most cost-effective, based on the weighted average cost per day of treatment across all three POS, followed by diclofenac drops (Pennsaid) and diclofenac patch (Flector). Results from the CMA and budget impact analyses (BIAs) showed that the scenario where Lidocaine patch (Lidoderm) and diclofenac gel (Voltaren) were designated UF, with diclofenac drops (Pennsaid) and patch (Flector) designated NF, was the most cost-effective for the MHS.

average cost per day of treatment across all three POS, followed by diclofenac drops (Pennsaid) and diclofenac patch (Flector). Results from the CMA and budget impact analyses (BIAs) showed that the scenario where Lidocaine patch (Lidoderm) and diclofenac gel (Voltaren) were designated UF, with diclofenac drops (Pennsaid) and patch (Flector) designated NF, was the most cost-effective for the MHS.

Topical Pain Agents—UF Recommendation

(Dr. Meade)

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following:) lidocaine 5% patch (Lidoderm) and diclofenac 1% gel (Voltaren) remain designated with formulary status on the UF, and recommended NF status for diclofenac 1.5% solution (Pennsaid drops) and diclofenac 1.3% patch (Flector), based on clinical and cost effectiveness.

Topical Pain Agents—Prior Authorization (PA) Criteria

(Dr. Meade)

The P&T Committee recommended (12 for, 4 opposed, 1 abstained, 0 absent) manual PA criteria apply to all current and new users of lidocaine 5% patch (Lidoderm). Coverage is approved for patients who have a diagnosis of postherpetic neuralgia, other peripheral neuropathic pain, and for patients with non-neuropathic pain where an occupational or clinical reason exists and other analgesics are contraindicated. Coverage is not approved for other uses of Lidoderm.

Topical Pain Agents—UF and PA Implementation Plan

(Dr. Meade)

The P&T Committee recommended (16 for, 1 opposed, 0 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS.

Topical Pain Agents—Committee Physician's Perspective

Dr. Kugler provided the Panel with the Committee physician's perspective on the recommendations in this drug class. He noted that although the drugs are administered topically they all have the same key ingredient. After reviewing the cost data the Committee recommended formulary status for the Lidoderm patch and Voltaren gel. Two products were recommended for NF status based on clinical and cost effectiveness considerations. Generic diclofenac tablets are also available on the UF.

The PA recommendations generated the most discussion. The Committee recommended PA criteria for all users of Lidoderm. Although there is no clinical data supporting off-label uses of

Topical Pain Agents—Panel Questions and Comments

Dr. Salom asked for an exception to the PA criteria for "occupational or clinical reasons" to the limitation for indicated use to postherpatic neuralgia and asked about the reason for that. Dr. Meade said that was discussed by the Committee and the sometime need to avoid narcotic use explained the decision.

Topical Pain Agents—Panel Vote on UF Recommendation

The Chair read the P&T Committee's UF recommendations for this class.

The P&T Committee recommended: lidocaine 5% patch (Lidoderm) and diclofenac 1% gel (Voltaren) remain designated with formulary status on the UF, and recommended NF status for diclofenac 1.5% solution (Pennsaid drops) and diclofenac 1.3% patch (Flector), based on clinical and cost effectiveness.

Without further discussion, the Panel voted as follows:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

Topical Pain Agents—Panel Vote on PA Criteria

Dr. Salom read the Committee's recommended PA criteria.

The P&T Committee recommended manual PA criteria apply to all current and new users of lidocaine 5% patch (Lidoderm). Coverage is approved for patients who have a diagnosis of postherpetic neuralgia, other peripheral neuropathic pain, and for patients with non-neuropathic pain where an occupational or clinical reason exists and other analgesics are contraindicated. Coverage is not approved for other uses of Lidoderm.

There was no discussion. The BAP vote on the PA criteria was:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

Topical Pain Agents—Panel Vote on Implementation Plan

The Chair read the implementation plan.

The P&T Committee recommended (16 for, 1 opposed, 0 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS.

Without discussion, the BAP vote was:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

II. UF CLASS REVIEWS—Oral Anticoagulant Drugs

(PEC Script)

Oral Anticoagulant Drugs—Relative Clinical Effectiveness

(Dr. Meade)

Background: The Oral Anticoagulant Drug Class is comprised of warfarin (Coumadin, generic), and the newer oral anticoagulants (NOACs) dabigatran (Pradaxa) and rivaroxaban (Xarelto). Another NOAC, apixaban (Eliquis) was approved in December 2012, and will be evaluated as a new drug at an upcoming meeting

Drugs in the GI-2 Drug Class are listed on page 4. The class has not been previously reviewed for UF placement. Figure 4 of the handout on page 4 shows the utilization of the agents.

The PORT provided the P&T Committee detailed analyses of current MHS prescribing patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- The NOACs dabigatran and rivaroxaban have advantages of predictable anticoagulant effect, fixed dosing, and fewer drug interactions compared to warfarin (Coumadin, generic). Advantages of warfarin include its long history of use, reliable reversal agent (vitamin K), and adverse effects that are predictable and manageable.
- The NOACs offer a convenience to patients; laboratory monitoring for efficacy and dietary restrictions are not required. More data is needed in patients with renal and hepatic impairment. No reversal agent is available with the NOACs.
- In non-valvular Afib, dabigatran and apixaban were superior to poorly controlled warfarin (time in therapeutic range < 65.5%) at preventing stroke and systemic embolism, including hemorrhagic stroke; rivaroxaban was non-inferior to poorly controlled warfarin for these outcomes. Intracranial bleeding was lower with dabigatran, rivaroxaban, and apixaban compared to warfarin.
- For VTE prevention following orthopedic surgery, rivaroxaban was superior to enoxaparin at preventing symptomatic DVT, but at the cost of increased bleeding. Dabigatran and apixaban were similar to enoxaparin at VTE prevention; no difference in bleeding was noticed with dabigatran, but a lower risk of bleeding was shown with apixaban versus enoxaparin.
- For prevention of VTE recurrence following DVT or PE, rivaroxaban in two trials was non-inferior to enoxaparin/warfarin for preventing recurrent VTE, with no difference in bleeding, and was superior to placebo in one trial for extended therapy. Dabigatran in one trial was non-inferior to enoxaparin/warfarin for preventing recurrent VTE, with no difference in bleeding. Apixaban was superior to placebo for prevention of recurrent VTE over 12 months (extended therapy) in one trial.
- Due to a lack of head-to-head trials, there is insufficient evidence to determine if one NOAC has advantages over the others for stroke prevention in non-valvular Afib, prophylaxis of VTE

following hip or knee replacement surgery, or for prevention of VTE recurrence following DVT or PE.

- Patients require education and clinical monitoring to ensure appropriate use and avoid adverse reactions with the NOACs. Bleeding is a concern with all the NOACs, and dabigatran is associated with dyspepsia and major GI bleeding. For warfarin, a high risk of falls is not associated with risk of subsequent major bleeding.
- It remains to be determined whether the NOACs will increase the numbers of patients currently undertreated for stroke prevention in Afib. Also unknown is whether NOACs will improve persistence rates for anticoagulation therapy.

Oral Anticoagulant Drugs—Relative Cost Effectiveness

(Dr. Meade):

The P&T Committee evaluated the relative cost-effectiveness of the anticoagulant agents for stroke prevention in non-valvular Afib and for prophylaxis of VTE in patients undergoing knee or hip replacement surgery. CMAs were performed for both indications. Additionally, a cost-effectiveness analysis (CEA) evaluated the agents for stroke prevention in AFib. For the BIAs, several of the model's key assumptions were varied, with corresponding sensitivity analyses conducted. BIA results were presented to the P&T Committee. The MHS projected budgetary impact varied depending on which medication was selected for BCF, UF, or NF status.

Committee Action: The P&T Committee concluded (17 for, 0 against, 0 abstained, 0 absent) the following:

- Anticoagulant agents for stroke prevention in non-valvular AFib—CMA results showed that, in all scenarios, warfarin (Coumadin, generic), including drug monitoring costs, was the least costly agent. CEA results showed that the ICERs per life year gained with dabigatran and rivaroxaban in relation to warfarin were in a range that could be considered cost-effective to the MHS.
- Anticoagulant agents for DVT/PE prophylaxis in hip and knee replacement surgery—CMA results demonstrated that rivaroxaban (Xarelto) was a cost-effective alternative compared to enoxaparin (Lovenox), based on analysis of the average weighted price per day of therapy at all three POS.
- BIA results—Scenarios where all drugs remain on the UF resulted in the greatest cost-avoidance to the MHS.

Oral Anticoagulant Drugs—UF Recommendation

(Dr. Meade):

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 0 absent) warfarin (Coumadin, generic), dabigatran (Pradaxa), and rivaroxaban (Xarelto) remain formulary on the UF.

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Oral Anticoagulant Drugs—Committee Physician's Perspective

Dr. Kugler briefed the BAP on the Committee physician's perspective regarding this drug class. He noted that warfarin has been around for a long time — over 50 years and is well known. The newer agents offer patients some clinical advantages. Warfarin is not well controlled and the newer drugs were clinically superior for treating atrial fibrillation and blood clots following surgery, and pulmonary embolism. Dr. Kugler said there was no controversy regarding the formulary decisions. He noted that warfarin had by far the greatest number of users in the MHS and that cost analysis showed that warfarin was the most cost-beneficial.

Oral Anticoagulant Drugs—Panel Questions and Comments

The BAP had no questions of the presenters concerning this drug class.

Oral Anticoagulant Drugs—Panel Vote on UF Recommendations

The Panel Chair then read the P&T Committee's UF recommendations for this drug class.

The P&T Committee recommended warfarin (Coumadin, generic), dabigatran (Pradaxa), and rivaroxaban (Xarelto) remain formulary on the UF.

Without further discussion, the BAP voted:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

III. RECENTLY APPROVED U.S. FDA AGENTS

Dr. Salom next opened the floor for the presentations on agents recently-approved by the FDA.

(PEC Script)

(Dr. Meade)

A. Newer Sedative Hypnotic-1 (SED-1s) Agents—Zolpidem Sublingual Low-Dose Tablets (Intermezzo) - Relative Clinical Effectiveness Conclusion

Background: Intermezzo is a new low-dose zolpidem sublingual (SL) formulation available in 1.75 mg and 3.5 mg tablets. Intermezzo is specifically approved for treatment of insomnia characterized by middle-of-the-night waking followed by difficulty returning to sleep. In one study, there was a statistically significant improvement in sleep latency and total sleep time with Intermezzo versus placebo for middle-of-the-night awakening, but another placebo-controlled trial found no differences in total sleep time. No studies have been completed with an active comparator.

Drugs in the Newer Sedative Hypnotic-1 (SED-1s) Agents are listed on page 3, Figure 3 of the handout, showing the utilization of the agents (by active ingredient). Zolpidem (generic), which

has approximately 2 million doses per month, has been removed from the graph so that differentiation could be seen in the less used products.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) despite its unique FDA labeling for middle-of-the-night awakening compared to the other SED-1s and the potential for less next-day impairment, zolpidem SL low dose (Intermezzo) does not offer a clinically compelling advantage over the other SED-1s included on the UF.

Newer Sedative Hypnotic-1 (SED-1s) Agents —Relative Cost- Effectiveness Analysis and Conclusion

A pharmacoeconomic analysis was performed. The weighted average cost per tablet at all three points of service (POS) was evaluated for Intermezzo in relation to other SED-1s products

The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that zolpidem SL low dose (Intermezzo) is not cost-effective when compared to other SED-1s included on the UF.

Newer Sedative Hypnotic-1 (SED-1s) Agents —UF Recommendation

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) zolpidem sublingual low dose (Intermezzo) be designated NF due to the lack of compelling clinical advantages and cost disadvantage compared to UF products.

Newer Sedative Hypnotic-1 (SED-1s) Agents – Prior Authorization

Existing automated prior authorization (step therapy) requires a trial of generic zolpidem IR or zaleplon, the step-preferred agents, prior to the other SED-1s in new users. The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) the following PA criteria should apply to Intermezzo. 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 Military Health System (MHS) pharmacy point of service (POS) [military treatment facilities (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.

Newer Sedative Hypnotic-1 (SED-1s) Agents —UF Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

Newer Sedative Hypnotic-1 (SED-1s) Agents — Committee Physician's Perspective

Dr. Kugler informed the BAP that there was no controversy over the Uniform Formulary recommendations for Intermezzo. It was the least cost-effective agent in the class. There are no head-to-head studies of its effectiveness and there are other zolpidem formulations on the UF.

Newer Sedative Hypnotic-1 (SED-1s) Agents — Panel Questions

Dr. Salom asked whether the MHS had the ability to restrict zolpidem prescriptions for women. Dr. Meade answered that that was suggested and said the subject would be addressed later in the presentation on Prior Authorizations.

Dr. Sampsel said if the Committee had considered asking to have the automated profile program adjusted to allow the differentiation, noting that they have had experience with some of the other agents. Dr. Meade replied that it is a question of "and/or" logic in the programming, which has been difficult to achieve operationally.

Dr. Salom asked the DFO whether it would be within the purview of the Panel to make a recommendation to the Department of Defense regarding making a change to the automated program. CDR Lawrence stated that it would be appropriate. Dr. Salom indicated he would raise that matter as a separate recommendation, after the scheduled vote.

Dr. Crum asked about the number of users of agents in this class, noting that the figures supplied and discussed in the presentation was in terms of number of doses.

Dr. Khurana asked whether it would help to change the PA in regard to immediate-release zolpidem ~~IR~~. Dr. Meade answered that most of the drugs on the PA are the lower-use drugs. The vast majority of users of these drugs are not subject to Prior Authorization.

Newer Sedative Hypnotic-1 (SED-1s) Agents — Panel Vote on UF Recommendations

The Chair then called for the vote on the P&T Committee's UF recommendation for Intermezzo.

The P&T Committee recommended zolpidem sublingual low dose (Intermezzo) be designated NF due to the lack of compelling clinical advantages and cost disadvantage compared to UF products.

The BAP voted:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

Newer Sedative Hypnotic-1 (SED-1s) Agents — Panel Vote on PA Recommendations

Dr. Salom next read the PA recommendations for this agent.

Existing automated prior authorization (step therapy) requires a trial of generic zolpidem IR or

zaleplon, the step-preferred agents, prior to the other SED-1s in new users. The P&T Committee recommended the following PA criteria should apply to Intermezzo. 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 Military Health System (MHS) pharmacy point of service (POS), military treatment facilities (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 affects, or has a contraindication to zolpidem IR or zaleplon.

The Panel vote was:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

Newer Sedative Hypnotic-1 (SED-1s) Agents — Panel Vote on Implementation Plan

The Chair read the implementation plan recommendation.

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

Without further discussion the BAP voted:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

Newer Sedative Hypnotic-1 (SED-1s) Agents — Additional BAP Recommendations

Dr. Salom then brought before the Panel the question of whether to recommend that the Department of Defense try to develop a step therapy process in which patients have to try more than one preferred agent before using a Non-Formulary agent. The Panel recognizes that this is operationally difficult to do.

Dr. Crum noted that there would be a lot of paperwork involved and said he would probably not be in favor of the recommendation. Dr. Sampsel said she would like to see it done by using the automated process to look back on more than one agent. Mr. Tackitt asked if it would be mandated that the patient try more than one preferred agent; Dr. Sampsel said she would recommend that because there are lots of formulary options. Mr. Tackitt asked whether that shouldn't be a clinical decision. Dr. Sampsel said she is concerned about working on the operational problem.

The Chair called for a Panel vote on submitting a recommendation that DoD try to develop a step therapy process that would have patients try more than one preferred formulary agent before using a Non-Formulary agent. The Panel voted:

Concur: 7 Non-concur: 1 Abstain: 0 Absent: 1

IV. UTILIZATION MANAGEMENT—PRIOR AUTHORIZATIONS

Dr. Salom then called for the utilization management presentations.

(PEC Script)

(Dr. Meade)

1. Tretinoin Age Limits

The P&T Committee reviewed the current age limits for tretinoin, which does not allow use in patients older than 35 years. While treatment for acne is covered by TRICARE benefits, cosmetic services and supplies are excluded from the benefit, including treatments for photoaging of the skin.

Tretinoin Age Limits—Committee Action

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) removing the age limit for tretinoin products that are not exclusively labeled for cosmetic use at all 3 MHS POS (MTF, Mail Order, and the Retail Network). Tretinoin products/derivatives specifically indicated for cosmetic use as a result of the aging process (e.g., Renova, Refissa, Avage) remain excluded from the Pharmacy benefit.

Tretinoin Age Limits—Committee Physician's Perspective

Dr. Kugler said there was some trepidation on the part of the Committee about removing the age limit but cosmetic uses will remain excluded from coverage. The Committee was unanimous in its approval.

Tretinoin Age Limits—Panel Questions

Ms. Buchta asked how MHS will verify that the product is not being used for cosmetic purposes. Dr. Meade replied that they won't be able to.

Other Panel members noted that MHS might be able to tell if the usage increases.

Tretinoin Age Limits—Panel Vote

The Chair read the Committee's recommendation.

The P&T Committee recommended removing the age limit for tretinoin products that are not exclusively labeled for cosmetic use at all 3 MHS POS (MTF, Mail Order, and the Retail Network).

Tretinoin products/derivatives specifically indicated for cosmetic use as a result of the aging process (e.g., Renova, Refissa, Avage) remain excluded from the Pharmacy benefit.

The BAP vote was:

Concur: 8 Non-concur: 0 Abstain: 0 Absent: 1

2. Zolpidem Gender-Based Dosing

(Dr. Meade)

This is an informational item not requiring BAP action.

The P&T Committee discussed whether PA criteria are needed for zolpidem products, given new recommendations from the FDA in January 2013 regarding dosing in women. For women, lower dosing is recommended, as blood levels in some patients may be high enough the morning after use to impair activities that require alertness, including driving. A review of MHS prescriptions in the last six months of 2012 showed significant use of the higher zolpidem dosages in women.

Zolpidem Gender-Based Dosing—Committee Action

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 0 absent) to not institute gender-based dosing PA criteria for zolpidem products, and to instead educate providers of the new recommendations, and notify patients via beneficiary newsletters of the concerns regarding impaired driving and activities requiring mental alertness the morning after use. The P&T Committee recommended re-evaluating this issue in six months to review MHS prescribing trends and whether additional measures are necessary.

Dr. Salom commented that he believes this is an extremely important issue.

Closing Statement

Dr. Salom thanked the presenters.

CDR Lawrence, the DFO, closed the meeting at 9:55 A.M.

Ira Salom, MD
Chair

Brief Listing of Acronyms Used in This Summary

Abbreviated terms are spelled out in full in this summary; when they are first used, the acronym is listed in parentheses immediately following the term. All of the terms commonly used as acronyms in Panel discussions are listed below for easy reference. The term "Panel" in this summary refers to the "Uniform Formulary Beneficiary Advisory Panel," the group whose meeting is the subject of this report.

- AE — Adverse event
- Afib—Non-Valvular Atrial Fibrillation
- APR — Automated Profile Review
- ASD(HA)—Assistant Secretary of Defense for Health Affairs
- BAP — Uniform Formulary Beneficiary Advisory Panel (the "Panel" referred to above)
- BCF — Basic Core Formulary
- BIA — Budget Impact Analysis
- CEA — Cost-effectiveness analysis
- CFR — Code of Federal Regulations
- CMA — Cost-Minimization Analysis
- CPG — Clinical Practice Guideline
- CR — Controlled Release (a drug formulation)
- DFO — Designated Federal Officer
- DoD — Department of Defense
- DVT—Deep Vein Thrombosis
- ECF — Extended Core Formulary
- ER — Extended Release (a drug formulation)
- ESI — Express-Scripts, Inc.
- FACA — Federal Advisory Committee Act
- FDA — U.S. Food and Drug Administration
- ICER—Incremental Cost-Effectiveness Ratio
- IR — Immediate Release (a drug formulation)
- MHS — Military Health System
- MN — Medical Necessity
- MTF — Military Treatment Facility
- NF — Non-formulary
- NIH — National Institutes of Health
- NOACs—Newer Oral Anticoagulants (a drug class)
- NSAID—Non-Steroidal Anti-Inflammatory Drug (a drug class)
- OTC — Over the counter
- PA — Prior Authorization
- P&T Committee — DoD Pharmacy and Therapeutics Committee
- PDTS — Pharmacy Data Transaction Service

- PEC — DoD Pharmacoeconomic Center
- PHN—Postherpatic neuralgia
- PORT — Pharmacy Outcomes Research Team
- POS — Point of Service
- RCTs — Randomized Control Trials
- SED-1s—Newer Sedative Hypnotic Agents (a drug class)
- SL—Sublingual (a drug formulation)
- SR — Sustained release (a drug formulation)
- TMA — TRICARE Management Activity
- TMOP — TRICARE Mail Order Pharmacy
- TPHARM — TRICARE Pharmacy Program
- TRRx — TRICARE Retail Pharmacy Program
- UF — DoD Uniform Formulary
- USC — United States Code
- VA — U.S. Department of Veterans Affairs
- VTE—Venous Thromboembolism