EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel (BAP)
March 27, 2019

UNIFORM FORMULARY DRUG CLASS REVIEWS

I. UF CLASS REVIEWS

A. MIGRAINE AGENTS – CALCITONIN GENE-RELATED PEPTIDE (CGRP) ANTAGONIST PROPHYLAXIS SUBCLASS

1. Migraine Agents – CGRP Antagonist Prophylaxis Subclass—UF Recommendation

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following for the CGRP Antagonist Prophylaxis agents, as outlined below, based on clinical and cost-effectiveness:

- UF
  a) erenumab (Aimovig)
  b) fremanezumab (Ajovy)
  c) galcanezumab (Emgality)

- NF
  - None

2. Migraine Agents – CGRP Antagonist Prophylaxis Subclass—Manual Prior Authorization (PA) Criteria

PA criteria currently apply to the CGRP products, requiring a trial of at least one drug from two oral classes used for migraine prophylaxis, including antiepileptic medications, beta-blockers or antidepressants. PA criteria were originally recommended when the individual CGRP products were first evaluated as new drugs. The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updates to the current manual PA criteria for all three CGRP antagonists in new users. The PA criteria and updates reflect the recommendations from the 2018 AHS Consensus Statement regarding candidates for a CGRP and assessment of response.

3. Aimovig, Ajovy, and Emgality
February 2019 updates are in BOLD and strikethrough.

Manual PA criteria apply to all new users of Aimovig, Ajovy, or Emgality.

Manual PA Criteria: Aimovig, Ajovy, or Emgality is approved if all criteria are met:

- Patient ≥ 18 years old and not pregnant
- Must be prescribed by or in consultation with a neurologist
- **The patient also meets one of the following:**
  - **Patient has episodic migraines at a rate of 4 to 7 migraine days per month for 3 months and has at least moderate disability shown by Migraine Disability Assessment (MIDAS) Test score > 11 or Headache Impact Test-6 (HIT-6) score > 50 OR**
  - Patient has **episodic migraine at a rate** of at least 8 migraine days per month for 3 months **OR**
  - **Patient has a diagnosis of chronic migraine**
- Patient has a contraindication to, intolerability to, or has failed a 2-month trial of at least ONE drug from TWO of the following migraine prophylactic drug classes:
  - Prophylactic antiepileptic medications: valproate, divalproic acid, topiramate
  - Prophylactic beta-blocker medications: metoprolol, propranolol, atenolol, nadolol, **timolol**
  - Prophylactic antidepressants: amitriptyline, **duloxetine, nortriptyline,** venlafaxine
- **Patient is not currently on botulinum toxin or patient must not have received a botulinum toxin injection within the last 2 months**
- Concurrent use with other CGRP inhibitors (e.g., Aimovig, Emgality) is not allowed
- For Emgality, a loading dose will be allowed

Non-FDA-approved uses are NOT approved.

PA expires after 6 months.

Renewal PA Criteria: Coverage will be approved indefinitely for continuation of therapy if **one of the following apply:**

- ~~The patient has shown improvement in migraine prevention (e.g., reduced migraine headache days, reduced migraine frequency, reduced use of acute abortive migraine medication)~~
- **The patient has had a reduction in mean monthly headache days of ≥ 50% relative to the pretreatment baseline (as shown by patient diary documentation or healthcare provider attestation) OR**
- **The patient has shown a clinically meaningful improvement in ANY of the following validated migraine-specific patient-reported outcome measures:**
  - **Migraine Disability Assessment (MIDAS)**
    - **Reduction of ≥ 5 points when baseline score is 11–20**
    - **Reduction of ≥ 30% when baseline score is > 20**
  - **Headache Impact Test (HIT-6)**
    - **Reduction of ≥ 5 points**
  - **Migraine Physical Functional Impact Diary (MPFID)**

- **Reduction of ≥ 5 points**

4. **Migraine Agents – CGRP Antagonist Prophylaxis Subclass—UF and PA Implementation Plan**

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) an effective date of the first Wednesday 30 days after the signing of the minutes in all points of service (POS).

Summary of Physician's Perspective:

This drug class is a good example of where all three drugs were first reviewed as new drugs soon after FDA-approval, and then the Committee was quickly able to do the full class review only a few months after the drugs had been launched. This helps with decreasing the number of patients who are established on therapy with having to switch products.

All three products are designated as UF. Since the CGRPs represent a new mechanism for treating migraine, having all three as UF will allow for us to see if providers will prefer one product over another. Additionally, if new safety or efficacy data does become available we can re-review the class.

PA criteria currently apply to all three drugs. We will continue to require a trial of the traditional oral preventive drugs before a CGRP. This in line with the recommendations from the American Academy of Neurology guidelines and the American Headache Society Consensus statement. Also, the ICER report did conclude that the traditional oral drugs are effective for preventing migraines.

For the PAs we will not require a trial of Botox first for chronic migraine, since the guidelines don't require this, plus when we talked with our neurologists, they did not recommend this either. However the clinical trials with the CGRPs excluded botulinum toxin for 2 to 4 months prior to initiation of therapy, so that is in the PA criteria.

This class represents a new mechanism for preventing migraine headache, and there has been a fast increase in utilization. However, we can't determine in advance who will respond to these medications, compared to the traditional oral drugs. Also there is no data yet on whether these drugs will actually decrease ER visits for migraine.

Summary of Panel Questions and Comments:

Mr. Hostettler asked how long it takes to get through manual PA for patients and requested feedback at the next meeting.

Lt Col Khoury follows-up with Mr. Hostettler regarding his question about length of time it takes a PA to process. Were you specifically interested in the CGRPs or the overall process? To make sure I heard that question right. You said, "can you tell us how long it takes for a PA to process?"

Mr. Hostettler said this is an on-going question. What is the length of time it takes for the prescription generation until the patient actually gets the medication. It takes longer for some drugs than others do. I am sure another week is not going to matter but sometimes it is longer than a week and in certain cases, I view that as problematic. I am curious about the data. The response can be more general.

Lt Col Khoury said, "According to our data, 99.7% of all PAs that are filled and submitted have a 5 day turnaround. Seventy-four percent of all Electronic PAs, have a turnaround time of a day or less. This data is approximately 6 months old.

Mr. Hostettler asked if the data provided is from the time the prescription is taken to the retail pharmacy.

Lt Col Khoury stated that is where the PA is driving the decision-making. The PA is required to be completed.

Mr. Hostettler provided an example for clarification. For instance, when the patient shows up at retail. The retail pharmacy says, "Sorry we can't do this thing it requires a PA," we send it off to corporate to get it started. Is this additional time that will be added to your numbers.

Lt Col Khoury responds yes. There are instances where the PA is not filled because the patient is switched to an alternative. It's a little bit more involved; it's not just the PA timeframe.

Mr. Hostettler said all of that is part of that timeframe, even up to the point of they never got the drug.

CDR Hellwig stated that the patient has received a drug. They may have received the alternative agent. Many times with our PAs, we are pushing patients to another agent. They would not necessarily receive the agent that the PA was submitted for.

Mr. Hostettler said regardless of whether the PA was completed and the patient received therapy as opposed to just never got it done. I believe all of these issues are a part of the process. What is the impact on the beneficiaries?

CDR Hellwig stated that we do not have the data. We can look to see if we can get it but it is going to be challenging.

Mr. Hostettler said, "It would behoove us to try to get to that information because that is the end-point, the patient impact. If the patient is not getting therapy, that is a big problem. If they are being changed to other alternatives properly, in a proper timeframe, that is fine. I just want to better understanding the process and ensure that everyone understands the process when we provide comments or make decisions.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation for the UF Recommendation, Manual PA Criteria, and UF and PA Implementation Plan for the Migraine Agents.

- **Migraine Agents – CGRP Antagonist Prophylaxis Subclass—UF Recommendation**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

  For Director, DHA:

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

- **Migraine Agents – CGRP Antagonist Prophylaxis Subclass—Manual PA Criteria**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

  For Director, DHA:

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

- **Migraine Agents – CGRP Antagonist Prophylaxis Subclass—UF and PA Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

  For Director, DHA:

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

ADDITIONAL PANEL QUESTIONS AND COMMENTS.

CDR Hellwig stated we do have something called a safety net. When we have step therapy in place, we do have a set-up where our mail order pharmacy will actually reach out to the patient if they have not gotten the other agent. This is specific to our step therapy process, not for our PAs. There is a safety net for patients in that situation or an intervention to make sure that they do get something.

Mr. Hostettler asked if that it is true if it is going through the mail order or is it true of both mail order and retail.

Lt Col Khoury stated we have to confirm if that is true for all.

Mr. Hostettler is not sure.

CDR Hellwig stated there are official steps that applies in certain situations when we do a drug class review. That is when this (the safety net) applies. Another thing that we've done, and you'll see in couple of our new drugs, some of our oncology agents we've added the option for the provider to write in the diagnosis cited in the NCCN guidelines. That's because things are changing so rapidly in the oncology world that once we've created a PA it may become outdated and so that's a way to keep patients from having to go through the drug process when there is good data available even if the product doesn't have that as a FDA indication. We have added that (the safety net) as well to ease the process there.

Mr. Hostettler noted and commended the additional controls in the process to address patient safety concerns.

B. ONCOLOGICAL AGENTS – CYP-17 INHIBITORS (CYP17) SUBCLASS AND 2ND-GENERATION ANTIANDROGENS (2ND-GEN AA) SUBCLASS

1. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—UF Recommendation

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following for the Prostate Cancer agents, as outlined below, based on clinical and cost-effectiveness:

CYP 17 Inhibitor Subclass

- UF and step-preferred
  - abiraterone acetate micronized (Yonsa)
- UF and non-step-preferred
  - abiraterone acetate (Zytiga, generics)
  -

- NF
  - None

2nd-Generation Antiandrogen Subclass

- UF and step-preferred
  - enzalutamide (Xtandi)
- UF and non-step-preferred
  - apalutamide (Erleada)
- NF
  - None

2. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—Manual PA Criteria

Updated manual PA criteria for all four prostate cancer drugs were recommended by the P&T Committee (18 for, 0 opposed, 0 abstained, 0 absent). For both Yonsa and Zytiga brand and generics, the prescription must be written by an oncologist or urologist, and off-label use for non-localized disease was added. The Zytiga PA criteria were also updated to include step therapy, requiring a trial of Yonsa first, unless there is a contraindication, inadequate response, or adverse reaction to Yonsa, for all new and current users of Zytiga brand or generics (i.e., "no grandfathering" scenario). Additionally, for Zytiga, the 250 mg tablets are the preferred formulation, based on cost-effectiveness. All new and current users of Zytiga brand or generic 500 mg tablets will need to try the 250 mg tablets first.

The Committee also recommended updating the current PAs for Xtandi and Erleada to include the Xtandi step-therapy requirements. All new users (i.e., "grandfathering" scenario) of Erleada will require a trial of Xtandi first, unless contraindicated or if the patient has had an inadequate response or adverse reaction to previous use of Xtandi. Additionally, for nmCRPC, both Xtandi and Erleada will require patients to have documented prostate-specific antigen doubling time (PSADT) of ≤ 10 months, consistent with the trial design of PROSPER and SPARTAN.

a) Yonsa
February 2019 updates are in BOLD and strikethrough.

Manual PA criteria apply to all new users of Yonsa.

Manual PA Criteria: Coverage is approved if all criteria are met:

- **Age ≥ 18 years**
- **Prescribed by or in consultation with an oncologist or urologist**

- Provider is aware that Yonsa may have different dosing and food effects than other abiraterone acetate products (medication errors and overdose warning)
- ~~Patient has documented diagnosis of metastatic castration-resistant prostate cancer (mCRPC)~~
- ~~Patient has documented diagnosis of metastatic high-risk castration-sensitive prostate cancer (mCSPC)~~
- **Patient has documented diagnosis of non-localized disease including:**
  - **Metastatic castration-resistant prostate cancer (mCRPC)**
  - **Metastatic castration-sensitive prostate cancer (mCSPC)**
  - **Regional disease (T_xN1M0) OR**
- **If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND**
  - **The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
- Patient must receive concomitant therapy with methylprednisolone
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy

Other non-FDA-approved uses are NOT approved.

PA does not expire.

b) **Zytiga Brand and Generics**
February 2019 updates are in BOLD and strikethrough.

Manual PA criteria apply to **all new and current users** of Zytiga and generics.

Manual PA Criteria: Coverage is approved if all criteria are met:

- **Yonsa is the Department of Defense's preferred CYP-17 Inhibitor agent.**
  - **Has the patient tried Yonsa?**

  OR
  - **Does the patient have or have they had a contraindication/inadequate response/adverse reaction to Yonsa that is not expected to occur with the requested agent?**
- **Age ≥ 18 years**
- **Prescribed by or in consultation with an oncologist or urologist**

- ~~Patient has documented diagnosis of metastatic castration-resistant prostate cancer (mCRPC)~~
- ~~Patient has documented diagnosis of metastatic high-risk castration-sensitive prostate cancer (mCSPC)~~
- **Patient has documented diagnosis of non-localized disease including:**
  - **Metastatic castration-resistant prostate cancer (mCRPC)**
  - **Metastatic castration-sensitive prostate cancer (mCSPC)**
  - **Regional disease (T_xN1M0) OR**
- **If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND**
  - **The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
- Patient must receive concomitant therapy with prednisone
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy
- **Zytiga 250 mg is the DoD's preferred strength. Is the prescription for Zytiga 250 mg OR will the prescription be changed to the 250 mg?**
  - **Note: If the prescription is being changed to the 250 mg strength, please submit a new prescription with this PA form**

    OR
  - **Please state why the patient cannot take multiple 250 mg tablets to achieve the patient's daily dose (fill-in blank)**

Other non-FDA-approved uses are NOT approved.

PA does not expire.

c) **Xtandi**
February 2019 updates are in BOLD.

Manual PA criteria apply to all new users of Xtandi.

Manual PA Criteria: Coverage is approved if all criteria are met:

- **Age ≥ 18 years**
- **Prescribed by or in consultation with an oncologist or urologist**
- Patient has documented diagnosis of **metastatic OR non-metastatic** castration-resistant prostate cancer (CRPC)

- If used in non-metastatic castration-resistant prostate cancer (nmCRPC), patient must have: prostate-specific antigen doubling time **(PSADT) ≤ 10 months OR**

- **If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND**
  - **The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy

Other non-FDA-approved uses are NOT approved.

PA does not expire.

d) Erleada
February 2019 updates are in BOLD.

Manual PA criteria apply to all new users of Erleada.

Manual PA Criteria: Coverage is approved if all criteria are met:

- **Xtandi is the Department of Defense's preferred 2nd-Generation Antiandrogen agent.**
  - **Has the patient tried Xtandi?**
    OR
  - **Does the patient have or have they had a contraindication/inadequate response/adverse reaction to Xtandi that is not expected to occur with Erleada?**
- **Age ≥ 18 years**
- Prescribed by or in consultation with an oncologist or urologist
- Patient has documented diagnosis of non-metastatic castration-resistant prostate cancer (nmCRPC) **AND**
  - Negative CT scan of abdomen/pelvis and/or negative bone scan, **AND**
  - **PSADT ≤ 10 months OR**
- **If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND**
  - **The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy

Other non-FDA-approved uses are NOT approved.

PA expires in 1 year.

Renewal PA Criteria: Coverage will be approved for 1 year for continuation of therapy if:

- Patient continues to be metastases-free
- No toxicities have developed
- Patient has not progressed onto subsequent therapy (such as abiraterone)

3. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—Tier 1 Cost-Share

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) lowering the current tier 2 cost-share for the CYP17 inhibitor Yonsa and the 2nd-generation AA Xtandi to the generic Tier 1 cost-share.

The authority for this recommendation is codified in 32 CFR 199.21(j)(3), which states that "when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the Pharmacy and Therapeutics Committee may also designate that the drug be cost-shared at the generic rate." Lowering the cost-share for both Yonsa and Xtandi will provide a greater incentive for beneficiaries to use the most cost-effective CYP 17 or 2nd-generation antiandrogen product, respectively, in the purchased care points of service.

4. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—UF and PA Implementation Plan

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) 1) an effective date of 90 days after signing of the P&T minutes at all points of service, and 2) DHA send letters to beneficiaries who are affected by the step decision in the CYP17 subclass (those patients currently on Zytiga brand or generics).

Summary of Physician's Perspective:

This is the first time that the Committee has recommended adding step therapy for an oncology drug. All four prostate cancer drugs will be UF, but Zytiga and Erleada will be behind a step. Note that there is manual PA criteria currently in place for all of these drugs, and the general PAs were updated.

The Committee recommended step therapy for the CYP 17 drugs, since Zytiga and Yonsa contain the same active ingredient. The step therapy criteria are included in the manual PA, which will apply to both new and current users of Zytiga ("no grandfathering"). Patients will be notified via letter of the upcoming requirements for step therapy. Currently, there about 1,200 patients who could be potentially affected by the step therapy for the CYP 17 drugs. However, the number of patients affected will likely be lower. Our data shows that about 34% of patients remain on therapy after 1 year, and only 10% of patients are on one of the CYP 17 drugs after 2 years. There is an implementation period of 90 days, so we expect the implementation date will be sometime in August 2019.

For the anti-androgens, the step therapy requiring Xtandi first will only apply to new patients. Therefore, all patients currently on Erleada will be allowed to continue therapy. Our data also shows that there is also low persistence for this subclass - only about 20% of patients remain on an anti-androgen after 2 years.

Xtandi has more indications than Erleada, and has been studied in more patients. The reason for having renewal criteria for Erleada but not Xtandi is due to the fact that Erleada is not approved for metastatic disease, and the PA takes that into account.

Summary of Panel Questions and Comments:

Mr. Hostettler asked for clarification on the manual PA criteria for Zytiga. More specifically, how does it affect new and current users? Why force patients who are doing well on their product to change to a different product.

MAJ Davies said the P&T Committee discussed this issue. The products have the same active ingredient. Theoretically, it would not be a change with switching that patient over to Yonsa, which is micronized abiraterone.

Dr. Peloquin asked if there was a change in dosage when the patient switched to the new product. There was some verbiage in the PA criteria about a dosage difference. Are there controls in place to address safety concerns?

Lt Col Khoury and MAJ Davies both believed that the verbiage in the PA would address safety concerns. Additionally the oncologist placing the order would know there is a difference in the formulation.

Mr. Hostettler believes that cancer patients using Xtandi, are very, very concerned about their treatment. If they are doing well with the product they are using, making a change due to cost is harmful to the patient. As you stated there are a percentage of patients who drop off the product for whatever reason. Not knowing the cost difference, overtime it does not seem to be that big a difference. It goes back to the discussion we had earlier about the humanistic aspect. We are putting a patient in a very serious situation and it is a hard decision.

MAJ Davis responded the current users of Xtandi are being grandfathered. This decision would only affect new patients. It is the Zytiga that will not be grandfathered. Zytiga is a metastatic disease and more progressive state of the disease state.

Mr. Hostettler stated that it makes the decision even harder because the patients are more concerned because they are at a higher risk. The change in product only adds to their concerns/problems. It is hard for me to say it is a good decision. I am simply asking the P&T Committee to take these comments into consideration.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation for the UF Recommendation, Manual PA Criteria, and UF and PA Implementation Plan for the Oncological Agents.

- **Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass —UF Recommendation**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

  for ***Director, DHA:***

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

- **Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass — Manual PA Criteria**

  Concur: 6 Non-Concur: 1 Abstain: 0 Absent: 2

  for ***Director, DHA:***

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

- **Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass Subclass —Tier 1 Cost-Share**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

  for ***Director, DHA:***

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

- **Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass Subclass —UF and PA Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

For Director, DHA:

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

II. NEWLY APPROVED DRUGS PER 32 CFR 199.21(G)(5)

1. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF Recommendation

The P&T Committee recommended (group 1 and group 3: 17 for, 0 opposed, 0 abstained, 1 absent; and group 2: 18 for, 0 opposed, 0 abstained, 0 absent) the following:

- UF:
  - amifampridine (Firdapse) – Miscellaneous Neurological Agent for Lambert-Eaton Myasthenic Syndrome (LEMS)
  - baloxavir (Xofluza) – Antiviral for Influenza
  - cenegermin-bkbj ophthalmic solution (Oxervate) – Anti-Inflammatory Immunomodulatory Ophthalmic Agent for Neurotrophic Keratitis
  - elapegademase-lvlr IM injection (Revcovi) – Miscellaneous Metabolic Agent for Adenosine Deaminase Severe Combined Immune Deficiency (ADA-SCID)
  - gilteritinib (Xospata) – Oncological Agent for Acute Myelogenous Leukemia (AML)
  - glasdegib (Daurismo) – Oncological Agent for AML
  - inotersen injection (Tegsedi) – Miscellaneous Neurological Agent for Hereditary Transthyretin Amyloidosis
  - larotrectinib (Vitrakvi) – Oncological Agent for Solid Tumors
  - lorlatinib (Lorbrena) – Oncological Agent for Non-Small Cell Lung Cancer (NSCLC)
  - loteprednol ophthalmic suspension (Inveltys) – Ophthalmic Corticosteroid for Postoperative Inflammation
  - pegfilgrastim-cbqv injection (Udenyca) – White Blood Cell Stimulant and Biosimilar to Neulasta
  - riluzole oral suspension (Tiglutik) – Miscellaneous Neurological Agent for Amyotrophic Lateral Sclerosis (ALS)

- tafenoquine 100 mg tablet (Arakoda) – Antimalarial Agent for Prophylaxis of Malaria
- tafenoquine 150 mg tablet (Krintafel) – Antimalarial Agent for Prevention of Relapse and Radical Cure of Malaria
- talazoparib (Talzenna) – Oncological Agent for Breast Cancer
- testosterone enanthate, subcutaneous (SQ) injection (Xyosted) – Androgens-Anabolic Steroids: Testosterone Replacement Therapies

- NF:
  - aripiprazole tablet with ingestible event marker (Abilify MyCite) – Atypical Antipsychotic
  - clobazam oral film (Sympazan) – Anticonvulsant-Antimania Agent for Lennox-Gastaut Syndrome
  - cyclosporine 0.09% ophthalmic solution (Cequa) – Anti-Inflammatory Immunomodulatory Ophthalmic Agent for Dry Eye Disease
  - desmopressin acetate sublingual (SL) tablet (Nocdurna) – Miscellaneous Endocrine Agent for Nocturia due to Nocturnal Polyuria
  - filgrastim vials (Granix) – White Blood Cell Stimulant and Biosimilar to Neupogen
  - halobetasol propionate 0.01% lotion (Bryhali) – High Potency Corticosteroid-Immune Modulator for Plaque Psoriasis
  - itraconazole 65 mg capsules (Tolsura) – Antifungal Agent
  - latanoprost (Xelpros) – Ophthalmic Prostaglandin
  - omadacycline (Nuzyra) – Tetracycline Antibiotic for Community-Acquired Bacterial Pneumonia (CABP) and Acute Bacterial Skin and Skin Structure Infections (ABSSSI)
  - revefenacin nebulized solution (Yupelri) – Pulmonary-2: Long Acting Anti-Muscarinic Agent (LAMA) for Chronic Obstructive Pulmonary Disease (COPD)
  - rifamycin (Aemcolo) – Miscellaneous Gastrointestinal Antibiotic for Traveler's Diarrhea
  - sarecycline (Seysara) – Tetracycline Antibiotic for Acne Vulgaris

2. Newly Approved Drugs per 32 CFR 199.21(g)(5)—PA Criteria

The P&T Committee recommended (group 1 and group 3: 17 for, 0 opposed, 0 abstained, 1 absent; and group 2: 18 for, 0 opposed, 0 abstained, 0 absent) the following:

- Oral Tetracycline Agents: Applying the same automated (step therapy) and manual PA criteria for sarecycline (Seysara) in new and current users that is currently in place for the other non-step-preferred oral tetracyclines. Patients must first try one generic doxycycline IR product, either the hyclate or

monohydrate salt and one generic minocycline IR product first, before Seysara.

- Androgens-Anabolic Steroids: Testosterone Replacement Therapies: Applying new manual PA criteria for Xyosted SQ in new and current users. In addition to a trial of the step-preferred testosterone 2% topical gel (Fortesta), patients must also try one injectable testosterone product and meet the Risk Evaluation and Mitigation Strategies (REMS) requirements listed in the Xyosted product label regarding the risk of increases in blood pressure and potential increase in the risk of major adverse cardiovascular events (MACE).
- Applying manual PA criteria to new users of Abilify MyCite, Arakoda, Daurismo, Firdapse, Lorbrena, Oxervate, Talzenna, Tegsedi, Tolsura, Vitrakvi, and Xospata.
- Applying manual PA criteria to new and current users of Aemcolo, Cequa, Nocdurna, Tiglutik, and Yupelri.

Full PA Criteria for the Newly Approved Drugs per 32 CFR 199.21(g)(5)

a) amifampridine (Firdapse)

Manual PA applies to all new users of Firdapse.

Manual PA Criteria: Firdapse is approved if:

- Age ≥ 18 years old
- Drug is prescribed by an oncologist or neurologist
- Has laboratory evidence of Lambert-Eaton myasthenic syndrome (LEMS)

Non-FDA-approved uses are NOT approved.

PA does not expire.

b) aripiprazole tablet with ingestible event marker (Abilify MyCite)

Manual PA criteria apply to all new users of Abilify MyCite.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient must have documented attempt to use generic aripiprazole tablets, with non-compliance documented in prescriber notes. Prescriber notes must also document the prescriber's attempted medication adherence counseling.
- Patient must have documented trial of at least 12 weeks of Abilify Maintena first

- Provider acknowledges that FDA labeling states the ability of Abilify MyCite to improve patient compliance or modify aripiprazole dosage has not been established.

Non-FDA-approved uses are NOT approved.

PA does not expire.

c) cenegermin-bkbj ophthalmic solution (Oxervate)

Manual PA criteria apply to all new users of Oxervate.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 2 years
- Patient has a documented diagnosis of neurotrophic keratitis
- Drug is prescribed by a cornea specialist or ophthalmologist
- Patient does not wear contact lenses during treatment course

Non-FDA-approved uses are NOT approved.

PA does not expire.

d) cyclosporine 0.09% ophthalmic solution (Cequa)

February 2019 criteria specific for Cequa are in BOLD for the PA form that also includes Xiidra and Restasis.

PA criteria apply to all **new and current** users. A new user is defined as a patient who has not filled a prescription for Restasis, **Cequa** or Xiidra in the past 120 days.

- If there is no Restasis, **Cequa**, or Xiidra prescription in the past 120 days, a manual PA is required.

Manual PA Criteria: Coverage is approved if all the criteria are met:

- The drug is prescribed by an ophthalmologist or optometrist
- **For Cequa: the patient is ≥ 18 years old**
- A diagnosis of moderate to severe dry eye disease is supported by both of the criteria below:
- Positive symptomatology screening for moderate to severe dry eye disease from an appropriate measure
- At least one positive diagnostic test (e.g., Tear Film Breakup Time, Osmolarity, Ocular Surface Staining, Schirmer Tear Test)
- Patient must try and fail the following:

- At least 1 month of one ocular lubricant used at optimal dosing and frequency (e.g., carboxymethylcellulose [Refresh, Celluvisc, Thera Tears, Genteal, etc.], polyvinyl alcohol [Liquitears, Refresh Classic, etc.], or wetting agents [Systane, Lacrilube])
- Followed by at least 1 month of a different ocular lubricant that is non-preserved at optimal dosing and frequency (e.g., carboxymethylcellulose, polyvinyl alcohol)

- Concomitant use of Restasis, **Cequa**, or Xiidra is NOT allowed.

Non-FDA-approved uses for Cequa are NOT approved.

PA expires in one year.

Renewal Criteria: Coverage will be approved indefinitely if all criteria are met:

- The drug is prescribed by an ophthalmologist or optometrist.
- The patient must have documented improvement in ocular discomfort.
- The patient must have documented improvement in signs of dry eye disease.

e) desmopressin acetate sublingual (SL) tablet (Nocdurna)

Manual PA criteria apply to all new and current users of Nocdurna.

Manual PA criteria apply to all new and current users of Nocdurna SL tablets. Updates are in BOLD for the PA that also has Noctiva nasal spray

Manual PA Criteria: Coverage is approved if all criteria are met:

- For Nocdurna: Age ≥ 18 years old
- For Nocdurna: For females: must use 27.7 mcg dosage; for males: must use 55.3 mcg dosage
- For Noctiva Nasal Spray: Age ≥ 50 years old (Only the low dose is allowed for pts > 65 years old)
- Patient has nocturia defined as having ≥ 2 nocturnal voids nightly for ≥ 6 months
- Causes of nocturia have been evaluated and nocturnal polyuria is confirmed with a 24-hour urine collection
- **Patient has tried non-pharmacologic techniques or lifestyle interventions to manage the nocturia (e.g., nighttime fluid restriction, avoidance of caffeine and alcohol, earlier timing of medications, leg elevation and/or use of compression stockings)**

- **The patient has tried oral desmopressin acetate tablets (DDAVP tablets, generics)**
- Patient is not currently taking <u>any of the following</u> medications:
  - Loop diuretics, alpha$_1$-adrenoceptor antagonists, 5-alpha reductase inhibitors (ARIs), thiazide diuretics, anticholinergics, antispasmodics, sedative/hypnotic agents, NSAIDs, SSRIs, SNRIs, antidepressants, anti-epileptics, opioids, or SGLT2s
  - Systemic or inhaled corticosteroids or lithium
- Prescribed by a urologist, a geriatrician, an endocrinologist, or a **nephrologist**
- **Provider must supply most recent serum sodium and date**
  - **Sodium _____mEq/mL Date_____**
- Patient has normal sodium (135-145 mEq/L) prior to initiation, recheck sodium after one week of therapy, and another sodium recheck at 1 month
- **Provider acknowledges that patients over 65 years old are at greater risk of hyponatremia and has advised the patient about this significant safety concern**
- Patient does not have the following conditions for both Noctiva Nasal Spray and Nocdurna:
  - **Renal impairment (eGFR < 50 mL/min)**
  - **Hyponatremia or history of hyponatremia**
  - **Polydipsia**
  - **Nocturnal enuresis**
  - **SIADH**
  - **Congestive heart failure**
  - **Uncontrolled hypertension or uncontrolled diabetes mellitus**
  - **Interstitial cystitis**
  - **Chronic prostatitis/chronic pelvic pain syndrome**
  - **Suspicion of bladder outlet obstruction (BOO) or urine flow < 5 mL/sec**
  - **Surgical treatment, including transurethral resection, for BOO or benign prostatic hyperplasia within the past 6 months**
  - **Urinary retention or a post-void residual volume in excess of 250 mL as confirmed by bladder ultrasound performed after suspicion of urinary retention**
  - **Current or a history of urologic malignancies (e.g., urothelium, prostate, or kidney cancer)**
  - **Genitourinary tract pathology (e.g., infection or stone in the bladder and urethra causing symptoms)**
  - **Neurogenic detrusor activity (detrusor overactivity)**
  - **Suspicion or evidence of cardiac failure**
  - **History of obstructive sleep apnea**
  - **Hepatic and/or biliary diseases**
  - **Treatment with another investigational product within 3 months prior to initiating therapy**
  - **Known alcohol or substance abuse**

- **Work or lifestyle that may have interfered with regular nighttime sleep**

AND

- **Patient does not have the following conditions for Noctiva Nasal Spray**
  - **acute or chronic rhinitis (for Noctiva nasal spray only)**
  - **atrophy of nasal mucosa (for Noctiva nasal spray only)**

Non-FDA-approved uses are NOT approved.

PA expires in ~~6 months~~ **4 months.**

Renewal Criteria: Coverage will be approved for an additional 6 months if all of the following apply:

- Patient has not developed any of the conditions above
- **Patient is not taking any of the medications mentioned above**
- Patient has shown a reduction in nocturia episodes

f) gilteritinib (Xospata)

Manual PA criteria apply to all new users of Xospata.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 18
- Has laboratory evidence of relapsed or refractory acute myeloid leukemia with a Ferline McDonough Sarcoma (FMS)-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test
- The patient will be monitored for posterior reversible encephalopathy syndrome (PRES), prolonged QTc, and pancreatitis
- Patient is not pregnant or actively trying to become pregnant
- Prescribed by or in consultation with a hematologist/oncologist

Non-FDA-approved uses are NOT approved.

PA does not expire.

g) glasdegib (Daurismo)

Manual PA criteria apply to all new users of Daurismo.

Manual PA criteria: Coverage is approved if all criteria are met:

- Treatment of newly diagnosed acute myeloid leukemia (in combination with low-dose cytarabine) in adult patients who are ≥ 75 years of age or who have comorbidities that preclude use of intensive induction chemotherapy.
- Provider acknowledges and patient has been informed that limitations of use include that this drug has not been studied in patients with severe renal impairment or moderate to severe hepatic impairment.
- Patient is not pregnant or actively trying to become pregnant
- Patient will be monitored for febrile neutropenia and QTc prolongation
- Prescribed by or in consultation with a hematologist/oncologist

Non-FDA-approved uses are NOT approved.

PA does not expire.

h) inotersen injection (Tegsedi)

Manual PA applies to all new users of Tegsedi.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 18 and has genetically confirmed transthyretin mutation resulting in familial amyloidotic polyneuropathy (FAP) stage 1 or 2 hereditary transthyretin-mediated amyloidosis (hTTRA)
- Has polyneuropathy secondary to hereditary transthyretin-mediated amyloidosis with either 1) a polyneuropathy disability (PND) score ≤ IIIB or 2) a Neuropathy Impairment Score between 10 and 130
- Provider and patient are both registered and enrolled with the Tegsedi Risk Evaluation and Mitigation Strategies (REMS) program
- Patient has no evidence of thrombocytopenia
- Patient does not have chronic kidney disease (CKD) stage 3b and has no history of glomerulonephritis
- The provider will monitor the patient's platelet counts and renal and hepatic function
- Patient will take an oral Vitamin A supplement at the recommended daily allowance
- Provider is aware and patient is informed of the following potential adverse drug reactions: stroke, encephalitis, carotid arterial dissection, hypercoagulability and thrombosis (venous and arterial), QRS prolongation and other arrhythmias, elevated liver-associated enzymes, autoimmune hepatitis, primary biliary cirrhosis, biliary obstruction, glomerulonephritis, nephrotic syndrome, interstitial nephritis, thrombocytopenia, idiopathic thrombocytopenia (ITP), antineutrophil cytoplasmic antibody-associated (ANCA) vasculitis, and hypersensitivity

- Prescribed by or in consultation with a specialist that manages hereditary transthyretin amyloidosis (e.g., cardiologist, geneticist, neurologist)
- Concomitant use of Onpattro and Tegsedi is not allowed

Non-FDA-approved uses are NOT approved.

PA does not expire.

i) itraconazole 65 mg capsules (Tolsura)

Manual PA criteria apply to all new users of Tolsura.

Manual PA Criteria: Tolsura is approved if:

- Patient has one of the following diagnoses:
  - Histoplasmosis
  - Pulmonary or Extrapulmonary Blastomycosis
  - Pulmonary or Extrapulmonary Aspergillosis

  AND
- For histoplasmosis or blastomycosis:
  - Patient has had serious side effects with generic itraconazole 100 mg tablets/capsules OR
  - Patient has failed drug treatment with generic itraconazole 100 mg tabs/capsules
- For aspergillosis
  - Patient has had serious side effects with generic itraconazole 100 mg tablets/capsules and amphotericin B OR
  - Patient has failed drug treatment with generic itraconazole 100 mg tabs/capsules and amphotericin B

Non-FDA-approved uses are NOT approved including onychomycosis.

PA does not expire.

j) larotrectinib (Vitrakvi) capsules and oral solution

Manual PA criteria apply to all new users of Vitrakvi capsules and oral solution.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient diagnosed with a solid tumor that:
  - has a neurotrophic tropomyosin receptor kinase (NTRK) gene fusion without a known acquired resistance mutation,

- is metastatic OR where surgical resection is likely to result in severe morbidity, AND
- has no satisfactory alternative treatments OR that has progressed following such treatment(s).

- Larotrectinib (Vitrakvi) is prescribed by or in consultation with a hematologist/oncologist
- For Vitrakvi oral solution: in addition to the above criteria, the patient has difficulty swallowing the capsules

Non-FDA-approved uses are NOT approved.

PA does not expire.

k) lorlatinib (Lorbrena)

Manual PA criteria apply to all new users of Lorbrena.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient is 18 years of age or older
- Drug is prescribed by or in consultation with hematologist or oncologist
- Patient has a diagnosis of metastatic anaplastic lymphoma kinase (ALK) positive non-small cell lung cancer
- Patient has experienced disease progression on one of the following treatments:
  - crizotinib (Xalkori) and at least one other ALK inhibitor
  - alectinib (Alecensa) as a first-line agent
  - ceritinib (Zykadia) as a first-line agent **OR**
- If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND
  - The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation

Non-FDA-approved uses NOT approved.

PA does not expire.

l) revefenacin nebulized solution (Yupelri)

Manual PA is required for all new and current users of Yupelri.

Manual PA Criteria: Yupelri is approved if all criteria are met:

- The patient has a diagnosis of chronic obstructive pulmonary disease

- The patient has tried and failed an adequate course of a nebulized Short-Acting Muscarinic Antagonist (e.g., ipratropium)
- The patient has tried and failed an adequate course of Spiriva Respimat
- The patient has tried and failed an adequate course of therapy with at least one of the following dry powder inhalers: Tudorza Pressair, Incruse Ellipta, Spiriva Handihaler, or Seebri Neohaler OR
- The patient cannot generate the peak inspiratory flow needed to activate at least one of the following dry powder inhalers: Tudorza Pressair, Incruse Ellipta, Spiriva Handihaler, or Seebri Neohaler

Non-FDA-approved uses are NOT approved.

PA does not expire.

m) rifamycin (Aemcolo)

Manual PA criteria apply to all new and current users of Aemcolo.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 18
- Patient has a diagnosis of traveler's diarrhea caused by noninvasive strains of *Escherichia coli*
- Patient does not have diarrhea complicated by fever and/or bloody stool
- Patient does not have diarrhea due to pathogens other than noninvasive strains of *E. coli*
- Patient has tried and failed a 3-day trial of ciprofloxacin unless a contraindication exists or patient has tried and failed azithromycin unless a contraindication exists

Non-FDA-approved uses are NOT approved including but not limited to diarrhea-predominant irritable bowel syndrome (IBS-D), non-alcoholic steatohepatitis (NASH), small intestine bacterial overgrowth (SIBO), and inflammatory bowel disease (IBD).

PA renewal not allowed. A new prescription will require a new PA to be submitted.

n) riluzole oral suspension (Tiglutik)

Manual PA criteria apply to all new and current users of Tiglutik.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient is diagnosed with amyotrophic lateral sclerosis
- Patient has dysphagia/swallowing dysfunction

Non-FDA-approved uses are NOT approved.

PA does not expire.

o) **sarecycline (Seysara)**
February 2019 criteria specific to Seysara are in BOLD.

PA applies to both new and current users of Seysara.

Automated PA Criteria:

- Patient has filled a prescription for one generic IR doxycycline (either hyclate or monohydrate salt; does not include doxycycline monohydrate 40 mg IR/DR) AND one generic minocycline IR product at any Military Treatment Facility (MTF), retail network pharmacy, or the mail order pharmacy in the previous 180 days

Manual PA Criteria: If automated PA criteria are not met, the non-step-preferred product is allowed if:

Acne Vulgaris or Rosacea

- For Solodyn or generic minocycline ER, Minolira, **or Seysara:** The patient has acne with inflammatory lesions AND
  - the patient cannot tolerate generic minocycline IR due to gastrointestinal adverse events

Non-FDA-approved uses are NOT approved.

PA expires in 1 year.

Renewal Criteria:

- **Seysara: PA renewal is not allowed; repeat courses will require a new PA to be submitted.**

p) **tafenoquine 100 mg tablet (Arakoda)**

Manual PA criteria apply to all new users of tafenoquine (Arakoda).

Manual PA Criteria: Coverage will be approved for tafenoquine (Arakoda) if all criteria are met:

- Age ≥ 18 and Arakoda is being prescribed for malaria chemoprophylaxis
- Patient has a contraindication or intolerance to both atovaquone-proguanil (Malarone) and doxycycline (e.g., pregnancy)
- Patient does not have a major psychiatric disorder to include but not limited to:
  - Active or recent history of depression
  - Generalized anxiety disorder
  - Psychosis or schizophrenia
  - Post-Traumatic Stress Disorder or Traumatic Brain Injury
- Patient does not have a history of seizures or vestibular disorders
- Patient does not have a cardiac conduction abnormality
- Patient has been tested and is negative for glucose 6 phosphate dehydrogenase (G6PD) deficiency
- The above information must be documented in the patient's medical record, and the patient must be educated on Arakoda adverse effects and dosing

Non-FDA-approved uses are NOT approved.

PA expires after 2 years. PA renewal is not allowed; repeat courses will require a new PA to be submitted.

q) talazoparib (Talzenna)

Manual PA criteria apply to all new users of Talzenna.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient is 18 years of age or older
- Drug is prescribed by or consultation with a hematologist or oncologist
- Patient has a diagnosis of deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) and human epidermal growth factor receptor 2-negative (HER2-) breast cancer

Non-FDA-approved uses are NOT approved.

PA does not expire.

r) testosterone enanthate injection (Xyosted)

February 2019 criteria specific to Xyosted are in BOLD for the PA that also includes topical testosterone replacement therapies.

Manual PA criteria apply to all new and current users of Xyosted.

Manual PA for Xyosted requires a trial of the step-preferred product, Fortesta, **and one injectable testosterone product.**

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 18 years and male
- Patient has documentation of experiencing signs and symptoms usually associated with hypogonadism
- **Xyosted is prescribed for the treatment of men with hypogonadal conditions associated with structural or genetic etiologies**
- Diagnosis of hypogonadism is confirmed and evidenced by morning total serum testosterone levels below 300 ng/dL taken on at least two separate occasions
- Patient has one of the following criteria:
  - Patient has tried Fortesta (testosterone 2% gel) **AND an injectable testosterone formulation for a minimum of 90 days AND** failed to achieve total serum testosterone levels above 400 ng/dL (labs drawn 2 hours after Fortesta application or the injectable testosterone formulation) **AND** without improvement in symptoms
    – OR –
  - **Patient has a contraindication to or has experienced a clinically significant adverse reaction to Fortesta that is not expected to occur with the Xyosted autoinjector**
- **The provider has considered the patient's baseline cardiovascular risk and ensured blood pressure is adequately controlled before initiating Xyosted and periodically during the course of treatment (based on the product's boxed warning of increased risk of major adverse cardiovascular events and hypertension).**
- **Patient does not have any of the following:**
  - **Carcinoma of the breast or suspected carcinoma of the prostate**

Non-FDA-approved uses are NOT approved.

Not approved for concomitant use with other testosterone products.

PA does not expire.

3. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF and PA Implementation Plan

The P&T Committee recommended (group 1 and group 3: 17 for, 0 opposed, 0 abstained, 1 absent; and group 2: 18 for, 0 opposed, 0 abstained, 0 absent) an effective date upon the first Wednesday 30 days after signing of the minutes in all points of service.

Summary of Physician's Perspective:

We've been reviewing about 30 new drugs each meeting, and this meeting was no exception. A total of 29 new drugs were reviewed, with 16 recommended for UF status, and 12 recommended for NF status. One new drug will be discussed in the upcoming Tier 4 section.

A total of 18 drugs were recommenced to have PAs. Six of these drugs are in classes where there are existing PA requirements. For 11 of the drugs, the PA will only apply to new users. Seven of the drugs have "no grandfathering" for the PA, so both new and current users will be affected. Two of the drugs (the acne drug Seysara and the testosterone drug Xyosted) already have step therapy in the class.

The Committee did have some specific comments for some of the new drugs:

- Xofluza for treatment of influenza: The Committee felt that the one time treatment course was of value, especially for readiness situations, compared to the 5 day treatment course with Tamiflu. So Xofluza was recommended for UF status.
- Omadycycline (Nuzyra) – This antibiotic was recommended for NF status. The manufacturer must conduct a trial in patients with community acquired pneumonia to determine if there is an increased risk of death. This clinical safety issues was enough of a concern to have the NF recommendation.
- Riluzole oral susp (Tiglutik) – This drug is approved for ALS. A review of DoD data led us to believe that there is the potential for off-label use. Therefore we did recommend a PA for the suspension only, which will apply to both new and current users. Note that the tablet formulation of the drug does not currently require a PA, only the new suspension will have the PA.

At the meeting the annual New Drug Update of the program was given. Over the past three years a total of 194 new drugs have been reviewed, with 52% (101 drugs) recommended for UF status and 48% (93 drugs) recommended for NF status. One challenge for the Committee will be keeping up with the increasing volume of new drug approvals from the FDA, and the increasing number of specialized products approved, particularly oncology products.

Summary of Panel Questions and Comments:

Mr. Hostettler stated that a new user was defined as a patient that has not used any of the products. It appears the current users would have already met the PA criteria for cyclosporine.

Lt Col Khoury referred to the prior class reviews of Restasis and Xiidra. The analysis showed that people come on and come off the product. Our intent was to ensure that patients were consistently on the drug. If they stop using the

product and start later, they are treated as a new user. That is how we clarify the timeline.

Mr. Hostettler further clarified, the patient is currently using the drug and they haven't stopped?

Lt Col Khoury responded that is what our data showed. The patient would start using the drug and over a period, they would stop.

Mr. Hostettler asked if the current users would be required to complete the PA process again. He also asked how many new and current users are affected by the decision for Yupelri.

Lt Col Khoury stated that currently 31 patients are on Yupelri. Cequa PA applies to new and current users if they have not completed.

Mr. Hostettler asked if the course of treatment for Amecolo was 10 or 3 days. He assumes it is a short course of therapy and not longer than a year.

CDR Hellwig stated that yes it is. It is unlikely patients would be affected by this decision.

Mr. Hostettler had the same questions on Arakoda. What is the normal course of treatment? Is it short again or long?

CDR Hellwig stated that Arakoda is a chemoprophylaxis agent. Patients could be on it for an extended period.

Mr. Hostettler clarified; new users are only affected by the decision?

Arakoda PA is for new users.

There were no questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, PA Criteria, and UF and PA Implementation Plan for the Newly Approved Drugs per 32 CRR 199.21(g)(5).

- **Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF Recommendation**

Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

For Director, DHA:

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

- **Newly Approved Drugs per 32 CFR 199.21(g)(5)—PA Criteria**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

  for Director, DHA:

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

- **Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF and PA Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

  for Director, DHA:

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

III. UTILIZATION MANAGEMENT

A. NEW MANUAL PA CRITERIA

New manual PA criteria were recommended for the following drugs, which will be discussed below.

1. Antihistamine-1: First generation and combinations – Dexchlorpheniramine 2 mg/5 mL oral solution (Ryclora)

Ryclora is a new liquid formulation of a dexchlorpheniramine, which had previously been removed from the market. Cost-effective generic formulations of chlorpheniramine are available on the UF without a PA required, and low-cost OTC liquid formulations for fexofenadine and loratadine are widely available.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for dexchlorpheniramine 2 mg/5 mL oral syrup (Ryclora) in new and current users, due to the significant cost differences and lack of clinically compelling benefits over generic alternatives.

Manual PA criteria apply to all new and current users of dexchlorpheniramine liquid (Ryclora). Coverage will be approved for dexchlorpheniramine liquid if all criteria are met:

Ryclora liquid has been identified as having cost-effective alternatives. The provider must describe why Ryclora is required as opposed to available alternatives (chlorpheniramine liquid, loratadine liquid, cetirizine liquid, and fexofenadine liquid).

Non-FDA-approved uses are NOT approved.

PA does not expire.

2. **Hepatitis C Agents: Direct-Acting Agents (HCV DAAs): generic ledipasvir/sofosbuvir (authorized generic for Harvoni) and generic sofosbuvir/velpatasvir (authorized generic for Epclusa)**

The P&T Committee most recently reviewed the HCV DAAs for formulary status in August 2018. Since the review, authorized generics for Harvoni and Epclusa entered the market in December 2018. An "authorized generic" is the brand company's own product repackaged and marketed as a generic drug. An authorized generic is considered therapeutically equivalent to the name brand drug because it is the same drug. The FDA does not consider authorized generics as AB-rated generic formulations.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for the authorized generic products ledipasvir/sofosbuvir and sofosbuvir/velpatasvir in new users, requiring a trial of the branded Harvoni or Epclusa, due to cost-effectiveness. The PA requirement will be removed when it is no longer cost advantageous.

Manual PA criteria apply to all new users of ledipasvir/sofosbuvir (authorized generic for Harvoni) or sofosbuvir/velpatasvir (authorized generic for Epclusa). Ledipasvir/sofosbuvir authorized generic products or sofosbuvir/velpatasvir authorized generic products are approved if all of the following criteria are met:

- For ledipasvir/sofosbuvir: The brand Harvoni formulation is preferred over the authorized generic product. The provider must provide a patient-specific justification as to why the brand Harvoni product cannot be used in this patient.
- For sofosbuvir/velpatasvir: The brand Epclusa formulation is preferred over the authorized generic product. The provider must provide a patient-specific justification as to why the brand Epclusa product cannot be used in this patient. AND the patient must meet the following criteria for a HCV DAA product:
- ≥ 18 years of age
- Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease physician, or a liver transplant physician
- Patient has laboratory evidence of hepatitis C virus infection
- The HCV genotype is documented. (Check box – GT1a, GT1b, GT2, GT3, GT4, GT5, GT6)

Coverage for the HCV DAA is only allowed for the FDA-approved indications or as outlined in the AASLD/IDSA HCV guidelines.

PA expires in 1 year.

3. **Skeletal Muscle Relaxants and Combinations: cyclobenzaprine 7.5 mg**

Generic formulations of the skeletal muscle relaxant cyclobenzaprine are available in 5 mg, 7.5 mg, and 10 mg tablets. Cyclobenzaprine 7.5 mg tablets are significantly less cost-effective compared to the 5 mg or 10 mg strengths. Cost-effective generic formulations of cyclobenzaprine 5 mg and 10 mg and multiple comparable muscle relaxants (e.g., baclofen, methocarbamol) are available on the UF without PA required. The Committee did note that skeletal muscle relaxants are not considered first-line therapy for musculoskeletal conditions.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for new and current users of cyclobenzaprine 7.5 mg tablets, due to the significant cost differences and lack of clinically compelling benefits compared with administering one and a half of a 5 mg tablet or using other generic muscle relaxants.

Manual PA criteria apply to all new and current users of cyclobenzaprine 7.5 mg tablets or capsules. Coverage will be approved for cyclobenzaprine 7.5 mg tablets if all criteria are met:

- Cyclobenzaprine 7.5 mg tablets have been identified as having cost-effective alternatives. The provider must describe why cyclobenzaprine 7.5 mg is required as opposed to available alternatives, including generic cyclobenzaprine 5 mg tablets and cyclobenzaprine 10 mg tablets

Non-FDA-approved uses are NOT approved.

PA does not expire.

4. **New PA Criteria—PA Implementation**

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) new PAs for Ryclora, cyclobenzaprine 7.5 mg, authorized generic ledipasvir/sofosbuvir and authorized generic sofosbuvir/velpatasvir become effective 90 days after the signing of the minutes. DHA will send letters to beneficiaries affected by the new PA requirements for the cyclobenzaprine 7.5 mg and Ryclora if applicable, as new and current users will be subject to the PA.

Summary of Physician's Perspective:

In regards to Ryclora syrup, this product is essentially a new twist on an old formulation, mainly that it is available as a syrup. There are other antihistamines that are available as oral syrups, both as prescription or OTC products. The Committee

could not come up with a clinical reason as to why Ryclora would be needed instead of the other widely available and low cost antihistamine syrups. Currently we don't have any utilization of this product.

In regards to Harvoni and Epclusa, the direction here is to prefer the branded Harvoni and Epclusa products over the authorized generics. The authorized generic and the branded products all come from the same manufacturer, however the branded products are more cost effective than the authorized generics. The PA will only apply to new users, so no letters will be sent.

In regards to cyclobenzaprine, cyclobenzaprine is available in 5 mg and 10 mg tablets, and the Committee felt that this "in-between-strength" offered no clinical value over the other tablet strengths. The Committee felt that it is reasonable for a patient to cut the 5 mg tablets in half, if a 7.5 mg dose is required. The 447 patients currently on the product will be receiving letters notifying them of the new PA requirements.

Summary of Panel Questions and Comments:

Mr. Hostettler asked if the 5mg tablet for cyclobenzaprine was scored.

CDR Hellwig stated that I have not seen all manufacturers' versions of it but the ones I have seen were not scored.

Mr. Hostettler stated that the two or three I have seen are not. Trying to break the pills usually results with a crumbled tablet. That is a problem.

CDR Hellwig thanked him for sharing and stated we would recommend using a tablet splitter.

Mr. Hostettler stated even with a pill splitter, there is the possibility of crushing the tablet.

There were no more questions or comments from the Panel. The Chair called for a vote on the Manual PA Criteria and PA Implementation Plan for the New PA Criteria.

- **New PA Criteria — PA Criteria**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Director, DHA:

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

- **New PA Criteria — PA Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Director, DHA:

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

Additional Panel Questions and Comments

Mr. Hostettler concurs with the implementation plan, but adds a comment on cyclobenzaprine. There is the potential that non-scored, 5 mg tablets will present a problem to patients. This leads to potential waste if the tablets are crushed and not usable, etc. There might be more cost in this decision than was considered.

B. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA

1. Updated PA Criteria

Updates to the manual PA criteria for several drugs were recommended by the P&T Committee due to a variety of reasons, including expanded FDA indications and safety. The updated manual PA as outlined below will apply to new users.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) updates to the manual PA criteria for Kalydeco, Noctiva nasal spray, Xifaxan, Doptelet, Humira, Kineret, Corlanor.

The updates are as follows:

a) **Cardiovascular Agents Miscellaneous: ivabradine (Corlanor)**—The Committee reviewed a request to allow an off-label use for ivabradine (Corlanor). The Committee recommended updating the PA criteria to include treatment of patients with symptomatic inappropriate sinus tachycardia (IST) or postural tachycardia syndrome (POTS). The recommendation was based on supporting clinical trial data and the 2015 guidelines from the American College of Cardiology/American Heart Association/Heart Rhythm Society, which state that Corlanor is reasonable for ongoing management in patients with these conditions.

b) **Cystic Fibrosis Agents: ivacaftor (Kalydeco)**—Kalydeco was first reviewed by the P&T Committee in July 2012, where PA was recommended, based on the package insert labeling. Additional updates were made in May 2014 and November 2018. The FDA has now approved Kalydeco for use in patients as young as 1 year

of age, and the PA criteria were updated to reflect the new FDA-approved age range.

c) **Gastrointestinal-2 Agents: Miscellaneous – rifaximin 200 mg (Xifaxan)**—Manual PA criteria were previously recommended for Xifaxan for Traveler's Diarrhea at the May 2013 P&T Committee meeting. The Xifaxan PA was updated to reflect the most recent update of the 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea, requiring a trial of azithromycin or ciprofloxacin.

d) **Hematological Agents – Platelets: avatrombopag (Doptelet)**—Avatrombopag (Doptelet) and lusutrombopag (Mulpleta) are pre-procedure regimens for patients with thrombocytopenia associated with liver disease. Mulpleta does not require dose adjustment; therefore, the P&T Committee updated the Doptelet PA criteria to require use of Mulpleta first, to reduce the risk of dosing errors with Doptelet.

e) **Immune Modulators Endocrine Agents: Miscellaneous – Desmopressin nasal spray (Noctiva)**—Noctiva nasal spray was most recently reviewed for formulary placement at the May 2018 DoD P&T Committee meeting. The PA criteria for Noctiva were updated to include a comprehensive list of safety concerns, and to mirror the PA criteria for the new drug desmopressin SL tablets (Nocdurna) discussed previously on page 22 to 24 of the BAP Background Information document.

f) **Targeted Immunomodulatory Biologics (TIBs): adalimumab (Humira) and anakinra (Kineret)**—The TIBs were most recently reviewed in August 2014, with step therapy requiring a trial of adalimumab (Humira) first. The FDA recently granted new indications for Humira for moderate to severe hidradenitis suppurativa in patients 12 years and older, and for Kineret for systemic juvenile idiopathic arthritis, and the respective PAs were updated for these additional indications.

2. Updated PA Criteria—Implementation Plan

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) updates to the current PA criteria for Kalydeco, Noctiva nasal spray, Xifaxan, Doptelet, Humira, Kineret, and Corlanor in new users become effective 60 days after the signing of the minutes.

Summary of Physician's Perspective:

At every meeting, we present updates to drugs with existing PAs to ensure the latest FDA indications or safety updates are included in our criteria. These updates to the existing PAs will only affect new patients.

For Corlanor, this is an example of where there is both clinical trial data and guideline recommendations to support an off label use. So the off-label use was added to the PA.

The other PA updates were due to due to safety issues (the Noctiva nasal spray for nocturia, and Doptelet), new indications (the TIBS Humira and Kineret, and the cystic fibrosis drug Kalydeco), or to ensure the PA criteria are in line with guidelines (the travelers' diarrhea indication for Xifaxin).

You will continue to see these types of updates at every meeting.

Summary of Panel Questions and Comments:

There were no questions or comments from the Panel. The Chair called for a vote on the Updated PA Criteria and the Updated PA Criteria Implementation Plan.

- **Updated PA Criteria**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Director, DHA:

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

- **Updated PA Criteria — Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Director, DHA:

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

IV. SECTION 703, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR (FY) 2008

At the November 2018 meeting, the P&T Committee designated Tobramycin Inhalation Solution Pak (NDC: 70644-0899-99) by Genericus, Inc. as not compliant with Section 703 requirements. After further review and comparison of tobramycin inhalation solution pak with the other available tobramycin inhalation products which do not include the nebulizer, the Committee recommended removing this drug from the Section 703 Non-Compliant Drug List and returning to its previous status of UF on the Uniform Formulary with no point of service (POS) restrictions.

1. Drugs Designated as NF

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) that the Section 703 non-compliant NDC of the following product return to its former UF status with no POS restrictions:

- Genericus, Inc.: tobramycin inhalation solution pak (*New Drug Application-authorized generic; NDC 70644-0899-99*) 300 mg/5 mL ampule-nebulizer

Summary of Physician's Perspective:

At the November meeting, the Committee reviewed Tobramycin Inhaler Solution as a 703 non-compliant drug and exempted the requirement to receive it from mail. However, we are now recommending to remove the Tobramycin Inhaler Solution Pak from the 703 Drug List, so the drug will remain UF and will not be forced to mail. The clinical reason for this is that there is not another alternative with a nebulizer handset packaged with it.

Summary of Panel Questions and Comments:

There were no questions or comments from the Panel. The Chair called for a vote to change the formulary status for the Section 703 NDAA FY 2008 Drugs Designated as NF.

- **Drugs Designed as NF**

Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Director, DHA:

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

V. SECTION 702, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR (FY) 2018: TRICARE TIER 4/NOT COVERED DRUGS PER 32 CFR 199.21(E)(3)

Background—An interim final rule implementing Section 702(b)(10) of the NDAA 2018 was published on December 11, 2018, and is found at: https://www.federalregister.gov/documents/2018/12/11/2018-26562/tricare-pharmacy-benefits-program-reforms. The interim rule allows for complete exclusion of drugs from TRICARE pharmacy benefit coverage when certain criteria are met.

The interim rule amends 32 CFR 199.21(e)(3). The P&T Committee may recommend, and the Director may, after considering the comments and recommendations of the Beneficiary

Advisory Panel approve uniform formulary actions to encourage use of pharmaceutical agents that provide the best clinical effectiveness to covered beneficiaries and DoD, including consideration of better care, healthier people, and smarter spending. Specifically, the P&T Committee may recommend complete exclusion of any pharmaceutical agent from the TRICARE pharmacy benefits program the Director determines provides very little or no clinical effectiveness relative to similar agents.

The P&T Committee was briefed on the above provisions at the February 2019 meeting. The Committee considered several factors when identifying candidates for complete exclusion from the TRICARE pharmacy benefit. These factors include, but are not limited to, the availability and quality of clinical efficacy evidence compared to alternative similar agents, determination of significant safety issues in which risks may outweigh potential benefit, identification of drugs that contain ingredients not covered by the TRICARE pharmacy benefit, or other negative concerns identified by regulatory authorities or nationally recognized expert organizations. The Committee also reviewed the practices regarding exclusion of drugs from several commercial, state, and Federal Government health care plans. Complete exclusion of drugs from the TRICARE pharmacy benefit will apply to both new and current users.

Relative Clinical and Cost-Effectiveness Summary/Rationale for Complete Exclusion—The Committee reviewed clinical efficacy, safety, and cost-effectiveness data for four candidates considered for Tier 4/Not Covered status under the TRICARE pharmacy benefit program.

- **Diabetes Non-Insulin Drugs – Biguanides Subclass: metformin ER (Glumetza brand and generics)** is an extended release formulation of metformin approved in 2005. It uses a polymer-based oral drug delivery system that makes the tablet swell, which causes retention in the stomach. Clinical trials show Glumetza is at least as efficacious as metformin immediate-release (IR) (Glucophage) in all measures of glycemic control. There is no evidence to suggest that differences in the extended-release properties of Glumetza confer any benefits in efficacy or safety compared to the other metformin ER formulations (Glucophage XR).

  Overall conclusion: A significant cost difference exists between Glumetza and other generic metformin ER formulations (Glucophage XR), with no additional clinical benefit. The P&T Committee concluded that the needs of TRICARE beneficiaries can be met by other metformin ER or metformin IR products available on the Uniform Formulary.

- **Pain Agents – Combinations Subclass: naproxen/esomeprazole (Vimovo)** is a fixed-dose combination of two over-the-counter (OTC) drugs, a nonsteroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor (PPI). The Committee agreed that use of fixed dose combination therapies offers patients a convenient formulation for improving adherence. However, this particular combination of an NSAID, which is typically targeted for short-term use, and a PPI, which has limited data to support use beyond eight weeks, is potentially harmful. There is no data to suggest that using other prescription or OTC NSAIDs concurrently with PPIs would not provide the claimed benefit of the individual ingredients found in Vimovo.

Overall conclusion: The Committee concluded that Vimovo is not cost-effective relative to other NSAIDs and PPIs used concurrently. The needs of TRICARE beneficiaries can be met by the concurrent use of similar single ingredient OTC or prescription NSAIDs and PPIs available on the Uniform Formulary.

- **Pancreatic Enzyme Replacement Therapy: pancrelipase (Zenpep)** and the other pancreatic enzyme replacement therapies (PERTs) were reviewed for formulary status in May 2018. The Committee concluded there is a high degree of therapeutic interchangeability among the PERT products, and having one on the formulary is sufficient to meet the needs of Military Health System (MHS) patients. Creon was designated as the sole step-preferred PERT, and the cost-share was lowered to the generic Tier 1 cost-share to provide a greater incentive for beneficiaries to use the more cost effective PERT formulation. Zenpep was designated nonformulary and non-step-preferred, requiring a trial of Creon in all users. Zenpep provides very little to no clinical effectiveness relative to Creon or the other PERTs.

  Overall conclusion: The needs of TRICARE beneficiaries can be met by Creon and the other available PERTs.

- **Targeted Immunomodulatory Biologics (TIBs): brodalumab (Siliq)** is an injectable TIB approved for treating plaque psoriasis and is the only TIB that carries a black box warning for suicide. An FDA safety review of all clinical trials with Siliq reported 36 patients with attempted suicide, or suicidal ideation, and 6 patients with completed suicides. This safety risk is comparable to other biologic agents that the FDA denied marketing approval, and is significantly greater than any of Siliq's clinical comparators. The drug also has Risk Evaluation and Mitigation Strategies (REMS) requirements that mandate certification of both prescribers and pharmacies.

  Siliq was reviewed as a newly approved drug at the August 2017 DoD P&T Committee meeting and recommended for nonformulary status, with PA criteria requiring a trial of adalimumab (Humira) and secukinumab (Cosentyx) first.

  Overall conclusion: The P&T Committee concluded that relative to the other nine TIBs that are FDA-approved to treat psoriasis, Siliq imposes a significant safety risk without offering any unique advantage in efficacy or in specific sub-populations. However, a subset of patients with plaque psoriasis will develop highly refractory disease, and Siliq may be of value as an alternate agent for patients who do not respond to other treatment options.

- **Corticosteroids-Immune Modulators – High Potency: Halobetasol propionate 0.05% foam (Lexette)** is a topical corticosteroid, which were reviewed for formulary placement in August 2013. There is a high degree of therapeutic interchangeability within a particular potency category and vehicle. There are currently 28 other high-potency topical corticosteroids on the formulary, including 12 products formulated in a hair-friendly vehicle, including foam, gel, lotion, shampoo, and solution. The new foam formulation of

Lexette offers no clinically meaningful advantages over the high-potency topical steroids available on the UF.

Overall conclusion: The P&T Committee concluded that Lexette provides little to no clinical benefit and its cost is prohibitive relative to the numerous formulary alternatives. Currently, the needs of TRICARE beneficiaries can be met by the 28 other formulary high-potency topical steroids.

1. **TRICARE Tier 4/Not Covered Recommendation**—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) designating the following products as Tier 4/Not Covered under the TRICARE pharmacy benefits program.

   - metformin ER (Glumetza) brand and generics
   - naproxen/esomeprazole (Vimovo)
   - pancrelipase (Zenpep)
   - halobetasol propionate 0.05% foam (Lexette)

2. **Recommendation Maintaining Current NF Status for Siliq**—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) maintaining the current formulary status for brodalumab (Siliq). The Committee acknowledged Siliq's place in therapy for highly selected patients who are refractory to other treatment options. Siliq will remain NF and non-step-preferred, requiring a trial of Humira, Cosentyx, Stelara, Tremfya, Ilumya and Taltz first. The current PA will remain in place to mitigate risk of suicidal ideation.

3. **Tier 4/Not Covered Implementation Period**—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) for Zenpep, Glumetza brand and generics, and Vimovo, and (17 for, 0 opposed, 0 abstained, 1 absent) for Lexette: 1) an effective date of the first Wednesday after a 120-day implementation period at all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/Not Covered recommendation.

Summary of Physician's Perspective:

For the drugs that were selected for Tier 4 status, the active ingredients for all the products are available in other formulations that are on the UF or OTC. For the impacted beneficiaries, about 400 patients will be affected by the Glumetza recommendation, 550 patients for the Vimovo recommendation; and about 600 patients for the Zenpep recommendation. Letters will be sent to the patients. Since this is a new regulation, we are allowing a longer implementation period of 120 days.

The P&T members felt that these drugs were good candidates for Tier 4 status, since it was difficult for the Committee to develop clinical medical necessity criteria that would warrant use of the Tier 4 product over the formulary alternatives. The Committee could not determine a valid clinical reason as to why these drugs should be used. The physician experts have concluded that there is no role for these drugs.

The Committee did take into consideration multiple factors when selecting the Tier 4 candidates. That is one reason why Siliq was recommended to not be placed on Tier 4 status, and will remain as NF.

Summary of Panel Questions and Comments:

Mr. Hostettler stated he has concerns regarding the P&T Committee decision for Zenpep. He understands the rationale and reason regarding the decision for the other drugs. However, approximately 600 patients completed the PA process for Zenpep. If they completed the process, there must have must have been some medical justification. He does not understand the decision to remove it from the pharmacy benefit and asks for an explanation.

Lt Col Khoury summarizes several reasons for the P&T Committee decision to move Zenpep to Tier 4.

- It is not a chronic medication and many of the patients come on and come off the drug;
- For the clinical evaluation, there is no information to support why Zenpep is being used over other alternatives, since it isn't typically a chronic medication that is being used over the long-term; and
- In class reviews, we highlighted some of the alternative options. We are trying to encourage behaviors in support of beneficiaries taking advantage of the Tier 1 agent. We suspect that is not being not fully effective but we do not' know why. It benefits patients to possibly shift to one that is both clinically effective and cost effective since it has Tier 1 copay.

Mr. Hostettler asked if the step therapy that was in place required trials of Creon first.

Lt Col Khoury stated there was no step therapy in that class. The PA was built to not require a PA for Creon but require a PA for the other drugs. There was no requirement to try all the agents; we were trying to encourage patients to shift to Creon. What appears to be happening is that the tools are not fully effective.

Mr. Hostettler stated, in his opinion, the better decision for patients is to implement an approach for Zenpep that is similar to the decision for Siliq. Placing Zenpep last on the PA or Step Therapy would give the patient the option to complete the steps and try the other drugs, if they need the drug. This is a better approach than having the patient with a chronic disease, change their treatment that is working. More importantly, this change may force a decision on the patient's families to change what is working or pay 100% of cost. I think the approach you took with Siliq makes perfect sense in this particular case as well. It is different from the 28 steroids and the metformin products; I think those are different but this one has a potential clinical need that cannot be fulfilled once this decision is made. I am concerned about this decision. It is rare that the BAP makes strong recommendations. If I can get my

colleagues to agree to recommend an approach for Zenpep that is similar to Siliq, it gives those patients who have tried everything else and it is not working the opportunity to get Zenpep. Make it non-formulary with the highest co-pay but give them the option as opposed to removing it from the pharmacy benefit.

Lt Col Khoury stated that providers do not see a clinical necessity for Zenpep. If there was data to support a decision similar to Siliq, I believe the P&T committee would have made that decision. We do not have any information to support that conclusion with Zenpep.

Mr. Hostettler stated I believe it is fair to appreciate that not every patient responds the same to every product. Approximately 600 patients complete the PA process for Zenpep. This recommendation is to move it to Tier 4 will require the patient to make another change in therapy. In my opinion, this is a situation where I believe we are going too far. I can understand making it last in line, like the Siliq approach, but I cannot understand removing it from the Pharmacy Benefit.

Dr. Peloquin asked how many other PERTs are there.

Lt Col Khoury responded that I believe there are approximately five including Creon. For example, with Siliq, in our analysis we looked at what patients had been on before. In many instances, they had not tried all of the alternatives. In our opinion, patients were potentially being put at risk. When we looked at Zenpep, patients had not been on other alternatives despite having multiple alternatives available. There was no clear clinical reason that we could find for not trying all the alternatives. I want to make sure that everyone understands that the majority of patients are not chronic, in our analysis; they are not on the drug for the long term. Most start taking the drug and they stop. They might have been on it in the past but this does not preclude them from trying again. It is in the patient's best interest, from a copay perspective, to try to shift to the drug that has the Tier 1 co-pay, if they have not tried the Creon.

Mr. Hostettler stated that I agree that they should try the other alternatives first, especially Creon at a lesser cost. As discussed in our executive meeting, there is no appeal process on Tier 4. Therefore, there are no options if the patient reaches a point where they need another option. In my opinion, it is hard to take away real, FDA-approved options when it is available. This decision affects 600 patients; I just do not fully appreciate that.

Dr. Bertin has a more general observation. We did have some discussion at our preliminary administrative meeting on this topic. Most of us agree that Tier 4 is probably a useful tool for this organization to promote rational drug therapy and we simply need to recognize that. Part of our issue is that this was rushed into implementation. It is still under an interim rule, the comments on the rule were due on February 11. We do not know whether there are significant comments that may lead to significant modifications for the final rule. I hope that the additional

comments are being considered. The other issue is simply information for beneficiaries and those that represent them and their interest. This was really the first opportunity that the BAP learned of this Tier 4 implementation and we are supposed to be representing the interests of our beneficiaries. It may be that extensive information, patient information, and organization information is being developed but it really is not out there yet and we would urge that information be developed and got out into the hands of beneficiaries who may well be significantly impacted, especially those who are faced with a situation. As my colleague pointed out, this is a no appeal denial. I believe that beneficiaries need to understand what they may be up against. We understand that there are not going to be lots and lots of drugs proposed for Tier 4 but we don't know that for sure. This could be affecting many, many of our beneficiaries.

Mr. Ostrowski stated that he is having a difficult time with this vote because the Panel did not have an issue with three of the four drugs. We only have concerns about Zenpep. Is it possible to split the vote and separately vote on the three drugs and Zenpep. This would allow the other three to move through the process.

Col Hoerner agreed that to split the vote. He also shared that there was a single provider from across the entire enterprise that came forward who saw potential use for Siliq. As a result, the Committee decided not to move it to Tier 4. This was not the case with Zenpep. Not a single voice or provider identified a potential need for this product. The beneficiaries we identified had not tried the Creon. It appears the the doctor just wrote a prescription and they just paid the higher copay and went straight to it.

Mr. Hostettler asked was there not a PA that prevents the patient from trying all the available alternatives.

Lt Col Khoury stated there is a PA but we do not understand the rational or reason why the patients did not try the alternatives. That data has not been available to us. There has been no patient or provider comments that are based on evidence that says these alternatives are all inappropriate. In my opinion, allowing it to exist harms patients in the sense of they do not necessarily know the cost until they have that copay. If they do not know the alternatives of those different copays, this agent will continue to be on there for them to be faced with a higher financial burden and not maintain any relative additional clinical benefit.

Mr. Hostettler said that I appreciate what you are saying but I still think it should be an option and if you want to build a step approach where it is last, I do not have a problem with that. At least it is available. If I am not mistaken, what I am also hearing is that you had a process in place, PA or step, to get there and it did not do the job. Either you wrote a bad process or the physicians filled it out in error. Something is array from what you are explaining to me and that to me does not mean we should throw the drug out.

Lt Col Khoury stated initially, all drugs are covered and that is part of the bad process. Other people have excluded Zenpep so patients do not get on it. We are dealing with this in between period where patients will be on drugs that either the provider does not necessarily know the details of the cost and/or the clinical efficacy. Their decision is predicated on historical data. The prescriber is used to prescribing the drug and all the information affecting the patient may not be driving the decision making whether it be cost and/or clinical

Mr. Hostettler stated that I wish we had the document that is in place for these 600 patients that completed the PA for Zenpep in front of us now so we that can see exactly what we're talking about. I appreciate your comments but I still think there should be an opportunity.

CDR Hellwig pulled the Zenpep PA and its criteria from the Formulary Search Tool ST and read it to the Panel. Although we have the PA in place requiring Creon, we have seen that quit a few of our patients on Zenpep have not tried Creon.

Mr. Hostettler asked when the requirement changed to a formulary status. You stated a change in formulary for new products.

Lt Col Khoury stated the PA was in effect since November.

Mr. Hostettler asked if the majority of these patient received Zenpep prior to November.

Lt Col Khoury stated that numbers you have were from last 12 months trailing.

Mr. Du Tiel stated that I appreciate everyone's comments regarding Zenpep and I understand the Tier 4 concept. He also appreciates Lt Col Khoury's comments that if it is not moved to Tier 4, it is still available and patients can get it if they want. However, if it is on Tier 4, the patient will have to pay full cost and we do not know how much that would be. I support my colleague in recommending making it the absolute last step, NF, etc. Do not put it out of reach for patients just yet. I encourage you to not throw people off drug that got onto it prior to these criteria in the first place and they are using it. I am a little nervous about it.

Dr. Dager stated I think it is an appropriate drug to have available but it would be nice to see it have a different PA than just the one-step. Have a step 2 or 3, maybe separate from the other agents.

Mr. Ostrowski stated we will split this decision so that the 3 drugs we do concur with can make it through this process. I concur with the remarks from the Panel regarding Zenpep. Rather than moving Zenpep to Tier 4, there must be other options available.

Dr. Peloquin stated one of the other concerns I am hearing is this decision to move it to Tier 4 is so close to the decision in November. Patients recently completed the

process in November and there is another change approximately 120 days after. From a beneficiary abrasion perspective, those patients are being moved again. That happens sometimes, I know, but relative to that as you look at it. It is something to consider from an abrasion perspective.

Mr. Ostrowski sends a request to the P&T Committee. Restructure the decision for Zenpep and present to the Panel at a meeting in the future.

There were no more comments from the Panel. The Chair called for a vote on the TRICARE Tier 4 recommendations for Glumetza, Vimovo, and Lexette.

- **TRICARE Tier 4/Not Covered Recommendation for Glumetza, Vimovo, and Lexette**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Director, DHA:

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

- **Recommendation Maintaining Current NF Status for Siliq**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Director, DHA:

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

- **Tier 4/Not Covered Implementation Period for Glumetza, Vimovo, and Lexette**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Director, DHA:

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

The Chair called for a vote on the TRICARE Tier 4 recommendations for Zenpep.

- **TRICARE Tier 4/Not Covered Recommendation for Zenpep**

  Concur: 0 Non-Concur: 7 Abstain: 0 Absent: 2

Director, DHA:

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

- **Tier 4/Not Covered Implementation Period for Zenpep**

  Concur: 0 Non-Concur: 7 Abstain: 0 Absent: 2

Director, DHA:

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

ADDITIONAL PANEL QUESTIONS AND COMMENTS.

Dr. Peloquin stated that the communication plan is vital to the Tier 4 Implementation Plan.

Mr. Hostettler stated, in the future, we anticipate tiering and pricing to drive patient decisions in the future. Unfortunately, patients, much like providers, do not know anything about the pricing and tiers until they go to a pharmacy and by then it is too late. The process is already in place. To go back and get it changed could possibly lead to lengthy delays getting another appointment, getting the physician involved again to re-write that prescription. Let us not forget that the tiering process, while it will drive decisions, is not the best way to go about it. More education, both to the patient and provider, is the best approach.

Mr. Ostrowski thanked everyone for coming and participating. He also thanked the Panel, the participation of new members, looks forward to seeing everyone again.

Appendix 1 – Informational Item – Summary of Recommendations and Beneficiary Impact February 2019
Appendix 2 – Brief Listing of Acronyms Used in this Summary

INFORMATIONAL ITEM—SUMMARY OF RECOMMENDATIONS AND BENEFICIARY IMPACT FEBRUARY 2019

Table of Implementation Status of UF Recommendations/Decisions Summary

DoD PEC Drug Class	UF Drugs	NF Drugs	Implement Date	Notes and Unique Users Affected
Migraine Agents – CGRP Antagonist Prophylaxis Subclass	▪ erenumab (Aimovig) ▪ fremanezumab (Ajovy) ▪ galcanezumab (Emgality)	▪ None	Pending signing of the minutes / 30 days	▪ Manual PA criteria applies to all new users Unique Users Affected not applicable; new users only
Oncological Agents: CYP-17 Inhibitors Subclass and 2nd-Generation Antiandrogen Subclass	CYP-17 Inhibitors *Step-preferred* ▪ abiraterone acetate micronized (Yonsa) *Non-step-preferred* ▪ abiraterone acetate (Zytiga, generics) 2nd-Generation Antiandrogens *Step-preferred* ▪ enzalutamide (Xtandi) *Non-step-preferred* ▪ apalutamide (Erleada)	▪ None	Pending signing of the minutes / 90 days	▪ Manual PA required ▪ Yonsa and Xtandi will be Tier 1 copay/cost-shared **CYP-17 Inhibitors Subclass** Unique Users Affected Mail – 464 MTF – 155 Retail – 620 Total – 1,239

Drugs with New Prior Authorization Criteria—Unique Utilizers Affected

Drug	MTF	Mail Order	Retail	Total
Antihistamine-1: First Generation and Combinations – dexchlorpheniramine maleate 2 mg/5 mL oral solution (Ryclora)	0	0	0	0
Skeletal Muscle Relaxants and Combinations: cyclobenzaprine 7.5 mg	16	52	379	447

Tier 4/Not Covered Drugs—Unique Utilizers Affected

Drug	MTF	Mail Order	Retail	Total
metformin ER (Glumetza brand) (Glumetza generic)	 24 28	 64 266	 5 17	 93 311

Drug	MTF	Mail Order	Retail	Total
naproxen/esomeprazole (Vimovo)	47	455	54	556
pancrelipase (Zenpep)	115	297	179	591

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 the Panel discussions are listed below for easy reference. The term "Pan" in this summary refers to the "Uniform Formulary Beneficiary Panel," the group who's meeting in the subject of this report.

- AA – Antiandrogen
- AAN – Academy of Neurology
- AASLD - American Association for the Study of Liver Diseases
- ABSSSI – Acute Bacterial Skin and Skin Structure Infection
- ADA-SCID – Adenosine Deaminase Severe Combined Immune Deficiency
- AHS – Academy of Headache Society
- ALS – Amyotrophic Lateral Sclerosis
- ALK – Anaplastic Lymphoma Kinase
- AML – Acute Myelogenous Leukemia
- ANCA – Antineutrphil Cytoplasmic Antibody-accociated.
- AUA – American Urological Association
- BAP – Beneficiary Advisory Panel
- BCF – Basic Core Formula
- BIA – Budget Impact Analysis
- BOO – Bladder Outlet Obstruction
- CABP – Community-Acquired Bacterial Pneumonia
- CDC –Center for Disease Control
- CFR – Code of Federal Regulations
- CGRP – Calcitonin Gene-Related Peptide
- CKD – Chronic Kidney Disease
- CMA – Cost-minimization Analysis
- COA – Commissioned Officers Association
- COPD – Chronic Obstructive Pulmonary Disease
- CR generics – Controlled-Released
- CRPC – Castration-resistant Prostate Cancer
- CV – Cardiovascular
- DAPA – Distribution and Pricing Agreement
- DDAVP – Desmopressin Acetate Tablets
- DFO - Designated Federal Officer
- DHA – Defense Health Agency
- DoD – Department of Defense
- ER – Extended Release
- FACA - Federal Advisory Committee Act
- FAP – Familial Amyloidotic polyneuropathy
- FDA – Federal Drug Administration
- FL – Follicular Lymphoma
- FMS – Ferline McDonough Sarcoma
- FY – Fiscal Year

- G6PD – Glucose 6 Phosphate Dehydrogenase
- gBRCAm – Germline BRCA-mutated
- GI – Gastrointestinal
- GnRH – Gonadotropin-releasing Hormone
- HCV DAA – Hepatitis C Agents: Direct-Acting Agents
- HER2- - Human Epidermal Growth Factor Receptor2-negative
- HSPC – Hormone-sensitive Prostate Cancer
- hTTRA – Hereditary Transthyretin-mediated amyloidosis
- IBD – Inflammatory Bowel Disease
- ICER – Institute for Clinical and Economic Review
- IDSA - Infectious Diseases Society of America
- IR – Immediate Release
- IST – Inappropriate Sinus Tachycardia
- ITP – Idiopathic Thrombocytopenia
- IV – Intravenous
- LAMA – Long-Acting Anti-Muscarinic Agent
- LEMS – Lambert-Eaton Myasthenic Syndrome
- MACE – Major Adverse Cardiovascular Events
- mCRPC – Metastatic Castration-Resistant Prostate Cancer
- MEK inhibitors – Chemical or drug that inhibits the mitogen-activated protein kinase enzymes
- MFS – Metastatis-free Survival
- Mg – Milligram
- MHS – Military Health Sytem
- MIDAS – Migraine Disability Assessment
- MN forms – Medical Necessity Form
- MMD – Monthly Migraine Days
- MPFID – Migraine Physical Functional Impact Diary
- MTF – Military Treatment Facility
- NASH – Non-Alcoholic Steatohepatisis
- NCCN – National Comprehensive Cancer Network
- NDAA – National Defense Authorization Act
- NDC – National Drug Code
- NF – Non Formulary
- nmCRPC – Non-Metastatic Castration-Resistant Prostate Cancer
- NSAID – Nonsteroidal Anti-Inflammatory Drugs
- NSCLC – Non-Small Cell Lung Cancer
- NTRK – Neurotrophic Tropomyosin Receptor Kinase
- OTC –Over the Counter
- P&T – Pharmacy & Therapeutics
- PA – Prior Authorization
- PERT – Pancreatic Enzyme Replacement Therapy
- pH – Potential Hydrogen
- POD – Pharmacy Operations Division
- POS – Point of Service
- POTS – Postural Tachycardia Syndrome
- PPI – Proton Pump Inhibitor

- PRES – Posterior Reversible Encephalopathy Syndrome
- PSA – Prostate-specific Antigen
- PSADT – Prostate-specific Antigen Doubling Time
- REMS program – Risk Evaluation and Mitigation Strategy
- Rx – Medical Prescription
- SIBO – Small Intestine Bacterial Overgrowth
- SL – Sublingual
- SQ - Subcutaneous
- TIB – Targeted Immunomodulatory Biologic
- TRICARE – Healthcare Network
- UF – Uniform Formulary
- USC – United States Code
- XR – Extended Release

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
March 27, 2019
Washington, D.C.

Present Panel Members

- Mr. John Ostrowski, Non Commissioned Officers Association, Chairperson
- Dr. Jay Peloquin, Express Scripts, Inc.
- Mr. John Du Teil, US Army Warrant Officers Association
- Mr. Charles Hostettler, AMSUS, The Society of Federal Health Professionals
- Mr. Richard Bertin, Commissioned Officers Association (COA) of the United States Public Health Service
- Dr. Lindsey Piirainen, USFHP Martin's Point Healthcare
- Dr. Karen Dager, Health Net Federal Services

Absent Panel Members

- Ms. Theresa Buchanan, National Military Family Association
- Ms. Suzanne Walker, Military Officers Association of America

The meeting was held at Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington D.C. and Col Paul Hoerner called the meeting to order at 9:04 A.M.

Agenda

The Agenda for the meeting of the Panel is as follows:

- Welcome and Opening Remarks
- Public Citizen Comments
- Therapeutic Class Reviews

    1. Drug Class Reviews

        a) Migraine Agents – Calcitonin Gene-Related Peptide (CGRP) Antogonists Subclass
        b) Oncological Agents – 2nd Generation Antiandrogens Subclass and CYP-17 Inhibitors Subclass

    2. Section 702, National Defense Authorization Act (NDAA) for Fiscal Year (FY) 2018: TRICARE Tier 4/Not Covered Drugs per 32 CFR 199.21(e)(3)

        a) Diabetes Non-Insulin – Biaguanides Subclass: metformin ER (Glumetza)
        b) Pain Agents – Combinations Subclass: naproxen/esomeprazole (Vimovo)
        c) Pancreatic Enzyme Replacement Therapy (PERT): pancrelipase (Zenpep)
        d) Targeted Immunomodulatory Bioligics: brodalumab (Siliq)

3. Newly Approved Drugs per 32 CFR 199.21(g)(5)

    a) amifampridine (Firdapse) – Miscellaneous Neurological Agent for Lambert-Eaton Myasthenic Syndrome (LEMS)
    b) aripiprazole tablet with ingestible even marker (Abilify MyCite) – Atypical Antipsychotic
    c) baloxavir (Xofluza) – Antiviral for Influenza
    d) cenegermin-bkbj ophthalmic solution (Oxervate) – Anti-Inflammatory Immunomodulatory Ophthalmic Agent for Neurotrophic Keratitis
    e) clobazam oral film (Sympazan) – Anticonvulsant-Antimania Agent for Lennox-Gastaut Syndrome
    f) cyclosporine 0.09% ophthalmic solution (Cequa) – Anti-Inflammatory Immunomodulatory Ophthalmic Agent for Dry Eye Disease
    g) desmopressin acetate sublingual (SL) tab (Nocdurna) – Miscellaneous Endocrine Agent for Nocturia due to Nocturnal Polyuria
    h) elapegademase-lvlr IM injection (Revcovi) – Miscellaneous Metabolic Agent for Adenosine Deaminase Severe Combined Immune Deficiency (ADA-SCID)
    i) filgrastim vials (Granix) – White Blood Cell Stimulant and Biosimilar to Neupogen
    j) gilteritinib (Xospata) – Oncological Agent for Acute Myelogenous Leukemia (AML)
    k) glasdegib (Daurismo) – Oncological Agent for AML
    l) halobetasol propionate 0.01% lotion (Bryhali) – High Potency Corticosteroid-Immune Modulator for Plaque Psoriasis
    m) halobetasol propionate 0.05% foam (Lexette) – corticosteroids-Immune Modulators – High Potency
    n) inotersen injection (Tegsedi) – Miscellaneous Neurological Agent for Hereditary Transthyretin Amyloidosis
    o) itraconazole 65 mg capsules (Tolsura) – Antifungal Agent
    p) larotrectinib (Vitrakvi) – Oncological Agent for Solid Tumors
    q) latanoprost (Xelpros) – Ophthalmic Prostaglandin
    r) lorlatinib (Lorbrena) – Oncological Agent for Non-Small Cell Lung Cancer (NSCLC)
    s) loteprednol ophthalmic suspension (Inveltys) – Ophthalmic Corticosteroid for Postoperative Inflammation
    t) omadacycline (Nuzyra) – Tetracycline Antibiotic for Community-Acquired Bacterial Pneumonia (CABP) and Acute Bacterial Skin and Skin Structure Infections (ABSSSIs)
    u) pegfilgrastim-cbqv injection (Udenyca) – White Blood Cell Stimulant and Biosimilar to Neulasta
    v) revefenacin nebulized solution (Yupelri) – Pulmonary-2: Long-Acting Anti-Muscarinic Agent (LAMA) for Chronic Obstructive Pulmonary Disease (COPD)
    w) rifamycin (Aemcolo) – Miscellaneous Gastrointestinal Antibiotic for Traveler's Diarrhea

x) riluzole oral suspension (Tiglutik) – Miscellaneous Neurological Agent for Amyotrophic Lateral Sclerosis (ALS)
y) sarecycline (Seysara) – Tetracycline Antibiotic for Acne Vulgaris
z) tafenoquine 100 mg tablet (Arakoda) – Antimalarial Agent for Prophylaxis of Malaria
aa) tafenoquine 150 mg tablet (Krintafel) – Antimalarial Agent for Prevention of Relapse and Radical Cure of Malaria
bb) talazoparib (Talzenna) – Oncological Agent for Breast Cancer
cc) testosterone enanthate, SQ injection (Xyosted) – Androgens-Anabolic Steroids: Testosterone Replacement Therapies

4. Utilization Management Issues

a) Prior Authorization Criteria – New Criteria

- Antihistamine-1: First Generation and Combinations – dexchlorpheniramine maleate 2 mg/5 mL oral solution (Ryclora)
- Hepatitis C Agents: Direct-Acting Agents: generic ledipasvir/sofosbuvir (Harvoni) and generic sofosbuvir/velpatasvir (Epclusa)
- Skeletal Muscle Relaxants and Combinations: Tricyclic Antidepressants: cyclobenzaprine 7.5 mg

b) Prior Authorization Criteria—Updated Criteria

- Cardiovascular Agents Miscellaneous: ivabradine (Corlanor)
- Cystic Fibrosis Agents: ivacaftor (Kalydeco)
- Gastrointestinal-2 Agents: Miscellaneous – rifaximin 200 mg (Xifaxan)
- Hematological Agents – Platelets: avatrombopag (Doptelet)
- Immune Modulators Endocrine Agents: Miscellaneous – desmopressin acetate nasal spray (Noctiva)
- Targeted Immunomodulatory Biologics (TIBs): adalimumab (Humira) and anakinra (Kineret)

5. Brand over Generic Authorization for Dihydroergotamine Spray/Pump (Migranal Nasal Spray)

6. Section 703, NDAA for FY 2008

7. Panel Discussions

The Beneficiary Advisory Panel members will have the opportunity to ask questions to each of the presenters. Upon completion of the presentation and any questions, the Panel will discuss the recommendations and vote to accept or reject them. The Panel will provide comments on their vote as directed by the Panel Chairman.

Opening Remarks

Col Paul Hoerner introduced himself as the Designated Federal Officer (DFO) for the Uniform Formulary (UF) Beneficiary Advisory Panel (BAP). The Panel has convened to comment on the recommendations of the DoD Pharmacy and Therapeutics (P&T) Committee meeting, which occurred on February 6-7, 2019.

Col Hoerner indicated Title 10, United States, (U.S.C.) section 1074g, subsection b requires the Secretary of Defense to establish a DoD Uniform Formulary (UF) of the pharmaceutical agent and established the P&T committee to review the formulary on a periodic basis to 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 Uniform Formulary. The Panel includes members that represent nongovernmental organizations and associations that represent the views and interests of a large number of eligible covered beneficiaries. The Panel's comments must be considered by the Director of the Defense Health Agency (DHA) before establishing the UF or implementing changes to the UF.

The Panel's meetings are conducted in accordance of the Federal Advisory Committee Act (FACA).

The duties of the Uniform Formulary Beneficiary Advisory Panel include the following:

- To review and comment on the recommendations of the P&T Committee concerning the establishment of the UF and subsequently recommending changes. Comments to the Director of the DHA 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 before making a final decision.
- To hold quarterly meetings in an open forum. The panel may not hold meetings except at the call or with the advance approval of the DFO and in consultation with the chairperson of the Panel.
- To prepare minutes of the proceedings and prepared comments of 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 of DHA. As guidance to the Panel regarding this meeting, Col Hoerner 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 maybe interested in the drug class they selected for review, drugs recommended for the basic core formula (BCF) or specific pricing data, these items do not fall under the purview of the BAP.
- The P&T Committee met for approximately 16 hours conducting this review of the drug class recommendation presented today. Since this meeting is considerably shorter, the Panel will not receive the same extensive information as 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.

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

The DFO provided ground rules for conducting the meeting:

- All discussions take place in an 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 Formulary Management Branch and 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.

Col Hoerner introduced the individual Panel members (see list above) and noted housekeeping considerations.

There were no individuals signed up this morning to provide comments to the BAP.

Chairman's Opening Remarks

Mr. Ostrowski welcomes everyone and thanks everyone for being here today. He also welcomes the newest panel members and thanks Col Hoerner and DHA representatives for their presentation.

DRUG CLASS REVIEW PRESENTATION

(POD Script – LT COL KHOURY)

GOOD MORNING. I am Lieutenant Colonel Ronald Khoury, Chief of the Formulary Management Branch of the DHA Pharmacy Operations Division. Joining me is doctor and retired Army Colonel John Kugler, the Chairman of the Pharmacy and Therapeutics Committee, who will provide the physician perspective and comments on the recommendations made by the P&T Committee. Also joining us from the Formulary Management Branch today is CDR Heather Hellwig, Chief of the P&T Section of the Formulary Management Branch of the DHA Pharmacy Operations Division and MAJ Adam Davies, the Managed Care Pharmacy Resident. I would also like to recognize Mr. Bryan Wheeler, Deputy General Counsel.

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

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:

- 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) and (g)(5). Also note that nonformulary medications are generally restricted to the mail order program according to amended section 199.21, revised paragraphs (h)(3)(i) and (ii), effective August 26, 2015.

- 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.

- The DoD P&T Committee's Uniform Formulary recommendation is based upon the Committee's collective professional judgment when considering the analyses from both the relative clinical and relative cost effectiveness evaluations.

  The Committee reviewed the following:

  1. The P&T Committee reviewed two Uniform Formulary Drug Classes:
     a. the Migraine Agents – Calcitonin Gene-Related Peptide (CGRP) Antagonist Prophylaxis subclass and

b. the Oncological Agents – CYP-17 Inhibitors Subclass and 2nd-Generation Antiandrogens Subclass.

   A summary table of the UF drug class recommendations and the numbers of affected utilizers is found on pages 39-40 of the background document.

2. The P&T Committee also evaluated 29 newly approved drugs per 32 CFR 199.21(g)(5), which are currently in pending status and available under terms comparable to nonformulary drugs.

   and

3. We also discussed prior authorizations (PAs) in the utilization management section for **11** drugs in **9** drug classes.

   a) Antihistamine-1: First generation and combinations
   b) Hepatitis C Agents: Direct-Acting Agents
   c) Skeletal Muscle Relaxants and Combinations
   d) Cardiovascular Agents Miscellaneous
   e) Cystic Fibrosis Agents
   f) Gastrointestinal-2 Agents: Miscellaneous
   g) Hematological Agents – Platelets
   h) Immune Modulators Endocrine Agents: Miscellaneous
   i) Targeted Immunomodulatory Biologics (TIBs)

4. We discussed one National Defense Authorization Act (NDAA) Section 703 non-compliant drug

   and

5. We evaluated four drugs for Tier 4/Not Covered status per amended 32 CFR 199.21(e)(3).

The DoD P&T Committee will make a recommendation as to the effective date of the agents being changed from the Uniform Formulary tier to Nonformulary tier. Based on 32 CFR 199.21, such change will not be longer than 180 days from the final decision date but may be less.

UNIFORM FORMULARY DRUG CLASS REVIEWS

I. UF CLASS REVIEWS

A. MIGRAINE AGENTS – CALCITONIN GENE-RELATED PEPTIDE (CGRP) ANTAGONIST PROPHYLAXIS SUBCLASS

(CDR HELLWIG)

1. Migraine Agents – CGRP Antagonist Prophylaxis Subclass—Relative Clinical Effectiveness Analysis and Conclusion

Background—The P&T Committee evaluated the relative clinical effectiveness of the CGRP antagonists, which provide a new mechanism for migraine headache prevention. The drugs in the subclass include erenumab (Aimovig), fremanezumab (Ajovy), and galcanezumab (Emgality). The CGRP antagonists are available as once monthly injections and were individually reviewed as new drugs at the August and November 2018 DoD P&T Committee meetings. All three products are FDA-approved for the preventive treatment of migraines in adults.

Relative Clinical Effectiveness Conclusion – The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

CGRP antagonists vs. oral preventive therapies

- Oral drugs, including the antiepileptics, beta-blockers and antidepressants, remain the first-line treatment for migraine headache prevention, based on the 2012/2015 American Academy of Neurology/American Headache Society (AHS) migraine prevention guidelines and the 2018 AHS consensus statement for instituting the new migraine treatments into clinical practice. CGRP antagonists are recommended following 2 or 3 trials of oral medications.
- A 2018 network meta-analysis from the Institute for Clinical and Economic Review (ICER) found that oral preventive treatment and CGRP antagonists decrease monthly migraine days (MMD) by approximately 2 days from baseline, compared to placebo. ICER also concluded that the evidence is inadequate to distinguish the net health benefit between treatment with the CGRP inhibitors versus oral preventive therapies (e.g., amitriptyline, topiramate, or propranolol).

CGRP antagonist vs. CGRP antagonist

- Although there are no head-to-head trials comparing Aimovig, Ajovy, or Emgality, there do not appear to be clinically relevant differences in efficacy, based on indirect comparisons. For episodic migraine, a meta-analysis showed similar improvements between the three CGRP antagonists in terms

of change from baseline in MMD and the patients who had a ≥ 50% reduction in migraine days (50% responders) *(Zhu, et al, Neurological Sciences 2018*).

- The 2018 ICER network meta-analysis reported reductions in MMDs ranging from 1.2 to 1.9 days with the CGRP inhibitors for episodic migraine, with the odds of achieving a 50% response rate ranging from 1.7 to 2.7. For chronic migraine, the decrease in MMDs ranged from 1.3 to 2.4 days. ICER concluded the evidence was inadequate to distinguish the net health benefits among the three CGRP inhibitors.
- The FDA review noted that some patients treated with a CGRP antagonist experienced relatively large reductions in migraine headache days. However, there are no clinical characteristics to prospectively identify those patients most likely to respond to therapy. Additionally, there was a high placebo response rate noted in the individual trials used to gain FDA approval.
- Some distinguishing characteristics among the CGRP inhibitors are as follows:
  - Aimovig is available in two dosages, 70 mg and 140 mg. There are no clear data to suggest that the two doses differ in their efficacy or safety.
  - Ajovy is the only CGRP inhibitor approved for quarterly dosing in addition to monthly dosing. However, administration of three pens at the same time is required.
  - Emgality requires a loading dose, administered as two pens at the same time.
  - All three products require refrigeration; however, advantages of Aimovig and Emgality include the ability to be stored up to 7 days at room temperature vs. only 24 hours with Ajovy.

Safety

- The CGRP antagonists have a relatively mild side effect profile, with injection site reactions the most commonly reported adverse event. Injection site reactions occurred at an incidence of 5.6% with Aimovig, 18%-23% with Emgality, and 45% with Ajovy.
- The ICER report concluded that there were no differences in the discontinuation rates due to adverse events among the CGRP inhibitors.
- There is concern for theoretical cardiovascular adverse events with long-term use of the CGRP antagonists. The FDA has required post marketing surveillance for myocardial infarction and stroke for the class.

Other Factors

- Botulinum toxin (Botox) injection is approved for prevention of chronic migraine, but is not part of the TRICARE pharmacy benefit. Botulinum toxin has similar efficacy to the oral preventive medications and CGRP antagonists in chronic migraine patients, based on the 2018 ICER review.

- There is a high degree of interchangeability between the CGRP antagonists. However, there remains uncertainty regarding the long-term efficacy and safety of this new class of therapy. At least one CGRP inhibitor should be on the UF to meet the needs of the majority of patients in the MHS.

2. Migraine Agents – CGRP Antagonist Prophylaxis Subclass—Relative Cost-Effectiveness Analysis and Conclusion

Cost-minimization analysis (CMA) and budget impact analysis (BIA) were performed to evaluate the CGRP Antagonist Prophylaxis agents. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA results showed that Emgality was the most cost-effective CGRP antagonist, followed by Aimovig, and Ajovy.
- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results found that designating Emgality, Aimovig, and Ajovy as uniform formulary demonstrated significant cost avoidance for the Military Health System (MHS).

3. Migraine Agents – CGRP Antagonist Prophylaxis Subclass—UF Recommendation

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following for the CGRP Antagonist Prophylaxis agents, as outlined below, based on clinical and cost-effectiveness:

- UF
  a) erenumab (Aimovig)
  b) fremanezumab (Ajovy)
  c) galcanezumab (Emgality)

- NF
  - None

4. Migraine Agents – CGRP Antagonist Prophylaxis Subclass—Manual Prior Authorization (PA) Criteria

PA criteria currently apply to the CGRP products, requiring a trial of at least one drug from two oral classes used for migraine prophylaxis, including antiepileptic medications, beta-blockers or antidepressants. PA criteria were originally recommended when the individual CGRP products were first evaluated as new drugs. The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updates to the current manual PA criteria for all three CGRP antagonists in new users. The PA criteria and updates reflect the recommendations from the 2018 AHS Consensus Statement regarding candidates for a CGRP and assessment of response.

5. Aimovig, Ajovy, and Emgality
February 2019 updates are in BOLD and strikethrough.

Manual PA criteria apply to all new users of Aimovig, Ajovy, or Emgality.

Manual PA Criteria: Aimovig, Ajovy, or Emgality is approved if all criteria are met:

- Patient ≥ 18 years old and not pregnant
- Must be prescribed by or in consultation with a neurologist
- **The patient also meets one of the following:**
  - **Patient has episodic migraines at a rate of 4 to 7 migraine days per month for 3 months and has at least moderate disability shown by Migraine Disability Assessment (MIDAS) Test score > 11 or Headache Impact Test-6 (HIT-6) score > 50 OR**
  - Patient has **episodic migraine at a rate** of at least 8 migraine days per month for 3 months **OR**
  - **Patient has a diagnosis of chronic migraine**
- Patient has a contraindication to, intolerability to, or has failed a 2-month trial of at least ONE drug from TWO of the following migraine prophylactic drug classes:
  - Prophylactic antiepileptic medications: valproate, divalproic acid, topiramate
  - Prophylactic beta-blocker medications: metoprolol, propranolol, atenolol, nadolol, **timolol**
  - Prophylactic antidepressants: amitriptyline, **duloxetine, nortriptyline,** venlafaxine
- **Patient is not currently on botulinum toxin or patient must not have received a botulinum toxin injection within the last 2 months**
- Concurrent use with other CGRP inhibitors (e.g., Aimovig, Emgality) is not allowed
- For Emgality, a loading dose will be allowed

Non-FDA-approved uses are NOT approved.

PA expires after 6 months.

Renewal PA Criteria: Coverage will be approved indefinitely for continuation of therapy if **one of the following apply:**

- ~~The patient has shown improvement in migraine prevention (e.g., reduced migraine headache days, reduced migraine frequency, reduced use of acute abortive migraine medication)~~
- **The patient has had a reduction in mean monthly headache days of ≥ 50% relative to the pretreatment baseline (as shown by patient diary documentation or healthcare provider attestation) OR**
- **The patient has shown a clinically meaningful improvement in ANY of the following validated migraine-specific patient-reported outcome measures:**

- **Migraine Disability Assessment (MIDAS)**
  - **Reduction of ≥ 5 points when baseline score is 11–20**
  - **Reduction of ≥ 30% when baseline score is > 20**
- **Headache Impact Test (HIT-6)**
  - **Reduction of ≥ 5 points**
- **Migraine Physical Functional Impact Diary (MPFID)**
  - **Reduction of ≥ 5 points**

6. Migraine Agents – CGRP Antagonist Prophylaxis Subclass—UF and PA Implementation Plan

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) an effective date of the first Wednesday 30 days after the signing of the minutes in all points of service (POS).

7. Physician's Perspective

This drug class is a good example of where all three drugs were first reviewed as new drugs soon after FDA-approval, and then the Committee was quickly able to do the full class review only a few months after the drugs had been launched. This helps with decreasing the number of patients who are established on therapy with having to switch products.

All three products are designated as UF. Since the CGRPs represent a new mechanism for treating migraine, having all three as UF will allow for us to see if providers will prefer one product over another. Additionally, if new safety or efficacy data does become available we can re-review the class.

PA criteria currently apply to all three drugs. We will continue to require a trial of the traditional oral preventive drugs before a CGRP. This in line with the recommendations from the American Academy of Neurology guidelines and the American Headache Society Consensus statement. Also, the ICER report did conclude that the traditional oral drugs are effective for preventing migraines.

For the PAs we will not require a trial of Botox first for chronic migraine, since the guidelines don't require this, plus when we talked with our neurologists, they did not recommend this either. However the clinical trials with the CGRPs excluded botulinum toxin for 2 to 4 months prior to initiation of therapy, so that is in the PA criteria.

This class represents a new mechanism for preventing migraine headache, and there has been a fast increase in utilization. However, we can't determine in advance who will respond to these medications, compared to the traditional oral drugs. Also there is no data yet on whether these drugs will actually decrease ER visits for migraine.

8. Panel Questions and Comments

Mr. Hostettler asked how long it takes to get through manual PA for patients and requested feedback at the next meeting.

Lt Col Khoury follows-up with Mr. Hostettler regarding his question about length of time it takes a PA to process. Were you specifically interested in the CGRPs or the overall process? To make sure I heard that question right. You said, "can you tell us how long it takes for a PA to process?"

Mr. Hostettler said this is an on-going question. What is the length of time it takes for the prescription generation until the patient actually gets the medication. It takes longer for some drugs than others do. I am sure another week is not going to matter but sometimes it is longer than a week and in certain cases, I view that as problematic. I am curious about the data. The response can be more general.

Lt Col Khoury said, "According to our data, 99.7% of all PAs that are filled and submitted have a 5 day turnaround. Seventy-four percent of all Electronic PAs, have a turnaround time of a day or less. This data is approximately 6 months old.

Mr. Hostettler asked if the data provided is from the time the prescription is taken to the retail pharmacy.

Lt Col Khoury stated that is where the PA is driving the decision-making. The PA is required to be completed.

Mr. Hostettler provided an example for clarification. For instance, when the patient shows up at retail. The retail pharmacy says, "Sorry we can't do this thing it requires a PA," we send it off to corporate to get it started. Is this additional time that will be added to your numbers.

Lt Col Khoury responds yes. There are instances where the PA is not filled because the patient is switched to an alternative. It's a little bit more involved; it's not just the PA timeframe.

Mr. Hostettler said all of that is part of that timeframe, even up to the point of they never got the drug.

CDR Hellwig stated that the patient has received a drug. They may have received the alternative agent. Many times with our PAs, we are pushing patients to another agent. They would not necessarily receive the agent that the PA was submitted for.

Mr. Hostettler said regardless of whether the PA was completed and the patient received therapy as opposed to just never got it done. I believe all of these issues are a part of the process. What is the impact on the beneficiaries?

CDR Hellwig stated that we do not have the data. We can look to see if we can get it but it is going to be challenging.

Mr. Hostettler said, "It would behoove us to try to get to that information because that is the end-point, the patient impact. If the patient is not getting therapy, that is a big problem. If they are being changed to other alternatives properly, in a proper timeframe, that is fine. I just want to better understanding the process and ensure that everyone understands the process when we provide comments or make decisions.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation for the UF Recommendation, Manual PA Criteria, and UF and PA Implementation Plan for the Migraine Agents.

- **Migraine Agents – CGRP Antagonist Prophylaxis Subclass—UF Recommendation**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **Migraine Agents – CGRP Antagonist Prophylaxis Subclass—Manual PA Criteria**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **Migraine Agents – CGRP Antagonist Prophylaxis Subclass—UF and PA Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

ADDITIONAL PANEL QUESTIONS AND COMMENTS.

CDR Hellwig stated we do have something called a safety net. When we have step therapy in place, we do have a set-up where our mail order pharmacy will actually reach out to the patient if they have not gotten the other agent. This is specific to our step therapy process, not for our PAs. There is a safety net for patients in that situation or an intervention to make sure that they do get something.

Mr. Hostettler asked if that it is true if it is going through the mail order or is it true of both mail order and retail.

Lt Col Khoury stated we have to confirm if that is true for all.

Mr. Hostettler is not sure.

CDR Hellwig stated there are official steps that applies in certain situations when we do a drug class review. That is when this (the safety net) applies. Another thing that we've done, and you'll see in couple of our new drugs, some of our oncology agents we've added the option for the provider to write in the diagnosis cited in the NCCN guidelines. That's because things are changing so rapidly in the oncology world that once we've created a PA it may become outdated and so that's a way to keep patients from having to go through the drug process when there is good data available even if the product doesn't have that as a FDA indication. We have added that (the safety net) as well to ease the process there.

Mr. Hostettler noted and commended the additional controls in the process to address patient safety concerns.

B. ONCOLOGICAL AGENTS – CYP-17 INHIBITORS (CYP17) SUBCLASS AND 2ND-GENERATION ANTIANDROGENS (2ND-GEN AA) SUBCLASS

(MAJ DAVIES)

1. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—Relative Clinical Effectiveness Analysis and Conclusion

Background—The P&T Committee evaluated the relative clinical effectiveness of two subclasses of drugs used for Prostate Cancer. The agents in the CYP17 inhibitor subclass include abiraterone acetate (Zytiga brand and generics) and abiraterone acetate micronized (Yonsa), while the 2nd-generation antiandrogen (AA) subclass is comprised of enzalutamide (Xtandi) and apalutamide (Erleada). The Committee reviewed new data available since the previous formulary decision in February 2015.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

CYP17 Inhibitors Subclass

- The 2018 guidelines from the National Comprehensive Cancer Network (NCCN) included updated recommendations for metastatic castration-resistant prostate cancer (mCRPC). Yonsa used with methylprednisolone was added to the mCRPC algorithm. The guidelines continue to recommend Zytiga, with prednisone for this indication.
- The American Urological Association (AUA) guidelines for mCRPC were updated in 2018 and continue to include abiraterone with prednisone.
- Zytiga and Yonsa contain the same active ingredient, abiraterone acetate. Both products must be co-administered with a corticosteroid to reduce the incidence and

severity of mineralocorticoid excess (hypertension, hypokalemia, and fluid retention). Differences include that Zytiga is given with prednisone while Yonsa is administered with methylprednisolone.

- There is no clinical trial data available with Yonsa; FDA approval was based upon the clinical trial data with Zytiga and bioequivalence studies.
- There are no head-to-head comparative trials between Zytiga and Yonsa. However, the NCCN guidelines recommend that either formulation can be used in place of the other.
- The micronized formulation of Yonsa results in a smaller tablet particle size; therefore, the dosages differ between the two preparations. Under fasting conditions, single doses of Yonsa 500 mg were equivalent to single doses of Zytiga 1,000 mg.
- Zytiga has an advantage of a lower tablet burden. Yonsa has an advantage in that it can be dosed without regard to meals, while Zytiga must be taken on an empty stomach.
- Generic formulations of Zytiga recently entered the market in December 2018, but the generics only include one tablet strength.
- Based on available safety data, the FDA review of Yonsa concluded that there is no evidence that there are differences in safety between Zytiga and Yonsa. Both products have similar warnings and precautions for mineralocorticoid excess, adrenocortical insufficiency, and hepatotoxicity. The FDA review noted that adverse events occurred at similar rates between the two formulations.
- Overall, there is a high degree of therapeutic interchangeability between Zytiga and Yonsa. At least one CYP17 inhibitor is required on the formulary in order to meet the needs of MHS patients.

2^{nd}-Generation AA Subclass

- Enzalutamide (Xtandi) and apalutamide (Erleada) are both FDA-approved for use in non-metastatic castration-resistant prostate cancer (nmCRPC). The 2018 NCCN and 2018 AUA guidelines also recommend both Xtandi and Erleada for nmCRPC. However, of the two 2^{nd}-generation antiandrogens, only Xtandi has FDA approval for use in metastatic CRPC and is included in both the NCCN and AUA guidelines for mCRPC.
- FDA approval for the 2^{nd}-generation AAs for non-metastatic CRPC was based on two randomized, placebo-controlled trials, PROSPER with Xtandi and SPARTAN with Erleada. Men with prostate-specific antigen (PSA) doubling times of ≤ 10 months were included in the trials.
    - Metastasis-free survival (MFS), defined as the delay in development of metastatic disease until metastasis is detected, was the primary endpoint used in both the PROSPER and SPARTAN trials. The study results showed that both Xtandi and Erleada provided a benefit in terms of MFS compared to placebo.

- An indirect comparison of the two trials showed a similar effect on MFS. For Xtandi the median MFS was 36.6 months vs. 14.7 months with placebo, resulting in a 71% risk reduction for the endpoint. In comparison, with Erleada the median MFS was 40.5 months vs. 16.2 months with placebo, corresponding with a 72% risk reduction in the primary endpoint.
- Although overall survival data are not yet mature, interim analyses indicate a trend toward improved survival with both drugs when compared to placebo.

- A 2018 ICER report concluded that, when compared to placebo, Erleada and Xtandi showed delays in disease progression and a trend toward improved survival in patients with non-metastatic CRPC, and were given an "A" rating.
- Xtandi and Erleada have relatively similar adverse effect profiles. Both drugs are associated with hypertension, fatigue, falls, fractures, and seizures.
- Although the PROSPER trial using Xtandi in patients with non-metastatic CRPC showed a disproportionate rate of adverse cardiac effects and death compared to placebo, this finding was not reproduced in other studies with Xtandi conducted in varying populations, including patients with non-metastatic hormone-sensitive prostate cancer (HSPC), metastatic HSPC, non-metastatic CRPC, and metastatic CRPC.
- Comparative effectiveness of Xtandi and Erleada, when used in non-metastatic CRPC, cannot be determined at this time, due to the lack of head-to-head trials.
- At least one 2nd-generation antiandrogen must be included on the formulary for MHS patients.

2. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—Relative Cost-Effectiveness Analysis and Conclusion

CMA and BIA were performed to evaluate the prostate cancer agents. The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

CYP17 Inhibitors

- CMA results for the CYP17 inhibitor subclass showed that Yonsa was more cost-effective than Zytiga brand and generics.
- BIA was performed for the CYP17 inhibitor subclass to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating Yonsa as formulary and step-preferred and Zytiga brand and generics as UF and non-step-preferred demonstrated the greatest cost avoidance for the MHS.

2nd-Generation AA Subclass

- CMA results for the 2nd-generation antiandrogen subclass showed that Xtandi was the most cost-effective 2nd-generation AA.

- BIA was performed for the 2nd-generation antiandrogen subclass to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating Xtandi as formulary and step-preferred and Erleada as UF and non-step-preferred demonstrated significant cost avoidance for the MHS.

3. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—UF Recommendation

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following for the Prostate Cancer agents, as outlined below, based on clinical and cost-effectiveness:

CYP 17 Inhibitor Subclass

- UF and step-preferred
  - abiraterone acetate micronized (Yonsa)
- UF and non-step-preferred
  - abiraterone acetate (Zytiga, generics)
- NF
  - None

2nd-Generation Antiandrogen Subclass

- UF and step-preferred
  - enzalutamide (Xtandi)
- UF and non-step-preferred
  - apalutamide (Erleada)
- NF
  - None

4. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—Manual PA Criteria

Updated manual PA criteria for all four prostate cancer drugs were recommended by the P&T Committee (18 for, 0 opposed, 0 abstained, 0 absent). For both Yonsa and Zytiga brand and generics, the prescription must be written by an oncologist or urologist, and off-label use for non-localized disease was added. The Zytiga PA criteria were also updated to include step therapy, requiring a trial of Yonsa first, unless there is a contraindication, inadequate response, or adverse reaction to Yonsa, for all new and current users of Zytiga brand or generics (i.e., "no grandfathering" scenario). Additionally, for Zytiga, the 250 mg tablets are

the preferred formulation, based on cost-effectiveness. All new and current users of Zytiga brand or generic 500 mg tablets will need to try the 250 mg tablets first.

The Committee also recommended updating the current PAs for Xtandi and Erleada to include the Xtandi step-therapy requirements. All new users (i.e., "grandfathering" scenario) of Erleada will require a trial of Xtandi first, unless contraindicated or if the patient has had an inadequate response or adverse reaction to previous use of Xtandi. Additionally, for nmCRPC, both Xtandi and Erleada will require patients to have documented prostate-specific antigen doubling time (PSADT) of ≤ 10 months, consistent with the trial design of PROSPER and SPARTAN.

a) Yonsa
February 2019 updates are in BOLD and strikethrough.

Manual PA criteria apply to all new users of Yonsa.

Manual PA Criteria: Coverage is approved if all criteria are met:

- **Age ≥ 18 years**
- **Prescribed by or in consultation with an oncologist or urologist**
- Provider is aware that Yonsa may have different dosing and food effects than other abiraterone acetate products (medication errors and overdose warning)
- ~~Patient has documented diagnosis of metastatic castration-resistant prostate cancer (mCRPC)~~
- ~~Patient has documented diagnosis of metastatic high-risk castration-sensitive prostate cancer (mCSPC)~~
- **Patient has documented diagnosis of non-localized disease including:**
  - **Metastatic castration-resistant prostate cancer (mCRPC)**
  - **Metastatic castration-sensitive prostate cancer (mCSPC)**
  - **Regional disease (T_xN1M0) OR**
- **If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND**
  - **The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
- Patient must receive concomitant therapy with methylprednisolone
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy

Other non-FDA-approved uses are NOT approved.

PA does not expire.

b) Zytiga Brand and Generics
February 2019 updates are in BOLD and strikethrough.

Manual PA criteria apply to **all new and current users** of Zytiga and generics.

Manual PA Criteria: Coverage is approved if all criteria are met:

- **Yonsa is the Department of Defense's preferred CYP-17 Inhibitor agent.**
  - **Has the patient tried Yonsa?**

  OR
  - **Does the patient have or have they had a contraindication/inadequate response/adverse reaction to Yonsa that is not expected to occur with the requested agent?**
- **Age ≥ 18 years**
- **Prescribed by or in consultation with an oncologist or urologist**
- ~~Patient has documented diagnosis of metastatic castration-resistant prostate cancer (mCRPC)~~
- ~~Patient has documented diagnosis of metastatic high-risk castration-sensitive prostate cancer (mCSPC)~~
- **Patient has documented diagnosis of non-localized disease including:**
  - **Metastatic castration-resistant prostate cancer (mCRPC)**
  - **Metastatic castration-sensitive prostate cancer (mCSPC)**
  - **Regional disease (T_xN1M0) OR**
- **If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND**
  - **The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
- Patient must receive concomitant therapy with prednisone
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy
- **Zytiga 250 mg is the DoD's preferred strength. Is the prescription for Zytiga 250 mg OR will the prescription be changed to the 250 mg?**
  - **Note: If the prescription is being changed to the 250 mg strength, please submit a new prescription with this PA form**

  OR

- **Please state why the patient cannot take multiple 250 mg tablets to achieve the patient's daily dose (fill-in blank)**

Other non-FDA-approved uses are NOT approved.

PA does not expire.

c) Xtandi
February 2019 updates are in BOLD.

Manual PA criteria apply to all new users of Xtandi.

Manual PA Criteria: Coverage is approved if all criteria are met:

- **Age ≥ 18 years**
- **Prescribed by or in consultation with an oncologist or urologist**
- Patient has documented diagnosis of **metastatic OR non-metastatic** castration-resistant prostate cancer (CRPC)
  - If used in non-metastatic castration-resistant prostate cancer (nmCRPC), patient must have: prostate-specific antigen doubling time **(PSADT) ≤ 10 months OR**
- **If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND**
  - **The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy

Other non-FDA-approved uses are NOT approved.

PA does not expire.

d) Erleada
February 2019 updates are in BOLD.

Manual PA criteria apply to all new users of Erleada.

Manual PA Criteria: Coverage is approved if all criteria are met:

- **Xtandi is the Department of Defense's preferred 2nd-Generation Antiandrogen agent.**
  - **Has the patient tried Xtandi?**

OR

- **Does the patient have or have they had a contraindication/inadequate response/adverse reaction to Xtandi that is not expected to occur with Erleada?**

- **Age ≥ 18 years**
- Prescribed by or in consultation with an oncologist or urologist
- Patient has documented diagnosis of non-metastatic castration-resistant prostate cancer (nmCRPC) **AND**
  - Negative CT scan of abdomen/pelvis and/or negative bone scan, **AND**
  - **PSADT ≤ 10 months OR**
- **If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND**
  - **The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy

Other non-FDA-approved uses are NOT approved.

PA expires in 1 year.

Renewal PA Criteria: Coverage will be approved for 1 year for continuation of therapy if:

- Patient continues to be metastases-free
- No toxicities have developed
- Patient has not progressed onto subsequent therapy (such as abiraterone)

5. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—Tier 1 Cost-Share

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) lowering the current tier 2 cost-share for the CYP17 inhibitor Yonsa and the 2nd-generation AA Xtandi to the generic Tier 1 cost-share.

The authority for this recommendation is codified in 32 CFR 199.21(j)(3), which states that "when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the Pharmacy and Therapeutics Committee may also designate that the drug be cost-shared at the generic rate."

Lowering the cost-share for both Yonsa and Xtandi will provide a greater incentive for beneficiaries to use the most cost-effective CYP 17 or 2nd-generation antiandrogen product, respectively, in the purchased care points of service.

6. Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass—UF and PA Implementation Plan

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) 1) an effective date of 90 days after signing of the P&T minutes at all points of service, and 2) DHA send letters to beneficiaries who are affected by the step decision in the CYP17 subclass (those patients currently on Zytiga brand or generics).

7. Physician's Perspective

This is the first time that the Committee has recommended adding step therapy for an oncology drug. All four prostate cancer drugs will be UF, but Zytiga and Erleada will be behind a step. Note that there is manual PA criteria currently in place for all of these drugs, and the general PAs were updated.

The Committee recommended step therapy for the CYP 17 drugs, since Zytiga and Yonsa contain the same active ingredient. The step therapy criteria are included in the manual PA, which will apply to both new and current users of Zytiga ("no grandfathering"). Patients will be notified via letter of the upcoming requirements for step therapy. Currently, there about 1,200 patients who could be potentially affected by the step therapy for the CYP 17 drugs. However, the number of patients affected will likely be lower. Our data shows that about 34% of patients remain on therapy after 1 year, and only 10% of patients are on one of the CYP 17 drugs after 2 years. There is an implementation period of 90 days, so we expect the implementation date will be sometime in August 2019.

For the anti-androgens, the step therapy requiring Xtandi first will only apply to new patients. Therefore, all patients currently on Erleada will be allowed to continue therapy. Our data also shows that there is also low persistence for this subclass - only about 20% of patients remain on an anti-androgen after 2 years.

Xtandi has more indications than Erleada, and has been studied in more patients. The reason for having renewal criteria for Erleada but not Xtandi is due to the fact that Erleada is not approved for metastatic disease, and the PA takes that into account.

8. Panel's Questions and Comments

Mr. Hostettler asked for clarification on the manual PA criteria for Zytiga. More specifically, how does it affect new and current users? Why force patients who are doing well on their product to change to a different product.

MAJ Davies said the P&T Committee discussed this issue. The products have the same active ingredient. Theoretically, it would not be a change with switching that patient over to Yonsa, which is micronized abiraterone.

Dr. Peloquin asked if there was a change in dosage when the patient switched to the new product. There was some verbiage in the PA criteria about a dosage difference. Are there controls in place to address safety concerns?

Lt Col Khoury and MAJ Davies both believed that the verbiage in the PA would address safety concerns. Additionally the oncologist placing the order would know there is a difference in the formulation.

Mr. Hostettler believes that cancer patients using Xtandi, are very, very concerned about their treatment. If they are doing well with the product they are using, making a change due to cost is harmful to the patient. As you stated there are a percentage of patients who drop off the product for whatever reason. Not knowing the cost difference, overtime it does not seem to be that big a difference. It goes back to the discussion we had earlier about the humanistic aspect. We are putting a patient in a very serious situation and it is a hard decision.

MAJ Davis responded the current users of Xtandi are being grandfathered. This decision would only affect new patients. It is the Zytiga that will not be grandfathered. Zytiga is a metastatic disease and more progressive state of the disease state.

Mr. Hostettler stated that it makes the decision even harder because the patients are more concerned because they are at a higher risk. The change in product only adds to their concerns/problems. It is hard for me to say it is a good decision. I am simply asking the P&T Committee to take these comments into consideration.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation for the UF Recommendation, Manual PA Criteria, and UF and PA Implementation Plan for the Oncological Agents.

- **Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass —UF Recommendation**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- Onc**ological Agents – CYP17 Subclass and 2nd-Gen AA Subclass — Manual PA Criteria**

  Concur: 6 Non-Concur: 1 Abstain: 0 Absent: 2

- **Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass Subclass —Tier 1 Cost-Share**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **Oncological Agents – CYP17 Subclass and 2nd-Gen AA Subclass Subclass —UF and PA Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

II. NEWLY APPROVED DRUGS PER 32 CFR 199.21(G)(5)

(Lt COL KHOURY)

1. **Newly Approved Drugs per 32 CFR 199.21(g)(5)—Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions**

   The P&T Committee agreed (group 1 and group 3: 17 for, 0 opposed, 0 abstained, 1 absent; and group 2: 18 for, 0 opposed, 0 abstained, 0 absent) with the relative clinical and cost-effectiveness analyses presented for the newly approved drugs reviewed according to 32 CFR 199.21(g)(5).

2. **Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF Recommendation**

   The P&T Committee recommended (group 1 and group 3: 17 for, 0 opposed, 0 abstained, 1 absent; and group 2: 18 for, 0 opposed, 0 abstained, 0 absent) the following:

   - UF:
     - amifampridine (Firdapse) – Miscellaneous Neurological Agent for Lambert-Eaton Myasthenic Syndrome (LEMS)
     - baloxavir (Xofluza) – Antiviral for Influenza
     - cenegermin-bkbj ophthalmic solution (Oxervate) – Anti-Inflammatory Immunomodulatory Ophthalmic Agent for Neurotrophic Keratitis
     - elapegademase-lvlr IM injection (Revcovi) – Miscellaneous Metabolic Agent for Adenosine Deaminase Severe Combined Immune Deficiency (ADA-SCID)
     - gilteritinib (Xospata) – Oncological Agent for Acute Myelogenous Leukemia (AML)
     - glasdegib (Daurismo) – Oncological Agent for AML
     - inotersen injection (Tegsedi) – Miscellaneous Neurological Agent for Hereditary Transthyretin Amyloidosis
     - larotrectinib (Vitrakvi) – Oncological Agent for Solid Tumors
     - lorlatinib (Lorbrena) – Oncological Agent for Non-Small Cell Lung Cancer (NSCLC)

- loteprednol ophthalmic suspension (Inveltys) – Ophthalmic Corticosteroid for Postoperative Inflammation
- pegfilgrastim-cbqv injection (Udenyca) – White Blood Cell Stimulant and Biosimilar to Neulasta
- riluzole oral suspension (Tiglutik) – Miscellaneous Neurological Agent for Amyotrophic Lateral Sclerosis (ALS)
- tafenoquine 100 mg tablet (Arakoda) – Antimalarial Agent for Prophylaxis of Malaria
- tafenoquine 150 mg tablet (Krintafel) – Antimalarial Agent for Prevention of Relapse and Radical Cure of Malaria
- talazoparib (Talzenna) – Oncological Agent for Breast Cancer
- testosterone enanthate, subcutaneous (SQ) injection (Xyosted) – Androgens-Anabolic Steroids: Testosterone Replacement Therapies

- NF:
  - aripiprazole tablet with ingestible event marker (Abilify MyCite) – Atypical Antipsychotic
  - clobazam oral film (Sympazan) – Anticonvulsant-Antimania Agent for Lennox-Gastaut Syndrome
  - cyclosporine 0.09% ophthalmic solution (Cequa) – Anti-Inflammatory Immunomodulatory Ophthalmic Agent for Dry Eye Disease
  - desmopressin acetate sublingual (SL) tablet (Nocdurna) – Miscellaneous Endocrine Agent for Nocturia due to Nocturnal Polyuria
  - filgrastim vials (Granix) – White Blood Cell Stimulant and Biosimilar to Neupogen
  - halobetasol propionate 0.01% lotion (Bryhali) – High Potency Corticosteroid-Immune Modulator for Plaque Psoriasis
  - itraconazole 65 mg capsules (Tolsura) – Antifungal Agent
  - latanoprost (Xelpros) – Ophthalmic Prostaglandin
  - omadacycline (Nuzyra) – Tetracycline Antibiotic for Community-Acquired Bacterial Pneumonia (CABP) and Acute Bacterial Skin and Skin Structure Infections (ABSSSI)
  - revefenacin nebulized solution (Yupelri) – Pulmonary-2: Long Acting Anti-Muscarinic Agent (LAMA) for Chronic Obstructive Pulmonary Disease (COPD)
  - rifamycin (Aemcolo) – Miscellaneous Gastrointestinal Antibiotic for Traveler's Diarrhea
  - sarecycline (Seysara) – Tetracycline Antibiotic for Acne Vulgaris

3. Newly Approved Drugs per 32 CFR 199.21(g)(5)—PA Criteria

The P&T Committee recommended (group 1 and group 3: 17 for, 0 opposed, 0 abstained, 1 absent; and group 2: 18 for, 0 opposed, 0 abstained, 0 absent) the following:

- Oral Tetracycline Agents: Applying the same automated (step therapy) and manual PA criteria for sarecycline (Seysara) in new and current users that is currently in place for the other non-step-preferred oral tetracyclines. Patients must first try one generic doxycycline IR product, either the hyclate or monohydrate salt and one generic minocycline IR product first, before Seysara.
- Androgens-Anabolic Steroids: Testosterone Replacement Therapies: Applying new manual PA criteria for Xyosted SQ in new and current users. In addition to a trial of the step-preferred testosterone 2% topical gel (Fortesta), patients must also try one injectable testosterone product and meet the Risk Evaluation and Mitigation Strategies (REMS) requirements listed in the Xyosted product label regarding the risk of increases in blood pressure and potential increase in the risk of major adverse cardiovascular events (MACE).
- Applying manual PA criteria to new users of Abilify MyCite, Arakoda, Daurismo, Firdapse, Lorbrena, Oxervate, Talzenna, Tegsedi, Tolsura, Vitrakvi, and Xospata.
- Applying manual PA criteria to new and current users of Aemcolo, Cequa, Nocdurna, Tiglutik, and Yupelri.

Full PA Criteria for the Newly Approved Drugs per 32 CFR 199.21(g)(5)

a) amifampridine (Firdapse)

Manual PA applies to all new users of Firdapse.

Manual PA Criteria: Firdapse is approved if:

- Age ≥ 18 years old
- Drug is prescribed by an oncologist or neurologist
- Has laboratory evidence of Lambert-Eaton myasthenic syndrome (LEMS)

Non-FDA-approved uses are NOT approved.

PA does not expire.

b) aripiprazole tablet with ingestible event marker (Abilify MyCite)

Manual PA criteria apply to all new users of Abilify MyCite.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient must have documented attempt to use generic aripiprazole tablets, with non-compliance documented in prescriber notes. Prescriber notes must also document the prescriber's attempted medication adherence counseling.
- Patient must have documented trial of at least 12 weeks of Abilify Maintena first
- Provider acknowledges that FDA labeling states the ability of Abilify MyCite to improve patient compliance or modify aripiprazole dosage has not been established.

Non-FDA-approved uses are NOT approved.

PA does not expire.

c) cenegermin-bkbj ophthalmic solution (Oxervate)

Manual PA criteria apply to all new users of Oxervate.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 2 years
- Patient has a documented diagnosis of neurotrophic keratitis
- Drug is prescribed by a cornea specialist or ophthalmologist
- Patient does not wear contact lenses during treatment course

Non-FDA-approved uses are NOT approved.

PA does not expire.

d) cyclosporine 0.09% ophthalmic solution (Cequa)

February 2019 criteria specific for Cequa are in BOLD for the PA form that also includes Xiidra and Restasis.

PA criteria apply to all **new and current** users. A new user is defined as a patient who has not filled a prescription for Restasis, **Cequa** or Xiidra in the past 120 days.

- If there is no Restasis, **Cequa**, or Xiidra prescription in the past 120 days, a manual PA is required.

Manual PA Criteria: Coverage is approved if all the criteria are met:

- The drug is prescribed by an ophthalmologist or optometrist
- **For Cequa: the patient is ≥ 18 years old**
- A diagnosis of moderate to severe dry eye disease is supported by both of the criteria below:
- Positive symptomatology screening for moderate to severe dry eye disease from an appropriate measure
- At least one positive diagnostic test (e.g., Tear Film Breakup Time, Osmolarity, Ocular Surface Staining, Schirmer Tear Test)
- Patient must try and fail the following:
  - At least 1 month of one ocular lubricant used at optimal dosing and frequency (e.g., carboxymethylcellulose [Refresh, Celluvisc, Thera Tears, Genteal, etc.], polyvinyl alcohol [Liquitears, Refresh Classic, etc.], or wetting agents [Systane, Lacrilube])
  - Followed by at least 1 month of a different ocular lubricant that is non-preserved at optimal dosing and frequency (e.g., carboxymethylcellulose, polyvinyl alcohol)
- Concomitant use of Restasis, **Cequa**, or Xiidra is NOT allowed.

Non-FDA-approved uses for Cequa are NOT approved.

PA expires in one year.

Renewal Criteria: Coverage will be approved indefinitely if all criteria are met:

- The drug is prescribed by an ophthalmologist or optometrist.
- The patient must have documented improvement in ocular discomfort.
- The patient must have documented improvement in signs of dry eye disease.

e) desmopressin acetate sublingual (SL) tablet (Nocdurna)

Manual PA criteria apply to all new and current users of Nocdurna.

Manual PA criteria apply to all new and current users of Nocdurna SL tablets. Updates are in BOLD for the PA that also has Noctiva nasal spray

Manual PA Criteria: Coverage is approved if all criteria are met:

- For Nocdurna: Age ≥ 18 years old

- For Nocdurna: For females: must use 27.7 mcg dosage; for males: must use 55.3 mcg dosage
- For Noctiva Nasal Spray: Age ≥ 50 years old (Only the low dose is allowed for pts > 65 years old)
- Patient has nocturia defined as having ≥ 2 nocturnal voids nightly for ≥ 6 months
- Causes of nocturia have been evaluated and nocturnal polyuria is confirmed with a 24-hour urine collection
- **Patient has tried non-pharmacologic techniques or lifestyle interventions to manage the nocturia (e.g., nighttime fluid restriction, avoidance of caffeine and alcohol, earlier timing of medications, leg elevation and/or use of compression stockings)**
- **The patient has tried oral desmopressin acetate tablets (DDAVP tablets, generics)**
- Patient is not currently taking <u>any of the following</u> medications:
  - Loop diuretics, alpha$_1$-adrenoceptor antagonists, 5-alpha reductase inhibitors (ARIs), thiazide diuretics, anticholinergics, antispasmodics, sedative/hypnotic agents, NSAIDs, SSRIs, SNRIs, antidepressants, anti-epileptics, opioids, or SGLT2s
  - Systemic or inhaled corticosteroids or lithium
- Prescribed by a urologist, a geriatrician, an endocrinologist, or a **nephrologist**
- **Provider must supply most recent serum sodium and date**
  - **Sodium _____mEq/mL Date_____**
- Patient has normal sodium (135-145 mEq/L) prior to initiation, recheck sodium after one week of therapy, and another sodium recheck at 1 month
- **Provider acknowledges that patients over 65 years old are at greater risk of hyponatremia and has advised the patient about this significant safety concern**
- Patient does not have the following conditions for both Noctiva Nasal Spray and Nocdurna:
  - **Renal impairment (eGFR < 50 mL/min)**
  - **Hyponatremia or history of hyponatremia**
  - **Polydipsia**
  - **Nocturnal enuresis**
  - **SIADH**
  - **Congestive heart failure**
  - **Uncontrolled hypertension or uncontrolled diabetes mellitus**
  - **Interstitial cystitis**
  - **Chronic prostatitis/chronic pelvic pain syndrome**
  - **Suspicion of bladder outlet obstruction (BOO) or urine flow < 5 mL/sec**
  - **Surgical treatment, including transurethral resection, for BOO or benign prostatic hyperplasia within the past 6 months**

- **Urinary retention or a post-void residual volume in excess of 250 mL as confirmed by bladder ultrasound performed after suspicion of urinary retention**
- **Current or a history of urologic malignancies (e.g., urothelium, prostate, or kidney cancer)**
- **Genitourinary tract pathology (e.g., infection or stone in the bladder and urethra causing symptoms)**
- **Neurogenic detrusor activity (detrusor overactivity)**
- **Suspicion or evidence of cardiac failure**
- **History of obstructive sleep apnea**
- **Hepatic and/or biliary diseases**
- **Treatment with another investigational product within 3 months prior to initiating therapy**
- **Known alcohol or substance abuse**
- **Work or lifestyle that may have interfered with regular nighttime sleep**

AND

- **Patient does not have the following conditions for Noctiva Nasal Spray**
  - **acute or chronic rhinitis (for Noctiva nasal spray only)**
  - **atrophy of nasal mucosa (for Noctiva nasal spray only**)

Non-FDA-approved uses are NOT approved.

PA expires in ~~6 months~~ **4 months.**

Renewal Criteria: Coverage will be approved for an additional 6 months if all of the following apply:

- Patient has not developed any of the conditions above
- **Patient is not taking any of the medications mentioned above**
- Patient has shown a reduction in nocturia episodes

f) gilteritinib (Xospata)

Manual PA criteria apply to all new users of Xospata.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 18
- Has laboratory evidence of relapsed or refractory acute myeloid leukemia with a Ferline McDonough Sarcoma (FMS)-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test
- The patient will be monitored for posterior reversible encephalopathy syndrome (PRES), prolonged QTc, and pancreatitis

- Patient is not pregnant or actively trying to become pregnant
- Prescribed by or in consultation with a hematologist/oncologist

Non-FDA-approved uses are NOT approved.

PA does not expire.

g) glasdegib (Daurismo)

Manual PA criteria apply to all new users of Daurismo.

Manual PA criteria: Coverage is approved if all criteria are met:

- Treatment of newly diagnosed acute myeloid leukemia (in combination with low-dose cytarabine) in adult patients who are ≥ 75 years of age or who have comorbidities that preclude use of intensive induction chemotherapy.
- Provider acknowledges and patient has been informed that limitations of use include that this drug has not been studied in patients with severe renal impairment or moderate to severe hepatic impairment.
- Patient is not pregnant or actively trying to become pregnant
- Patient will be monitored for febrile neutropenia and QTc prolongation
- Prescribed by or in consultation with a hematologist/oncologist

Non-FDA-approved uses are NOT approved.

PA does not expire.

h) inotersen injection (Tegsedi)

Manual PA applies to all new users of Tegsedi.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 18 and has genetically confirmed transthyretin mutation resulting in familial amyloidotic polyneuropathy (FAP) stage 1 or 2 hereditary transthyretin-mediated amyloidosis (hTTRA)
- Has polyneuropathy secondary to hereditary transthyretin-mediated amyloidosis with either 1) a polyneuropathy disability (PND) score ≤ IIIB or 2) a Neuropathy Impairment Score between 10 and 130
- Provider and patient are both registered and enrolled with the Tegsedi Risk Evaluation and Mitigation Strategies (REMS) program
- Patient has no evidence of thrombocytopenia

- Patient does not have chronic kidney disease (CKD) stage 3b and has no history of glomerulonephritis
- The provider will monitor the patient's platelet counts and renal and hepatic function
- Patient will take an oral Vitamin A supplement at the recommended daily allowance
- Provider is aware and patient is informed of the following potential adverse drug reactions: stroke, encephalitis, carotid arterial dissection, hypercoagulability and thrombosis (venous and arterial), QRS prolongation and other arrhythmias, elevated liver-associated enzymes, autoimmune hepatitis, primary biliary cirrhosis, biliary obstruction, glomerulonephritis, nephrotic syndrome, interstitial nephritis, thrombocytopenia, idiopathic thrombocytopenia (ITP), antineutrophil cytoplasmic antibody-associated (ANCA) vasculitis, and hypersensitivity
- Prescribed by or in consultation with a specialist that manages hereditary transthyretin amyloidosis (e.g., cardiologist, geneticist, neurologist)
- Concomitant use of Onpattro and Tegsedi is not allowed

Non-FDA-approved uses are NOT approved.

PA does not expire.

i) itraconazole 65 mg capsules (Tolsura)

Manual PA criteria apply to all new users of Tolsura.

Manual PA Criteria: Tolsura is approved if:

- Patient has one of the following diagnoses:
  - Histoplasmosis
  - Pulmonary or Extrapulmonary Blastomycosis
  - Pulmonary or Extrapulmonary Aspergillosis

  AND
- For histoplasmosis or blastomycosis:
  - Patient has had serious side effects with generic itraconazole 100 mg tablets/capsules OR
  - Patient has failed drug treatment with generic itraconazole 100 mg tabs/capsules
- For aspergillosis
  - Patient has had serious side effects with generic itraconazole 100 mg tablets/capsules and amphotericin B OR
  - Patient has failed drug treatment with generic itraconazole 100 mg tabs/capsules and amphotericin B

Non-FDA-approved uses are NOT approved including onychomycosis.

PA does not expire.

j) larotrectinib (Vitrakvi) capsules and oral solution

Manual PA criteria apply to all new users of Vitrakvi capsules and oral solution.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient diagnosed with a solid tumor that:
  - has a neurotrophic tropomyosin receptor kinase (NTRK) gene fusion without a known acquired resistance mutation,
  - is metastatic OR where surgical resection is likely to result in severe morbidity, AND
  - has no satisfactory alternative treatments OR that has progressed following such treatment(s).
- Larotrectinib (Vitrakvi) is prescribed by or in consultation with a hematologist/oncologist
- For Vitrakvi oral solution: in addition to the above criteria, the patient has difficulty swallowing the capsules

Non-FDA-approved uses are NOT approved.

PA does not expire.

k) lorlatinib (Lorbrena)

Manual PA criteria apply to all new users of Lorbrena.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient is 18 years of age or older
- Drug is prescribed by or in consultation with hematologist or oncologist
- Patient has a diagnosis of metastatic anaplastic lymphoma kinase (ALK) positive non-small cell lung cancer
- Patient has experienced disease progression on one of the following treatments:
  - crizotinib (Xalkori) and at least one other ALK inhibitor
  - alectinib (Alecensa) as a first-line agent
  - ceritinib (Zykadia) as a first-line agent **OR**
- If patient has a diagnosis other than those listed above, list the diagnosis: _____. AND

- The diagnosis is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation

Non-FDA-approved uses NOT approved.

PA does not expire.

l) revefenacin nebulized solution (Yupelri)

Manual PA is required for all new and current users of Yupelri.

Manual PA Criteria: Yupelri is approved if all criteria are met:

- The patient has a diagnosis of chronic obstructive pulmonary disease
- The patient has tried and failed an adequate course of a nebulized Short-Acting Muscarinic Antagonist (e.g., ipratropium)
- The patient has tried and failed an adequate course of Spiriva Respimat
- The patient has tried and failed an adequate course of therapy with at least one of the following dry powder inhalers: Tudorza Pressair, Incruse Ellipta, Spiriva Handihaler, or Seebri Neohaler OR
- The patient cannot generate the peak inspiratory flow needed to activate at least one of the following dry powder inhalers: Tudorza Pressair, Incruse Ellipta, Spiriva Handihaler, or Seebri Neohaler

Non-FDA-approved uses are NOT approved.

PA does not expire.

m) rifamycin (Aemcolo)

Manual PA criteria apply to all new and current users of Aemcolo.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 18
- Patient has a diagnosis of traveler's diarrhea caused by noninvasive strains of *Escherichia coli*
- Patient does not have diarrhea complicated by fever and/or bloody stool
- Patient does not have diarrhea due to pathogens other than noninvasive strains of *E. coli*

- Patient has tried and failed a 3-day trial of ciprofloxacin unless a contraindication exists or patient has tried and failed azithromycin unless a contraindication exists

Non-FDA-approved uses are NOT approved including but not limited to diarrhea-predominant irritable bowel syndrome (IBS-D), non-alcoholic steatohepatitis (NASH), small intestine bacterial overgrowth (SIBO), and inflammatory bowel disease (IBD).

PA renewal not allowed. A new prescription will require a new PA to be submitted.

n) riluzole oral suspension (Tiglutik)

Manual PA criteria apply to all new and current users of Tiglutik.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient is diagnosed with amyotrophic lateral sclerosis
- Patient has dysphagia/swallowing dysfunction

Non-FDA-approved uses are NOT approved.

PA does not expire.

o) sarecycline (Seysara)
February 2019 criteria specific to Seysara are in BOLD.

PA applies to both new and current users of Seysara.

Automated PA Criteria:

- Patient has filled a prescription for one generic IR doxycycline (either hyclate or monohydrate salt; does not include doxycycline monohydrate 40 mg IR/DR) AND one generic minocycline IR product at any Military Treatment Facility (MTF), retail network pharmacy, or the mail order pharmacy in the previous 180 days

Manual PA Criteria: If automated PA criteria are not met, the non-step-preferred product is allowed if:

Acne Vulgaris or Rosacea

- For Solodyn or generic minocycline ER, Minolira, **or Seysara:** The patient has acne with inflammatory lesions AND
  - the patient cannot tolerate generic minocycline IR due to gastrointestinal adverse events

Non-FDA-approved uses are NOT approved.

PA expires in 1 year.

Renewal Criteria:

- **Seysara: PA renewal is not allowed; repeat courses will require a new PA to be submitted.**

p) tafenoquine 100 mg tablet (Arakoda)

Manual PA criteria apply to all new users of tafenoquine (Arakoda).

Manual PA Criteria: Coverage will be approved for tafenoquine (Arakoda) if all criteria are met:

- Age ≥ 18 and Arakoda is being prescribed for malaria chemoprophylaxis
- Patient has a contraindication or intolerance to both atovaquone-proguanil (Malarone) and doxycycline (e.g., pregnancy)
- Patient does not have a major psychiatric disorder to include but not limited to:
  - Active or recent history of depression
  - Generalized anxiety disorder
  - Psychosis or schizophrenia
  - Post-Traumatic Stress Disorder or Traumatic Brain Injury
- Patient does not have a history of seizures or vestibular disorders
- Patient does not have a cardiac conduction abnormality
- Patient has been tested and is negative for glucose 6 phosphate dehydrogenase (G6PD) deficiency
- The above information must be documented in the patient's medical record, and the patient must be educated on Arakoda adverse effects and dosing

Non-FDA-approved uses are NOT approved.

PA expires after 2 years. PA renewal is not allowed; repeat courses will require a new PA to be submitted.

q) talazoparib (Talzenna)

Manual PA criteria apply to all new users of Talzenna.

Manual PA Criteria: Coverage is approved if all criteria are met:

- Patient is 18 years of age or older
- Drug is prescribed by or consultation with a hematologist or oncologist
- Patient has a diagnosis of deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) and human epidermal growth factor receptor 2-negative (HER2-) breast cancer

Non-FDA-approved uses are NOT approved.

PA does not expire.

r) testosterone enanthate injection (Xyosted)

February 2019 criteria specific to Xyosted are in BOLD for the PA that also includes topical testosterone replacement therapies.

Manual PA criteria apply to all new and current users of Xyosted.

Manual PA for Xyosted requires a trial of the step-preferred product, Fortesta, **and one injectable testosterone product.**

Manual PA Criteria: Coverage is approved if all criteria are met:

- Age ≥ 18 years and male
- Patient has documentation of experiencing signs and symptoms usually associated with hypogonadism
- **Xyosted is prescribed for the treatment of men with hypogonadal conditions associated with structural or genetic etiologies**
- Diagnosis of hypogonadism is confirmed and evidenced by morning total serum testosterone levels below 300 ng/dL taken on at least two separate occasions
- Patient has one of the following criteria:
  - Patient has tried Fortesta (testosterone 2% gel) **AND an injectable testosterone formulation for a minimum of 90 days AND** failed to achieve total serum testosterone levels above 400 ng/dL (labs drawn 2 hours after Fortesta application or the injectable testosterone formulation) **AND** without improvement in symptoms
    – OR –
  - **Patient has a contraindication to or has experienced a clinically significant adverse reaction to Fortesta that is not expected to occur with the Xyosted autoinjector**

- **The provider has considered the patient's baseline cardiovascular risk and ensured blood pressure is adequately controlled before initiating Xyosted and periodically during the course of treatment (based on the product's boxed warning of increased risk of major adverse cardiovascular events and hypertension).**
- **Patient <u>does not have any</u> of the following:**
  - **Carcinoma of the breast or suspected carcinoma of the prostate**

Non-FDA-approved uses are NOT approved.

Not approved for concomitant use with other testosterone products.

PA does not expire.

4. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF and PA Implementation Plan

The P&T Committee recommended (group 1 and group 3: 17 for, 0 opposed, 0 abstained, 1 absent; and group 2: 18 for, 0 opposed, 0 abstained, 0 absent) an effective date upon the first Wednesday 30 days after signing of the minutes in all points of service.

5. Physician's Perspective

We've been reviewing about 30 new drugs each meeting, and this meeting was no exception. A total of 29 new drugs were reviewed, with 16 recommended for UF status, and 12 recommended for NF status. One new drug will be discussed in the upcoming Tier 4 section.

A total of 18 drugs were recommenced to have PAs. Six of these drugs are in classes where there are existing PA requirements. For 11 of the drugs, the PA will only apply to new users. Seven of the drugs have "no grandfathering" for the PA, so both new and current users will be affected. Two of the drugs (the acne drug Seysara and the testosterone drug Xyosted) already have step therapy in the class.

The Committee did have some specific comments for some of the new drugs:

- Xofluza for treatment of influenza: The Committee felt that the one time treatment course was of value, especially for readiness situations, compared to the 5 day treatment course with Tamiflu. So Xofluza was recommended for UF status.
- Omadycycline (Nuzyra) – This antibiotic was recommended for NF status. The manufacturer must conduct a trial in patients with community acquired pneumonia to determine if there is an increased risk of death. This clinical safety issues was enough of a concern to have the NF recommendation.

- Riluzole oral susp (Tiglutik) – This drug is approved for ALS. A review of DoD data led us to believe that there is the potential for off-label use. Therefore we did recommend a PA for the suspension only, which will apply to both new and current users. Note that the tablet formulation of the drug does not currently require a PA, only the new suspension will have the PA.

At the meeting the annual New Drug Update of the program was given. Over the past three years a total of 194 new drugs have been reviewed, with 52% (101 drugs) recommended for UF status and 48% (93 drugs) recommended for NF status. One challenge for the Committee will be keeping up with the increasing volume of new drug approvals from the FDA, and the increasing number of specialized products approved, particularly oncology products.

6. Panel Questions and Comments

Mr. Hostettler stated that a new user was defined as a patient that has not used any of the products. It appears the current users would have already met the PA criteria for cyclosporine.

Lt Col Khoury referred to the prior class reviews of Restasis and Xiidra. The analysis showed that people come on and come off the product. Our intent was to ensure that patients were consistently on the drug. If they stop using the product and start later, they are treated as a new user. That is how we clarify the timeline.

Mr. Hostettler further clarified, the patient is currently using the drug and they haven't stopped?

Lt Col Khoury responded that is what our data showed. The patient would start using the drug and over a period, they would stop.

Mr. Hostettler asked if the current users would be required to complete the PA process again. He also asked how many new and current users are affected by the decision for Yupelri.

Lt Col Khoury stated that currently 31 patients are on Yupelri. Cequa PA applies to new and current users if they have not completed.

Mr. Hostettler asked if the course of treatment for Amecolo was 10 or 3 days. He assumes it is a short course of therapy and not longer than a year.

CDR Hellwig stated that yes it is. It is unlikely patients would be affected by this decision.

Mr. Hostettler had the same questions on Arakoda. What is the normal course of treatment? Is it short again or long?

CDR Hellwig stated that Arakoda is a chemoprophylaxis agent. Patients could be on it for an extended period.

Mr. Hostettler clarified; new users are only affected by the decision?

Arakoda PA is for new users.

There were no questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, PA Criteria, and UF and PA Implementation Plan for the Newly Approved Drugs per 32 CRR 199.21(g)(5).

- **Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF Recommendation**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **Newly Approved Drugs per 32 CFR 199.21(g)(5)—PA Criteria**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF and PA Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

III. UTILIZATION MANAGEMENT

A. NEW MANUAL PA CRITERIA

(CDR HELLWIG)

New manual PA criteria were recommended for the following drugs, which will be discussed below.

1. Antihistamine-1: First generation and combinations – Dexchlorpheniramine 2 mg/5 mL oral solution (Ryclora)

Ryclora is a new liquid formulation of a dexchlorpheniramine, which had previously been removed from the market. Cost-effective generic formulations of chlorpheniramine are available on the UF without a PA required, and low-cost OTC liquid formulations for fexofenadine and loratadine are widely available.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for dexchlorpheniramine 2 mg/5 mL oral syrup (Ryclora) in new and current users, due to the significant cost differences and lack of clinically compelling benefits over generic alternatives.

Manual PA criteria apply to all new and current users of dexchlorpheniramine liquid (Ryclora). Coverage will be approved for dexchlorpheniramine liquid if all criteria are met:

Ryclora liquid has been identified as having cost-effective alternatives. The provider must describe why Ryclora is required as opposed to available alternatives (chlorpheniramine liquid, loratadine liquid, cetirizine liquid, and fexofenadine liquid).

Non-FDA-approved uses are NOT approved.

PA does not expire.

2. Hepatitis C Agents: Direct-Acting Agents (HCV DAAs): generic ledipasvir/sofosbuvir (authorized generic for Harvoni) and generic sofosbuvir/velpatasvir (authorized generic for Epclusa)

The P&T Committee most recently reviewed the HCV DAAs for formulary status in August 2018. Since the review, authorized generics for Harvoni and Epclusa entered the market in December 2018. An "authorized generic" is the brand company's own product repackaged and marketed as a generic drug. An authorized generic is considered therapeutically equivalent to the name brand drug because it is the same drug. The FDA does not consider authorized generics as AB-rated generic formulations.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for the authorized generic products ledipasvir/sofosbuvir and sofosbuvir/velpatasvir in new users, requiring a trial of the branded Harvoni or Epclusa, due to cost-effectiveness. The PA requirement will be removed when it is no longer cost advantageous.

Manual PA criteria apply to all new users of ledipasvir/sofosbuvir (authorized generic for Harvoni) or sofosbuvir/velpatasvir (authorized generic for Epclusa). Ledipasvir/sofosbuvir authorized generic products or sofosbuvir/velpatasvir authorized generic products are approved if all of the following criteria are met:

- For ledipasvir/sofosbuvir: The brand Harvoni formulation is preferred over the authorized generic product. The provider must provide a patient-specific justification as to why the brand Harvoni product cannot be used in this patient.
- For sofosbuvir/velpatasvir: The brand Epclusa formulation is preferred over the authorized generic product. The provider must provide a patient-specific justification as to why the brand Epclusa product cannot be used in this patient.

AND the patient must meet the following criteria for a HCV DAA product:

- ≥ 18 years of age
- Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease physician, or a liver transplant physician
- Patient has laboratory evidence of hepatitis C virus infection
- The HCV genotype is documented. (Check box – GT1a, GT1b, GT2, GT3, GT4, GT5, GT6)

Coverage for the HCV DAA is only allowed for the FDA-approved indications or as outlined in the AASLD/IDSA HCV guidelines.

PA expires in 1 year.

3. Skeletal Muscle Relaxants and Combinations: cyclobenzaprine 7.5 mg

Generic formulations of the skeletal muscle relaxant cyclobenzaprine are available in 5 mg, 7.5 mg, and 10 mg tablets. Cyclobenzaprine 7.5 mg tablets are significantly less cost-effective compared to the 5 mg or 10 mg strengths. Cost-effective generic formulations of cyclobenzaprine 5 mg and 10 mg and multiple comparable muscle relaxants (e.g., baclofen, methocarbamol) are available on the UF without PA required. The Committee did note that skeletal muscle relaxants are not considered first-line therapy for musculoskeletal conditions.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for new and current users of cyclobenzaprine 7.5 mg tablets, due to the significant cost differences and lack of clinically compelling benefits compared with administering one and a half of a 5 mg tablet or using other generic muscle relaxants.

Manual PA criteria apply to all new and current users of cyclobenzaprine 7.5 mg tablets or capsules. Coverage will be approved for cyclobenzaprine 7.5 mg tablets if all criteria are met:

- Cyclobenzaprine 7.5 mg tablets have been identified as having cost-effective alternatives. The provider must describe why cyclobenzaprine 7.5 mg is required as opposed to available alternatives, including generic cyclobenzaprine 5 mg tablets and cyclobenzaprine 10 mg tablets

Non-FDA-approved uses are NOT approved.

PA does not expire.

4. New PA Criteria—PA Implementation

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) new PAs for Ryclora, cyclobenzaprine 7.5 mg, authorized generic ledipasvir/sofosbuvir and authorized generic sofosbuvir/velpatasvir become effective 90 days after the signing of the minutes. DHA will send letters to beneficiaries affected by the new PA requirements for the cyclobenzaprine 7.5 mg and Ryclora if applicable, as new and current users will be subject to the PA.

5. Physician's Perspective

In regards to Ryclora syrup, this product is essentially a new twist on an old formulation, mainly that it is available as a syrup. There are other antihistamines that are available as oral syrups, both as prescription or OTC products. The Committee could not come up with a clinical reason as to why Ryclora would be needed instead of the other widely available and low cost antihistamine syrups. Currently we don't have any utilization of this product.

In regards to Harvoni and Epclusa, the direction here is to prefer the branded Harvoni and Epclusa products over the authorized generics. The authorized generic and the branded products all come from the same manufacturer, however the branded products are more cost effective than the authorized generics. The PA will only apply to new users, so no letters will be sent.

In regards to cyclobenzaprine, cyclobenzaprine is available in 5 mg and 10 mg tablets, and the Committee felt that this "in-between-strength" offered no clinical value over the other tablet strengths. The Committee felt that it is reasonable for a patient to cut the 5 mg tablets in half, if a 7.5 mg dose is required. The 447 patients currently on the product will be receiving letters notifying them of the new PA requirements.

6. Panel Questions and Comments

Mr. Hostettler asked if the 5mg tablet for cyclobenzaprine was scored.

CDR Hellwig stated that I have not seen all manufacturers' versions of it but the ones I have seen were not scored.

Mr. Hostettler stated that the two or three I have seen are not. Trying to break the pills usually results with a crumbled tablet. That is a problem.

CDR Hellwig thanked him for sharing and stated we would recommend using a tablet splitter.

Mr. Hostettler stated even with a pill splitter, there is the possibility of crushing the tablet.

There were no more questions or comments from the Panel. The Chair called for a vote on the Manual PA Criteria and PA Implementation Plan for the New PA Criteria.

- **New PA Criteria — PA Criteria**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **New PA Criteria — PA Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

Additional Panel Questions and Comments

Mr. Hostettler concurs with the implementation plan, but adds a comment on cyclobenzaprine. There is the potential that non-scored, 5 mg tablets will present a problem to patients. This leads to potential waste if the tablets are crushed and not usable, etc. There might be more cost in this decision than was considered.

B. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA

(CDR HELLWIG)

1. Updated PA Criteria

Updates to the manual PA criteria for several drugs were recommended by the P&T Committee due to a variety of reasons, including expanded FDA indications and safety. The updated manual PA as outlined below will apply to new users.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) updates to the manual PA criteria for Kalydeco, Noctiva nasal spray, Xifaxan, Doptelet, Humira, Kineret, Corlanor.

The updates are as follows:

a) **Cardiovascular Agents Miscellaneous: ivabradine (Corlanor)—**The Committee reviewed a request to allow an off-label use for ivabradine (Corlanor). The Committee recommended updating the PA criteria to include treatment of patients with symptomatic inappropriate sinus tachycardia (IST) or postural tachycardia syndrome (POTS). The recommendation was based on supporting clinical trial data and the 2015 guidelines from the American College of Cardiology/American Heart Association/Heart Rhythm Society, which state that Corlanor is reasonable for ongoing management in patients with these conditions.

b) **Cystic Fibrosis Agents: ivacaftor (Kalydeco)**—Kalydeco was first reviewed by the P&T Committee in July 2012, where PA was recommended, based on the package insert labeling. Additional updates were made in May 2014 and November 2018. The FDA has now approved Kalydeco for use in patients as young as 1 year of age, and the PA criteria were updated to reflect the new FDA-approved age range.

c) **Gastrointestinal-2 Agents: Miscellaneous – rifaximin 200 mg (Xifaxan)—** Manual PA criteria were previously recommended for Xifaxan for Traveler's Diarrhea at the May 2013 P&T Committee meeting. The Xifaxan PA was updated to reflect the most recent update of the 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea, requiring a trial of azithromycin or ciprofloxacin.

d) **Hematological Agents – Platelets: avatrombopag (Doptelet)**—Avatrombopag (Doptelet) and lusutrombopag (Mulpleta) are pre-procedure regimens for patients with thrombocytopenia associated with liver disease. Mulpleta does not require dose adjustment; therefore, the P&T Committee updated the Doptelet PA criteria to require use of Mulpleta first, to reduce the risk of dosing errors with Doptelet.

e) **Immune Modulators Endocrine Agents: Miscellaneous – Desmopressin nasal spray (Noctiva)**—Noctiva nasal spray was most recently reviewed for formulary placement at the May 2018 DoD P&T Committee meeting. The PA criteria for Noctiva were updated to include a comprehensive list of safety concerns, and to mirror the PA criteria for the new drug desmopressin SL tablets (Nocdurna) discussed previously on page 22 to 24 of the BAP Background Information document.

f) **Targeted Immunomodulatory Biologics (TIBs): adalimumab (Humira) and anakinra (Kineret)—**The TIBs were most recently reviewed in August 2014, with step therapy requiring a trial of adalimumab (Humira) first. The FDA recently granted new indications for Humira for moderate to severe hidradenitis suppurativa in patients 12 years and older, and for Kineret for systemic juvenile idiopathic arthritis, and the respective PAs were updated for these additional indications.

2. Updated PA Criteria—Implementation Plan

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) updates to the current PA criteria for Kalydeco, Noctiva nasal spray, Xifaxan, Doptelet, Humira, Kineret, and Corlanor in new users become effective 60 days after the signing of the minutes.

3. Physician's Perspective

At every meeting, we present updates to drugs with existing PAs to ensure the latest FDA indications or safety updates are included in our criteria. These updates to the existing PAs will only affect new patients.

For Corlanor, this is an example of where there is both clinical trial data and guideline recommendations to support an off label use. So the off-label use was added to the PA.

The other PA updates were due to due to safety issues (the Noctiva nasal spray for nocturia, and Doptelet), new indications (the TIBS Humira and Kineret, and the cystic fibrosis drug Kalydeco), or to ensure the PA criteria are in line with guidelines (the travelers' diarrhea indication for Xifaxin).

You will continue to see these types of updates at every meeting.

4. Panel Questions and Comments

There were no questions or comments from the Panel. The Chair called for a vote on the Updated PA Criteria and the Updated PA Criteria Implementation Plan.

- **Updated PA Criteria**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **Updated PA Criteria — Implementation Plan**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

IV. SECTION 703, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR (FY) 2008

(CDR HELLWIG)

At the November 2018 meeting, the P&T Committee designated Tobramycin Inhalation Solution Pak (NDC: 70644-0899-99) by Genericus, Inc. as not compliant with Section 703 requirements. After further review and comparison of tobramycin inhalation solution pak with the other available tobramycin inhalation products which do not include the nebulizer, the Committee recommended removing this drug from the Section 703 Non-Compliant Drug List and returning to its previous status of UF on the Uniform Formulary with no point of service (POS) restrictions.

1. Drugs Designated as NF

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) that the Section 703 non-compliant NDC of the following product return to its former UF status with no POS restrictions:

- Genericus, Inc.: tobramycin inhalation solution pak (*New Drug Application-authorized generic; NDC 70644-0899-99*) 300 mg/5 mL ampule-nebulizer

2. Physician's Perspective

At the November meeting, the Committee reviewed Tobramycin Inhaler Solution as a 703 non-compliant drug and exempted the requirement to receive it from mail. However, we are now recommending to remove the Tobramycin Inhaler Solution Pak from the 703 Drug List, so the drug will remain UF and will not be forced to mail. The clinical reason for this is that there is not another alternative with a nebulizer handset packaged with it.

3. Panel Questions and Comments

There were no questions or comments from the Panel. The Chair called for a vote to change the formulary status for the Section 703 NDAA FY 2008 Drugs Designated as NF.

- **Drugs Designed as NF**

Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

V. SECTION 702, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR (FY) 2018: TRICARE TIER 4/NOT COVERED DRUGS PER 32 CFR 199.21(E)(3)

(LT COL KHOURY)

Please go back to page 14 of the background document.
Background—An interim final rule implementing Section 702(b)(10) of the NDAA 2018 was published on December 11, 2018, and is found at: https://www.federalregister.gov/documents/2018/12/11/2018-26562/tricare-pharmacy-benefits-program-reforms. The interim rule allows for complete exclusion of drugs from TRICARE pharmacy benefit coverage when certain criteria are met.

The interim rule amends 32 CFR 199.21(e)(3). The P&T Committee may recommend, and the Director may, after considering the comments and recommendations of the Beneficiary Advisory Panel approve uniform formulary actions to encourage use of pharmaceutical agents that provide the best clinical effectiveness to covered beneficiaries and DoD, including consideration of better care, healthier people, and smarter spending. Specifically, the P&T

Committee may recommend complete exclusion of any pharmaceutical agent from the TRICARE pharmacy benefits program the Director determines provides very little or no clinical effectiveness relative to similar agents.

The P&T Committee was briefed on the above provisions at the February 2019 meeting. The Committee considered several factors when identifying candidates for complete exclusion from the TRICARE pharmacy benefit. These factors include, but are not limited to, the availability and quality of clinical efficacy evidence compared to alternative similar agents, determination of significant safety issues in which risks may outweigh potential benefit, identification of drugs that contain ingredients not covered by the TRICARE pharmacy benefit, or other negative concerns identified by regulatory authorities or nationally recognized expert organizations. The Committee also reviewed the practices regarding exclusion of drugs from several commercial, state, and Federal Government health care plans. Complete exclusion of drugs from the TRICARE pharmacy benefit will apply to both new and current users.

Relative Clinical and Cost-Effectiveness Summary/Rationale for Complete Exclusion—The Committee reviewed clinical efficacy, safety, and cost-effectiveness data for four candidates considered for Tier 4/Not Covered status under the TRICARE pharmacy benefit program.

- **Diabetes Non-Insulin Drugs – Biguanides Subclass: metformin ER (Glumetza brand and generics)** is an extended release formulation of metformin approved in 2005. It uses a polymer-based oral drug delivery system that makes the tablet swell, which causes retention in the stomach. Clinical trials show Glumetza is at least as efficacious as metformin immediate-release (IR) (Glucophage) in all measures of glycemic control. There is no evidence to suggest that differences in the extended-release properties of Glumetza confer any benefits in efficacy or safety compared to the other metformin ER formulations (Glucophage XR).

  Overall conclusion: A significant cost difference exists between Glumetza and other generic metformin ER formulations (Glucophage XR), with no additional clinical benefit. The P&T Committee concluded that the needs of TRICARE beneficiaries can be met by other metformin ER or metformin IR products available on the Uniform Formulary.

- **Pain Agents – Combinations Subclass: naproxen/esomeprazole** (**Vimovo**) is a fixed-dose combination of two over-the-counter (OTC) drugs, a nonsteroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor (PPI). The Committee agreed that use of fixed dose combination therapies offers patients a convenient formulation for improving adherence. However, this particular combination of an NSAID, which is typically targeted for short-term use, and a PPI, which has limited data to support use beyond eight weeks, is potentially harmful. There is no data to suggest that using other prescription or OTC NSAIDs concurrently with PPIs would not provide the claimed benefit of the individual ingredients found in Vimovo.

  Overall conclusion: The Committee concluded that Vimovo is not cost-effective relative to other NSAIDs and PPIs used concurrently. The needs of TRICARE beneficiaries can be

met by the concurrent use of similar single ingredient OTC or prescription NSAIDs and PPIs available on the Uniform Formulary.

- **Pancreatic Enzyme Replacement Therapy: pancrelipase (Zenpep)** and the other pancreatic enzyme replacement therapies (PERTs) were reviewed for formulary status in May 2018. The Committee concluded there is a high degree of therapeutic interchangeability among the PERT products, and having one on the formulary is sufficient to meet the needs of Military Health System (MHS) patients. Creon was designated as the sole step-preferred PERT, and the cost-share was lowered to the generic Tier 1 cost-share to provide a greater incentive for beneficiaries to use the more cost effective PERT formulation. Zenpep was designated nonformulary and non-step-preferred, requiring a trial of Creon in all users. Zenpep provides very little to no clinical effectiveness relative to Creon or the other PERTs.

  Overall conclusion: The needs of TRICARE beneficiaries can be met by Creon and the other available PERTs.

- **Targeted Immunomodulatory Biologics (TIBs): brodalumab** (**Siliq**) is an injectable TIB approved for treating plaque psoriasis and is the only TIB that carries a black box warning for suicide. An FDA safety review of all clinical trials with Siliq reported 36 patients with attempted suicide, or suicidal ideation, and 6 patients with completed suicides. This safety risk is comparable to other biologic agents that the FDA denied marketing approval, and is significantly greater than any of Siliq's clinical comparators. The drug also has Risk Evaluation and Mitigation Strategies (REMS) requirements that mandate certification of both prescribers and pharmacies.

  Siliq was reviewed as a newly approved drug at the August 2017 DoD P&T Committee meeting and recommended for nonformulary status, with PA criteria requiring a trial of adalimumab (Humira) and secukinumab (Cosentyx) first.

  Overall conclusion: The P&T Committee concluded that relative to the other nine TIBs that are FDA-approved to treat psoriasis, Siliq imposes a significant safety risk without offering any unique advantage in efficacy or in specific sub-populations. However, a subset of patients with plaque psoriasis will develop highly refractory disease, and Siliq may be of value as an alternate agent for patients who do not respond to other treatment options.

- **Corticosteroids-Immune Modulators – High Potency**: **Halobetasol propionate 0.05% foam (Lexette)** is a topical corticosteroid, which were reviewed for formulary placement in August 2013. There is a high degree of therapeutic interchangeability within a particular potency category and vehicle. There are currently 28 other high-potency topical corticosteroids on the formulary, including 12 products formulated in a hair-friendly vehicle, including foam, gel, lotion, shampoo, and solution. The new foam formulation of Lexette offers no clinically meaningful advantages over the high-potency topical steroids available on the UF.

Overall conclusion: The P&T Committee concluded that Lexette provides little to no clinical benefit and its cost is prohibitive relative to the numerous formulary alternatives. Currently, the needs of TRICARE beneficiaries can be met by the 28 other formulary high-potency topical steroids.

1. **TRICARE Tier 4/Not Covered Recommendation—**The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) designating the following products as Tier 4/Not Covered under the TRICARE pharmacy benefits program.

   - metformin ER (Glumetza) brand and generics
   - naproxen/esomeprazole (Vimovo)
   - pancrelipase (Zenpep)
   - halobetasol propionate 0.05% foam (Lexette)

2. **Recommendation Maintaining Current NF Status for Siliq**—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) maintaining the current formulary status for brodalumab (Siliq). The Committee acknowledged Siliq's place in therapy for highly selected patients who are refractory to other treatment options. Siliq will remain NF and non-step-preferred, requiring a trial of Humira, Cosentyx, Stelara, Tremfya, Ilumya and Taltz first. The current PA will remain in place to mitigate risk of suicidal ideation.

3. **Tier 4/Not Covered Implementation Period**—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) for Zenpep, Glumetza brand and generics, and Vimovo, and (17 for, 0 opposed, 0 abstained, 1 absent) for Lexette: 1) an effective date of the first Wednesday after a 120-day implementation period at all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/Not Covered recommendation.

4. **Physician's Perspective**

   For the drugs that were selected for Tier 4 status, the active ingredients for all the products are available in other formulations that are on the UF or OTC. For the impacted beneficiaries, about 400 patients will be affected by the Glumetza recommendation, 550 patients for the Vimovo recommendation; and about 600 patients for the Zenpep recommendation. Letters will be sent to the patients. Since this is a new regulation, we are allowing a longer implementation period of 120 days.

   The P&T members felt that these drugs were good candidates for Tier 4 status, since it was difficult for the Committee to develop clinical medical necessity criteria that would warrant use of the Tier 4 product over the formulary alternatives. The Committee could not determine a valid clinical reason as to why these drugs should be used. The physician experts have concluded that there is no role for these drugs.

   The Committee did take into consideration multiple factors when selecting the Tier 4 candidates. That is one reason why Siliq was recommended to not be placed on Tier 4 status, and will remain as NF.

5. Panel Questions and Comments

Mr. Hostettler stated he has concerns regarding the P&T Committee decision for Zenpep. He understands the rationale and reason regarding the decision for the other drugs. However, approximately 600 patients completed the PA process for Zenpep. If they completed the process, there must have must have been some medical justification. He does not understand the decision to remove it from the pharmacy benefit and asks for an explanation.

Lt Col Khoury summarizes several reasons for the P&T Committee decision to move Zenpep to Tier 4.

- It is not a chronic medication and many of the patients come on and come off the drug;
- For the clinical evaluation, there is no information to support why Zenpep is being used over other alternatives, since it isn't typically a chronic medication that is being used over the long-term; and
- In class reviews, we highlighted some of the alternative options. We are trying to encourage behaviors in support of beneficiaries taking advantage of the Tier 1 agent. We suspect that is not being not fully effective but we do not' know why. It benefits patients to possibly shift to one that is both clinically effective and cost effective since it has Tier 1 copay.

Mr. Hostettler asked if the step therapy that was in place required trials of Creon first.

Lt Col Khoury stated there was no step therapy in that class. The PA was built to not require a PA for Creon but require a PA for the other drugs. There was no requirement to try all the agents; we were trying to encourage patients to shift to Creon. What appears to be happening is that the tools are not fully effective.

Mr. Hostettler stated, in his opinion, the better decision for patients is to implement an approach for Zenpep that is similar to the decision for Siliq. Placing Zenpep last on a PA or Step Therapy would give the patient the option to complete the steps and try the other drugs, if they need the drug. This is a better approach than having the patient with a chronic disease, change their treatment that is working. More importantly, this change may force a decision on the patients' families to change what is working or pay 100% of cost. I think the approach you took with Siliq makes perfect sense in this particular case as well. It is different from the 28 steroids and the metformin products; I think those are different but this one has a potential clinical need that cannot be fulfilled once this decision is made. I am concerned about this decision. It is rare that the BAP makes strong recommendations. If I can get my colleagues to agree to recommend an approach for Zenpep that is similar to Siliq, it gives those patients who have tried everything else and it is not working the opportunity to get Zenpep. Make it non-formulary with the highest co-pay but give them the option as opposed to removing it from the pharmacy benefit.

Lt Col Khoury stated that providers do not see a clinical necessity for Zenpep. If there was data to support a decision similar to Siliq, I believe the P&T committee would have made that decision. We do not have any information to support that conclusion with Zenpep.

Mr. Hostettler stated I believe it is fair to appreciate that not every patient responds the same to every product. Approximately 600 patients complete the PA process for Zenpep. This recommendation is to move it to Tier 4 will require the patient to make another change in therapy. In my opinion, this is a situation where I believe we are going too far. I can understand making it last in line, like the Siliq approach, but I cannot understand removing it from the Pharmacy Benefit.

Dr. Peloquin asked how many other PERTs are there.

Lt Col Khoury responded that I believe there are approximately five including Creon. For example, with Siliq, in our analysis we looked at what patients had been on before. In many instances, they had not tried all of the alternatives. In our opinion, patients were potentially being put at risk. When we looked at Zenpep, patients had not been on other alternatives despite having multiple alternatives available. There was no clear clinical reason that we could find for not trying all the alternatives. I want to make sure that everyone understands that the majority of patients are not chronic, in our analysis; they are not on the drug for the long term. Most start taking the drug and they stop. They might have been on it in the past but this does not preclude them from trying again. It is in the patient's best interest, from a copay perspective, to try to shift to the drug that has the Tier 1 co-pay, if they have not tried the Creon.

Mr. Hostettler stated that I agree that they should try the other alternatives first, especially Creon at a lesser cost. As discussed in our executive meeting, there is no appeal process on Tier 4. Therefore, there are no options if the patient reaches a point where they need another option. In my opinion, it is hard to take away real, FDA-approved options when it is available. This decision affects 600 patients; I just do not fully appreciate that.

Dr. Bertin has a more general observation. We did have some discussion at our preliminary administrative meeting on this topic. Most of us agree that Tier 4 is probably a useful tool for this organization to promote rational drug therapy and we simply need to recognize that. Part of our issue is that this was rushed into implementation. It is still under an interim rule, the comments on the rule were due on February 11. We do not know whether there are significant comments that may lead to significant modifications for the final rule. I hope that the additional comments are being considered. The other issue is simply information for beneficiaries and those that represent them and their interest. This was really the first opportunity that the BAP learned of this Tier 4 implementation and we are supposed to be representing the interests of our beneficiaries. It may be that extensive information, patient information, and organization information is being developed but

it really is not out there yet and we would urge that information be developed and got out into the hands of beneficiaries who may well be significantly impacted, especially those who are faced with a situation. As my colleague pointed out, this is a no appeal denial. I believe that beneficiaries need to understand what they may be up against. We understand that there are not going to be lots and lots of drugs proposed for Tier 4 but we don't know that for sure. This could be affecting many, many of our beneficiaries.

Mr. Ostrowski stated that he is having a difficult time with this vote because the Panel did not have an issue with three of the four drugs. We only have concerns about Zenpep. Is it possible to split the vote and separately vote on the three drugs and Zenpep. This would allow the other three to move through the process.

Col Hoerner agreed that to split the vote. He also shared that there was a single provider from across the entire enterprise that came forward who saw potential use for Siliq. As a result, the Committee decided not to move it to Tier 4. This was not the case with Zenpep. Not a single voice or provider identified a potential need for this product. The beneficiaries we identified had not tried the Creon. It appears the the doctor just wrote a prescription and they just paid the higher copay and went straight to it.

Mr. Hostettler asked was there not a PA that prevents the patient from trying all the available alternatives.

Lt Col Khoury stated there is a PA but we do not understand the rational or reason why the patients did not try the alternatives. That data has not been available to us. There has been no patient or provider comments that are based on evidence that says these alternatives are all inappropriate. In my opinion, allowing it to exist harms patients in the sense of they do not necessarily know the cost until they have that copay. If they do not know the alternatives of those different copays, this agent will continue to be on there for them to be faced with a higher financial burden and not maintain any relative additional clinical benefit.

Mr. Hostettler said that I appreciate what you are saying but I still think it should be an option and if you want to build a step approach where it is last, I do not have a problem with that. At least it is available. If I am not mistaken, what I am also hearing is that you had a process in place, PA or step, to get there and it did not do the job. Either you wrote a bad process or the physicians filled it out in error. Something is array from what you are explaining to me and that to me does not mean we should throw the drug out.

Lt Col Khoury stated initially, all drugs are covered and that is part of the bad process. Other people have excluded Zenpep so patients do not get on it. We are dealing with this in between period where patients will be on drugs that either the provider does not necessarily know the details of the cost and/or the clinical efficacy. Their decision is predicated on historical data. The prescriber is used to prescribing

the drug and all the information affecting the patient may not be driving the decision making whether it be cost and/or clinical

Mr. Hostettler stated that I wish we had the document that is in place for these 600 patients that completed the PA for Zenpep in front of us now so we that can see exactly what we're talking about. I appreciate your comments but I still think there should be an opportunity.

CDR Hellwig pulled the Zenpep PA and its criteria from the Formulary Search Tool ST and read it to the Panel. Although we have the PA in place requiring Creon, we have seen that quit a few of our patients on Zenpep have not tried Creon.

Mr. Hostettler asked when the requirement changed to a formulary status. You stated a change in formulary for new products.

Lt Col Khoury stated the PA was in effect since November.

Mr. Hostettler asked if the majority of these patient received Zenpep prior to November.

Lt Col Khoury stated that numbers you have were from last 12 months trailing.

Mr. Du Tiel stated that I appreciate everyone's comments regarding Zenpep and I understand the Tier 4 concept. He also appreciates Lt Col Khoury's comments that if it is not moved to Tier 4, it is still available and patients can get it if they want. However, if it is on Tier 4, the patient will have to pay full cost and we do not know how much that would be. I support my colleague in recommending making it the absolute last step, NF, etc. Do not put it out of reach for patients just yet. I encourage you to not throw people off drug that got onto it prior to these criteria in the first place and they are using it. I am a little nervous about it.

Dr. Dager stated I think it is an appropriate drug to have available but it would be nice to see it have a different PA than just the one-step. Have a step 2 or 3, maybe separate from the other agents.

Mr. Ostrowski stated we will split this decision so that the 3 drugs we do concur with can make it through this process. I concur with the remarks from the Panel regarding Zenpep. Rather than moving Zenpep to Tier 4, there must be other options available.

Dr. Peloquin stated one of the other concerns I am hearing is this decision to move it to Tier 4 is so close to the decision in November. Patients recently completed the process in November and there is another change approximately 120 days after. From a beneficiary abrasion perspective, those patients are being moved again. That happens sometimes, I know, but relative to that as you look at it. It is something to consider from an abrasion perspective.

Mr. Ostrowski sends a request to the P&T Committee. Restructure the decision for Zenpep and present to the Panel at a meeting in the future.

There were no more comments from the Panel. The Chair called for a vote on the TRICARE Tier 4 recommendations for Glumetza, Vimovo, and Lexette.

- **TRICARE Tier 4/Not Covered Recommendation for Glumetza, Vimovo, and Lexette**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **Recommendation Maintaining Current NF Status for Siliq**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

- **Tier 4/Not Covered Implementation Period for Glumetza, Vimovo, and Lexette**

  Concur: 7 Non-Concur: 0 Abstain: 0 Absent: 2

The Chair called for a vote on the TRICARE Tier 4 recommendations for Zenpep.

- **TRICARE Tier 4/Not Covered Recommendation for Zenpep**

  Concur: 0 Non-Concur: 7 Abstain: 0 Absent: 2

- **Tier 4/Not Covered Implementation Period for Zenpep**

  Concur: 0 Non-Concur: 7 Abstain: 0 Absent: 2

ADDITIONAL PANEL QUESTIONS AND COMMENTS.

Dr. Peloquin stated that the communication plan is vital to the Tier 4 Implementation Plan.

Mr. Hostettler stated, in the future, we anticipate tiering and pricing to drive patient decisions in the future. Unfortunately, patients, much like providers, do not know anything about the pricing and tiers until they go to a pharmacy and by then it is too late. The process is already in place. To go back and get it changed could possibly lead to lengthy delays getting another appointment, getting the physician involved again to re-write that prescription. Let us not forget that the tiering process, while it will drive decisions, is not the best way to go about it. More education, both to the patient and provider, is the best approach.

Mr. Ostrowski thanked everyone for coming and participating. He also thanked the Panel, the participation of new members, looks forward to seeing everyone again.

Meeting Concludes

Appendix 1 – Informational Item – Summary of Recommendations and Beneficiary Impact February 2019

Appendix 2 – Brief Listing of Acronyms Used in this Summary

Mr. Jon Ostrowski
UF BAP Chairperson

INFORMATIONAL ITEM—SUMMARY OF RECOMMENDATIONS AND BENEFICIARY IMPACT FEBRUARY 2019

Table of Implementation Status of UF Recommendations/Decisions Summary

DoD PEC Drug Class	UF Drugs	NF Drugs	Implement Date	Notes and Unique Users Affected
Migraine Agents – CGRP Antagonist Prophylaxis Subclass	▪ erenumab (Aimovig) ▪ fremanezumab (Ajovy) ▪ galcanezumab (Emgality)	▪ None	Pending signing of the minutes / 30 days	▪ Manual PA criteria applies to all new users Unique Users Affected not applicable; new users only
Oncological Agents: CYP-17 Inhibitors Subclass and 2nd-Generation Antiandrogen Subclass	CYP-17 Inhibitors *Step-preferred* ▪ abiraterone acetate micronized (Yonsa) *Non-step-preferred* ▪ abiraterone acetate (Zytiga, generics) 2nd-Generation Antiandrogens *Step-preferred* ▪ enzalutamide (Xtandi) *Non-step-preferred* ▪ apalutamide (Erleada)	▪ None	Pending signing of the minutes / 90 days	▪ Manual PA required ▪ Yonsa and Xtandi will be Tier 1 copay/cost-shared **CYP-17 Inhibitors Subclass** Unique Users Affected Mail – 464 MTF – 155 Retail – 620 Total – 1,239

Drugs with New Prior Authorization Criteria—Unique Utilizers Affected

Drug	MTF	Mail Order	Retail	Total
Antihistamine-1: First Generation and Combinations – dexchlorpheniramine maleate 2 mg/5 mL oral solution (Ryclora)	0	0	0	0
Skeletal Muscle Relaxants and Combinations: cyclobenzaprine 7.5 mg	16	52	379	447

Tier 4/Not Covered Drugs—Unique Utilizers Affected

Drug	MTF	Mail Order	Retail	Total
metformin ER (Glumetza brand) (Glumetza generic)	24 28	64 266	5 17	93 311

Drug	MTF	Mail Order	Retail	Total
naproxen/esomeprazole (Vimovo)	47	455	54	556
pancrelipase (Zenpep)	115	297	179	591

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 the Panel discussions are listed below for easy reference. The term "Pan" in this summary refers to the "Uniform Formulary Beneficiary Panel," the group who's meeting in the subject of this report.

- AA – Antiandrogen
- AAN – Academy of Neurology
- AASLD - American Association for the Study of Liver Diseases
- ABSSSI – Acute Bacterial Skin and Skin Structure Infection
- ADA-SCID – Adenosine Deaminase Severe Combined Immune Deficiency
- AHS – Academy of Headache Society
- ALS – Amyotrophic Lateral Sclerosis
- ALK – Anaplastic Lymphoma Kinase
- AML – Acute Myelogenous Leukemia
- ANCA – Antineutrphil Cytoplasmic Antibody-accociated.
- AUA – American Urological Association
- BAP – Beneficiary Advisory Panel
- BCF – Basic Core Formula
- BIA – Budget Impact Analysis
- BOO – Bladder Outlet Obstruction
- CABP – Community-Acquired Bacterial Pneumonia
- CDC –Center for Disease Control
- CFR – Code of Federal Regulations
- CGRP – Calcitonin Gene-Related Peptide
- CKD – Chronic Kidney Disease
- CMA – Cost-minimization Analysis
- COA – Commissioned Officers Association
- COPD – Chronic Obstructive Pulmonary Disease
- CR generics – Controlled-Released
- CRPC – Castration-resistant Prostate Cancer
- CV – Cardiovascular
- DAPA – Distribution and Pricing Agreement
- DDAVP – Desmopressin Acetate Tablets
- DFO - Designated Federal Officer
- DHA – Defense Health Agency
- DoD – Department of Defense
- ER – Extended Release
- FACA - Federal Advisory Committee Act
- FAP – Familial Amyloidotic polyneuropathy
- FDA – Federal Drug Administration
- FL – Follicular Lymphoma
- FMS – Ferline McDonough Sarcoma
- FY – Fiscal Year

- G6PD – Glucose 6 Phosphate Dehydrogenase
- gBRCAm – Germline BRCA-mutated
- GI – Gastrointestinal
- GnRH – Gonadotropin-releasing Hormone
- HCV DAA – Hepatitis C Agents: Direct-Acting Agents
- HER2- - Human Epidermal Growth Factor Receptor2-negative
- HSPC – Hormone-sensitive Prostate Cancer
- hTTRA – Hereditary Transthyretin-mediated amyloidosis
- IBD – Inflammatory Bowel Disease
- ICER – Institute for Clinical and Economic Review
- IDSA - Infectious Diseases Society of America
- IR – Immediate Release
- IST – Inappropriate Sinus Tachycardia
- ITP – Idiopathic Thrombocytopenia
- IV – Intravenous
- LAMA – Long-Acting Anti-Muscarinic Agent
- LEMS – Lambert-Eaton Myasthenic Syndrome
- MACE – Major Adverse Cardiovascular Events
- mCRPC – Metastatic Castration-Resistant Prostate Cancer
- MEK inhibitors – Chemical or drug that inhibits the mitogen-activated protein kinase enzymes
- MFS – Metastatis-free Survival
- Mg – Milligram
- MHS – Military Health Sytem
- MIDAS – Migraine Disability Assessment
- MN forms – Medical Necessity Form
- MMD – Monthly Migraine Days
- MPFID – Migraine Physical Functional Impact Diary
- MTF – Military Treatment Facility
- NASH – Non-Alcoholic Steatohepatisis
- NCCN – National Comprehensive Cancer Network
- NDAA – National Defense Authorization Act
- NDC – National Drug Code
- NF – Non Formulary
- nmCRPC – Non-Metastatic Castration-Resistant Prostate Cancer
- NSAID – Nonsteroidal Anti-Inflammatory Drugs
- NSCLC – Non-Small Cell Lung Cancer
- NTRK – Neurotrophic Tropomyosin Receptor Kinase
- OTC –Over the Counter
- P&T – Pharmacy & Therapeutics
- PA – Prior Authorization
- PERT – Pancreatic Enzyme Replacement Therapy
- pH – Potential Hydrogen
- POD – Pharmacy Operations Division
- POS – Point of Service
- POTS – Postural Tachycardia Syndrome
- PPI – Proton Pump Inhibitor

- PRES – Posterior Reversible Encephalopathy Syndrome
- PSA – Prostate-specific Antigen
- PSADT – Prostate-specific Antigen Doubling Time
- REMS program – Risk Evaluation and Mitigation Strategy
- Rx – Medical Prescription
- SIBO – Small Intestine Bacterial Overgrowth
- SL – Sublingual
- SQ - Subcutaneous
- TIB – Targeted Immunomodulatory Biologic
- TRICARE – Healthcare Network
- UF – Uniform Formulary
- USC – United States Code
- XR – Extended Release