EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel Comments
26 March 2015

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

1. NEWER SEDATIVE HYPNOTICS (SED-1s) DRUG CLASS - Tasimelteon (Hetlioz):

A. The Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** Hetlioz be designated NF due to the lack of compelling clinical advantages, other than its unique indication, and cost disadvantage compared to SED-1 agents on the Uniform Formulary.

B. Hetlioz Prior Authorization (PA) Criteria:

Automated (step therapy) and manual PA criteria were recommended at the August 2014 DoD P&T Committee meeting and implemented December 10, 2014 for tasimelteon, requiring a trial of zolpidem immediate release (IR) or zaleplon first, and a diagnosis of blindness. The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** updating the PA criteria for tasimelteon, including removing the step therapy requirement, and requiring all new patients to undergo the manual PA process.

The full PA criteria are as follows:

The previous automated (step therapy) criteria for Hetlioz that requires a trial of zolpidem IR or zaleplon no longer apply. Manual PA criteria apply to all new users of Hetlioz.

Manual PA criteria: Hetlioz is approved if:

1. The patient is totally blind and has a documented diagnosis of non-24 sleep wake disorder,
   AND
2. The patient has had a trial of melatonin and either failed or had an adverse event,
   AND
3. The patient is not taking a drug that will interact with tasimelteon (i.e., beta blockers or strong CYP3A4 inducers).

PA Criteria will expire after 6 months. If a patient has not responded after 6 months, they will be deemed a non-responder.

E. Hetlioz's Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1) An effective date of the first Wednesday after a **60-day** implementation period in all points of service; and,
2) The DHA will send a letter to the beneficiaries affected by the Uniform Formulary decision.

Summary of Physician's Perspective:

The Committee recommended non-formulary placement for Hetlioz, since it is not cost-effective. The Committee did recognize the unique indication for Hetlioz. However, for non-24 sleep wake disorder, the usual standard of treatment is to try a melatonin supplement. This was why the PA criteria were revised to include a trial of melatonin, and then allow Hetlioz if a patient doesn't respond to or has an adverse reaction to the supplement. The Committee did recommend removing the previous step therapy criteria (where a trial of generic Ambien or Sonata was previously required), since there was the potential that a patient with insomnia could meet the requirement to receive Hetlioz. Other products on the Uniform Formulary [for example Ambien, Sonata or Lunesta)] should be prescribed for insomnia instead of Hetlioz. The Committee felt that manualPA criteria was the most appropriate method to ensure Hetlioz is used in the patients for which it is indicated. Additionally, other civilian healthcare plans do require a trial of melatonin and prior authorization for Hetlioz. Currently there are six patients in the MHS who are receiving Hetlioz. These patients will be "grandfathered," and not required to go through the new manual PA criteria.

Summary of Panel Questions and Comments:

There were no questions or comments or comment from the Panel members. Without further discussion, the Chair asked for a vote on the UF recommendation, PA Criteria, and UF and PA Implementation Plan for Tasimelteon (Hetlioz).

1. **Tasimelteon (Hetlioz) - UF Recommendation:**

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

Director, DHA: 5 May 15

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

2. **Tasimelteon (Hetlioz) - PA Criteria:**

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

Director, DHA: 5 May 15

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

3. **Tasimelteon (Hetlioz) –UF and PA Implementation Plan:**

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

Director, DHA: 5 May 15

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

2. SODIUM-GLUCOSE CO-TRANSPORTER 2 (SGLT-2) INHIBITOR drug class - Empagliflozin (Jardiance):

A. The Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** Jardiance to be designated Non-Formulary due to the lack of compelling clinical advantages, safety concerns, lack of long-term outcomes, and cost disadvantage compared to the oral Uniform Formulary products used for treating diabetes.

B. Prior Authorization Criteria for Jardiance:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** a trial of metformin or a sulfonylurea and a DPP-4 inhibitor in all new and current users of Jardiance, consistent with the Prior Authorization requirements in place for Invokana and Farxiga.

The full PA criteria are as follows:

All new and current users of Jardiance are required to try metformin or a sulfonylurea, and a DPP-4 inhibitor before Jardiance.

Automated PA criteria: The patient has filled a prescription for metformin or a sulfonylurea, AND a DPP-4 inhibitor at any Military Health System (MHS) pharmacy point of service [this includes Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

AND

Manual PA criteria: If automated criteria are not met, Jardiance is approved AND a trial of metformin or suflonylurea AND a DPP-4 inhibitor is NOT required if:

The patient has experienced any of the following issues on metformin:
a. impaired renal function precluding treatment with metformin
b. history of lactic acidosis

2. The patient has experienced any of the following issues on a sulfonylurea:
a. hypoglycemia requiring medical treatment

3. The patient has had inadequate response to metformin or a sulfonylurea or a DPP-4 inhibitor.

4. The patient has a contraindication to metformin or a sulfonylurea or DPP-4 inhibitor.

C. The Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. an effective date of the first Wednesday after a **90-day** implementation period in all Points of Service; and,
2. DHA send a letter to beneficiaries affected by the Uniform Formulary decision.

Summary of Physicians Perspective:

There was no controversy with the recommendation for non-formulary status. This is the third SGLT2 inhibitor that the Committee has reviewed. The three drugs in this class all have similar effects on lowering blood glucose levels, and also similar adverse effect profiles. The long-term safety with these drugs is not known at this time.

The same PA criteria that apply to the other SGLT-2 inhibitors were recommended for Jardiance. Additionally, all the oral diabetes drugs have the requirement for a trial of metformin or a sulfonylurea first.

There are combinations of an SGLT2 inhibitor with other diabetes drugs, including metformin and the DPP-4 inhibitors, that have recently been approved, and more are in the pipeline. Because of this, the SGLT2- inhibitors will be reviewed by the Committee in August 2015.

Summary of Panel Questions and Comments:

Dr. Anderson asked for clarification regarding the PA Criteria for the SFLT2 inhibitors, the 90-day implementation plan and the beneficiary notification letters. More specifically, he asks if the PA criteria applied to all the SGLT2 inhibitors and if the other 2 were also designated non-formulary? Also, would new users be allowed to get a

prescription for Jardiance during the 90-day implementation period as well as receive a beneficiary notification letter?

CAPT Down stated that the PA criteria did apply to all of the SGLT2 inhibitors and that the other two (2) are designated non-formulary. He further states that after the minutes are signed, we have 90-days to complete the implementation plan. This includes notifying the beneficiary of the change and what needs to be done to either continue or change the medication. Beneficiaries who just stated the medication will receive a beneficiary notification letter.

Dr. Kugler interjected the same process/procedure that we are currently using.

Dr. Delgado asked how many beneficiaries are currently on this medication.

Dr. Allerman responded that the information is located on page 3 of the handout. There are 913 beneficiaries currently on the medication.

There were no further questions or comments from the Panel. The Chair asked for a vote on the UF recommendation, PA criteria, and UF and PA Implementation Plan for Empagliflozin (Jardiance).

1. **Empagliflozin Jardiance UF Recommendation:**

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

   Director, DHA: 5 May 15

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

2. **Empagliflozin Jardiance PA Criteria:**

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

   Director, DHA: 5 May 15

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

3. **Empagliflozin Jardiance Implementation Plan:**

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

   Director, DHA: 5 May 15

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

3. **ANTIPLATELET AGENTS - Vorapaxar (Zontivity):**

A. Zontivity's Uniform Formulary Recommendation:

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** Zontivity be designated Non-Formulary based on clinical and cost effectiveness.

B. The Uniform Formulary Implementation Plan:

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** to following:

1. An effective date of the first Wednesday after a **90-day** implementation period in all POS; and,
2. DHA sends a letter to the beneficiaries affected by the UF decision

Summary of Physician's Perspective:

The Committee recommended non-formulary placement, due to the risk of bleeding and also cost-effectiveness. All the other antiplatelets are available on the formulary.

We did ask for input from the cardiology consultants from the three services (army, navy, air force). Overall, they felt that Zontivity should not be added to the formulary, due to the high bleeding risk, and limited number of clinical trials.

The Committee did feel that the Medical Necessity process would be the best mechanism to allow a co-pay reduction for those patients who are appropriate candidates for Zontivity, and that a prior authorization was not needed.

Summary of Panel Questions and Comments:

There were no questions or comments or comment from the Panel members. Without further discussion, the Chair asked for a vote on the UF recommendation and the UF Implementation Plan for Vorapaxar (Zontivity).

1. **Vorapaxar (Zontivity) - UF Recommendation:**

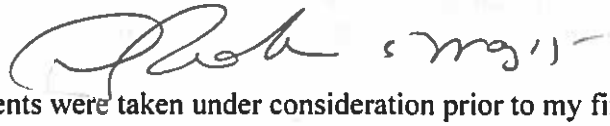
Concur: 6 Non-Concur: 0 Abstain: 0 Absent: 1

Director, DHA: 5 May 15

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

2. **Vorapaxar (Zontivity) – UF Implementation Plan:**

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

Director, DHA: 

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

3. **PHOSPHODIESTERASE-5 (PDE-5) INHIBITORS FOR ERECTILE DYSFUNCTION (ED) - Avanafil (Stendra):**

A. Stendra's Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** Stendra be designated Non-Formulary due to the lack of compelling clinical advantages and the cost disadvantage compared to the step-preferred product, sildenafil (Viagra).

B. Stendra's PA Criteria:

Existing automated PA criteria (step therapy) for the PDE-5 inhibitors used for the treatment of ED requires a trial of sildenafil (Viagra), prior to receiving another PDE-5 inhibitor. The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** PA criteria for all current users of avanafil (Stendra), similar to the existing PA criteria for the class.

The full PA criteria are as follows:

PA criteria apply to all current users of avanafil.

Automated PA criteria: Coverage approved for treatment of ED if:

1. The patient has received a prescription for sildenafil (Viagra) at any Military Health System pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days, AND
2. The patient is a male aged 40 years or older.

Manual PA criteria: A trial of sildenafil (Viagra) is not required if:

1. Patient has tried sildenafil (Viagra) and has had an inadequate response or was unable to tolerate treatment due to adverse effects.
2. Treatment with sildenafil (Viagra) is contraindicated.
3. Patient is between 18 and 39 years of age and is being treated for ED of organic or mixed organic/psychogenic origin. [Must try sildenafil (Viagra) first or indicate inability to due to reasons stated above in 1 or 2.]
4. Patient is between 18 and 39 years of age and is being treated for drug-induced ED where the causative drug cannot be altered or discontinued. [Must try sildenafil (Viagra) first or indicate inability to due to reasons stated above.]

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

Use of sildenafil, tadalafil, or avanafil (Stendra) for preservation/restoration of erectile dysfunction after prostatectomy. PA expires after one year.

C. The Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. Effective date of the first Wednesday after a 90-day implementation period in all points of service.

Summary of Physician's Perspective:

Once again, there is no controversy here for non-formulary placement. The other PDE-5 inhibitors have been available for over 10 years, so this product is very late to the market. Although it has a slighter faster onset of action than the other PDE-5s, since there are no head to head trials, there is no data to show that Stendra would be more effective than the other products for erectile dysfunction.

The recommended PA criteria for Stendra reflect what is already in place for the other products (Viagra, Cialis and Levitra). In addition to treatment for erectile dysfunction, the Committee did recognize the one trial available that evaluated Stendra following prostatectomy, so this was added to the PA criteria, in addition to ED.

Summary of Panel Questions and Comments:

Dr. Delgado recognizes that there was a differentiation on the automated versus the manual PA criteria with regard to age. Is that some reason that the automated PA can't be 18 and over? It appears to be redundant based on the fact that the PA criteria requires the beneficiary to try one of the other medications.

Dr. Allerman states that this particular set of PA criteria for Viagra has been in place for several years. Basically, if a male is 40 years or older, it's almost like it's an automatic pass. Several years ago it was a requirement for a male to be aged 45 and over. That was lowered to 40. However, there was a lot of discussion about decreasing the age even more. There was also concern that younger patients, who didn't have any type of organic disease, would want to get a PDE-5 because of performance anxiety. This is the particular criteria that has been applied to Cialis, Avetra, and Viagra dating back to 2011. Additionally, If the patient already has a PA criteria for erectile dysfunction, there's no expiration date. If they tried it, that would be in the profile and won't hit the prior authorization. It was Just for the following prostatectomy, the data just shows that after one year, there is no data.

Dr. Anderson asks if quantity limits are required with the ED therapies in addition to the PA?

Dr. Allerman responded yes. There have been quantity limits for several years. It is a collective quantity limits of 6 per month. For example, one month the patient is on Viagra, then the next month the patient changes to Cialis. It's still 6 months collectively. Part of the purview of the BAP is actually not to comment on quantity limits, but we do have these in place. However, she adds for patients who need daily use of a PDE-5 inhibitor for indication such as prostatectomy, pulmonary hypertension and Raynaud's for those indications can get daily therapy. The quantity limit can be overridden.

There were no further questions or comments from the Panel. The Chair asked for a vote on the UF recommendation and the UF Implementation Plan for Avanafil (Stendra).

1. **Avanafil (Stendra) - UF Recommendation:**

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

Director, DHA: 5 May 15

☐ ~~These~~ comments were taken under consideration prior to my final decision

2. **Avanafil (Stendra) - UF Implementation Plan:**

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

Director, DHA: 5 May 15

☐ ~~These~~ comments were taken under consideration prior to my final decision

5. PROTON PUMP INHIBITORS (PPIs) - Esomeprazole Strontium:

A. Esomeprazole Strontium's Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** esomeprazole strontium be designated Non-Formulary due to the lack of compelling clinical advantages and the cost disadvantage compared to the other PPIs on the Uniform Formulary.

B. Esomeprazole Strontium's PA Criteria:

Existing automated PA criteria (step therapy) for the PPIs requires a trial of Nexium or omeprazole first, prior to receiving another PPI. The P&T Committee recommended **(14 for,**

0 opposed, 1 abstained, 1 absent) PA criteria for all new and current users of esomeprazole strontium similar to the existing PA criteria for the class.
The full PA criteria are as follows:

PA criteria apply to all new and current users of esomeprazole strontium.

Automated PA criteria: The patient has filled a prescription for omeprazole (Prilosec or its generics), pantoprazole tablets (Protonix or its generics), or esomeprazole magnesium (Nexium) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order), during the previously 180 days.

AND

Manual PA criteria: A trial of omeprazole (Prilosec or its generics), pantoprazole tablets (Protonix or its generics), or esomeprazole magnesium (Nexium) is NOT required if:

1. The patient has tried omeprazole, pantoprazole tablets, and esomeprazole magnesium (Nexium) and had an inadequate response.
2. The patient has tried omeprazole, pantoprazole tablets, and esomeprazole magnesium (Nexium) and was unable to tolerate it due to adverse effects.
3. Treatment with omeprazole, pantoprazole tablets, and esomeprazole magnesium (Nexium) is contraindicated (e.g., hypersensitivity; moderate to severe hepatic insufficiency).

C. The Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. An effective date of the first Wednesday after a 90-day implementation period in all POS; and,
2. DHA sends a letter to beneficiaries affected by the UF decision

Summary of Physician's Perspective:

This product is simply Nexium, with a different salt. The package insert largely reflects what is found in the Nexium package insert, and data from the Nexium trials was used to gain FDA approval for this product.

The PPIs are another drug class that have been on the market for over 10 years, and now both generic products and over-the-counter formulations are available.

The Committee recommended non-formulary placement, due to the lack of clinical trials and also due to the higher cost of the product, compared with the other PPIs.

There are no advantages of this product compared to the other PPIs available on the formulary.

The PA criteria recommended for esomeprazole strontium are consistent with what is already in place for the class.

Summary of Panel Questions and Comments:

Dr. Anderson asks if the generic is considered AB rated to Nexium. Is it a generic or not?

Dr. Allerman states that it isn't because the salt form is different. She also states that it is strange because it doesn't have a brand name, but it's not generic.

There were no further from the Panel. The Chair asked for a vote on the UF recommendation, PA criteria, and UF and PA Implementation Plan for Esomeprazole Strontium.

1. **Esomeprazole Strontium - UF Recommendation:**

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

   Director, DHA: 5 May 11

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

2. **Esomeprazole Strontium - PA Criteria:**

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

   Director, DHA: 5 May 11

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

3. **Esomeprazole Strontium – UF and PA Implementation Plan:**

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

   Director, DHA: 5 May 11

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

UNIFORM FORMULARY CLASS REVIEWS

1. PULMONARY ARTERIAL HYPERTENSION (PAH) AGENTS:

A. Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. Endothelial Receptor Agonists: designate Tracleer, Letairis, and Opsumit as Uniform Formulary.
2. Prostacyclins: designate treprostinil nebulized solution (Tyvaso), treprostinil tablets (Orenitram ER), and iloprost (Ventavis) as Uniform Formulary.
3. Nitric Oxide Drugs:
   a. Uniform Formulary and step-preferred: sildenafil 20mg generic and sildenafil brand (Revatio)
   b. Uniform Formulary and non-step-preferred: Adcirca and Adempas
   c. This recommendation includes step therapy, which requires a trial of sildenafil 20 mg generic or branded sildenafil (Revatio) in all new users of Adcirca or Adempas.

B. The PA Criteria for Pulmonary Hypertension:

Existing manual PA criteria apply to sildenafil 20 mg (Revatio) or tadalafil (Adcirca) for patients with primary PAH. The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** automated (step therapy) criteria for all new users of the non-preferred nitric oxide PAH drugs [Adcirca and Adempas], requiring a trial of sildenafil 20 mg generic or sildenafil brand (Revatio) first.

The full PA criteria are as follows:

Prior Authorization criteria apply to all new users of Adempas and Adcirca.

Automated PA criteria: The patient has filled a prescription for sildenafil 20mg generic or sildenafil brand (Revatio) at any Military Health System pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria: Adempas and Adcirca is approved and a trial of sildenafil is NOT required if:

1. For Adempas:

   a. Patient has a documented diagnosis of chronic thromboembolic pulmonary hypertension
   b. Patient has tried a PDE-5 inhibitor and failed or did not respond to therapy

c. Patient has experienced significant adverse effects from the PDE-5 inhibitor

2. For Adcirca:

   a. Patient has tried a sildenafil 20 mg generic or sildenafil brand (Revatio) and failed or did not respond to therapy

3. For both Adempas and Adcirca:

   a. Patient is not taking a nitrate drug.

C. The Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** an effective date of the first Wednesday after a 90-day implementation period in all Points of Service.

Summary of Physician's Perspective:

This is the first time that the Committee has reviewed a more specialized drug class. The pulmonary hypertension drugs were reviewed due to increasing expenditures, and new entrants to the class. The PDE-5 inhibitors for PAH were previously reviewed in November 2009, but this was the first review for the other two subclasses (prostacyclins and endothelin receptor antagonists).

The cost analysis compared Adempas with the PDE-5 inhibitors because these are nitric oxide drugs that have a similar mechanism of action. Step therapy was recommended for the subclass, requiring a trial of either sildenafil generic or Revatio brand before Adcirca or Adempas, since it resulted in the lowest budget impact. The sildenafil products approved for PAH have a different dosage strength than the sildenafil product (Viagra) used for erectile dysfunction.

Adcirca was previously non-formulary, but now it moves to Uniform Formulary status, behind the sildenafil and Revatio step. If the automated step therapy criteria are not met, then the patient can undergo the manual PA criteria process. The manual PA criteria for Adempas do recognize its unique indication for CTEPH (chronic thromboembolic pulmonary hypertension).

The cost effectiveness review supported inclusion of all the PAH drugs on the Uniform Formulary, which clinically allows a wide range of options to treat DoD patients.

Summary of Panel Questions and Comments:

Dr. Anderson asks if there are any national guidelines available to inform providers about first-line treatment since there are no head-to-head comparisons among the

Pulmonary Hypertension Agents. He asks for further clarification regarding the step therapy algorithms.

CAPT Downs responds that there is an algorithm, but it doesn't rate them above the other. Step therapy only restricts to the PDE-5s. You can pick any from general class. In the classes, one is not recommended over the other. The step edit only applies to the nitrous oxide class and the PDE-5s.

There were no further from the Panel. The Chair asked for a vote on the UF recommendation and PA Criteria and the UF and PA Implementation Plan for Pulmonary Arterial Hypertension Agents.

1. **Pulmonary Arterial Hypertension Agents - UF Recommendation:**

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

   Director, DHA: 5 May 15

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

2. **Pulmonary Arterial Hypertension Agents - PA Criteria:**

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

   Director, DHA: 5 May 15

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

3. **Pulmonary Arterial Hypertension Agents - PA Criteria:**

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

   Director, DHA: 5 May 15

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

2. ORAL ONCOLOGY DRUGS: PROSTATE CANCER

A. The Uniform Formulary Recommendation:

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** the following:

1. Uniform Formulary:
   a. Flutamide (Eulexin; generic)

b. Bicalutamide (Casodex; generic)
c. Nilutamide (Nilandron)
d. Abiraterone (Zytiga)
e. Enzalutamide (Xtandi)

2. Non-Formulary: None

B. The PA Criteria:

A manual PA criteria is currently apply to enzalutamide (Xtandi) and abiraterone (Zytiga). The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** maintaining the current PA criteria for Xtandi and Zytiga. The P&T Committee also recommended a manual PA criteria for all new users of nilutamide due to its limited indication.

The full PA criteria are as follows:

1. For nilutamide:

Manual PA criteria: PA criteria apply to all new users of nilutamide.

Nilutamide is approved if any of the following:

a. The patient has experienced significant adverse effects or contraindication from bicalutamide or flutamide; or
b. The patient has experienced therapeutic failure with bicalutamide or flutamide; or
c. The patient has a diagnosis of metastatic prostate cancer (stage D2) disease and the patient has undergone orchiectomy.

2. For enzalutamide (Xtandi): Coverage is approved if:

a. Documented diagnosis of metastatic castration-resistant prostate cancer

No expiration date for the PA.

3. For abiraterone (Zytiga): Coverage is approved if

a. Documented diagnosis of metastatic castration-resistant prostate cancer, AND
b. Patient is receiving concomitant therapy with prednisone.

No expiration date for the PA.

C. The Uniform Formulary and PA Implementation Plan:

P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** an effective date of the first Wednesday after a 90-day implementation period in all Points of Service.

Summary of Physician's Perspective:

This is the first time that the Committee has reviewed the oral oncology drugs for formulary placement and solicited pricing concessions from manufacturers. Previously, the Committee has only recommended Prior Authorization or quantity limits for the oncology drugs.

Several oral chemotherapy drugs are now available to treat patients with cancer on an outpatient basis. These products are very expensive, and have unique indications. The P&T Committee will also review the drugs for chronic myelogenous leukemia (CML) at the August 2015 meeting, so you will see more class reviews in the area of cancer. For the Prostate Cancer drugs, we did survey several MTF and civilian oncologists to get their opinions on how these drugs are used. We also looked at whether civilian healthcare plans had step therapy or prior authorization criteria.

All of the Prostate Cancer drugs were recommended for Uniform Formulary placement. Step therapy for the survival-prolonging drugs Xtandi and Zytiga was considered, but the cost-effectiveness review did not support having one drug as preferred over the other. There is currently a manual prior authorization criteria in place for both Xtandi and Zytiga, which reflect their FDA-approved indications. No changes were recommended to the existing PA criteria for these two drugs.

The Committee did recommend manual PA criteria for one of the anti-androgens, nilutamide (Nilandron). This product has a unique indication (for surgical castration), and has safety concerns. The PA criteria would only apply to new patients. Currently there are 41 patients in the MHS receiving nilutamide.

Summary of Panel Questions and Comments:

There were no questions or comments or comment from the Panel members. Without further discussion, the Chair asked for a vote on the UF recommendation, PA Criteria, and UF and PA Implementation Plan for Oral Oncology Drugs: Prostate Cancer.

1. **Oral Oncology Drugs: Prostate Cancer - UF Recommendation:**

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

Director, DHA:

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

2. **Oral Oncology Drugs: Prostate Cancer - PA Criteria:**

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

Director, DHA:

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

3. **Oral Oncology Drugs: Prostate Cancer – UF and PA Implementation Plan:**

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

Director, DHA:

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

2. TRANSMUCOSAL IMMEDIATE RELEASE FENTANYL PRODUCTS (TIRFs):

A. The Uniform Formulary Recommendation:

The P&T Committee recommended **(9 for, 5 opposed, 1 abstained, 1 absent)** the following:

1. Uniform Formulary: fentanyl transmucosal lozenge (Actiq, generics)

2. Non-Formulary:
   a. Fentanyl sublingual tablet (Abstral)
   b. Fentanyl buccal tablet (Fentora)
   c. Fentanyl nasal spray (Lazanda)
   d. Fentanyl sublingual spray (Subsys)

B. The Uniform Formulary Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. An effective date of the first Wednesday after a 90-day implementation period in all Points of Service; and,
2. DHA sends a letter to beneficiaries affected by the Uniform Formulary decision.

Summary of Physician's Perspective:

These products all contain fentanyl, and are used for breakthrough cancer pain. Other narcotics are also used for breakthrough pain, and are available on the Uniform Formulary (for example immediate release morphine).

These products do have a role for some patients who have difficulty swallowing or persistent nausea and vomiting. But currently the TIRFs are not widely used in the MHS – in the past year there were approximately 600 unique patients receiving one of these products, at a cost of $23 million dollars.

The FDA does have strict safety requirements for prescribing the TIRFs, including a Risk Evaluation and Mitigation Safety program (REMS), which ensures the drugs are not abused or misused, and are prescribed for the appropriate patients. Additionally, the MHS has an opioid safety edit, which is a type of Prior Authorization that makes sure these products are used in patients who are already receiving a narcotic. If a TIRF is prescribed in an opiate-naïve patient, there is a risk of respiratory depression.

The P&T Committee recommended (9 for, 5 opposed) that generic Actiq would be the only product available on the Uniform Formulary, and that the other four products (Abstral, Fentora, Lazanda, and Subsys) be non-formulary. The nonformulary recommendations affect about 355 patients. Step-therapy was not recommended, because not having step-therapy would disrupt the least amount of patients. These products are controlled schedule II drugs, and if step-therapy had been considered, a patient could potentially walk away from the pharmacy without anything.

There was a lot of discussion on the formulary decision. The P&T Committee members who dissented were in favor of a step-therapy scenario, since it could potentially result in a greater cost-avoidance. However, if step-therapy had been recommended, the formulary decision would have affected 71% of the new patients receiving a TIRF, and patients would be required to go back to their providers to obtain a new prescription, since controlled schedule II drugs cannot be changed over the phone with the pharmacist.

Summary of Panel Questions and Comments:

Dr. Anderson asks for a clarification regarding step therapy. Although the process many not be known as step therapy he is glad to hear that an opioid safety edit exists to ensure that patients get other opioids therapy before receiving access to the drugs. He also asks if the drugs are only approved for cancer pain and if the current controls in place are successful?

Dr. Allerman responds that we don't call it step therapy. It's a fentanyl safety edit. It's done manually at the MTF and at the retail network. At the retail network and the mail order, it's actually a hard stop with a look back of the patient's profile. We have a designated list of narcotics. If the patient had 3 days of vicodin for dental, then that does not count. If the

profile does not have a narcotic, it's a hard stop. The pharmacist cannot continue to process the prescription. They have to talk to the patient. Do you have cancer? Have you been on something before? Or they have to call the provider. The pharmacist cannot override for some of the edits.

Yes, the transmucosal fentanyl products are only approved for cancer and not for back pain. That is the intent of the REMS program from the FDA because of the risk of diversion and misuse. The FDA is trying to ensure it is used only for cancer patients and not neuropathic pain. Yes, we do believe the safety controls in place are successful. A group within the PEC, a clinical group within the operation, routinely looks and reviews the safety edit as well as our clinical contact at ESI. When new narcotics come out, we will consider whether they will be added to the safety edit. Just recently we did update the list. This is something we feel very important about because there have been some deaths several years ago when the fentanyl patch was used after dental pain. This is a high visibility item, and we do keep track of it.

Dr. Delgado asks if current patients taking other medication would be grandfathered and if the beneficiary notification letters would explain if there is a process for grandfathering in place or not.

Dr. Allerman clarified the question by stating "now that we are having non-formulary recommendations, would they be grandfathered? Grandfathering only applies in the setting of a prior authorization. This has no PA criteria recommended. Those products will go to non-formulary status. They would not be able to be grandfathered. We would send them a letter notifying that as of the 90 days your co-pay would be increasing. There is the opportunity if they wanted to try the product or we have medical necessity criteria where the patient would continue to stay on the non-formulary but get the co-pay reduced to a formulary co-pay. That so happens that the medical necessity criteria does not fall under the purview of your committee's recommendations. The letter explains what the drugs are and the class, when the co-pays will increase, what the co-pays will increase to, and the mechanism of medical necessity.

There were no further questions or comments from the Panel. The Chair asked for a vote on the UF recommendation and the UF Implementation Plan for the Transmucosal Immediate Release Fentanyl Products (TIRFs).

1. **Transmuscosal Immediate Release Fentanyl Products - UF Recommendation:**

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

Director, DHA:

☐ ~~These~~ comments were taken under consideration prior to my final decision

2. **Transmuscosal Immediate Release Fentanyl Products – UF Implementation Plan:**

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

Director, DHA: 5 May 15

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

UTILIZATION MANAGEMENT

1. HEPATITIS C VIRUS (HCV) AGENTS, DIRECT ACTING ANTIVIRALS (DAAs):

A. HCV Agents, DAAs: Paritaprevir/Ritonavir/Ombitasvir with Dasbuvir (Viekira Pak)—PA Criteria:

The combination product Viekira Pak contains paritaprevir 75 mg, ritonavir 50 mg, and ombitasvir 12.5 mg (dosed two tablets once daily), packaged with dasbuvir 250 mg (dosed twice daily). Viekira Pak was approved by the FDA in December 2014 and is the third FDA approved interferon-free regimen indicated to treat HCV genotype 1.

PA criteria currently apply to the DAAs. The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for new users of paritaprevir/ritonavir/ombitasvir with dasbuvir (Viekira Pak), consistent with FDA-approved labeling. Prior authorization will expire after 12–24 weeks, based on the treatment regimen.

The full PA criteria are as follows:

Paritaprevir/ritonavir/ombitasvir with dasbuvir (Viekira Pak)

1. Direct Acting Antiviral Subclass

a. New users of paritaprevir/ritonavir/ombitasvir with dasbuvir (Viekira Pak) are required to undergo the PA process.
b. Current users are not affected by PA; they can continue therapy uninterrupted.
c. Patients are encouraged to use the Mail Order Pharmacy or MTFs to fill their Viekira Pak prescriptions.
d. Consult the AASLD/IDSA HCV guidelines (www.hcvguidelines.org) for the most up-to-date and comprehensive treatment for HCV. Unique patient populations are also addressed and treatment recommendations may differ from those for the general population.

2. **Manual PA Criteria**:

   a. Age ≥ 18
   b. Has laboratory evidence of chronic HCV genotype 1 infection
      1. State the HCV genotype and HCV RNA viral load on the PA form
   c. Paritaprevir/ritonavir/ombitasvir + dasbuvir (Viekira Pak) is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.
   d. The patient is not co-infected with Hepatitis B virus (HBV).

3. **Treatment Regimens and Duration of Therapy**

   a. Treatment and duration of therapy are approved for one of the following regimens outlined below, based on HCV genotype, prior treatment, and presence of cirrhosis.
   b. Prior authorization will expire after 12 weeks or 24 weeks, based on the treatment regimen selected.

Genotype 1 Patient Populations[1,2]	*Treatment*	*Duration*
GT1a without cirrhosis	Viekira Pak + ribavirin bid	12 weeks
GT1a with cirrhosis	Viekira Pak + ribavirin bid	24 weeks[3]
GT1b without cirrhosis	Viekira Pak	12 weeks
GT1b with cirrhosis	Viekira Pak + ribavirin bid	12 weeks
Liver transplant recipients with normal hepatic function and mild fibrosis (Metavir ≤2)	Viekira Pak + ribavirin bid	24 weeks
[1]Follow GT1a dosing recommendation in patients with an unknown GT1 or mixed GT1 infection [2]Treatment naïve or treatment-experienced with peginterferon alpha plus ribavirin [3]For treatment naïve OR prior IFN+RBV relapser/partial responder, consider 12 weeks		

Summary of Panel Questions and Comments:

Dr. Anderson asks if all the Hepatitis C agents designated as covered under the formulary. He also asked if the other new combination drug for Hepatitis C was in the review process.

Dr. Downs responds that all the ones that are available. That will be reviewed in the May P&T Committee meeting. All the drugs that all have prior authorizations restrict their use for the update.

There were no further questions or comments from the Panel. The Chair asked for a vote on the PA Criteria for the HCV Agents, DAAs: Paritaprevir/Ritonavir/Ombitasvir with Dasbuvir (Viekira Pak).

1. **HCV Agents, DAAs: Paritaprevir/Ritonavir/Ombitasvir with Dasbuvir (Viekira Pak)—PA Criteria:**

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

Director, DHA: 5 Mg 15

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

2. **TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs):**

A. TIBs: Secukinumab (Cosentyx)—PA Criteria:

Secukinumab (Cosentyx) is a new TIB indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. The TIBs were reviewed by the P&T Committee in August 2014 and automated PA (step therapy) and manual PA criteria were recommended for the class (implemented on December 17, 2014).

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria and step therapy for secukinumab (Cosentyx), consistent with the FDA-approved indication.

The full PA criteria are as follows:

PA criteria apply to all new and current users of Cosentyx.

Automated PA criteria: The patient has filled a prescription for adalimumab (Humira) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria:

If automated criteria are not met, coverage is approved for Cosentyx if:

a. Contraindications exist to Humira
b. Inadequate response to Humira (need for different anti-TNF or non-TNF)
c. Adverse reactions to Humira not expected with requested non-step preferred TIB

AND

Coverage approved for patients > 18 years with:

a. Active moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy

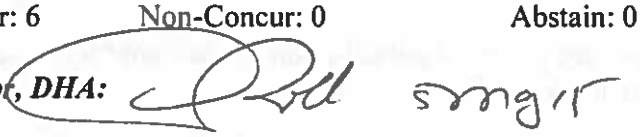
Coverage is NOT provided for concomitant use.

Summary of Panel Questions and Comments:

There were no further questions or comments from the Panel. The Chair asked for a vote on the PA Criteria for the Targeted Immunomodulatory Biologics.

1. **Targeted Immunomodulatory Biologics (TIBs) - PA Criteria:**

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

Director, DHA: 

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

3. TOPICAL ANTIFUNGALS

A. Topical Antifungals: Efinaconazole 10% (Jublia) and Tavaborole 5% (Kerydin) Topical Solutions—PA Criteria:

Jublia and Kerydin are indicated for the topical treatment of toenail onychomycosis. Both products are dosed once daily for 48 weeks. The P&T Committee reviewed the current recommended treatment guidelines, FDA-approved indications, efficacy data, safety information, and utilization and cost data for the topical antifungals for toenail onychomycosis.

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for efinaconazole 10% (Jublia) and tavaborole 5% (Kerydin) in all new and current users of the products. PA criteria were recommended due to the modest efficacy of the products, lack of head-to-head clinical trials, limited efficacy and safety data, and high cost.

The full PA criteria are as follows:

PA criteria apply to all new and current users of Jublia and Kerydin.

Manual PA criteria:
Jublia and Kerydin are approved if all of the following criteria apply:

1. The patient must have diagnostically confirmed onychomycosis by either potassium hydroxide preparation, fungal culture, nail biopsy, or other assessment to confirm diagnosis.

2. The patient is immunocompromised, has diabetes mellitus, or peripheral vascular disease and has swelling and/or redness in the surrounding nail tissue or pain in affected nail(s).

3. The patient has history of one of the following (therapeutic failure, contraindication or adverse events, or intolerance) to one of the following antifungals: itraconazole, terbinafine, or ciclopirox.

    a. therapeutic failure
    b. contraindication (e.g., renal impairment, pre-existing liver disease, or evidence of ventricular dysfunction such as congestive heart failure)
    c. adverse event/intolerance to one of the following antifungal agents

4. Treatment is requested due to a medical condition and not for cosmetic purposes. Examples include the following:

    a. history of cellulitis of the lower extremity who have ipsilateral toenail onychomycosis
    b. diabetic patients with additional risk factors for cellulitis
    c. patients who experience pain/discomfort associated with the infected nail

5. The patient's condition is causing debility or a disruption in their activities of daily living.

6. Jublia or Kerydin have not been used in the previous 24 months.

    PA expires after 1 year.

B. Topical Antifungals: Efinaconazole 10% (Jublia) and Tavaborole 5% (Kerydin) Topical Solutions—PA Implementation Plan:

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)**

1. An effective date of the first Wednesday after a 90-day implementation period in all POS; and.
2. DHA sends a letter to beneficiaries affected by the PA.

Summary of Panel Questions and Comments:

There were no questions or comments from the Panel. The Chair asked for a vote on the UF recommendation, PA Criteria and PA Implementation Plan for the Topical Antifungals.

1. **Topical Antifungals - PA Criteria:**

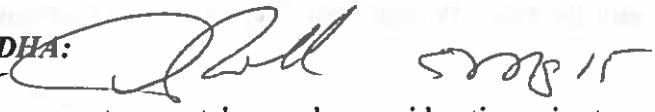
Concur: 6 Non-Concur: 0 Abstain: 0 Absent: 1

Director, DHA: 

☐ ~~These~~ comments were taken under consideration prior to my final decision

2. **Topical Antifungals – PA Implementation Plan:**

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

Director, DHA: 

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

4. CYSTIC FIBROSIS DRUGS

A. Cystic Fibrosis Drugs: Ivacaftor (Kalydeco)—PA Criteria:

Ivacaftor (Kalydeco) is indicated for the treatment of cystic fibrosis. PA criteria were recommended at the February 2012 meeting, updated in May 2014, and reflect the FDA-approved indication for various mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. In December 2014, Kalydeco received an additional indication for the R117H mutation in the CFTR gene.

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** updated manual PA criteria for Kalydeco to include the expanded FDA-approved indication.

The full PA criteria are as follows:

Manual PA Criteria apply to all new and current users of Ivacaftor (Kalydeco).

1. Coverage will be approved for the treatment of CF patients aged 6 years and older who have a G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R or **for R117H** mutation in the CFTR gene, detected by an FDA-approved test.
2. Coverage is not approved for patients who are homozygous for the F508del mutation in the CFTR gene. We do have 32 patients receiving Kalydeco.

Summary of Panel Questions and Comments:

There were no questions or comments from the Panel. The Chair asked for a vote on the PA Criteria for the Cystic Fibrosis Drugs: Ivacaftor (Kalydeco) .

1. **Cystic Fibrosis Drug: Ivacaftor (Kalydeco) - PA Criteria:**

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

   Director, DHA:

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

NON-INSULIN DIABETES MELLITUS DRUGS: GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST (GLP1RAs)

A. **GLP1RAs : Exenatide Once Weekly Pen (Bydureon Pen)—Removal of PA Criteria:**

Exenatide (Bydureon) is now available in a pre-filled pen in addition to the original vial formulation. Manual PA criteria were recommended at the November 2014 P&T Committee meeting due to the significant price difference between the Bydureon Pen formulation and the Bydureon vials. The cost of the Bydureon pen is now comparable to the vial formulation.

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** to remove the following manual PA criteria for the Bydureon pen, requiring use of Bydureon vials first. The existing step therapy PA, requiring a trial of metformin or a sulfonylurea first, will remain for the formulation.

Manual PA criteria from the November 2014 P&T Committee meeting recommended to be removed:

Exenatide once weekly (Bydureon pen)

1. Coverage approved if patient has first tried Bydureon 2mg vial/cartridge first,

   AND

2. Patient has dexterity issues and cannot assemble the Bydureon vial/cartridge

The existing step therapy PA, requiring a trial of metformin or a sulfonylurea first, that will remain is as follows:

New GLP1RA users are required to try metformin or a sulfonylurea before receiving Byetta, Bydureon, or Victoza.

<u>Automated PA criteria</u>: The patient has received a prescription for metformin or sulfonylurea at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria, if automated criteria are not met: Byetta, Bydureon, or Victoza is approved and a trial of metformin or sulfonylrea is NOT required) if:

1. The patient has a confirmed diagnosis of Type 2 Diabetes Mellitus
2. The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.
3. The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.
4. The patient has a contraindication to both metformin and a SU.
5. The patient has had an inadequate response to metformin and a SU.

Summary of Panel Questions and Comments:

There were no questions or comments from the Panel. The Chair asked for a vote on the PA Criteria for the Non-Insulin Diabetes Mellitus Drugs: Glucagon-like Peptide-1 Receptor Agonists (GLP1RAs)

1. **Non-Insulin Diabetes Mellitus Drugs: Glucagon-like Peptide-1 Receptor Agonists (GLP1RAs) - PA Criteria:**

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

   Director, DHA:

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

Brief Listing of Acronyms Used in this Summary

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

- AASLD – American Association for the Study of Liver Diseases
- BAP – Beneficiary Advisory Panel
- BCF – Basic Core Formula
- CFR – Code of Federal Regulations
- CFTR – Cystic Fibrosis Transmembrane Conductance Regulator
- CMA – Cost-Minimization Analysis
- CYP3A4 – Cytochrome P450 3A4
- DAA – Direct Acting Antivirals
- DFO – Designated Federal Officer
- DHA – Defense Health Agency
- DoD – Department of Defense
- DPP-4 – Dipetidase-4
- ED – Erectile Dysfunction
- ERAs – Endothelin Receptor Antagonists
- FACA – Federal Advisory Committee Act
- FDA – Food and Drug Administration
- G1224E – Cystic Fibrosis Mutation
- G1392D - Cystic Fibrosis Mutation
- G178R - Cystic Fibrosis Mutation
- G551D - Cystic Fibrosis Mutation
- G551S - Cystic Fibrosis Mutation
- GLP-1RAs – Glucagon-Like Peptide-1 Receptor Agonists
- GT1 – Genotype 1
- HBV – Hepatitis B Virus
- HCV – Hepatitis C Virus
- HCV RNA – Genetic materials
- IDSA – Infectious Diseases Society of America
- IFN+RBV – Interferon + Ribavirin
- IR – Immediate Release
- MHS – Military Health System
- MI – Myocardial Infarction
- MTF – Military Treatment Facility
- NDAA – National Defense Authorization Act
- P&T – Pharmacy & Therapeutic
- PA – Prior Authorization
- PAH – Pulmonary Arterial Hypertension

- PDE-5 – Phosphodiesterase-5
- PEC – Pharmacoeconomic Center
- POS – Point of Sale
- PPIs – Proton Pump Inhibitors
- R117H - Cystic Fibrosis Mutation
- S1251N - Cystic Fibrosis Mutation
- S549R - Cystic Fibrosis Mutation
- S549R - Cystic Fibrosis Mutation
- SED-1s – Sedative Hynotics
- SGLT2 – Sodium-Glucose Co-Transporter 2
- TIBs – Targeted Immunomodulatory Biologics
- TIRF – Transmucosal Immediate Release Fentanyl
- TNF – Tumor Necrosis Factor
- TRICARE – Military Health Care System
- UF – Uniform Formulary
- USC – United States Code

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
March 26, 2015
Washington, D.C.

Present Panel Members

- Michael Anderson, United Healthcare, Acting Chairperson
- Theresa Buchanan, the National Military Family Association
- Sandra S. Delgado, Humana
- Robert L. Lewis, Chief Warrant and Warrant Officers Association
- Katherine O'Neill-Tracy, The Military Officers Association of America
- John Wagoner, HealthNet Federal Services

Absent:

- Mr. Robert Duane Tackitt, the Association of Military Surgeons US

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. Mr. William Blanche called the proceedings to order at 9:00 A.M.

Agenda

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

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

  - Designated Newly Approved Drugs
    - Newer Sedative Hypnotic Drugs – Tasimelteon (Hetlioz)
    - Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors – empagliflozin (Jardiance)
    - Antiplatelet Agents – vorapaxar (Zontivity)
    - Phosphodiesterase-5 Inhibitors – avanafil (Stendra)
    - Proton Pump Inhibitors – esomeprazole sodium

  - Drug Class Reviews
    - Pulmonary Arterial Hypertension (PAH) Agents
    - Oral Oncology Drugs – Prostate Cancer
    - Transmucosal Immediate Release Fentanyl (TRIF) Products

  - Utilization Management Issues
    - Prior Authorization Criteria

- Hepatitis C Virus Drugs: Direct Acting Antivirals – Paritaprevir/Ritonavir/Ombitasivir with Dabuvir (Viekira Pak)
- Targeted Immunomodulatory Biologics (TIBs) – Secukinumab (Cosentyx)
- Topical Antifungals – Efinaconazole 10% (Jublia) and Tavaborole 5% (Keydin) Topical Solutions
- Cystic Fibrosis Drugs – Ivacaftor (Kalydeco)
- Non-insulin Diabetes Mellitus Drugs: Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RAs) – exenatide once weekly pen formulation (Bydureon pen) – Removal of PA criteria

➢ Panel Discussions

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

Opening Remarks

Mr. Blanche introduces himself as the alternate Designated Federal Officer (DFO) for the Uniform Formulary Beneficiary Advisory Panel. The panel has convened to comment on the recommendations of the DoD P&T Committee meeting, which occurred in February 2015.

Mr. Blanche indicated Title 10, United States Code, (USC) 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 and make additional recommendations regarding the formulary as the committee determines necessary and appropriate.

In addition, 10 U.S.C. Section 1074g, subsection c, also requires the Secretary to establish a UF Beneficiary Advisory Panel (BAP) to review and comment on the development of the Uniform Formulary. The panel includes members that represent non-governmental organizations and associations that represent the views and interests of a large number of eligible covered beneficiaries. Comments of the Panel must be considered by the Director of the Defense Health Agency (DHA) before establishing the UF or implementing changes to the UF.

The panels 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 prepare 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, Mr. Blanche 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 the selected for review, drugs recommended for the basic core formula (BCF) or specific pricing data, these titles do not fall under the purview of the BAP.

The P&T Committee met for approximately 12 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 Pharmacoeconomic 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.

Mr. Blanche introduced the individual Panel members (see list above) and noted house-keeping considerations.

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

Chairman's Opening Remarks

Dr. Michael Anderson greets the BAP and audience and states he's the alternate Chair for the BAP. He states today should be a shorter meeting and gives the floor to CAPT Downs.

DRUG CLASS REVIEW PRESENTATION:

(PEC Script – CAPT Downs)

GOOD MORNING. I am CAPT Walter Downs, Chief of the Formulary Management Branch. Joining me is doctor and retired Army Colonel John Kugler, the Chairman of the Pharmacy & 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 Dr. Angela Allerman, a clinical pharmacist and Deputy Chief of the P&T Operations; LTC Kevin Ridderhoff, Deputy Chief of the Formulary Management Branch; CDR Edward Von Berg, Formulary Management Branch clinical pharmacist and manage care resident, and CAPT Edward Norton, Deputy Chief of the Pharmacy Operations Division. I would also like to recognize Mr. Bryan Wheeler, Associate Deputy General Counsel for the DHA.

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 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:

1. A brief overview of the relative clinical effectiveness analyses considered by the DoD P & T Committee. All reviews include but are not limited to the sources of information listed in 32 CFR 199.21 (e)(1).

2. A brief general overview of the relative cost effectiveness analyses. This overview will be general in nature since we are unable to disclose the actual costs used in the economic models. This overview will include the factors used to evaluate the costs of the agents in relation to the safety, effectiveness, and clinical outcomes.

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

4. 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 Non-formulary 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.

We have given you a handout that includes the Uniform Formulary recommendations for all the drugs discussed today; these are found on pages 2 through 6. We will be using trade names as much as possible, so you can refer to your handout throughout the presentation.

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

1. NEWER SEDATIVE HYPNOTICS (SED-1s) DRUG CLASS - Tasimelteon (Hetlioz)

(Dr. Downs)

A. The Relative Clinical Effectiveness and Conclusion:

Hetlioz is a melatonin receptor agonist indicated solely for treatment of the non-24 sleep wake disorder, a circadian rhythm disorder sometimes found in blind patients. Many limitations exist with the two placebo-controlled studies used to gain FDA approval, including the small numbers of patients enrolled (less than 100 patients), the inclusion of patients shown to previously respond to Hetlioz (RESET trial), and the high patient discontinuation rate (SET trial).

Two agents with a similar structure as tasimelteon [melatonin supplement and ra-melt-e-on (Rozerem)] are marketed to treat insomnia caused by difficulties with sleep onset.

The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** that other than its unique indication for treating blind patients with non-24 sleep wake disorder, tasimelteon offers no clinically compelling advantages over the existing SED-1 drugs on the UF that are used to treat sleep disorders.

B. Relative Cost-Effectiveness Analysis and Conclusion:

A Cost-minimization analysis (CMA) was performed. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** Hetlioz is more costly than the formulary and non-formulary SED-1 agents and melatonin.

C. The Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** Hetlioz be designated NF due to the lack of compelling clinical advantages, other than its unique indication, and cost disadvantage compared to SED-1 agents on the Uniform Formulary.

D. Hetlioz Prior Authorization (PA) Criteria:

Automated (step therapy) and manual PA criteria were recommended at the August 2014 DoD P&T Committee meeting and implemented December 10, 2014 for tasimelteon, requiring a trial of zolpidem immediate release (IR) or zaleplon first, and a diagnosis of blindness. The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** updating the PA criteria for tasimelteon, including removing the step therapy requirement, and requiring all new patients to undergo the manual PA process.

The full PA criteria are as follows:

The previous automated (step therapy) criteria for Hetlioz that requires a trial of zolpidem IR or zaleplon no longer apply. Manual PA criteria apply to all new users of Hetlioz.

Manual PA criteria: Hetlioz is approved if:

1. The patient is totally blind and has a documented diagnosis of non-24 sleep wake disorder,
   AND
2. The patient has had a trial of melatonin and either failed or had an adverse event,
   AND
3. The patient is not taking a drug that will interact with tasimelteon (i.e., beta blockers or strong CYP3A4 inducers).

PA Criteria will expire after 6 months. If a patient has not responded after 6 months, they will be deemed a non-responder.

E. Hetlioz's Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1) An effective date of the first Wednesday after a **60-day** implementation period in all points of service; and,
2) The DHA will send a letter to the beneficiaries affected by the Uniform Formulary decision.

F. Physician's Perspective:

The Committee recommended non-formulary placement for Hetlioz, since it is not cost-effective. The Committee did recognize the unique indication for Hetlioz. However, for non-24 sleep wake disorder, the usual standard of treatment is to try a melatonin supplement. This was why the PA criteria were revised to include a trial of

melatonin, and then allow Hetlioz if a patient doesn't respond to or has an adverse reaction to the supplement. The Committee did recommend removing the previous step therapy criteria (where a trial of generic Ambien or Sonata was previously required), since there was the potential that a patient with insomnia could meet the requirement to receive Hetlioz. Other products on the Uniform Formulary [for example Ambien, Sonata or Lunesta)] should be prescribed for insomnia instead of Hetlioz. The Committee felt that manualPA criteria was the most appropriate method to ensure Hetlioz is used in the patients for which it is indicated. Additionally, other civilian healthcare plans do require a trial of melatonin and prior authorization for Hetlioz. Currently there are six patients in the MHS who are receiving Hetlioz. These patients will be "grandfathered," and not required to go through the new manual PA criteria.

G. *BAP Comments:*

There were no questions or comments or comment from the Panel members. Without further discussion, the Chair asked for a vote on the UF recommendation, PA Criteria, and UF and PA Implementation Plan for Tasimelteon (Hetlioz).

1. **Tasimelteon (Hetlioz) - UF Recommendation**:

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

2. **Tasimelteon (Hetlioz) - PA Criteria:**

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

3. **Tasimelteon (Hetlioz) –UF and PA Implementation Plan:**

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

2. SODIUM-GLUCOSE CO-TRANSPORTER 2 (SGLT-2) INHIBITOR drug class - Empagliflozin (Jardiance)

(Dr. Downs)

A. The Relative Clinical Effectiveness and Conclusion:

Jardiance is the third FDA-approved SGLT2 inhibitor. It is similar to canagliflozin (Invokana) and dapagliflozin (Farxiga) in terms of its effects on lowering hemoglobin A1c, and increasing low-density lipoprotein cholesterol, increasing high-density lipoprotein cholesterol, and decreasing systolic blood pressure and body weight. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** empagliflozin offers no clinically compelling advantages over the existing Uniform Formulary non-insulin diabetes drugs, given the modest decrease in A1c, risk of adverse

reactions, including female genital fungal infections and urinary tract infections, and unknown long-term cardiovascular safety profile.

B. The Relative Cost-Effectiveness Analysis and Conclusion:

A Cost-minimization analysis (CMA) was performed to evaluate Jardiance with other oral products on the Uniform Formulary used in the treatment of diabetes. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** the following:

1. The Cost-minimization analysis showed Jardiance was not cost effective compared to existing formulary agents in the non-insulin diabetes class including metformin, sulfonylureas, thiazolidinediones, and dipeptidyl-dipeptidase-4 (DPP-4) inhibitors.

2. Current costs for Jardiance show it was comparable to Invokana and Farxiga, the other agents available in the SGLT2 subclass.

C. The Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** Jardiance to be designated Non-Formulary due to the lack of compelling clinical advantages, safety concerns, lack of long-term outcomes, and cost disadvantage compared to the oral Uniform Formulary products used for treating diabetes.

D. Prior Authorization Criteria for Jardiance:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** a trial of metformin or a sulfonylurea and a DPP-4 inhibitor in all new and current users of Jardiance, consistent with the Prior Authorization requirements in place for Invokana and Farxiga.

The full PA criteria are as follows:

All new and current users of Jardiance are required to try metformin or a sulfonylurea, and a DPP-4 inhibitor before Jardiance.

Automated PA criteria: The patient has filled a prescription for metformin or a sulfonylurea, AND a DPP-4 inhibitor at any Military Health System (MHS) pharmacy point of service [this includes Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

AND

Manual PA criteria: If automated criteria are not met, Jardiance is approved AND a trial of metformin or suflonylurea AND a DPP-4 inhibitor is NOT required if:

1. The patient has experienced any of the following issues on metformin:
   a. impaired renal function precluding treatment with metformin
   b. history of lactic acidosis

2. The patient has experienced any of the following issues on a sulfonylurea:
   a. hypoglycemia requiring medical treatment
3. The patient has had inadequate response to metformin or a sulfonylurea or a DPP-4 inhibitor.
4. The patient has a contraindication to metformin or a sulfonylurea or DPP-4 inhibitor.

E. The Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. an effective date of the first Wednesday after a **90-day** implementation period in all Points of Service; and,
2. DHA send a letter to beneficiaries affected by the Uniform Formulary decision.

F. Physician's Perspective:

There was no controversy with the recommendation for non-formulary status. This is the third SGLT2 inhibitor that the Committee has reviewed. The three drugs in this class all have similar effects on lowering blood glucose levels, and also similar adverse effect profiles. The long-term safety with these drugs is not known at this time.

The same PA criteria that apply to the other SGLT-2 inhibitors were recommended for Jardiance. Additionally, all the oral diabetes drugs have the requirement for a trial of metformin or a sulfonylurea first.

There are combinations of an SGLT2 inhibitor with other diabetes drugs, including metformin and the DPP-4 inhibitors, that have recently been approved, and more are in the pipeline. Because of this, the SGLT2- inhibitors will be reviewed by the Committee in August 2015.

G. Panel Questions and Comments:

Dr. Anderson asked for clarification regarding the PA Criteria for the SFLT2 inhibitors, the 90-day implementation plan and the beneficiary notification letters. More specifically, he asks if the PA criteria applied to all the SGLT2 inhibitors and if the other 2 were also designated non-formulary? Also, would new users be allowed to get a prescription for Jardiance during the 90-day implementation period as well as receive a beneficiary notification letter?

CAPT Down stated that the PA criteria did apply to all of the SGLT2 inhibitors and that the other two (2) are designated non-formulary. He further states that after the minutes are signed, we have 90-days to complete the implementation plan. This includes

notifying the beneficiary of the change and what needs to be done to either continue or change the medication. Beneficiaries who just stated the medication will receive a beneficiary notification letter.

Dr. Kugler interjected the same process/procedure that we are currently using.

Dr. Delgado asked how many beneficiaries are currently on this medication.

Dr. Allerman responded that the information is located on page 3 of the handout. There are 913 beneficiaries currently on the medication.

There were no further questions or comments from the Panel. The Chair asked for a vote on the UF recommendation, PA criteria, and UF and PA Implementation Plan for Empagliflozin (Jardiance).

1. **Empagliflozin Jardiance UF Recommendation**:

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

2. **Empagliflozin Jardiance PA Criteria:**

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

3. **Empagliflozin Jardiance Implementation Plan:**

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

3. **ANTIPLATELET AGENTS - Vorapaxar (Zontivity)**

(Dr. Allerman)

A. The Relative Clinical Effectiveness and Conclusion:

Zontivity is a new antiplatelet with a novel mechanism of action. It is approved in the setting of secondary prevention for the reduction of cardiovascular events (including cardiovascular death, myocardial infarction (MI), and stroke) in patients with a history of MI or with peripheral artery disease. It remains unknown whether adding Zontivity to aspirin and or clopidogrel offers benefits similar to that seen with other antiplatelet agents.

The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** that clinically, the place in therapy for Zontivity is limited due to the significantly increased bleeding risk. Zontivity should be reserved for those patients with stable atherosclerotic disease who have failed other antiplatelet therapies.

B. The Relative Cost-Effectiveness Analysis and Conclusion:

A cost-minimization analysis (CMA) was performed to evaluate Zontivity with other oral antiplatelet agents on the Uniform Formulary. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** that Zontivity was not cost effective compared to other oral antiplatelet agents on the UF.

C. Zontivity's Uniform Formulary Recommendation:

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** Zontivity be designated Non-Formulary based on clinical and cost effectiveness.

D. The Uniform Formulary Implementation Plan:

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** to following:

1. An effective date of the first Wednesday after a **90-day** implementation period in all POS; and,
2. DHA sends a letter to the beneficiaries affected by the UF decision

E. Physician's Perspective:

The Committee recommended non-formulary placement, due to the risk of bleeding and also cost-effectiveness. All the other antiplatelets are available on the formulary.

We did ask for input from the cardiology consultants from the three services (army, navy, air force). Overall, they felt that Zontivity should not be added to the formulary, due to the high bleeding risk, and limited number of clinical trials.

The Committee did feel that the Medical Necessity process would be the best mechanism to allow a co-pay reduction for those patients who are appropriate candidates for Zontivity, and that a prior authorization was not needed.

F. Panel Questions and Comments:

There were no questions or comments or comment from the Panel members. Without further discussion, the Chair asked for a vote on the UF recommendation and the UF Implementation Plan for Vorapaxar (Zontivity).

1. **Vorapaxar (Zontivity) - UF Recommendation**:

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

2. Vorapaxar (Zontivity) – UF Implementation Plan:

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

3. PHOSPHODIESTERASE-5 (PDE-5) INHIBITORS FOR ERECTILE DYSFUNCTION (ED) - Avanafil (Stendra):

(Dr. Allerman)

A. The Relative Clinical Effectiveness and Conclusion:

Stendra is the fourth PDE-5 inhibitor for Erectile Dysfunction to enter the market. The change in efficacy endpoints for Erectile Dysfunction with Stendra and the safety profile appears similar to the other PDE-5 inhibitors. In one study, the higher doses of Stendra were effective in improving Erectile Dysfunction after prostatectomy, compared to placebo.

The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** that although Stendra differs from the other PDE-5 inhibitors in that it has a 15-minute onset of action, only one PDE-5 is required on the Uniform Formulary to meet the needs of the Military Health System.

B. The Relative Cost-Effectiveness Analysis and Conclusion:

A Cost-minimization analysis (CMA) was performed. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** Stendra was more costly than the other Uniform Formulary and Non-Formulary PDE-5 inhibitors.

C. Stendra's Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** Stendra be designated Non-Formulary due to the lack of compelling clinical advantages and the cost disadvantage compared to the step-preferred product, sildenafil (Viagra).

D. Stendra's PA Criteria:

Existing automated PA criteria (step therapy) for the PDE-5 inhibitors used for the treatment of ED requires a trial of sildenafil (Viagra), prior to receiving another PDE-5 inhibitor. The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** PA criteria for all current users of avanafil (Stendra), similar to the existing PA criteria for the class.

The full PA criteria are as follows:

PA criteria apply to all current users of avanafil.

Automated PA criteria: Coverage approved for treatment of ED if:

1. The patient has received a prescription for sildenafil (Viagra) at any Military Health System pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days, AND

2. The patient is a male aged 40 years or older.

Manual PA criteria: A trial of sildenafil (Viagra) is not required if:

1. Patient has tried sildenafil (Viagra) and has had an inadequate response or was unable to tolerate treatment due to adverse effects.
2. Treatment with sildenafil (Viagra) is contraindicated.
3. Patient is between 18 and 39 years of age and is being treated for ED of organic or mixed organic/psychogenic origin. [Must try sildenafil (Viagra) first or indicate inability to due to reasons stated above in 1 or 2.]
4. Patient is between 18 and 39 years of age and is being treated for drug-induced ED where the causative drug cannot be altered or discontinued. [Must try sildenafil (Viagra) first or indicate inability to due to reasons stated above.]

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

   Use of sildenafil, tadalafil, or avanafil (Stendra) for preservation/restoration of erectile dysfunction after prostatectomy. PA expires after one year.

E. The Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. Effective date of the first Wednesday after a 90-day implementation period in all points of service.

F. Physician's Perspective:

Once again, there is no controversy here for non-formulary placement. The other PDE-5 inhibitors have been available for over 10 years, so this product is very late to the market. Although it has a slighter faster onset of action than the other PDE-5s, since there are no head to head trials, there is no data to show that Stendra would be more effective than the other products for erectile dysfunction.

The recommended PA criteria for Stendra reflect what is already in place for the other products (Viagra, Cialis and Levitra). In addition to treatment for erectile dysfunction, the Committee did recognize the one trial available that evaluated Stendra following prostatectomy, so this was added to the PA criteria, in addition to ED.

G. Panel Questions and Comments:

Dr. Delgado recognizes that there was a differentiation on the automated versus the manual PA criteria with regard to age. Is that some reason that the automated PA can't be 18 and over? It appears to be redundant based on the fact that the PA criteria requires the beneficiary to try one of the other medications.

Dr. Allerman states that this particular set of PA criteria for Viagra has been in place for several years. Basically, if a male is 40 years or older, it's almost like it's an automatic pass. Several years ago it was a requirement for a male to be aged 45 and over. That was lowered to 40. However, there was a lot of discussion about decreasing the age even more. There was also concern that younger patients, who didn't have any type of organic disease, would want to get a PDE-5 because of performance anxiety. This is the particular criteria that has been applied to Cialis, Avetra, and Viagra dating back to 2011. Additionally, If the patient already has a PA criteria for erectile dysfunction, there's no expiration date. If they tried it, that would be in the profile and won't hit the prior authorization. It was Just for the following prostatectomy, the data just shows that after one year, there is no data.

Dr. Anderson asks if quantity limits are required with the ED therapies in addition to the PA?

Dr. Allerman responded yes. There have been quantity limits for several years. It is a collective quantity limits of 6 per month. For example, one month the patient is on Viagra, then the next month the patient changes to Cialis. It's still 6 months collectively. Part of the purview of the BAP is actually not to comment on quantity limits, but we do have these in place. However, she adds for patients who need daily use of a PDE-5 inhibitor for indication such as prostatectomy, pulmonary hypertension and Raynaud's for those indications can get daily therapy. The quantity limit can be overridden.

There were no further questions or comments from the Panel. The Chair asked for a vote on the UF recommendation and the UF Implementation Plan for Avanafil (Stendra).

1. **Avanafil (Stendra) - UF Recommendation**:

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

2. Avanafil (Stendra) - UF Implementation Plan:

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

5. PROTON PUMP INHIBITORS (PPIs) - Esomeprazole Strontium

(Dr. Downs)

A. The Relative Clinical Effectiveness and Conclusion:

Esomeprazole strontium (it does not have a brand name) is the 8th PPI to reach the market. It was approved via section 505(b)(2) of the Federal Food, Drug, and Cosmetic

Act using efficacy and safety data primarily obtained from information contained in the package insert for esomeprazole magnesium (Nexium).

The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** that esomeprazole strontium offers no clinically compelling advantages compared to esomeprazole magnesium (Nexium) or the other PPIs.

B. The Relative Cost-Effectiveness Analysis and Conclusion:

A Cost Minimization Analysis was performed. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** that esomeprazole strontium is not cost effective compared to other PPIs on the Uniform Formulary.

C. Esomeprazole Strontium's Uniform Formulary Recommendation

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** esomeprazole strontium be designated Non-Formulary due to the lack of compelling clinical advantages and the cost disadvantage compared to the other PPIs on the Uniform Formulary.

D. Esomeprazole Strontium's PA Criteria

Existing automated PA criteria (step therapy) for the PPIs requires a trial of Nexium or omeprazole first, prior to receiving another PPI. The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** PA criteria for all new and current users of esomeprazole strontium similar to the existing PA criteria for the class.
The full PA criteria are as follows:

PA criteria apply to all new and current users of esomeprazole strontium.

Automated PA criteria: The patient has filled a prescription for omeprazole (Prilosec or its generics), pantoprazole tablets (Protonix or its generics), or esomeprazole magnesium (Nexium) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order), during the previously 180 days.

AND

Manual PA criteria: A trial of omeprazole (Prilosec or its generics), pantoprazole tablets (Protonix or its generics), or esomeprazole magnesium (Nexium) is NOT required if:

1. The patient has tried omeprazole, pantoprazole tablets, and esomeprazole magnesium (Nexium) and had an inadequate response.
2. The patient has tried omeprazole, pantoprazole tablets, and esomeprazole magnesium (Nexium) and was unable to tolerate it due to adverse effects.
3. Treatment with omeprazole, pantoprazole tablets, and esomeprazole magnesium

(Nexium) is contraindicated (e.g., hypersensitivity; moderate to severe hepatic insufficiency).

E. The Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. An effective date of the first Wednesday after a 90-day implementation period in all POS; and,
2. DHA sends a letter to beneficiaries affected by the UF decision

F. Physician's Perspective:

This product is simply Nexium, with a different salt. The package insert largely reflects what is found in the Nexium package insert, and data from the Nexium trials was used to gain FDA approval for this product.

The PPIs are another drug class that have been on the market for over 10 years, and now both generic products and over-the-counter formulations are available.

The Committee recommended non-formulary placement, due to the lack of clinical trials and also due to the higher cost of the product, compared with the other PPIs. There are no advantages of this product compared to the other PPIs available on the formulary.

The PA criteria recommended for esomeprazole strontium are consistent with what is already in place for the class.

G. **Panel Questions and Comments:**

Dr. Anderson asks if the generic is considered AB rated to Nexium. Is it a generic or not?

Dr. Allerman states that it isn't because the salt form is different. She also states that it is strange because it doesn't have a brand name, but it's not generic.

There were no further from the Panel. The Chair asked for a vote on the UF recommendation, PA criteria, and UF and PA Implementation Plan for Esomeprazole Strontium.

1. **Esomeprazole Strontium - UF Recommendation**:

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

2. **Esomeprazole Strontium - PA Criteria:**

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

3. **Esomeprazole Strontium – UF and PA Implementation Plan:**

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

UNIFORM FORMULARY CLASS REVIEWS

1. PULMONARY ARTERIAL HYPERTENSION (PAH) AGENTS

(Dr. Downs)

A. The Relative Clinical Effectiveness and Conclusion for Pulmonary Arterial Hypertension agents:

The P&T Committee reviewed the clinical effectiveness of the Pulmonary Hypertension Agents, which is divided into the three subclasses outlined below.

1. **Prostacyclins that include**: treprostinil nebulized solution (Tyvaso), treprostinil oral tablets [Orenitram extended release (ER)], and iloprost nebulized solution (Ventavis);

2. **Endothelin Receptor Antagonists (ERAs) that include**: bosentan (Tracleer), ambrisentan (Letairis), and macitentan (Opsumit);

3. **Nitric Oxide Drugs that include**: the soluble guanylate cyclase stimulator, riociguat (Adempas); and, the PDE-5 inhibitors, sildenafil generic, branded sildenafil (Revatio), and tadalafil (Adcirca).

The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** the following for the Pulmonary Hypertension agents:

1. There are no head-to-head comparisons among the Pulmonary Hypertension drugs; therefore, no evidence-based first-line treatment can be proposed.

2. For the PDE-5 inhibitors, there was no new data to change the conclusion from the previous Uniform Formulary review in November 2009. These conclusion were

    a. Sildenafil and tadalafil show similar improvements in 6-minute walking distance (it is an indirect measure of the severity of pulmonary hypertension). This was based on indirect comparisons of clinical trial results.
    b. Tadalafil (Adcirca) is dosed once daily, which is more convenient compared to the three-times daily dosing required with sildenafil (Revatio).

3. In one systematic review (CHEST 2014), all the Pulmonary Hypertension drugs increased the 6-minute walking distance by 27.9 meters to 39.9 meters when compared to placebo; however, comparisons between agents are inconclusive. Of note, the minimal clinically important difference for the 6-minute walking distance is a distance of at least 33 meters.
4. In their individual trials, Orenitram ER, Opsumit, and Adempas caused statistically significant improvements in the 6-minute walking distance compared to placebo. Orenitram ER and Adempas have not shown mortality benefits. Orenitram ER showed a significant reduction in the endpoint of time to clinical worsening. Adempas has an additional indication for chronic thromboembolic pulmonary hypertension.
5. Within and among the subclasses, the Pulmonary Hypertension drugs have distinct adverse reaction profiles. The Endothelial Receptor Agonists and Adempas are pregnancy category X.

The overall relative clinical effectiveness conclusion: The P&T Committee concluded the choice of drug for Pulmonary Arterial Hypertension depends on a variety of factors including indication, product labeling, mechanism of action, route of administration, side effect profile, drug interactions, patient preference, and physician experience.

B. The Relative Cost-Effectiveness Analysis and Conclusion:

A Cost Minimization Analysis and budget impact analysis was performed to evaluate the PAH subclasses. The budget impact analysis was performed to evaluate the potential impact of designating selected agents in various formulary scenarios. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** the following:

Endothelial Receptor Agonists:

1. The Cost-minimization analysis (CMA) results showed that Letairis was the most cost-effective agent in this subclass, followed by Opsumit and Tracleer.
2. The budget impact analysis results showed that the scenario with Letairis, Opsumit, and Tracleer designated with Uniform Formulary status and no step requirement yielded the lowest budget impact for the Military Health System.

Prostacyclins:

1. Cost-minimization analysis (CMA) results showed that treprostinil tablets (Orenitram ER) was the most cost-effective agent in this subclass, followed by treprostinil nebulized solution (Tyvaso) and iloprost (Ventavis).
2. The budget impact analysis results showed that the scenario with Orenitram ER, Tyvaso, and Ventavis designated with Uniform Formulary status and no step requirement yielded the lowest budget impact for the Military Health System.

Nitric Oxide Drugs:

1. A Cost-minimization analysis (CMA) results showed that sildenafil generic was the most cost-effective agent in this subclass, followed by tadalafil (Adcirca), sildenafil brand (Revatio), and riociguat (Adempas).
2. The budget impact analysis results showed that the scenario with sildenafil generic and branded sildenafil (Revatio) as step-preferred and on the Uniform Formulary, with tadalafil (Adcirca) and riociguat (Adempas) as non-step-preferred and on the Uniform Formulary, yielded the lowest budget impact for the Military Health System.

C. Uniform Formulary Recommendation:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. Endothelial Receptor Agonists: designate Tracleer, Letairis, and Opsumit as Uniform Formulary.
2. Prostacyclins: designate treprostinil nebulized solution (Tyvaso), treprostinil tablets (Orenitram ER), and iloprost (Ventavis) as Uniform Formulary.
3. Nitric Oxide Drugs:
   a. Uniform Formulary and step-preferred: sildenafil 20mg generic and sildenafil brand (Revatio)
   b. Uniform Formulary and non-step-preferred: Adcirca and Adempas
   c. This recommendation includes step therapy, which requires a trial of sildenafil 20 mg generic or branded sildenafil (Revatio) in all new users of Adcirca or Adempas.

D. The PA Criteria for Pulmonary Hypertension:

Existing manual PA criteria apply to sildenafil 20 mg (Revatio) or tadalafil (Adcirca) for patients with primary PAH. The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** automated (step therapy) criteria for all new users of the non-preferred nitric oxide PAH drugs [Adcirca and Adempas], requiring a trial of sildenafil 20 mg generic or sildenafil brand (Revatio) first.

The full PA criteria are as follows:

Prior Authorization criteria apply to all new users of Adempas and Adcirca.

Automated PA criteria: The patient has filled a prescription for sildenafil 20mg generic or sildenafil brand (Revatio) at any Military Health System pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria: Adempas and Adcirca is approved and a trial of sildenafil is NOT required if:

1. For Adempas:

    a. Patient has a documented diagnosis of chronic thromboembolic pulmonary hypertension
    b. Patient has tried a PDE-5 inhibitor and failed or did not respond to therapy
    c. Patient has experienced significant adverse effects from the PDE-5 inhibitor

2. For Adcirca:

    a. Patient has tried a sildenafil 20 mg generic or sildenafil brand (Revatio) and failed or did not respond to therapy

3. For both Adempas and Adcirca:

    a. Patient is not taking a nitrate drug.

E. The Uniform Formulary and PA Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** an effective date of the first Wednesday after a 90-day implementation period in all Points of Service.

G. Physician's Perspective:

This is the first time that the Committee has reviewed a more specialized drug class. The pulmonary hypertension drugs were reviewed due to increasing expenditures, and new entrants to the class. The PDE-5 inhibitors for PAH were previously reviewed in November 2009, but this was the first review for the other two subclasses (prostacyclins and endothelin receptor antagonists).

The cost analysis compared Adempas with the PDE-5 inhibitors because these are nitric oxide drugs that have a similar mechanism of action. Step therapy was recommended for the subclass, requiring a trial of either sildenafil generic or Revatio brand before Adcirca or Adempas, since it resulted in the lowest budget impact. The sildenafil products approved for PAH have a different dosage strength than the sildenafil product (Viagra) used for erectile dysfunction.

Adcirca was previously non-formulary, but now it moves to Uniform Formulary status, behind the sildenafil and Revatio step. If the automated step therapy criteria are not met, then the patient can undergo the manual PA criteria process. The manual PA criteria for Adempas do recognize its unique indication for CTEPH (chronic thromboembolic pulmonary hypertension).

The cost effectiveness review supported inclusion of all the PAH drugs on the Uniform Formulary, which clinically allows a wide range of options to treat DoD patients.

F. **Panel Questions and Comments:**

Dr. Anderson asks if there are any national guidelines available to inform providers about first-line treatment since there are no head-to-head comparisons among the Pulmonary Hypertension Agents. He asks for further clarification regarding the step therapy algorithms.

CAPT Downs responds that there is an algorithm, but it doesn't rate them above the other. Step therapy only restricts to the PDE-5s. You can pick any from general class. In the classes, one is not recommended over the other. The step edit only applies to the nitrous oxide class and the PDE-5s.

There were no further from the Panel. The Chair asked for a vote on the UF recommendation and PA Criteria and the UF and PA Implementation Plan for Pulmonary Arterial Hypertension Agents.

1. **Pulmonary Arterial Hypertension Agents - UF Recommendation**:

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

2. **Pulmonary Arterial Hypertension Agents - PA Criteria:**

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

3. **Pulmonary Arterial Hypertension Agents - PA Criteria:**

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

2. ORAL ONCOLOGY DRUGS: PROSTATE CANCER

(Dr. Allerman)

A. The Relative Clinical Effectiveness and Conclusion of Oral Oncology Drugs: Prostate Cancer.

The P&T Committee evaluated the relative clinical effectiveness of the Prostate Cancer drugs, which is comprised of the following:

1. **Subclass I (Anti-Androgen Agents) including**: bicalutamide (Casodex; generic), flutamide (Eulexin; generic), and nilutamide (Nilandron)

2. **Subclass II (Survival-Prolonging Drugs)**: enzalutamide (Xtandi) and abiraterone (Zytiga)

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** the following conclusions for the Prostate Cancer drugs:

1. Subclass I (Anti-Androgen Agents):

a. There is only limited data regarding clinical benefits of the Subclass I agents (bicalutamide, flutamide, and nilutamide). The guidelines also stated that the three anti-androgens demonstrate unknown survival and quality of life benefit.
b. Flutamide has a higher incidence of gastrointestinal side effects than bicalutamide, and has warnings for hepatotoxicity. Nilutamide has a black box warning for pulmonary toxicity and delays visual light-to-dark adaptation that can limit its use.
c. Bicalutamide is considered the initial drug of choice, based on its dosing frequency (once daily dosing, compared to three times daily dosing with flutamide), toxicity profile, and clinical trial data.
d. Although Nilutamide has no compelling advantages compared with flutamide or bicalutamide and has the least favorable safety profile, it is required on the Uniform Formulary due to its unique indication for use in combination with surgical castration.

2. **Subclass II (Survival Prolonging Drugs)**:

a. For the Subclass II agents, abiraterone (Zytiga) and enzalutamide (Xtandi) have independently been shown to improve overall survival and progression-free survival when compared to placebo, both in the post-chemotherapy and chemotherapy-naïve settings.
b. Zytiga requires the co-administration of prednisone to help mitigate the mineralocorticoid excess that can result from its mechanism of action. Xtandi does not require concomitant administration of steroids, but 30%–47% of patients were receiving some form of steroids therapy in the two phase 3 studies that led to its FDA approval.
c. The Subclass II agents have differing safety profiles. Zytiga can cause adrenocortical insufficiency, hypertension, hypokalemia, and edema, which requires close monitoring for these complications. Xtandi has been associated with seizures as well as hypertension or increases blood pressure when compared to placebo.

Overall relative clinical effectiveness conclusion: The P&T Committee concluded the choice of prostate cancer agent depends on clinical considerations, patient preferences, prior treatment, presence or absence of visceral disease, patient symptoms, and drug side effect profiles.

A. The Relative Cost-Effectiveness Analysis and Conclusion:

A Cost-minimization analysis and Budget Impact Analysis were performed to evaluate the Prostate Cancer drugs. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** the following:

1. The Cost-minimization analysis showed that in Subclass I, bicalutamide was the most cost-effective agent, followed by flutamide and nilutamide. In Subclass II, abiraterone (Zytiga) was more cost effective than enzalutamide (Xtandi).
2. Budget Impact Analysis results showed that designating all the prostate cancer drugs as formulary on the Uniform Formulary, with no step-preferred agents in either subclass, demonstrated significant cost avoidance for the Military Health System.

B. The Uniform Formulary Recommendation:

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** the following:

1. Uniform Formulary:
   a. Flutamide (Eulexin; generic)
   b. Bicalutamide (Casodex; generic)
   c. Nilutamide (Nilandron)
   d. Abiraterone (Zytiga)
   e. Enzalutamide (Xtandi)

2. Non-Formulary: None

C. The PA Criteria:

A manual PA criteria is currently apply to enzalutamide (Xtandi) and abiraterone (Zytiga). The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** maintaining the current PA criteria for Xtandi and Zytiga. The P&T Committee also recommended a manual PA criteria for all new users of nilutamide due to its limited indication.

The full PA criteria are as follows:

1. For nilutamide:

   Manual PA criteria: PA criteria apply to all new users of nilutamide.

   Nilutamide is approved if any of the following:

   a. The patient has experienced significant adverse effects or contraindication from bicalutamide or flutamide; or

b. The patient has experienced therapeutic failure with bicalutamide or flutamide; or
c. The patient has a diagnosis of metastatic prostate cancer (stage D2) disease and the patient has undergone orchiectomy.

2. For enzalutamide (Xtandi): Coverage is approved if:

a. Documented diagnosis of metastatic castration-resistant prostate cancer

No expiration date for the PA.

3. For abiraterone (Zytiga): Coverage is approved if

a. Documented diagnosis of metastatic castration-resistant prostate cancer, AND
b. Patient is receiving concomitant therapy with prednisone.

No expiration date for the PA.

E. The Uniform Formulary and PA Implementation Plan:

P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** an effective date of the first Wednesday after a 90-day implementation period in all Points of Service.

F. **Physician's Perspective:**

This is the first time that the Committee has reviewed the oral oncology drugs for formulary placement and solicited pricing concessions from manufacturers. Previously, the Committee has only recommended Prior Authorization or quantity limits for the oncology drugs.

Several oral chemotherapy drugs are now available to treat patients with cancer on an outpatient basis. These products are very expensive, and have unique indications. The P&T Committee will also review the drugs for chronic myelogenous leukemia (CML) at the August 2015 meeting, so you will see more class reviews in the area of cancer. For the Prostate Cancer drugs, we did survey several MTF and civilian oncologists to get their opinions on how these drugs are used. We also looked at whether civilian healthcare plans had step therapy or prior authorization criteria.

All of the Prostate Cancer drugs were recommended for Uniform Formulary placement. Step therapy for the survival-prolonging drugs Xtandi and Zytiga was considered, but the cost-effectiveness review did not support having one drug as preferred over the other. There is currently a manual prior authorization criteria in place for both Xtandi and Zytiga, which reflect their FDA-approved indications. No changes were recommended to the existing PA criteria for these two drugs.

The Committee did recommend manual PA criteria for one of the anti-androgens, nilutamide (Nilandron). This product has a unique indication (for surgical castration), and has safety concerns. The PA criteria would only apply to new patients. Currently there are 41 patients in the MHS receiving nilutamide.

G. **Panel Questions and Comments:**

There were no questions or comments or comment from the Panel members. Without further discussion, the Chair asked for a vote on the UF recommendation, PA Criteria, and UF and PA Implementation Plan for Oral Oncology Drugs: Prostate Cancer.

1. **Oral Oncology Drugs: Prostate Cancer - UF Recommendation**:

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

2. **Oral Oncology Drugs: Prostate Cancer - PA Criteria:**

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

3. **Oral Oncology Drugs: Prostate Cancer – UF and PA Implementation Plan:**

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

2. TRANSMUCOSAL IMMEDIATE RELEASE FENTANYL PRODUCTS (TIRFs)

(Dr. Allerman)

A. The Relative Clinical Effectiveness and Conclusion of the TIRFs:

The TIRF subclass is comprised of the following formulations of transmucosal fentanyl: oral lozenge (Actiq, generics), buccal tablet (Fentora), sublingual tablet (Abstral), nasal spray (Lazanda), and sublingual spray (Subsys).

All of the TIRFs are indicated for the management of breakthrough cancer pain in patients who are already receiving opioids, and who are tolerant to around-the-clock therapy.

The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 1 absent)** the following for the TIRF formulations:

1. No head-to-head comparisons of the various TIRF formulations have been conducted to date. Indirect comparisons between products are difficult to make.
2. Evidence from a network meta-analysis and a Cochrane systematic review demonstrate that all the TIRFs provide rapid onset of analgesia, with clinically

meaningful differences in pain intensity achieved after 30 minutes following administration.
3. Minor pharmacokinetic differences (such as bioavailability and onset of analgesia) do not result in clinically relevant differences in pain relief.
4. Adverse effects are similar for all the TIRFs and are consistent with opioid therapy in cancer patients. Unique application site reactions include dental cavities with the lozenge (Actiq) and nasal irritation with the nasal spray (Lazanda).
5. Unique advantages of the products include the following: administration of the lozenge (Actiq) can be interrupted in case of toxicity and it is approved for adolescents 16 years and older. The sublingual tablet (Abstral) and spray (Subsys) have faster dissolution rates than the lozenge (Actiq) and buccal (Fentora) formulations. The nasal spray (Lazanda) is convenient and can be administered by caregivers.
6. Unique disadvantages include the following: the sugar content in the lozenge (Actiq) may cause formation of dental cavities and subsequent tooth loss. Lazanda may be unsuitable for patients with respiratory illnesses. Co-administration of Lazanda with a vasoconstrictive nasal decongestant (e.g., oxymetazoline) may lead to reduced fentanyl plasma concentrations.

Overall Clinical-Effectiveness Conclusion—In the absence of direct comparative trials, TIRF selection should be based on individual patient characteristics, likelihood of adherence, and patient preferences.

B. The Relative Cost-Effectiveness Analysis and Conclusion:

A Cost-minimization analysis and Budget Impact Analysis were performed to evaluate the TIRF subclass. The P&T Committee concluded **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. The Cost-minimization analysis showed that generic fentanyl citrate lozenge (Actiq) was the most cost-effective TIRF, followed by Fentora, Lazanda, and Abstral. Subsys was the least cost effective.
2. Budget Impact Analysis results showed that all modeled scenarios demonstrated a cost avoidance for the Military Health System, compared to the current baseline formulary status. The scenario with generic fentanyl lozenge (Actiq) with no step requirement and formulary on the Uniform Formulary, and all other branded agents Non-Formulary, demonstrated a cost avoidance for the Military Health System, with the smallest impact to patients from disruption in therapy.

C. The Uniform Formulary Recommendation:

The P&T Committee recommended **(9 for, 5 opposed, 1 abstained, 1 absent)** the following:

1. Uniform Formulary: fentanyl transmucosal lozenge (Actiq, generics)

2. Non-Formulary:
   a. Fentanyl sublingual tablet (Abstral)
   b. Fentanyl buccal tablet (Fentora)
   c. Fentanyl nasal spray (Lazanda)
   d. Fentanyl sublingual spray (Subsys)

D. The Uniform Formulary Implementation Plan:

The P&T Committee recommended **(14 for, 0 opposed, 1 abstained, 1 absent)** the following:

1. An effective date of the first Wednesday after a 90-day implementation period in all Points of Service; and,
2. DHA sends a letter to beneficiaries affected by the Uniform Formulary decision.

E. **Physician's Perspective:**

These products all contain fentanyl, and are used for breakthrough cancer pain. Other narcotics are also used for breakthrough pain, and are available on the Uniform Formulary (for example immediate release morphine).

These products do have a role for some patients who have difficulty swallowing or persistent nausea and vomiting. But currently the TIRFs are not widely used in the MHS – in the past year there were approximately 600 unique patients receiving one of these products, at a cost of $23 million dollars.

The FDA does have strict safety requirements for prescribing the TIRFs, including a Risk Evaluation and Mitigation Safety program (REMS), which ensures the drugs are not abused or misused, and are prescribed for the appropriate patients. Additionally, the MHS has an opioid safety edit, which is a type of Prior Authorization that makes sure these products are used in patients who are already receiving a narcotic. If a TIRF is prescribed in an opiate-naïve patient, there is a risk of respiratory depression.

The P&T Committee recommended (9 for, 5 opposed) that generic Actiq would be the only product available on the Uniform Formulary, and that the other four products (Abstral, Fentora, Lazanda, and Subsys) be non-formulary. The nonformulary recommendations affect about 355 patients. Step-therapy was not recommended, because not having step-therapy would disrupt the least amount of patients. These

products are controlled schedule II drugs, and if step-therapy had been considered, a patient could potentially walk away from the pharmacy without anything.

There was a lot of discussion on the formulary decision. The P&T Committee members who dissented were in favor of a step-therapy scenario, since it could potentially result in a greater cost-avoidance. However, if step-therapy had been recommended, the formulary decision would have affected 71% of the new patients receiving a TIRF, and patients would be required to go back to their providers to obtain a new prescription, since controlled schedule II drugs cannot be changed over the phone with the pharmacist.

F. **Panel Questions and Comments:**

Dr. Anderson asks for a clarification regarding step therapy. Although the process many not be known as step therapy he is glad to hear that an opioid safety edit exists to ensure that patients get other opioids therapy before receiving access to the drugs. He also asks if the drugs are only approved for cancer pain and if the current controls in place are successful?

Dr. Allerman responds that we don't call it step therapy. It's a fentanyl safety edit. It's done manually at the MTF and at the retail network. At the retail network and the mail order, it's actually a hard stop with a look back of the patient's profile. We have a designated list of narcotics. If the patient had 3 days of vicodin for dental, then that does not count. If the profile does not have a narcotic, it's a hard stop. The pharmacist cannot continue to process the prescription. They have to talk to the patient. Do you have cancer? Have you been on something before? Or they have to call the provider. The pharmacist cannot override for some of the edits.

Yes, the transmucosal fentanyl products are only approved for cancer and not for back pain. That is the intent of the REMS program from the FDA because of the risk of diversion and misuse. The FDA is trying to ensure it is used only for cancer patients and not neuropathic pain. Yes, we do believe the safety controls in place are successful. A group within the PEC, a clinical group within the operation, routinely looks and reviews the safety edit as well as our clinical contact at ESI. When new narcotics come out, we will consider whether they will be added to the safety edit. Just recently we did update the list. This is something we feel very important about because there have been some deaths several years ago when the fentanyl patch was used after dental pain. This is a high visibility item, and we do keep track of it.

Dr. Delgado asks if current patients taking other medication would be grandfathered and if the beneficiary notification letters would explain if there is a process for grandfathering in place or not.

Dr. Allerman clarified the question by stating "now that we are having non-formulary recommendations, would they be grandfathered? Grandfathering only applies in the setting of a prior authorization. This has no PA criteria recommended. Those products will go to

non-formulary status. They would not be able to be grandfathered. We would send them a letter notifying that as of the 90 days your co-pay would be increasing. There is the opportunity if they wanted to try the product or we have medical necessity criteria where the patient would continue to stay on the non-formulary but get the co-pay reduced to a formulary co-pay. That so happens that the medical necessity criteria does not fall under the purview of your committee's recommendations. The letter explains what the drugs are and the class, when the co-pays will increase, what the co-pays will increase to, and the mechanism of medical necessity.

There were no further questions or comments from the Panel. The Chair asked for a vote on the UF recommendation and the UF Implementation Plan for the Transmucosal Immediate Release Fentanyl Products (TIRFs).

1. **Transmuscosal Immediate Release Fentanyl Products - UF Recommendation**:

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

2. **Transmuscosal Immediate Release Fentanyl Products – UF Implementation Plan:**

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

UTILIZATION MANAGEMENT

1. HEPATITIS C VIRUS (HCV) AGENTS, DIRECT ACTING ANTIVIRALS (DAAs)

(Dr. Downs)

A. HCV Agents, DAAs: Paritaprevir/Ritonavir/Ombitasvir with Dasbuvir (Viekira Pak)—PA Criteria

The combination product Viekira Pak contains paritaprevir 75 mg, ritonavir 50 mg, and ombitasvir 12.5 mg (dosed two tablets once daily), packaged with dasbuvir 250 mg (dosed twice daily). Viekira Pak was approved by the FDA in December 2014 and is the third FDA approved interferon-free regimen indicated to treat HCV genotype 1.

PA criteria currently apply to the DAAs. The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for new users of paritaprevir/ritonavir/ombitasvir with dasbuvir (Viekira Pak), consistent with FDA-approved labeling. Prior authorization will expire after 12–24 weeks, based on the treatment regimen.

The full PA criteria are as follows:

Paritaprevir/ritonavir/ombitasvir with dasbuvir (Viekira Pak)

1. Direct Acting Antiviral Subclass

a. New users of paritaprevir/ritonavir/ombitasvir with dasbuvir (Viekira Pak) are required to undergo the PA process.
b. Current users are not affected by PA; they can continue therapy uninterrupted.
c. Patients are encouraged to use the Mail Order Pharmacy or MTFs to fill their Viekira Pak prescriptions.
d. Consult the AASLD/IDSA HCV guidelines (www.hcvguidelines.org) for the most up-to-date and comprehensive treatment for HCV. Unique patient populations are also addressed and treatment recommendations may differ from those for the general population.

2. **Manual PA Criteria**:

a. Age ≥ 18
b. Has laboratory evidence of chronic HCV genotype 1 infection
    1. State the HCV genotype and HCV RNA viral load on the PA form
c. Paritaprevir/ritonavir/ombitasvir + dasbuvir (Viekira Pak) is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.
d. The patient is not co-infected with Hepatitis B virus (HBV).

3. Treatment Regimens and Duration of Therapy

a. Treatment and duration of therapy are approved for one of the following regimens outlined below, based on HCV genotype, prior treatment, and presence of cirrhosis.
b. Prior authorization will expire after 12 weeks or 24 weeks, based on the treatment regimen selected.

Genotype 1 Patient Populations[1,2]	***Treatment***	***Duration***
GT1a without cirrhosis	Viekira Pak + ribavirin bid	12 weeks
GT1a with cirrhosis	Viekira Pak + ribavirin bid	24 weeks[3]
GT1b without cirrhosis	Viekira Pak	12 weeks
GT1b with cirrhosis	Viekira Pak + ribavirin bid	12 weeks
Liver transplant recipients with normal hepatic function and mild fibrosis (Metavir ≤2)	Viekira Pak + ribavirin bid	24 weeks
[1]Follow GT1a dosing recommendation in patients with an unknown GT1 or mixed GT1 infection [2]Treatment naïve or treatment-experienced with peginterferon alpha plus ribavirin [3]For treatment naïve OR prior IFN+RBV relapser/partial responder, consider 12 weeks		

B. Panel Questions and Comments:

Dr. Anderson asks if all the Hepatitis C agents designated as covered under the formulary. He also asked if the other new combination drug for Hepatitis C was in the review process.

Dr. Downs responds that all the ones that are available. That will be reviewed in the May P&T Committee meeting. All the drugs that all have prior authorizations restrict their use for the update.

C. There were no further questions or comments from the Panel. The Chair asked for a vote on the PA Criteria for the HCV Agents, DAAs: Paritaprevir/Ritonavir/Ombitasvir with Dasbuvir (Viekira Pak).

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1. **HCV Agents, DAAs: Paritaprevir/Ritonavir/Ombitasvir with Dasbuvir (Viekira Pak)—PA Criteria**

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

2. TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs)

(Dr. Downs)

A. TIBs: Secukinumab (Cosentyx)—PA Criteria:

Secukinumab (Cosentyx) is a new TIB indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. The TIBs were reviewed by the P&T Committee in August 2014 and automated PA (step therapy) and manual PA criteria were recommended for the class (implemented on December 17, 2014).

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria and step therapy for secukinumab (Cosentyx), consistent with the FDA-approved indication.

The full PA criteria are as follows:

PA criteria apply to all new and current users of Cosentyx.

Automated PA criteria: The patient has filled a prescription for adalimumab (Humira) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria:

If automated criteria are not met, coverage is approved for Cosentyx if:

a. Contraindications exist to Humira
b. Inadequate response to Humira (need for different anti-TNF or non-TNF)
c. Adverse reactions to Humira not expected with requested non-step preferred TIB

AND

Coverage approved for patients > 18 years with:

a. Active moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy

Coverage is NOT provided for concomitant use.

B. **Panel Questions and Comments:**

There were no further questions or comments from the Panel. The Chair asked for a vote on the PA Criteria for the Targeted Immunomodulatory Biologics.

1. **Targeted Immunomodulatory Biologics (TIBs) - PA Criteria**:

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

3. TOPICAL ANTIFUNGALS

(Dr. Allerman)

A. Topical Antifungals: Efinaconazole 10% (Jublia) and Tavaborole 5% (Kerydin) Topical Solutions—PA Criteria:

Jublia and Kerydin are indicated for the topical treatment of toenail onychomycosis. Both products are dosed once daily for 48 weeks. The P&T Committee reviewed the current recommended treatment guidelines, FDA-approved indications, efficacy data, safety information, and utilization and cost data for the topical antifungals for toenail onychomycosis.

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for efinaconazole 10% (Jublia) and tavaborole 5% (Kerydin) in all new and current users of the products. PA criteria were recommended due to the modest efficacy of the products, lack of head-to-head clinical trials, limited efficacy and safety data, and high cost.

The full PA criteria are as follows:

PA criteria apply to all new and current users of Jublia and Kerydin.

Manual PA criteria:
Jublia and Kerydin are approved if all of the following criteria apply:

1. The patient must have diagnostically confirmed onychomycosis by either potassium hydroxide preparation, fungal culture, nail biopsy, or other assessment to confirm diagnosis.

2. The patient is immunocompromised, has diabetes mellitus, or peripheral vascular disease and has swelling and/or redness in the surrounding nail tissue or pain in affected nail(s).

3. The patient has history of one of the following (therapeutic failure, contraindication or adverse events, or intolerance) to one of the following antifungals: itraconazole, terbinafine, or ciclopirox.

    a. therapeutic failure
    b. contraindication (e.g., renal impairment, pre-existing liver disease, or evidence of ventricular dysfunction such as congestive heart failure)
    c. adverse event/intolerance to one of the following antifungal agents

4. Treatment is requested due to a medical condition and not for cosmetic purposes. Examples include the following:

a. history of cellulitis of the lower extremity who have ipsilateral toenail onychomycosis
b. diabetic patients with additional risk factors for cellulitis
c. patients who experience pain/discomfort associated with the infected nail

5. The patient's condition is causing debility or a disruption in their activities of daily living.

6. Jublia or Kerydin have not been used in the previous 24 months.

PA expires after 1 year.

B. Topical Antifungals: Efinaconazole 10% (Jublia) and Tavaborole 5% (Kerydin) Topical Solutions—PA Implementation Plan

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)**

1. An effective date of the first Wednesday after a 90-day implementation period in all POS; and.
2. DHA sends a letter to beneficiaries affected by the PA.

C. Panel Questions and Comments.

There were no questions or comments from the Panel. The Chair asked for a vote on the UF recommendation, PA Criteria and PA Implementation Plan for the Topical Antifungals.

1. **Topical Antifungals - PA Criteria**:

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

2. **Topical Antifungals – PA Implementation Plan**:

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

4. CYSTIC FIBROSIS DRUGS

A. Cystic Fibrosis Drugs: Ivacaftor (Kalydeco)—PA Criteria

Ivacaftor (Kalydeco) is indicated for the treatment of cystic fibrosis. PA criteria were recommended at the February 2012 meeting, updated in May 2014, and reflect the FDA-approved indication for various mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. In December 2014, Kalydeco received an additional indication for the R117H mutation in the CFTR gene.

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent)** updated manual PA criteria for Kalydeco to include the expanded FDA-approved indication.

The full PA criteria are as follows:

Manual PA Criteria apply to all new and current users of Ivacaftor (Kalydeco).

1. Coverage will be approved for the treatment of CF patients aged 6 years and older who have a G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R or **for R117H** mutation in the CFTR gene, detected by an FDA-approved test.
2. Coverage is not approved for patients who are homozygous for the F508del mutation in the CFTR gene. We do have 32 patients receiving Kalydeco.

B. Panel Questions and Comments.

There were no questions or comments from the Panel. The Chair asked for a vote on the PA Criteria for the Cystic Fibrosis Drugs: Ivacaftor (Kalydeco) .

1. **Cystic Fibrosis Drug: Ivacaftor (Kalydeco) - PA Criteria**:

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

5. NON-INSULIN DIABETES MELLITUS DRUGS: GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST (GLP1RAs)

A. GLP1RAs : Exenatide Once Weekly Pen (Bydureon Pen)—Removal of PA Criteria

Exenatide (Bydureon) is now available in a pre-filled pen in addition to the original vial formulation. Manual PA criteria were recommended at the November 2014 P&T Committee meeting due to the significant price difference between the Bydureon Pen formulation and the Bydureon vials. The cost of the Bydureon pen is now comparable to the vial formulation.

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 1 absent**) to remove the following manual PA criteria for the Bydureon pen, requiring use of Bydureon vials first. The existing step therapy PA, requiring a trial of metformin or a sulfonylurea first, will remain for the formulation.

Manual PA criteria from the November 2014 P&T Committee meeting recommended to be removed:

Exenatide once weekly (Bydureon pen)

1. Coverage approved if patient has first tried Bydureon 2mg vial/cartridge first,

AND

2. Patient has dexterity issues and cannot assemble the Bydureon vial/cartridge

The existing step therapy PA, requiring a trial of metformin or a sulfonylurea first, that will remain is as follows:

New GLP1RA users are required to try metformin or a sulfonylurea before receiving Byetta, Bydureon, or Victoza.

Automated PA criteria: The patient has received a prescription for metformin or sulfonylurea at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria, if automated criteria are not met: Byetta, Bydureon, or Victoza is approved and a trial of metformin or sulfonylrea is NOT required) if:

1. The patient has a confirmed diagnosis of Type 2 Diabetes Mellitus
2. The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.
3. The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.
4. The patient has a contraindication to both metformin and a SU.
5. The patient has had an inadequate response to metformin and a SU.

C. Panel Questions and Comments.

There were no questions or comments from the Panel. The Chair asked for a vote on the PA Criteria for the Non-Insulin Diabetes Mellitus Drugs: Glucagon-like Peptide-1 Receptor Agonists (GLP1RAs)

1. Non-Insulin Diabetes Mellitus Drugs: Glucagon-like Peptide-1 Receptor Agonists (GLP1RAs) - PA Criteria:

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

Mr. Blanche thanks the panel and concludes the meeting.

Dr. Michael J. Anderson

Brief Listing of Acronyms Used in this Summary

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

- AASLD – American Association for the Study of Liver Diseases
- BAP – Beneficiary Advisory Panel
- BCF – Basic Core Formula
- CFR – Code of Federal Regulations
- CFTR – Cystic Fibrosis Transmembrane Conductance Regulator
- CMA – Cost-Minimization Analysis
- CYP3A4 – Cytochrome P450 3A4
- DAA – Direct Acting Antivirals
- DFO – Designated Federal Officer
- DHA – Defense Health Agency
- DoD – Department of Defense
- DPP-4 – Dipetidase-4
- ED – Erectile Dysfunction
- ERAs – Endothelin Receptor Antagonists
- FACA – Federal Advisory Committee Act
- FDA – Food and Drug Administration
- G1224E – Cystic Fibrosis Mutation
- G1392D - Cystic Fibrosis Mutation
- G178R - Cystic Fibrosis Mutation
- G551D - Cystic Fibrosis Mutation
- G551S - Cystic Fibrosis Mutation
- GLP-1RAs – Glucagon-Like Peptide-1 Receptor Agonists
- GT1 – Genotype 1
- HBV – Hepatitis B Virus
- HCV – Hepatitis C Virus
- HCV RNA – Genetic materials
- IDSA – Infectious Diseases Society of America
- IFN+RBV – Interferon + Ribavirin
- IR – Immediate Release
- MHS – Military Health System
- MI – Myocardial Infarction
- MTF – Military Treatment Facility
- NDAA – National Defense Authorization Act
- P&T – Pharmacy & Therapeutic
- PA – Prior Authorization
- PAH – Pulmonary Arterial Hypertension

- PDE-5 – Phosphodiesterase-5
- PEC – Pharmacoeconomic Center
- POS – Point of Sale
- PPIs – Proton Pump Inhibitors
- R117H - Cystic Fibrosis Mutation
- S1251N - Cystic Fibrosis Mutation
- S549R - Cystic Fibrosis Mutation
- S549R - Cystic Fibrosis Mutation
- SED-1s – Sedative Hynotics
- SGLT2 – Sodium-Glucose Co-Transporter 2
- TIBs – Targeted Immunomodulatory Biologics
- TIRF – Transmucosal Immediate Release Fentanyl
- TNF – Tumor Necrosis Factor
- TRICARE – Military Health Care System
- UF – Uniform Formulary
- USC – United States Code