DEPARTMENT OF DEFENSE PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

INFORMATION FOR THE UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL

I. UNIFORM FORMULARY REVIEW PROCESS

Under 10 United States Code § 1074g, as implemented by 32 Code of Federal Regulations 199.21, the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee is responsible for developing the Uniform Formulary (UF). Recommendations to the Director, Defense Health Agency (DHA), on formulary status, pre-authorizations, and the effective date for a drug's change from formulary to nonformulary (NF) status receive comments from the Beneficiary Advisory Panel (BAP), which must be reviewed by the Director before making a final decision.

II. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—NEWER SEDATIVE HYPNOTICS (SED-1s)

P&T Comments

A. SED-1s: Tasimelteon (Hetlioz)—Relative Clinical Effectiveness and Conclusion

Tasimelteon (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 tasimelteon (RESET trial), and the high patient discontinuation rate (SET trial).

Two agents with a similar structure as tasimelteon [melatonin supplement and ramelteon (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. SED-1s: Tasimelteon (Hetlioz)—Relative Cost-Effectiveness Analysis and Conclusion

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

C. SED-1s: Tasimelteon (Hetlioz)—UF Recommendation

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) tasimelteon

(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 UF.

D. SED-1s: Tasimelteon (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 tasimelteon (Hetlioz) (requiring a trial of zolpidem IR or zaleplon) no longer apply. Manual PA criteria apply to all new users of tasimelteon (Hetlioz).

Manual PA criteria: Tasimelteon (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 patient has not responded after 6 months, they will be deemed a non-responder).

E. SED-1s: Tasimelteon (Hetlioz)—UF and PA Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service (POS); and, 2) DHA send a letter to beneficiaries affected by the UF decision.

III. RECENTLY APPROVED U.S. FDA AGENTS—SED-1s

BAP Comments

A. SED-1s: Tasimelteon (Hetlioz)—UF Recommendation, PA Criteria, UF and PA Implementation Plan

The P&T Committee's recommendations for tasimelteon (Hetlioz) are listed above. This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissention

IV. RECENTLY APPROVED U.S. FDA AGENTS—SODIUM-GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITORS

P&T Comments

A. SGLT2 Inhibitors: Empagliflozin (Jardiance)—Relative Clinical Effectiveness and Conclusion

Empagliflozin (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 (A1c), 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 UF non-insulin diabetes drugs, given the modest decrease in A1c, risk of adverse reactions, including female genital mycotic infections and urinary tract infections, and unknown long-term cardiovascular safety profile.

B. SGLT2 Inhibitors: Empagliflozin (Jardiance)—Relative Cost-Effectiveness Analysis and Conclusion

CMA was performed to evaluate empagliflozin (Jardiance) with other oral products on the UF used in the treatment of diabetes. The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA results showed empagliflozin (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.
- Current costs for empagliflozin (Jardiance) show it was comparable to canagliflozin (Invokana) and dapagliflozin (Farxiga), the other agents available in the SGLT2 subclass.

C. SGLT2 Inhibitors: Empagliflozin (Jardiance)—UF Recommendation

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

D. SGLT2 Inhibitors: Empagliflozin (Jardiance)—PA Criteria

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 empagliflozin (Jardiance), consistent with the PA requirements in place for canagliflozin and dapagliflozin.

The full PA criteria are as follows:

All new and current users of empagliflozin (Jardiance) are required to try metformin or a sulfonylurea (SU), and a dipeptidyl-dipeptidase-4 (DPP-4) inhibitor before empagliflozin (Jardiance).

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

AND

Manual PA criteria: If automated criteria are not met, empagliflozin (Jardiance) is approved (e.g., trial of metformin or SU AND a DPP-4 inhibitor is NOT required) if:

- The patient has experienced any of the following issues on metformin:
  - impaired renal function precluding treatment with metformin
  - history of lactic acidosis
- The patient has experienced any of the following issues on a sulfonylurea:
  - hypoglycemia requiring medical treatment
- The patient has had inadequate response to metformin or a SU or a DPP-4 inhibitor.
- The patient has a contraindication to metformin or a SU or DPP-4 inhibitor.

E. SGLT2 Inhibitors: Empagliflozin (Jardiance)—UF and PA Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS; and, 2) DHA send a letter to beneficiaries affected by the UF decision.

V. RECENTLY APPROVED U.S. FDA AGENTS—SGLT2 INHIBITORS

BAP Comments

A. SGLT2 Inhibitors: Empagliflozin (Jardiance)—UF Recommendation, PA Criteria, UF and PA Implementation Plan

The P&T Committee's recommendations for empagliflozin (Jardiance) are listed above. This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissention

VI. RECENTLY APPROVED U.S. FDA AGENTS—ANTIPLATELET AGENTS

P&T Comments

A. Antiplatelet Agents: Vorapaxar (Zontivity)—Relative Clinical Effectiveness and Conclusion

Vorapaxar (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 (CV) events (including CV death, myocardial infarction (MI), and stroke) in patients with a history of MI or with peripheral artery disease. It remains unknown whether adding vorapaxar 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 vorapaxar is limited due to the significantly increased bleeding risk. Vorapaxar should be reserved for those patients with stable atherosclerotic disease who have failed other antiplatelet therapies.

B. Antiplatelet Agents: Vorapaxar (Zontivity)—Relative Cost-Effectiveness Analysis and Conclusion

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

C. Antiplatelet Agents: Vorapaxar (Zontivity)—UF Recommendation

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

D. Antiplatelet Agents: Vorapaxar (Zontivity)—UF 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 send a letter to beneficiaries affected by the UF decision.

VII. RECENTLY APPROVED U.S. FDA AGENTS—ANTIPLATELET AGENTS

BAP Comments

A. Antiplatelet Agents: Vorapaxar (Zontivity)—UF Recommendation and UF Implementation Plan

The P&T Committee's recommendations for vorapaxar (Zontivity) are listed above. This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissention

VIII. RECENTLY APPROVED U.S. FDA AGENTS—PHOSPHODIESTERASE-5 (PDE-5) INHIBITORS FOR ERECTILE DYSFUNCTION (ED)

P&T Comments

A. PDE-5 Inhibitors for ED: Avanafil (Stendra)—Relative Clinical Effectiveness and Conclusion

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

The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) that although avanafil 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 UF to meet the needs of the MHS.

B. PDE-5 Inhibitors for ED: Avanafil (Stendra)—Relative Cost-Effectiveness Analysis and Conclusion

CMA was performed. The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) avanafil (Stendra) was more costly than the other UF and NF PDE-5 inhibitors.

C. PDE-5 Inhibitors for ED: Avanafil (Stendra)—UF Recommendation

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

D. PDE-5 Inhibitors for ED: Avanafil (Stendra)—PA Criteria

Existing automated (step therapy) PA criteria for the PDE-5 inhibitors used for the treatment of ED requires a trial of sildenafil (Viagra) first, 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 MHS 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:

- Patient has tried sildenafil (Viagra) and has had an inadequate response or was unable to tolerate treatment due to adverse effects.
- Treatment with sildenafil (Viagra) is contraindicated.
- 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.]
- 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 in 1 or 2.]

  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. PDE-5 Inhibitors for ED: Avanafil (Stendra)—UF and PA Implementation Plan

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS.

IX. RECENTLY APPROVED U.S. FDA AGENTS—PDE-5 INHIBITORS FOR ED

BAP Comments

A. PDE-5 Inhibitors for ED: Avanafil (Stendra)—UF Recommendation and UF Implementation Plan

The P&T Committee's recommendations for avanafil (Stendra) are listed above. This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

X. RECENTLY APPROVED U.S. FDA AGENTS—PROTON PUMP INHIBITORS (PPIs)

P&T Comments

A. PPIs: Esomeprazole Strontium—Relative Clinical Effectiveness and Conclusion

Esomeprazole strontium (no brand name) is the eighth 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. PPIs: Esomeprazole Strontium—Relative Cost-Effectiveness Analysis and Conclusion

CMA 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 UF.

C. PPIs: Esomeprazole Strontium—UF Recommendation

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

D. PPIs: Esomeprazole Strontium—PA Criteria

Existing automated (step therapy) PA criteria 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, generics), pantoprazole tablets (Protonix, 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, generics), pantoprazole tablets (Protonix, generics), or esomeprazole magnesium (Nexium) is NOT required if:

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

E. PPIs: Esomeprazole Strontium—UF and PA Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) an 1) an effective date of the first Wednesday after a 90-day implementation period in all POS; and, 2) DHA send a letter to beneficiaries affected by the UF decision.

XI. RECENTLY APPROVED U.S. FDA AGENTS—PPIs

BAP Comments

A. PPIs: Esomeprazole Strontium—UF Recommendation, PA Criteria, and UF and PA Implementation Plan

The P&T Committee's recommendations for esomeprazole strontium are listed above. This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissention

XII. UF CLASS REVIEWS—PULMONARY ARTERIAL HYPERTENSION (PAH) AGENTS

P&T Comments

A. PAH—Relative Clinical Effectiveness and Conclusion

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

- **Prostacyclins**: treprostinil nebulized solution (Tyvaso), treprostinil oral tablets [Orenitram extended release (ER)], and iloprost nebulized solution (Ventavis);
- **Endothelin Receptor Antagonists (ERAs)**: bosentan (Tracleer), ambrisentan (Letairis), and macitentan (Opsumit);
- **Nitric Oxide Drugs**: the soluble guanylate cyclase stimulator, riociguat (Adempas); and, the PDE-5 inhibitors, sildenafil generic, sildenafil brand (Revatio), and tadalafil (Adcirca).

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

1. There are no head-to-head comparisons among the PAH 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 UF review (November 2009).
    - Sildenafil and tadalafil show similar improvements in 6-minute walking distance (6MWD), based on indirect comparisons of clinical trial results.
    - 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 PAH drugs increased the 6MWD 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 6MWD is a distance of at least 33 meters.
4. In their individual trials, treprostinil (Orenitram ER), macitentan (Opsumit), and riociguat (Adempas) caused statistically significant improvements in the 6MWD 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 (CTEPH).

5. Within and among the subclasses, the PAH drugs have distinct adverse reaction profiles. The ERAs and riociguat are pregnancy category X.

Overall relative clinical effectiveness conclusion: The P&T Committee concluded the choice of drug for PAH 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. PAH—Relative Cost-Effectiveness Analysis and Conclusion

CMA and budget impact analysis (BIA) was performed to evaluate the PAH subclasses. BIA 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:

ERAs:

- CMA results showed that ambrisentan (Letairis) was the most cost-effective agent in this subclass, followed by macitentan (Opsumit) and bosentan (Tracleer).
- BIA results showed that the scenario with Letairis, Opsumit, and Tracleer designated with UF status and no step requirement yielded the lowest budget impact for the MHS.

Prostacyclins:

- 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).
- BIA results showed that the scenario with Orenitram ER, Tyvaso, and Ventavis designated with UF status and no step requirement yielded the lowest budget impact for the MHS.

Nitric Oxide Drugs:

- 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).
- BIA results showed that the scenario with sildenafil generic and sildenafil brand (Revatio) as step-preferred and formulary on the UF, with tadalafil (Adcirca) and riociguat (Adempas) as non step-preferred and formulary on the UF, yielded the lowest budget impact for the MHS.

C. PAH—UF Recommendation

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

- ERAs: designate bosentan (Tracleer), ambrisentan (Letairis), and macitentan (Opsumit) as UF.
- Prostacyclins: designate treprostinil nebulized solution (Tyvaso), treprostinil tablets (Orenitram ER), and iloprost (Ventavis) as UF.
- Nitric Oxide Drugs:
    - UF and step-preferred: sildenafil 20mg generic and sildenafil brand (Revatio)
    - UF and non step-preferred: tadalafil (Adcirca) and riociguat (Adempas)
    - This recommendation includes step therapy, which requires a trial of sildenafil 20 mg generic or sildenafil brand (Revatio) in all new users of tadalafil (Adcirca) or riociguat (Adempas).

D. PAH—PA Criteria

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 [tadalafil (Adcirca) and riociguat (Adempas)], requiring a trial of sildenafil 20 mg generic or sildenafil brand (Revatio) first.

The full PA criteria are as follows:

PA 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 MHS 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 (e.g., a trial of sildenafil is NOT required) if:

- For Adempas:
    - Patient has a documented diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH)
    - Patient has tried a PDE-5 inhibitor and failed or did not respond to therapy
    - Patient has experienced significant adverse effects from the PDE-5 inhibitor
- For Adcirca:

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

- For both Adempas and Adcirca:
  - Patient is not taking a nitrate drug.

E. PAH—UF 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 POS.

XIII. UF CLASS REVIEWS—PAH

BAP Comments

A. PAH—UF Recommendation, PA Criteria, UF and PA Implementation Plan

The P&T Committee's recommendations for the PAH Drug Class are listed above. This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissention

XIV. UF CLASS REVIEWS—ORAL ONCOLOGY DRUGS: PROSTATE CANCER

P&T Comments

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

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

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

- **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:

- **Subclass I (Anti-Androgen Agents):**

    1. 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.
    2. Flutamide has a higher incidence of gastrointestinal side effects than bicalutamide, and has warnings for hepatotoxicity. Nilutamide (Nilandron) has a black box warning for pulmonary toxicity and delays visual light-to-dark adaptation that can limit its use.
    3. 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.
    4. Although nilutamide (Nilutamide) has no compelling advantages compared with flutamide or bicalutamide and has the least favorable safety profile, it is required on the UF due to its unique indication for use in combination with surgical castration.

- **Subclass II (Survival Prolonging Drugs)**:

    1. 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.
    2. 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.
    3. 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 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.

B. Oral Oncology Drugs: Prostate Cancer—Relative Cost-Effectiveness Analysis and Conclusion

CMA and BIA were performed to evaluate the Prostate Cancer drugs. The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA results 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).
- BIA results showed that designating all the prostate cancer drugs as formulary on the UF, with no step-preferred agents in either subclass, demonstrated significant cost avoidance for the MHS.

C. Oral Oncology Drugs: Prostate Cancer—UF Recommendation

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

- UF:
  - Flutamide (Eulexin; generic)
  - Bicalutamide (Casodex; generic)
  - Nilutamide (Nilandron)
  - Abiraterone (Zytiga)
  - Enzalutamide (Xtandi)
- NF: None

D. Oral Oncology Drugs: Prostate Cancer—PA Criteria

Manual PA criteria 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 manual PA criteria for all new users of nilutamide (Nilandron) due to its limited indication.

The full PA criteria are as follows:

- For nilutamide (Nilandron):

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

  Nilutamide is approved if any of the following:

  - Patient has experienced significant adverse effects or contraindication from bicalutamide or flutamide; or
  - Patient has experienced therapeutic failure with bicalutamide or flutamide; or
  - Patient has a diagnosis of metastatic prostate cancer (stage D2) disease and the patient has undergone orchiectomy.
- For enzalutamide (Xtandi):

Coverage is approved if:

- Documented diagnosis of metastatic castration-resistant prostate cancer

No expiration date for the PA.

- For abiraterone (Zytiga):

  Coverage is approved if:

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

  No expiration date for the PA.

E. Oral Oncology Drugs: Prostate Cancer—UF 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 POS.

XV. UF CLASS REVIEWS—ORAL ONCOLOGY DRUGS: PROSTATE CANCER

BAP Comments

A. Oral Oncology Drugs: Prostate Cancer—UF Recommendation, PA Criteria, UF and PA Implementation Plan

The P&T Committee's recommendations regarding the Oral Oncology Drugs for Prostate Cancer are listed above. This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

XVI. UF CLASS REVIEWS—TRANSMUCOSAL IR FENTANYL PRODUCTS (TIRFs)

P&T Comments

A. TIRFs—Relative Clinical Effectiveness and Conclusion

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 caries 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 caries 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. TIRFs—Relative Cost-Effectiveness Analysis and Conclusion

CMA and BIA were performed to evaluate the TIRF subclass. The P&T Committee concluded (14 for, 0 opposed, 1 abstained, 1 absent) the following:

- CMA results 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.
- BIA results showed that all modeled scenarios demonstrated a cost avoidance for the MHS, compared to the current baseline formulary status. The scenario with generic fentanyl lozenge (Actiq) with no step requirement and formulary on the UF, and all other branded agents NF, demonstrated a cost avoidance for the MHS, with the smallest impact to patients from disruption in therapy.

C. TIRFs—UF Recommendation

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

- UF: fentanyl transmucosal lozenge (Actiq, generics)

- NF:
  - Fentanyl sublingual tablet (Abstral)
  - Fentanyl buccal tablet (Fentora)
  - Fentanyl nasal spray (Lazanda)
  - Fentanyl sublingual spray (Subsys)

D. TIRFs—UF Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS; and, 2) DHA send a letter to beneficiaries affected by the UF decision.

XVII. UF CLASS REVIEWS—TIRFs

BAP Comments

A. TIRFs—UF Recommendation and UF Implementation Plan

The P&T Committee's recommendations for the TIRFs drug subclass are listed above. This section is reserved for BAP discussion and comments.

XVIII. UTILIZATION MANAGEMENT—HEPATITIS C VIRUS (HCV) AGENTS, DIRECT ACTING ANTIVIRALS (DAAs)

P&T Comments

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)
Direct Acting Antiviral Subclass

- New users of paritaprevir/ritonavir/ombitasvir with dasbuvir (Viekira Pak) are required to undergo the PA process.
- Current users are not affected by PA; they can continue therapy uninterrupted.
- Patients are encouraged to use the Mail Order Pharmacy or MTFs to fill their Viekira Pak prescriptions.
- 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.

Manual PA Criteria:

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

Treatment Regimens and Duration of Therapy

- 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.
- 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

XIX. UTILIZATION MANAGEMENT—HCV AGENTS, DAAs

BAP Comments

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

The P&T Committee's recommendation for paritaprevir/ritonavir/ombitasvir with dasbuvir (Viekira Pak) is listed above.

This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

XX. UTILIZATION MANAGEMENT—TARGETED IMMUNOMODULATORY BIOLOGICS (TIBs)

P&T Comments

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:

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

AND

Coverage approved for patients > 18 years with:

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

Coverage is NOT provided for concomitant use with other TIBs.

XXI. UTILIZATION MANAGEMENT—TIBs

BAP Comments

A. TIBs: Secukinumab (Cosentyx)—PA Criteria

The P&T Committee's recommendation for secukinumab (Cosentyx) is listed above.

This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

XXII. UTILIZATION MANAGEMENT—TOPICAL ANTIFUNGALS

P&T Comments

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
    - therapeutic failure
    - contraindication (e.g., renal impairment, pre-existing liver disease, or evidence of ventricular dysfunction such as congestive heart failure)
    - 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:
    - history of cellulitis of the lower extremity who have ipsilateral toenail onychomycosis
    - diabetic patients with additional risk factors for cellulitis
    - 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 send a letter to beneficiaries affected by the PA.

XXIII. UTILIZATION MANAGEMENT—TOPICAL ANTIFUNGALS

BAP Comments

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

The P&T Committee's recommendations for efinaconazole 10% (Jublia) and tavaborole 5% (Kerydin) topical solutions are listed above.

This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissention

XXIV. UTILIZATION MANAGEMENT—CYSTIC FIBROSIS DRUGS

P&T Comments

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 (changes highlighted in bold):

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.

XXV. UTILIZATION MANAGEMENT—CYSTIC FIBROSIS DRUGS

BAP Comments

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

The P&T Committee's recommendation for the ivacaftor (Kalydeco) is listed above.

This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissention

XXVI. UTILIZATION MANAGEMENT—NON-INSULIN DIABETES MELLITUS DRUGS: GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST (GLP1RAs)

P&T Comments

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)

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

AND

- 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 (SU) before receiving Byetta, Bydureon, or Victoza.

Automated PA criteria: The patient has received a prescription for metformin or SU 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 (e.g., trial of metformin or SU 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.

XXVII. UTILIZATION MANAGEMENT—GLP1RAs

BAP Comments

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

The P&T Committee's recommendation for exenatide once weekly pen (Bydureon Pen) is listed above.

This section is reserved for BAP discussion and comments.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention