EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel Comments
June 11, 2015

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

1. NEWER SEDATIVE HYPNOTICS (SED-1s)

A. SED-1s: Suvorexant (Belsomra) - UF Recommendation

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) Belsomra be designated NF, due to the lack of compelling clinical advantages and cost disadvantage compared to the existing sedative hypnotics on the UF.

B. SED-1s: Suvorexant (Belsomra) – Prior Authroization for PA Criteria

Existing automated PA criteria or step therapy for the SED-1s require a trial of immediate release (IR) zolpidem or zaleplon. The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) that the existing automated PA criteria for the SED-1s apply to Belsomra.

The full PA criteria are as follows: A trial of generic zolpidem IR or zaleplon is required for new users of Belsomra.

Automated PA: The patient has filled a prescription for zolpidem IR or zaleplon at any Military Health System pharmacy point of service (Military Treatment Facility, retail network pharmacies, or mail order) during the previous 180 days.

Manual PA Criteria: The patient has an inadequate response to, been unable to tolerate due to adverse effects, or has a contraindication to zolpidem IR or zaleplon.

C. SED-1s: Suvorexant (Belsomra) – UF and PA Implementation

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 points of service and the DHA will send a letter to beneficiaries affected by the UF decision.

Summary Physician's Perspective:

Belsomra has the same FDA indications as Ambien CR and Lunesta, which are both on the Uniform Formulary. Although the mechanism of action is unique, Belsomra's side effect profile is similar to the other drugs in the class, and it is a controlled schedule drug.

The Committee did unanimously recommend non-formulary placement for Belsomra, as it was not cost effective.

From the period of February 2015 to April 2015, there were 756 patients receiving Belsomra in the DoD. Automated prior authorization (step therapy) has been applied to the Sedative Hypnotics class for several years, and the recommendation was for Belsomra to follow the same requirements. Patients would need a trial of generic Ambien immediate release or generic Sonata before using Belsomra.

Summary of Panel Questions and Comments:

There were no questions or comments from the Panel. Without further discussion, the Chair called for the vote on UF recommendation, PA Criteria, and UF and PA Implementation for SED-1s for Suvorexant (Belsomra).

1. **SED-1s: Suvorexant (Belsomra) – 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. **SED-1s: Suvorexant (Belsomra) – 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. **SED-1s: Suvorexant (Belsomra) – 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. MULTIPLE SCLEROSIS (MS) DRUGS

A. MS Drugs: Peginterferon Beta-1a (Plegridy) – UF Recommendation

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) Plegridy be designated NF based on clinical and cost effectiveness.

B. MS Drugs: Peginterferon Beta-1a (Plegridy) – UF 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 points of service and the DHA will send a letter to beneficiaries affected by the UF decision.

Summary of Physician Perspective:

The MS drugs were most recently reviewed in November 2014, and all the drugs, both injectables and orals are on the Uniform Formulary.

Plegridy is manufactured by the same company that makes Avonex. Plegridy and Avonex contain the same active ingredient; however, Plegridy is pegylated, which allows it to be administered every two weeks.

The recommendation for Plegridy was that it should be non-formulary, since it is not cost effective compared to the other MS drugs. An analysis of DoD data shows that most patients who are newly diagnosed with MS are being started on one of the oral drugs, and overall, the use of injectables is decreasing. There is no data that has evaluated efficacy in patients who have switched from another interferon product or an oral MS drug to Plegridy. Currently there are about 106 patients on Plegridy in the DoD.

Summary of Panel Questions and Comments:

Dr. Anderson asked if the 106 patients that are currently on Plegridy be grandfathered.

Dr. Downs replied that grandfathering is usually step-therapy.

Dr. Allerman interjected that this decision did not have prior authorization of step-therapy. The medical necessity pathway is not addressed by the BAP committee. That is the pathway to get the co-pay reduced.

There were no more questions or comments from the Panel. Without further discussion, the Chair called for the vote on UF recommendation and UF Implementation Plan for MS Drugs: Peginterferon Beta-1a (Plegridy).

1. **MS Drugs: Peginterferon Beta-1a (Plegridy) – 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. **MS Drugs: Peginterferon Beta-1a (Plegridy) – 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. **ANTIEMETICS/ANTIVERTIGO AGENTS**

   A. Antiemetics/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis)—UF Recommendation

   The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) doxylamine succinate and pyridoxine hydrochloride (Diclegis) be designated NF due to the lack of compelling clinical advantages, aside from its pregnancy Category A rating, and its cost disadvantage when compared to the individual OTC components and the formulary agents available to treat NVP.

   B. Antiemetics/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochlordie (Diclegis) – PA Criteria

   Manual PA criteria were recommended at the February 2013 DoD P&T Committee meeting and implemented in August 2013 for doxylamine succinate and pyridoxine hydrochloride (Diclegis), requiring a trial of nonpharmacologic interventions and OTC pyridoxine, and consideration of alternate antiemetics. The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) maintaining the PA criteria for doxylamine succinate and pyridoxine hydrochloride (Diclegis).

   The full PA criteria are as follows: All new users of Diclegis are required to try a nonpharmacologic method for management of nausea and vomiting during pregnancy AND over-the-counter pyridoxine before receiving doxylamine succinate and pyridoxine hydrochloride (Diclegis).

   Manual PA Criteria—Doxylamine succinate and pyridoxine hydrochloride (Diclegis) is approved if:

- The patient has not had relief of symptoms after trying a nonpharmacologic method to manage nausea and vomiting during pregnancy,

  AND

- The patient has not had relief of symptoms after trying over-the-counter pyridoxine for management of nausea and vomiting during pregnancy.
- Providers are encouraged to consider an alternate antiemetic (e.g., ondansetron) prior to prescribing doxylamine succinate and pyridoxine hydrochloride (Diclegis).

  Prior Authorization will expire after 9 months.

C. **Antiemetics/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis) – UF and PA Implementation Plan**

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) 1) an effective date of the first Wednesday after a 90-day implementation period in all points of service (POS); and, 2) DHA send a letter to beneficiaries affected by the UF decision.

Summary of Physician's Perspective

Diclegis is an example of a new twist on an old drug. It contains the same active ingredient as the product Bendectin, which was available years ago and subsequently removed from the market. Bendectin continued to be available in Canada, and a Canadian company received FDA approval to market the drug in the US under the brand name Diclegis.

The individual ingredients, which are found in the OTC products Unisom and Vitamin B6, have been used for years to treat nausea and vomiting of pregnancy. The guidelines from the OB-GYN professional group continue to recommend vitamin B6 and doxylamine as first line. Additionally, other treatments, including Zofran, are also in the guidelines.

A gynecologist is a member of the P&T Committee, and she relayed that the main benefit of Diclegis to the patient is convenience. However, many MTFs routinely carry Vitamin B6, and Unisom is widely available from grocery stores and pharmacies in inexpensive formulations. Generic Unisom can be found at a cost of about $4 for a one-month supply. A review of several civilian health care plans found that Diclegis is either not covered, or non-formulary. The Committee did recommend Diclegis be designated as non-formulary.

Manual Prior Authorization had previously been placed on Diclegis, and the Committee recommended continuing the same criteria. The PA requires use of other treatments, including non-pharmacologic therapies, prior to use of Diclegis.

***Summary of Panel Questions and Comments*:**

Dr. Delgado stated that she was confused about the drug being available over the counter (OTC). She asked why it was being approved for the formulary.

Dr. Allerman made the correction that the recommendation is for non-formulary. She states the fixed-dose combination is only prescription and the physical components are widely available OTC.

Dr. Delgado stated she couldn't imagine a scenario where the drug would be prescribed if it is available OTC.

There were no more questions or comments from the Panel. Without further discussion, the Chair called for the vote on UF recommendation, PA Criteria, and UF Implementation Plan for Antiemetics/Antivertigo Agents: Doxylamin Succinate and Pyridoxine Hydrochloride (Diclegis)

1. **Antiemetic/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis) – UF Remmendations**

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

   Director, DHA:

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

2. **Antiemetic/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis) – 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. **Antiemetic/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis) – 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

UNIFORM FORMULARY CLASS REVIEWS

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

A. HCV Drugs: DAAs - UF Recommendation

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

- Uniform Formulary:
  - Ledipasvir/sofosbuvir (Harvoni)
  - Paritaprevir/ritonavir/ombitasvir + dasabuvir (Viekira Pak)
  - Sofosbuvir (Sovaldi)
  - Simeprevir (Olysio)
  - Boceprevir (Victrelis), until market withdrawal in December 2015
- Non Formulary: None

B. HCV Drugs: DAAs – Sofosbuvir (Sovaldi) PA Criteria

Manual PA criteria for the individual Direct Acting Antivirals were recommended previously. The P&T Committee recommended (**16 for, 0 opposed, 1 abstained, 1 absent**) minor revisions to the Sovaldi manual PA criteria to include the table of the recommended treatments for each HCV genotype and duration of therapy.

The full PA criteria are as follows:

Sofosbuvir (Sovaldi)

- New users of **Sovaldi** are required to undergo the PA process.
- Current users are not affected by PA; they can continue therapy uninterrupted.
- Consult the AASLD/IDSA Hepatitis C 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 $\geq$ 18
- Has laboratory evidence of chronic HCV infection
- Has laboratory evidence of HCV genotype 1, 2, 3, or 4 HCV infection
  - State the HCV genotype and HCV RNA viral load on the PA form
- Sovaldi is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
- Sovaldi is not prescribed as monotherapy

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 or unique population.
- Prior authorization will expire after 12 to 24 weeks, based on the treatment regimen selected.

Table of Recommended Treatment Regimens and Duration of Therapy for Sofosbuvir (Sovaldi)

HCV genotype	Treatment	Duration
Genotype 1	SOFOSBUVIR + peginterferon alfa + ribavirin	12 weeks
	SIMEPREVIR 150 mg once daily + SOFOSBUVIR 400 mg once daily (treatment naïve or experienced* without cirrhosis)	12 weeks
	SIMEPREVIR 150 mg once daily + SOFOSBUVIR 400 mg once daily (treatment naïve or experienced* with cirrhosis)	24 weeks
Genotype 2	SOFOSBUVIR + ribavirin	12 weeks
	SOFOSBUVIR + ribavirin (cirrhotic or treatment experienced)	16 weeks
Genotype 3	SOFOSBUVIR + ribavirin	24 weeks
	SOFOSBUVIR + peginterferon alfa + ribavirin (cirrhotic or treatment experienced)	12 weeks
Genotype 4, 5, 6	SOFOSBUVIR + peginterferon alfa + ribavirin	12 weeks
Hepatocellular carcinoma awaiting transplant	SOFOSBUVIR + ribavirin	up to 48 weeks or at transplant
***Treatment-experienced patients who have failed treatment with peginterferon alfa + ribavirin but not a HCV protease inhibitor**		

Regimen other than those listed: Please explain the rationale for treatment and duration of therapy. Consult the AASLD/IDSA HCV guidelines for new updates and guidelines.

C. **HCV Drugs: DAAs – UF and PA Implementation Plan**

The P&T Committee recommended (**16 for, 0 opposed, 1 abstained, 1 absent**) the UF and PA implementation become effective upon signing of the minutes in all POS.

Summary of Physician's Perspective:

The hepatitis C drugs were last reviewed for Uniform Formulary placement in November 2012, and since then there has been significant changes to the direct acting anti-virals (or DAAs), so this subclass was reviewed. The introduction of the second generation DAAs has significantly impacted the treatment of hepatitis C, in that now there is a very high response rate, a shortened treatment duration, and no need for injectable therapies.

The Committee recommended that all the DAAs remain on the Uniform Formulary, and did not recommend step therapy. The one dissenting vote was that the member felt a step-therapy scenario should have been chosen.

The formulary recommendation will allow for availability of all the DAAs for DoD patients, but will still generate cost-avoidance to the system.

The Prior Authorization criteria have been applied to the new DAA's as they have been approved. Since this drug class continues to evolve, the Committee will continue to monitor the guidelines, and update the PA criteria as necessary.

Summary of Panel Questions and Comments:

Dr. Buchanan asked if Victrelis is the standard of care, then why does it remain on the uniform formulary.

Dr. Downs replied that it will be withdrawn from the market. Considering the process, it is easier to implement with a formulary change. They have one patient that is on the drug and they should still get it because they are on therapy. It doesn't impact anybody.

There were no more questions or comments from the Panel. Without further discussion, the Chair called for the vote on UF recommendation, PA Criteria, and UF Implementation Plan for HCV Drugs: DAAs

1. **HCV Drugs: DAAs - UF Recommendations:**

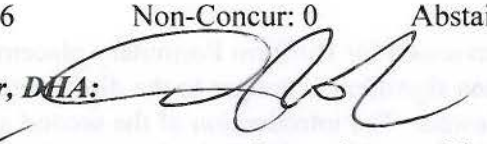
Concur: 6	Non-Concur: 0	Abstain: 0	Absent: 1

Director, DHA:

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

2. **HCV Drugs: DAAs – Sofosbuvir (Sovaldi) PA Criteria**

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

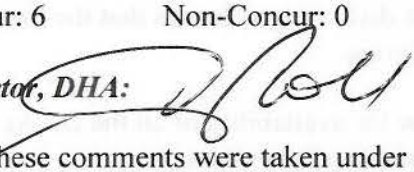


Director, DHA:

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

3. **HCV Drugs: DAAs – 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. ORAL ANTICOAGULANTS

A. Oral Anticoagulants—UF Recommendation

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

- Uniform Formulary:
  - Warfarin (Coumadin; generic)
  - Apixaban (Eliquis)
  - Dabigatran (Pradaxa)
  - Edoxaban (Savaysa)
  - Rivaroxaban (Xarelto)
- Non Formulary: None

No implementation needed here due to no change in formulary status, and there is no recommendation for prior authorization criteria.

Summary of Physician's Perspective

The Committee most recently reviewed the oral anticoagulants in February 2013, and since then two new products have reached the market.

There are several advantages of the newer agents over warfarin, and a review of DoD data does show a decline in warfarin utilization. However, warfarin still represents about 60% of DoD utilization. Additionally, there are many clinical reasons to consider

warfarin for a patient, including the fact that a reliable antidote is available. Antidotes to the newer anticoagulants are currently under review at the FDA.

A review of DoD data found that the majority of use of the newer oral anticoagulants was for stroke prevention in patients with atrial fibrillation, so this was the focus of the clinical review. The clinical data for the other indications was also reviewed.

For the Uniform Formulary recommendation, there was no controversy here. All of the oral anticoagulants were recommended to remain on the Uniform Formulary. As the newer agents continue to gain additional indications, or if head-to-head trials become available, the class will likely be reviewed again.

Summary of Panel Questions and Comments:

Dr Anderson asked if Savaysa was being added to the formulary and if there was any consideration for a step therapy edit.

Dr Allerman replied that yes, Savaysa had not previously been reviewed. By default, it was on the uniform formulary until it could be reviewed. That is the major change from the previous decision from 2013.

In response to the question regarding the step therapy edit, Dr. Allerman replied that part of the condition sets did include the option for step therapy. When all the modeling was done and the cost effective analysis, the recommendation was stated that to place everything on the uniform formulary without the step therapy. There are no new indications or an antidote; it is likely that this class will be reviewed again in the near future.

There were no more questions or comments from the Panel. The Chair called for the vote on UF recommendation, PA Criteria, and UF Implementation Plan for Oral Anticoagulants.

1. Oral Anticoagulants – UF Recommendation

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

Director, DHA:

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

UTILIZATION MANAGEMENT

1. TESTOSTERONE REPLACEMENT THERAPY (TRT)

A. TRT: Testosterone Nasal Gel (Natesto)—PA Criteria

Natesto is a new formulation of testosterone that is administered intranasally. It is dosed as one pump actuation per nostril, three times daily, six to eight hours apart. The TRT products were reviewed by the P&T Committee in August 2012 and automated PA (step therapy) and manual PA criteria were recommended for the class (implemented March 2013).

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) step therapy and manual PA criteria for testosterone nasal gel (Natesto), consistent with the rest of the class and its FDA-approved indication.

The full PA criteria are as follows: PA criteria apply to all new and current users of Natesto.

Automated PA Criteria: The patient has filled a prescription for transdermal 2% gel pump (Fortesta) at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order pharmacy) during the previous 180 days

AND

Manual PA Criteria: If automated criteria are not met, coverage is approved for Natesto if:

- Contraindications exist to Fortesta (hypersensitivity to a component)
- Inadequate response to Fortesta (minimum of 90 days **AND** failed to achieve testosterone levels above 400 ng/dL **AND** the patient has denied improvement in symptoms)
- Clinically significant adverse reactions to Fortesta not expected with Natesto

AND

Coverage approved for male patients aged 17 years or older with:

- A diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism

Coverage for use in women or in adolescent males under the age of 17 is not approved and will be considered upon appeal only.

Dr. Allerman mentioned that for the Prior Authorization criteria, they normally do not have comments from Dr. Kugler.

Summary of Panel Questions and Comments:

There were no more questions or comments from the Panel. Without further discussion, the Chair called for the vote on PA Criteria for the TRT: Testosterone Nasal Gel (Natesto)

1. **TRT: Testosterone Nasal Gel (Natesto) – 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. **CYSTIC FIBROSIS (CF) DRUGS**

A. CF: Ivacaftor (Kalydeco)—PA Criteria

Ivacaftor (Kalydeco) is indicated for the treatment of CF. PA criteria were recommended at the February 2012 meeting, updated in May 2014 and December 2014 to reflect the FDA-approved indication for various mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. In March 2015, the FDA-approved indication for Kalydeco was further expanded to include pediatric patients aged 2 years and older. Along with this expanded indication, a new dosage form was launched in the form of oral granules that are mixed with either soft food or liquid every 12 hours for weight-based pediatric dosing.
The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 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).

- Coverage will be approved for the treatment of CF patients aged 2 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.

- Coverage is not approved for patients who are homozygous for the F508del mutation in the CFTR gene.

***Summary of Panel Questions and Comments*:**

There were no more questions or comments from the Panel. Without further discussion, the Chair called for the vote on PA Criteria for the CF: Ivacaftor (Kalydeco)

1. **CF: 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

3. RENIN ANGIOTENSIN ANTIHYPERTENSIVES (RAAS)

A. RAAs: Perindopril/Amlodipine (Prestalia)—PA Criteria

The FDA recently approved the combination product perindopril and amlodipine (Prestalia). It is indicated for the treatment of hypertension as monotherapy or as initial therapy in patients requiring multiple drugs to achieve their blood pressure goals. The RAAs class was reviewed in August 2010; step therapy was implemented in January 2011 and applies to all drugs in the class.

The P&T Committee recommended **(17 for, 0 opposed, 1 abstained, 0 absent)** step therapy criteria for perindopril/amlodipine (Prestalia), consistent with the current criteria for the RAAs class.

The full PA criteria are as follows: PA criteria apply to all new and current users of Prestalia.

Automated PA Criteria—The patient has filled a prescription for one of the preferred agents (generic angiotensin-converting enzyme inhibitors, generic losartan, losartan/HCTZ, Diovan, Diovan HCT, Exforge, Exforge HCT, Micardis, Micardis HCT, or Twynsta) 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, coverage is approved for Prestalia if:

- Contraindications exist to one step-preferred RAA agent not expected to occur with Prestalia

- The patient has had an inadequate response to one step-preferred RAA agent
- The patient has been unable to tolerate one step preferred RAA agents, due to adverse effects.

Summary of Panel Questions BAP Comments:

There were no more questions or comments from the Panel. Without further discussion, the Chair called for the vote on PA Criteria for the RAA's: Perindopril/Amlodipine (Prestalia)

1. **RAAs: Perindopril/Amlodipine (Prestalia) – PA Criteria**

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

Director, DHA:

These comments were taken under consideration prior to my final decision

4. INSULINS

A. Insulins: Inhaled Insulin (Afrezza)—PA Criteria

Afrezza is rapid-acting inhaled insulin indicated to improve glycemic control in adult patients with Type 1 or Type 2 diabetes mellitus. It is available as single-use cartridges of 4, 8, and 12 units, administered via oral inhalation at the beginning of a meal. Dosing must be individualized. Manual PA criteria were recommended to ensure appropriate use of the drug in Type 1 and Type 2 diabetic patients, including failure of or inability to tolerate an adequate trial (90 days) of a rapid or short-acting subcutaneous insulin product.

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) manual PA criteria for Afrezza, consistent with the FDA-approved product labeling for use in Type 1 and Type 2 diabetic patients.

The full PA criteria are as follows: Manual PA criteria apply to all new and current users of Afrezza. Coverage is approved for non-smoking patients with either:

- **Type 1 Diabetes Mellitus (diagnosed)**
  - Failure to achieve hemoglobin A1C ≤ 7 % in 90 days of use of a rapid or short-acting subcutaneous (SC) insulin product or clinically significant adverse effects experienced with SC rapid or short-acting insulin unexpected to occur with inhaled insulin
  - Afrezza is used as adjunctive treatment to current basal insulin therapy
  - Spirometry testing [baseline forced expiratory volume in the first second

- (FEV1) upon initiation with repeated FEV1 at 6 months after initiation and repeated annually thereafter] has been performed

- **Type 2 Diabetes Mellitus (diagnosed)**

  - Failure to achieve hemoglobin A1C ≤ 7 % in 90 days of use of a rapid or short-acting SC insulin product or clinically significant adverse effects experienced with SC rapid or short-acting insulin unexpected to occur with inhaled insulin
  - Failure of or clinically significant adverse effect to two oral anti-diabetic agents [i.e. sulfonylurea, thiazolidinedione, or dipeptidyl peptidase-4 inhibitor] if metformin is contraindicated
  - Spirometry testing (baseline FEV1 upon initiation with repeated FEV1 at 6 months after initiation and repeated annually thereafter) has been performed

  Contraindications to the use of Afrezza: hypoglycemia, chronic lung disease (asthma, COPD), hypersensitivity to regular human insulin, or any Afrezza excipients

Summary of Panel Questions and Comments:

There were no more questions or comments from the Panel. The Chair called for the vote on PA Criteria for the Insulin: Inhaled Insulin (Afrezza).

1. **Insulins: Inhaled Insulin (Afrezza) – PA Criteria**

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

Director, DHA:

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

SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS

A. SMBGS Test Strips: ACCU-CHEK Aviva Plus Test Strips – PA Criteria

The SMBGS test strips were evaluated at the November 2014 P&T Committee Meeting. Step therapy and MN criteria were recommended with an implementation date of August 5, 2015. PA and MN criteria allow for use of a non-preferred, NF test strip if the patient uses an insulin pump and requires a specific test strip that communicates wirelessly with a specific meter.

The ACCU-CHEK Aviva Plus test strips are designated non-preferred and NF. However, the ACCU-CHEK Aviva Plus test strips are used in the ACCU-CHEK Combo meter, which communicates wirelessly with the ACCU-CHEK Spirit Combo insulin pump.

The P&T Committee recommended (**17 for, 0 opposed, 1 abstain, 0 absent**) adding the ACCU-CHEK Aviva Plus test strips to the SMBGS Test Strips PA criteria for patients using the ACCU-CHEK Aviva Combo meter with the ACCU-CHEK Spirit Combo pump.

The PA criteria are as follows: New and current users of the NF test strips are required to try FreeStyle Lite or Precision Xtra.

Manual PA Criteria—Non-preferred test strip allowed if: patient uses an insulin pump and requires a specific test strip that communicates wirelessly with a specific meter

- CONTOUR NEXT strip with CONTOUR NEXT Link meter for Medtronic pump
- Nova Max strip with Nova Max Link meter for Medtronic pump
- ACCU-CHEK Aviva Plus test strip with the ACCU-CHEK Combo meter for the ACCU-CHEK Spirit Combo pump

B. *BAP Comments*

There were no more questions or comments from the Panel. Without further discussion, the Chair called for the vote on PA Criteria the SMBGS Test Strips: ACCU-CHEK Aviva Plus Test Strips

1. **SMBGS Test Strips: ACCU-CHEK Aviva Plus Test Strips – 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 uses 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.

- BAP – Beneficiary Advisory Panel
- DFO – Designated Federal Officer
- A1C – hemoglobin
- AASLD – American Association for the Study of Liver Diseases
- BCF – Basic Core Formula
- BIA – Budget Impact Analysis
- CEA – Cost-Effectiveness Analysis
- CF – Cystic Fibrosis
- CFR – Code of Federal Regulations
- CFTR – Cystic Fibrosis Transmembrane Conductance Regulator
- CMA – Cost Minimization Analysis
- COPD – Chronic Obstructive Pulmonary Disease
- DAA – Direct Acting Antiviral
- DHA – Defense Health Agency
- DoD – Department of Defense
- FACA – Federal Advisory Committee Act
- FEV1 – Forced Expiratory Volume in the First Second
- FDA – Food & Drug Administration
- G1244E - Cystic Fibrosis Mutation
- G1339D - Cystic Fibrosis Mutation
- G178R 0 Cystic Fibrosis Mutation
- G55ID – Cystic Fibrosis Mutation
- G551S - Cystic Fibrosis Mutation
- GI – Gastrointestinal
- HCT – Hematocrit
- HCTZ – Diuretic
- HCV – Hepatitis C Virus
- HIV – Human Immunodeficiency Virus
- IDSA – Infectious Diseases Society of America
- IM – Intramuscular
- LMWH – Low-Molecular Weight Heparin
- MS – Multiple Sclerosis
- NDAA – National Defense Authorization Act
- NF – Non-Formulary
- NVAF – Non-Valvular Atrial Fibrillation

- NVP – Nausea and Vomiting during Pregnancy
- OTC – Over-the-Counter
- PE – Pulmonary Embolism
- P&T – Pharmacy & Therapeutic
- R117H - Cystic Fibrosis Mutation
- S1251N - Cystic Fibrosis Mutation
- S1255P - Cystic Fibrosis Mutation
- S549N - Cystic Fibrosis Mutation
- S549R - Cystic Fibrosis Mutation
- SC – Subcutaneous
- SED-1s – Sedative Hypnotic Agents
- SMBGS – Self-Monitoring Blood Glucose Systems
- SVR12 – Sustained Virologic Response at 12 weeks
- TRICARE – Military Health Care System
- TSOACs – Targeted-Specific Oral Anticoagulants
- UF – Uniform Formulary
- USC – United States Code
- VTE – Venous Thromboembolism

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
June 11, 2015
Washington, D.C.

Present Panel Members

- Robert Duane Tackitt, the Association of Military Surgeons US, Chairperson
- Michael Anderson, United Healthcare
- Theresa Buchanan, the National Military Family Association
- Sandra S. Delgado, Humana
- Katherine O'Neill-Tracy, the Military Officers Association of America
- John Wagoner, HealthNet Federal Services

Absent:
- Robert Lewis, Chief Warrant and Warrant Officers Association

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C. CAPT Edward Norton 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 Review
- Designated Newly Approved Drugs

    1. Newer Sedative Hypnotic Drugs – Suvorexant (Belsomra)
    2. Multiple Sclerosis Drugs – Peginterferon beta-1a (Plegridy)
    3. Antiemetics/Antivertigo Agents – Doxylamine succinate and pyridoxine hydrochloride (Diclegis)

- Drug Class Reviews

    1. Hepatitis C Virus Drugs: Direct Acting Antivirals
    2. Oral Anticoagulants

- Utilization Management Issues - Prior Authorization Criteria

    1. Testosterone Replacement Therapy – Testosterone Nasal Gel (Natesto)
    2. Cystic Fibrosis Drugs – Ivacaftor (Kalydeco)
    3. Renin Angiotensin Antihypertensives – Perindopril/amlodipine (Prestalia)
    4. Insulins – Inhaled Insulin (Afrezza)

5. Self-Monitoring Blood Glucose System Test Strips – ACCU-CHEK Aviva Plus Test Strips

- 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

CAPT Edward Norton introduces himself as the Designated Federal Officer (DFO) for the Uniform Formulary Advisory Panel. The panel has convened to comment on the recommendations of the DoD P&T Committee meeting, which occurred on May 13-14, 2015.

CAPT Norton indicated Title 10, United States, (U.S.C.) section 1074g, subsection b requires the Secretary of Defense to establish a DoD Uniform Formulary (UF) of the pharmaceutical agent and established the P&T committee to review the formulary on a periodic basis to make additional recommendations regarding the formulary as the committee determines necessary and appropriate.

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

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

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

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

As guidance to the Panel regarding this meeting, CAPT Norton 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.

CAPT Norton 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

Mr. Tackitt welcomes CAPT Norton and greets the audience.

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; I would also like to recognize Mr. David Hurt, Associate 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

    a. Three (3) newly approved drugs. They are:

        1. Suvorexant (Belsomra) in the Newer Sedative Hypnotic Agents (SED-1s) drug class;
        2. Peginterferon beta1a (Plegridy) in the Multiple Sclerosis (MS) drug class;
        3. Doxylamine succinate and pyridoxine hydrochloride (Diclegis) in the Antiemetic Agent drug class;

b. Two (2) Uniform Formulary Drug Classes:

1. Hepatitis C Virus (HCV) Drugs, Direct Acting Antiviral (DAA) agent subclass and
2. Oral Anitcoagulants, Target-Specific Oral Anticoagulants (TSPACs) subclass.

c. Five (5) Prior Authorizations (PA):

1. Testosterone Replacement Therapy (TRT): testosterone nasal gel Natesto**;**
2. Cystic Fibrosis Drug: ivacaftor (Kalydeco) adding expanded indication to include the pediatric patient aged 2 and older;
3. Renin Angiotension Antihypertensive (RAAs): perindopril / amlodipine (Prestalia)
4. Inhaled Insulin: Afrezza
5. Self-Monitoring Blood Glucose Systems (SMBGS) Test Strips: ACCU-CHEK Aviva Plus Test Strips

d. There were no NDAA Section 703 drugs reviewed at this meeting.

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 4. 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 ADMINSTRATION (FDA) AGENTS

1. NEWER SEDATIVE HYPNOTICS (SED-1s)

(Dr. Downs)

A. SED-1s: Suvorexant (Belsomra) – Relative Clinical Effectiveness and Conclusion
Belsomra is a first-in-class orexin receptor antagonist indicated for the treatment of insomnia characterized by difficulties with sleep onset and sleep maintenance. Its mechanism of action antagonizes orexin receptors, which turns off the wakefulness signal in the brain.

- There are no head-to-head studies with Belsomra and other sedative hypnotic agents.

- Belsomra reduced the time to sleep onset by approximately 10 minutes and increased the total sleep time by approximately 30 minutes compared to placebo.

- The 5 mg dose has not been studied in clinical trials and is meant for patients with drug interaction concerns.

- Belsomra is generally well tolerated. The most common adverse effects include next-day somnolence, headache, and fatigue.

- Somnolence was more common in the non-elderly treatment group, was mild to moderate, and occurred earlier in the course of therapy.

- Similar to other agents in the class, Belsomra is a controlled substance or DEA Schedule IV, has several drug interactions, and carries the same warnings regarding sleep-related behaviors.

  The P&T Committee concluded (**18 for, 0 opposed, 0 abstained, 0 absent**) despite its unique mechanism of action, Belsomra offers no clinically compelling advantages over the existing newer sedative hypnotic agents on the UF. Other SED-1 drugs on the UF also have the same FDA-approved indications as Belsomra.

B. SED-1s: Suvorexant (Blesomra) - Relative Cost-Effectiveness Analysis and Conclusion

A cost minimization analysis or CMA was performed to evaluate Belsomra with other agents on the UF used in the treatment of insomnia. The P&T Committee concluded (**18 for, 0 opposed, 0 abstained, 0 absent**) that Belsomra was not cost effective.

C. SED-1s: Suvorexant (Belsomra) - UF Recommendation

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) Belsomra be designated NF, due to the lack of compelling clinical advantages and cost disadvantage compared to the existing sedative hypnotics on the UF.

D. SED-1s: Suvorexant (Belsomra) – Prior Authorization for PA Criteria

Existing automated PA criteria or step therapy for the SED-1s require a trial of immediate release (IR) zolpidem or zaleplon. The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) that the existing automated PA criteria for the SED-1s apply to Belsomra.

The full PA criteria are as follows: A trial of generic zolpidem IR or zaleplon is required for new users of Belsomra.

Automated PA: The patient has filled a prescription for zolpidem IR or zaleplon at any Military Health System pharmacy point of service (Military Treatment Facility, retail network pharmacies, or mail order) during the previous 180 days.

Manual PA Criteria: The patient has an inadequate response to, been unable to tolerate due to adverse effects, or has a contraindication to zolpidem IR or zaleplon.

E. SED-1s: Suvorexant (Belsomra) – UF and PA Implementation

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 points of service and the DHA will send a letter to beneficiaries affected by the UF decision.

F. Physician's Perspective

Belsomra has the same FDA indications as Ambien CR and Lunesta, which are both on the Uniform Formulary. Although the mechanism of action is unique, Belsomra's side effect profile is similar to the other drugs in the class, and it is a controlled schedule drug.

The Committee did unanimously recommend non-formulary placement for Belsomra, as it was not cost effective.

From the period of February 2015 to April 2015, there were 756 patients receiving Belsomra in the DoD. Automated prior authorization (step therapy) has been applied to the Sedative Hypnotics class for several years, and the recommendation was for Belsomra to follow the same requirements. Patients would need a trial of generic Ambien immediate release or generic Sonata before using Belsomra.

G. BAP Comments

There were no questions or comments from the Panel. The Chair called for the vote on UF recommendation, PA Criteria, and UF and PA Implementation for SED-1s for Suvorexant (Belsomra).

1. **SED-1s: Suvorexant (Belsomra) – UF Recommendation**

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

2. **SED-1s: Suvorexant (Belsomra) – PA Criteria**

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

3. **SED-1s: Suvorexant (Belsomra) – UF and PA Implementation Plan**

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

2. MULTIPLE SCLEROSIS (MS) DRUGS

(Dr. Downs)

A. MS Drugs: Peginterferon Beta-1a (Plegridy) - Relative Clinical Effectiveness and Conclusion:

Plegridy is a new pegylated interferon that is dosed every two weeks and administered subcutaneously. It is a disease-modifying agent approved for patients with relapsing forms of MS. There are no head-to-head trials comparing Plegridy with oral or injectable drugs for MS.

- Compared to interferon beta-1a (Avonex), Plegridy offers the advantage of less frequent dosing (every 2 weeks instead of once weekly dosing) and subcutaneous administration, instead of intramuscular (IM) dosing. However, Avonex is now available in an autoinjector, which can ease IM administration.

- Plegridy's safety profile is similar to that of established interferons on the market, but it has a higher incidence of injection-site reactions than Avonex or placebo.

- While Plegridy offers the patient the convenience of every two-weeks administration, there is no data in patients who have received long-term prior treatment with another beta interferon or an oral agent.

The P&T Committee concluded (**18 for, 0 opposed, 0 abstained, 0 absent**) that the place in therapy for Plegridy is limited because the oral MS agents and the other disease-modifying drugs for MS, including Avonex, are on the UF and available to patients. Plegridy should be reserved for those patients who are not able to tolerate the currently available oral medications or injectable for MS.

B. MS Drugs: Peginterferon Beta-1a (Plegridy) – Relative Cost-Effectiveness Analysis and Conclusion

A CMA was performed to evaluate Plegridy with other injectable disease-modifying agents that are used to treat MS. The P&T Committee concluded (**18 for, 0 opposed, 0 abstained, 0 absent**) that Plegridy was NOT cost effective.

C. MS Drugs: Peginterferon Beta-1a (Plegridy) – UF Recommendation

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) Plegridy be designated NF based on clinical and cost effectiveness.

D. **MS Drugs: Peginterferon Beta-1a (Plegridy) – UF 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 points of service and the DHA will send a letter to beneficiaries affected by the UF decision.

F. **Physician's Perspective**

The MS drugs were most recently reviewed in November 2014, and all the drugs, both injectables and orals are on the Uniform Formulary.

Plegridy is manufactured by the same company that makes Avonex. Plegridy and Avonex contain the same active ingredient; however, Plegridy is pegylated, which allows it to be administered every two weeks.

The recommendation for Plegridy was that it should be non-formulary, since it is not cost effective compared to the other MS drugs. An analysis of DoD data shows that most patients who are newly diagnosed with MS are being started on one of the oral drugs, and overall, the use of injectables is decreasing. There is no data that has evaluated efficacy in patients who have switched from another interferon product or an oral MS drug to Plegridy. Currently there are about 106 patients on Plegridy in the DoD.

G. **BAP Comments**

Dr. Anderson asked would the 106 patients that are on Plegridy be grandfathered.

Dr. Downs replied that grandfathering is usually step-therapy.

Dr. Allerman interjected that this decision did not have prior authorization of step-therapy. The medical necessity pathway is not addressed by the BAP committee. That is the pathway to get the co-pay reduced.

There were no more questions or comments from the Panel. The Chair called for the vote on UF recommendation and UF Implementation Plan for MS Drugs: Peginterferon Beta-1a (Plegridy).

1. **MS Drugs: Peginterferon Beta-1a (Plegridy) – UF Recommendation**

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

2. **MS Drugs: Peginterferon Beta-1a (Plegridy) – UF Implementation Plan**

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

3. ANTIEMETICS/ANTIVERTIGO AGENTS

(Dr. Allerman)

A. Antiemetics/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis)—Relative Clinical Effectiveness and Conclusion

Diclegis is a delayed-release product containing doxylamine succinate, an antihistamine, and pyridoxine hydrochloride, or vitamin-. Diclegis is indicated for treatment of nausea and vomiting during pregnancy (NVP) in women who do not respond to conservative therapies.

- The individual components of Diclegis are available over-the-counter (OTC) in inexpensive formulations of the sleep aid Unisom and vitamin B6.

- The components of Diclegis were previously available in a formulation known as Bendectin, which was approved in 1956. Bendectin was voluntarily removed from the market in 1983 due to litigation concerns. The FDA New Drug Application for Diclegis references the data for Bendectin. Since the market withdrawal of Bendectin, OTC doxylamine and vitamin B6 continue to be available and are frequently used for NVP.

- Current treatment guidelines from the American College of Obstetrics and Gynecology state vitamin B6 or use of doxylamine with vitamin B6 are safe and effective, and are the recommended first-line treatments for NVP (nausea and vomiting during pregnancy). Other treatments, including acupressure and ginger, other antihistamines, and ondansetron are also recommended.

- In the 15-day small clinical trial used to obtain FDA approval, Diclegis showed a statistically significant benefit over placebo in emesis but the clinical difference was small.

- A 2013 Cochrane review found that there was limited evidence to support use of vitamin B6, antihistamines, and other antiemetics for mild to moderate nausea and vomiting during pregnancy. However, there are no significant head-to-head trials available to compare the agents currently used for NVP nausea and vomiting during pregnancy.

- No studies have suggested a definitive link between fetal malformations and the drugs typically used for treating NVP, including Diclegis, the equivalent OTC components, or the other commonly used antiemetics.

  The P&T Committee concluded (**18 for, 0 opposed, 0 abstained, 0 absent**) the combination prescription product of doxylamine succinate and pyridoxine hydrochloride (Diclegis) offers no clinically compelling advantages when compared to the individual OTC components or other antiemetic available on the UF.

B. Antiemetics/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis)—Relative Cost-Effectiveness Analysis and Conclusion

CMA was performed. The P&T Committee concluded (**18 for, 0 opposed, 0 abstained, 0 absent**) Diclegis is more costly than the individual OTC components and the formulary agents used in the treatment of nausea and vomiting during pregnancy.

C. Antiemetics/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis)—UF Recommendation

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) doxylamine succinate and pyridoxine hydrochloride (Diclegis) be designated NF due to the lack of compelling clinical advantages, aside from its pregnancy Category A rating, and its cost disadvantage when compared to the individual OTC components and the formulary agents available to treat NVP.

D. Antiemetics/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochlordie (Diclegis) – PA Criteria

Manual PA criteria were recommended at the February 2013 DoD P&T Committee meeting and implemented in August 2013 for doxylamine succinate and pyridoxine hydrochloride (Diclegis), requiring a trial of nonpharmacologic interventions and OTC pyridoxine, and consideration of alternate antiemetics. The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) maintaining the PA criteria for doxylamine succinate and pyridoxine hydrochloride (Diclegis).

The full PA criteria are as follows: All new users of Diclegis are required to try a nonpharmacologic method for management of nausea and vomiting during pregnancy AND over-the-counter pyridoxine before receiving doxylamine succinate and pyridoxine hydrochloride (Diclegis).

Manual PA Criteria—Doxylamine succinate and pyridoxine hydrochloride (Diclegis) is approved if:

- The patient has not had relief of symptoms after trying a nonpharmacologic method to manage nausea and vomiting during pregnancy,

  AND

- The patient has not had relief of symptoms after trying over-the-counter pyridoxine for management of nausea and vomiting during pregnancy.

- Providers are encouraged to consider an alternate antiemetic (e.g., ondansetron) prior to prescribing doxylamine succinate and pyridoxine hydrochloride (Diclegis).

  Prior Authorization will expire after 9 months.

E. **Antiemetics/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis) – UF and PA Implementation Plan**

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) 1) an effective date of the first Wednesday after a 90-day implementation period in all points of service (POS); and, 2) DHA send a letter to beneficiaries affected by the UF decision.

F. **Physician's Perspective**

Diclegis is an example of a new twist on an old drug. It contains the same active ingredient as the product Bendectin, which was available years ago and subsequently removed from the market. Bendectin continued to be available in Canada, and a Canadian company received FDA approval to market the drug in the US under the brand name Diclegis.

The individual ingredients, which are found in the OTC products Unisom and Vitamin B6, have been used for years to treat nausea and vomiting of pregnancy. The guidelines from the OB-GYN professional group continue to recommend vitamin B6 and doxylamine as first line. Additionally, other treatments, including Zofran, are also in the guidelines.

A gynecologist is a member of the P&T Committee, and she relayed that the main benefit of Diclegis to the patient is convenience. However, many MTFs routinely carry Vitamin B6, and Unisom is widely available from grocery stores and pharmacies in inexpensive formulations. Generic Unisom can be found at a cost of about $4 for a one-month supply. A review of several civilian health care plans found that Diclegis is either not covered, or non-formulary. The Committee did recommend Diclegis be designated as non-formulary.

Manual Prior Authorization had previously been placed on Diclegis, and the Committee recommended continuing the same criteria. The PA requires use of other treatments, including non-pharmacologic therapies, prior to use of Diclegis.

G. **BAP Comments**

Dr. Delgado stated that she was confused about the drug being available over the counter (OTC). She asked why it was being approved for the formulary.

Dr. Allerman made the correction that the recommendation is for non-formulary. She states the fixed-dose combination is only prescription and the physical components is widely available OTC.

Dr. Delgado stated she couldn't imagine a scenario where the drug would be prescribed if it is available OTC.

The Chair called for the vote on UF recommendation, PA Criteria, and UF Implementation Plan for Antiemetics/Antivertigo Agents: Doxylamin Succinate and Pyridoxine Hydrochloride (Diclegis)

1. **Antiemetic/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis) – UF Remmendations**

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

2. **Antiemetic/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis) – PA Criteria**

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

3. **Antiemetic/Antivertigo Agents: Doxylamine Succinate and Pyridoxine Hydrochloride (Diclegis) – UF and PA Implementation Plan**

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

UNIFORM FORMULARY CLASS REVIEWS

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

(Dr. Downs)

A. HCV Drugs: DAAs – Relative Clinical Effectiveness and Conclusion

Simeprevir or Olysio, sofosbuvir or Sovaldi,, ledipasvir & sofosbuvir combination or Harvoni, and ombitasvir/paritaprevir/ritonavir/dasabuvir co-packaged tablets or Viekira Pak, are Direct Acting Antivirals with an FDA indications for the treatment of genotype 1 chronic HCV in adults. Additionally, Sovaldi is indicated for the treatment of adults with genotypes 2, 3, and 4 chronic Hepatitis C. Boceprevir or Victrelis is a first generation Direct Acting Antivirals and is no longer the standard of care. Market withdrawal is expected in December 2015.

Due to the rapidly evolving Hepatitis C field, use of the Direct Acting Antivirals outside of their FDA-labeled indications is not uncommon. The American Association for the Study of Liver Diseases/ Infectious Diseases Society of America or AASLD/IDSA, updated the Hepatitis C treatment guidelines on April 8, 2015. The AASLD/IDSA Hepatitis C treatment guidelines recommend an all-oral, interferon-free options whenever feasible for patients with Hepatitis C. Harvoni and Viekira Pak are now prominently featured in the guidelines as recommended regimens for patients with genotype 1 and 4 chronic Hepatitis C. Sovaldi in combination with Olysio is also a recommended regimen in patients with genotype 1 Hepatitis C. Sovaldi with ribavirin is recommended for

patients with non-genotype 1 chronic Hepatitis C, in most situations. Consult the guidelines for the most up-to-date recommendations at: www.HCVguidelines.org.
The P&T Committee concluded (**17 for, 0 against, 0 abstained, 1 absent**) the following:

- There are no studies directly comparing Harvoni, Sovaldi in combination with Olysio, or Viekira Pak. In general, when making indirect comparisons across similar patient populations, efficacy (assessed as sustained virologic response at 12 weeks (SVR12) as the primary endpoint) appears similar among these products.

- In general, the rate of SVR12 across clinical trials in patients with genotype 1 chronic Hepatitis C treated with any Direct Acting Antivirals except Victrelis is **> 90%**. With Harvoni and Viekira Pak, SVR12 rates are > 95% in most instances.

- Harvoni and Viekira Pak represent all-oral, interferon-free therapies that have demonstrated high rates of clinical cure or SVR12 in large populations across Phase III clinical trials.

- Sovaldi, when used with Olysio, represents an all-oral option for patients with genotype 1 chronic Hepatitis C; however, data are limited to one small Phase IIa study.

- Harvoni is the only one of these three regimens (Harvoni, Sovaldi with Olysio, and Viekira Pak) that has been studied in previous Hepatitis C protease inhibitor treatment failures.

- Viekira Pak with ribavirin was evaluated in Hepatitis C genotype 1 patients with liver transplant and patients co-infected with HIV. There is a potential for significant drug-drug interactions with Viekira Pak.

- Sovaldi remains as an important therapy that allows for interferon-free options in patients with genotypes 2 or 3 chronic Hepatitis C.

- In the absence of head-to-head trials, Hepatitis C treatment should be based on current AASLD/IDSA treatment guideline recommendations, individual patient characteristics, likelihood of adherence, and patient preferences, as well as cost.

B. HCV Drugs: DAAs - Relative Cost-Effectiveness Analysis and Conclusion

A cost-effectiveness analysis or CEA and Budget Impact Analysis or BIA were performed to evaluate the HCV drugs. The P&T Committee concluded (**17 for, 0 opposed, 0 abstained, 1 absent**) the following:

- The CEA showed that all Direct Acting Antiviral agents were within a range considered cost-effective to the Military Health System.

- The BIA was performed to evaluate the potential impact of designating selected agents as step-preferred, formulary, or NF on the UF. BIA results showed that designating all agents, UF, with no step-therapy, demonstrated significant cost avoidance for the Military Health System.

C. HCV Drugs: DAAs - UF Recommendation

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

- Uniform Formulary:

  - Ledipasvir/sofosbuvir (Harvoni)
  - Paritaprevir/ritonavir/ombitasvir + dasabuvir (Viekira Pak)
  - Sofosbuvir (Sovaldi)
  - Simeprevir (Olysio)
  - Boceprevir (Victrelis), until market withdrawal in December 2015

- Non Formulary: None

D. HCV Drugs: DAAs – Sofosbuvir (Sovaldi) PA Criteria

A manual PA criteria for the individual Direct Acting Antivirals were recommended previously. The P&T Committee recommended (**16 for, 0 opposed, 1 abstained, 1 absent**) minor revisions to the Sovaldi manual PA criteria to include the table of the recommended treatments for each HCV genotype and duration of therapy.

The full PA criteria are as follows:

Sofosbuvir (Sovaldi)

- New users of **Sovaldi** are required to undergo the PA process.
- Current users are not affected by PA; they can continue therapy uninterrupted.
- Consult the AASLD/IDSA Hepatitis C 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 infection
- Has laboratory evidence of HCV genotype 1, 2, 3, or 4 HCV infection
  - State the HCV genotype and HCV RNA viral load on the PA form
- Sovaldi is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
- Sovaldi is not prescribed as monotherapy

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 or unique population.
- Prior authorization will expire after 12 to 24 weeks, based on the treatment regimen selected.

Table of Recommended Treatment Regimens and Duration of Therapy for Sofosbuvir (Sovaldi)

HCV genotype	Treatment	Duration
	SIMEPREVIR 150 mg once daily + SOFOSBUVIR 400 mg once daily (treatment naïve or experienced* without cirrhosis)	12 weeks
Genotype 2	SOFOSBUVIR + ribavirin	12 weeks
Genotype 3	SOFOSBUVIR + ribavirin	24 weeks
Genotype 4, 5, 6	SOFOSBUVIR + peginterferon alfa + ribavirin	12 weeks
***Treatment-experienced patients who have failed treatment with peginterferon alfa + ribavirin but not a HCV protease inhibitor**		

Regimen other than those listed: Please explain the rationale for treatment and duration of therapy. Consult the AASLD/IDSA HCV guidelines for new updates and guidelines.

E. HCV Drugs: DAAs – UF and PA Implementation Plan

The P&T Committee recommended (**16 for, 0 opposed, 1 abstained, 1 absent**) the UF and PA implementation become effective upon signing of the minutes in all POS.

F. **Physician's Perspective**

The hepatitis C drugs were last reviewed for Uniform Formulary placement in November 2012, and since then there has been significant changes to the direct acting anti-virals (or DAAs), so this subclass was reviewed. The introduction of the second generation DAAs has significantly impacted the treatment of hepatitis C, in that now there is a very high response rate, a shortened treatment duration, and no need for injectable therapies.

The Committee recommended that all the DAAs remain on the Uniform Formulary, and did not recommend step therapy. The one dissenting vote was that the member felt a step-therapy scenario should have been chosen.

The formulary recommendation will allow for availability of all the DAAs for DoD patients, but will still generate cost-avoidance to the system.

The Prior Authorization criteria have been applied to the new DAA's as they have been approved. Since this drug class continues to evolve, the Committee will continue to monitor the guidelines, and update the PA criteria as necessary.

G. **BAP Comments**

Dr. Buchanan asked if Victrelis is the standard of care, then why does it remain on the uniform formulary.

Dr. Downs replied that it will be withdrawn from the market. Considering the process, it is easier to implement with a formulary changes. They have one patient that is on the drug and they should still get it because they are on therapy. It doesn't impact anybody.

There were no more questions or comments from the Panel. The Chair called for the vote on UF recommendation, PA Criteria, and UF Implementation Plan for HCV Drugs: DAAs

1. **HCV Drugs: DAAs - UF Recommendations:**

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

2. HCV Drugs: DAAs – Sofosbuvir (Sovaldi) PA Criteria

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

3. **HCV Drugs: DAAs – UF and PA Implementation Plan**

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

2. ORAL ANTICOAGULANTS

(Dr. Allerman)

A. Oral Anticoagulants—Relative Clinical Effectiveness and Conclusion

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

- **Target-Specific Oral Anticoagulants (TSOACs)**: apixaban (Eliquis), dabigatran (Pradaxa), edoxaban (Savaysa), and rivaroxaban (Xarelto)

- **Vitamin K Antagonists**: warfarin (Coumadin, generic)

The P&T Committee recommended (**18 for, 0 opposed, 0 abstained, 0 absent**) the following conclusions:

- **Non-valvular Atrial Fibrillation (NVAF):**

  - In NVAF, dabigatran and apixaban were superior to not optimally controlled warfarin, while edoxaban and rivaroxaban were non-inferior.

  - Intracranial bleeding was lower with all four TSOACs compared with warfarin in the major trials used to obtain FDA approval for apixaban, dabigatran, edoxaban, and rivaroxaban.

  - Edoxaban advantages include once daily dosing and an overall lower rate of bleeding versus warfarin. Disadvantages include a higher rate of gastrointestinal (GI) bleeding, and a higher risk of stroke in patients with normal renal function (creatinine clearance greater than 95 mL/min).

  - Dabigatran was the only TSOAC to show superior ischemic stroke reduction, but it has a higher incidence of GI bleeding than warfarin, causes dyspepsia, and is highly dependent on renal clearance.

- Rivaroxaban advantages include once daily dosing, but it has an increased incidence of GI bleeding and major bleeding compared to warfarin. The patient population studied with rivaroxaban had more comorbidities than the other three TSOACs.

- Apixaban had significantly less major bleeding than warfarin, and was the only TSOAC to show a reduction in mortality, but the confidence interval approached one. The point estimates and confidence intervals for all the TSOACs are similar for mortality.

- **Venous Thromboembolism (VTE) or Pulmonary Embolism (PE)**

  - For acute VTE, no overlap with low-molecular weight heparin (LMWH) is required with apixaban or rivaroxaban. All four TSOACs were non-inferior to LMWH and/or warfarin for the composite endpoint of recurrent VTE, nonfatal pulmonary embolism (PE), or death.

  - Apixaban and rivaroxaban had significantly less major bleeding than LMWH and/or warfarin.

- **VTE Prevention following Orthopedic Surgery (Hip or Knee Replacement)**

  - The TSOACs offer a convenience to patients in that LMWH injections are not required.

  - Rivaroxaban and apixaban are FDA approved, while edoxaban and dabigatran are not approved for this use.

Due to a lack of head-to-head trials, the P&T Committee concluded there is insufficient evidence to determine if one TSOAC has advantages over the others. The TSOACs have advantages over warfarin of predictable anticoagulant effect, fixed dosing, fewer drug interactions, and lack of laboratory monitoring and dietary restrictions. However, overall warfarin remains a viable therapy option due to its large number of FDA-approved indications, long history of use, preferred choice for patients with severe renal dysfunction, and availability of an antidote.

B. Oral Anticoagulants—Relative Cost-Effectiveness Analysis and Conclusion

CMA, CEA, and BIA were performed to evaluate the oral anticoagulants. The P&T Committee concluded (**17 for, 0 opposed, 1 abstained, 0 absent**) the following:

- CMA and CEA results showed generic warfarin was the most cost-effective oral anticoagulant, followed by all branded TSOACs (apixaban, dabigatran, edoxaban and rivaroxaban).

- BIA was performed to evaluate the potential impact of designating selected TSOACs with formulary or NF status on the UF. BIA results showed that modeled scenarios where generic warfarin is BCF, with all other branded TSOACs designated as

formulary on the UF, demonstrated lower cost avoidance for the MHS compared to the current baseline formulary status.

C. Oral Anticoagulants—UF Recommendation

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

- Uniform Formulary:
  - Warfarin (Coumadin; generic)
  - Apixaban (Eliquis)
  - Dabigatran (Pradaxa)
  - Edoxaban (Savaysa)
  - Rivaroxaban (Xarelto)

- Non Formulary: None

No implementation needed here due to no change in formulary status, and there is no recommendation for prior authorization criteria.

D. **Physician's Perspective**

The Committee most recently reviewed the oral anticoagulants in February 2013, and since then two new products have reached the market.

There are several advantages of the newer agents over warfarin, and a review of DoD data does show a decline in warfarin utilization. However, warfarin still represents about 60% of DoD utilization. Additionally, there are many clinical reasons to consider warfarin for a patient, including the fact that a reliable antidote is available. Antidotes to the newer anticoagulants are currently under review at the FDA.

A review of DoD data found that the majority of use of the newer oral anticoagulants was for stroke prevention in patients with atrial fibrillation, so this was the focus of the clinical review. The clinical data for the other indications was also reviewed.

For the Uniform Formulary recommendation, there was no controversy here. All of the oral anticoagulants were recommended to remain on the Uniform Formulary. As the newer agents continue to gain additional indications, or if head-to-head trials become available, the class will likely be reviewed again.

E. **BAP Comments**

Dr Anderson asked in terms of what is changing, is it just the Savaysa being added to the formulary.

Dr Allerman replied that yes, Savaysa had not previously been reviewed. By default, it was on the uniform formulary until it could be reviewed. That is the major change from the previous decision from 2013.

Dr. Anderson asked if there was any consideration for a step therapy edit.

Dr. Allerman replied that part of the condition sets did include the option for step therapy. When all the modeling was done and the cost effective analysis, the recommendation was stated that to place everything on the uniform formulary without the step therapy. There are no new indications or an antidote; it is likely that this class will be reviewed again in the near future.

There were no more questions or comments from the Panel. The Chair called for the vote on UF recommendation, PA Criteria, and UF Implementation Plan for Oral Anticoagulants.

1. Oral Anticoagulants – UF Recommendation

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

UTILIZATION MANAGEMENT

1. TESTOSTERONE REPLACEMENT THERAPY (TRT)

(Dr. Allerman)

A. TRT: Testosterone Nasal Gel (Natesto)—PA Criteria

Natesto is a new formulation of testosterone that is administered intranasally. It is dosed as one pump actuation per nostril, three times daily, six to eight hours apart. The TRT products were reviewed by the P&T Committee in August 2012 and automated PA (step therapy) and manual PA criteria were recommended for the class (implemented March 2013).

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) step therapy and manual PA criteria for testosterone nasal gel (Natesto), consistent with the rest of the class and its FDA-approved indication.

The full PA criteria are as follows: PA criteria apply to all new and current users of Natesto.

Automated PA Criteria: The patient has filled a prescription for transdermal 2% gel pump (Fortesta) at any Military Health System pharmacy point of service (Military

Treatment Facilities, retail network pharmacies, or mail order pharmacy) during the previous 180 days

AND

Manual PA Criteria: If automated criteria are not met, coverage is approved for Natesto if:

- Contraindications exist to Fortesta (hypersensitivity to a component)
- Inadequate response to Fortesta (minimum of 90 days **AND** failed to achieve testosterone levels above 400 ng/dL **AND** the patient has denied improvement in symptoms)
- Clinically significant adverse reactions to Fortesta not expected with Natesto

AND

Coverage approved for male patients aged 17 years or older with:

- A diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism

Coverage for use in women or in adolescent males under the age of 17 is not approved and will be considered upon appeal only.

Dr. Allerman mentioned that for the Prior Authorization criteria, they normally do not have comments from Dr. Kugler.

B. **BAP Comments**

There were no more questions or comments from the Panel. The Chair called for the vote on PA Criteria for the TRT: Testosterone Nasal Gel (Natesto)

1. TRT: Testosterone Nasal Gel (Natesto) – PA Criteria

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

2. CYSTIC FIBROSIS (CF) DRUGS

(Dr. Allerman)

A. CF: Ivacaftor (Kalydeco)—PA Criteria

Ivacaftor (Kalydeco) is indicated for the treatment of CF. PA criteria were recommended at the February 2012 meeting, updated in May 2014 and December 2014 to reflect the FDA-approved indication for various mutations in the cystic fibrosis transmembrane conductance regulator

(CFTR) gene. In March 2015, the FDA-approved indication for Kalydeco was further expanded to include pediatric patients aged 2 years and older. Along with this expanded indication, a new dosage form was launched in the form of oral granules that are mixed with either soft food or liquid every 12 hours for weight-based pediatric dosing.
The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 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).

- Coverage will be approved for the treatment of CF patients aged 2 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.

- Coverage is not approved for patients who are homozygous for the F508del mutation in the CFTR gene.

B. **BAP Comments**

There were no more questions or comments from the Panel. The Chair called for the vote on PA Criteria for the CF: Ivacaftor (Kalydeco)

1. **CF: Ivacaftor (Kalydeco) – PA Criteria:**

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

3. RENIN ANGIOTENSIN ANTIHYPERTENSIVES (RAAS)

(Dr. Allerman)

A. RAAs: Perindopril/Amlodipine (Prestalia)—PA Criteria

The FDA recently approved the combination product perindopril and amlodipine (Prestalia). It is indicated for the treatment of hypertension as monotherapy or as initial therapy in patients requiring multiple drugs to achieve their blood pressure goals. The RAAs class was reviewed in August 2010; step therapy was implemented in January 2011 and applies to all drugs in the class.

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) step therapy criteria for perindopril/amlodipine (Prestalia), consistent with the current criteria for the RAAs class.

The full PA criteria are as follows: PA criteria apply to all new and current users of

Prestalia.

Automated PA Criteria—The patient has filled a prescription for one of the preferred agents (generic angiotensin-converting enzyme inhibitors, generic losartan, losartan/HCTZ, Diovan, Diovan HCT, Exforge, Exforge HCT, Micardis, Micardis HCT, or Twynsta) 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, coverage is approved for Prestalia if:

- Contraindications exist to one step-preferred RAA agent not expected to occur with Prestalia
- The patient has had an inadequate response to one step-preferred RAA agent
- The patient has been unable to tolerate one step preferred RAA agents, due to adverse effects.

B. **BAP Comments**

There were no more questions or comments from the Panel. The Chair called for the vote on PA Criteria for the RAA's: Perindopril/Amlodipine (Prestalia)

1. **RAAs: Perindopril/Amlodipine (Prestalia) – PA Criteria**

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

4. INSULINS

(Dr. Allerman)

A. Insulins: Inhaled Insulin (Afrezza)—PA Criteria

Afrezza is rapid-acting inhaled insulin indicated to improve glycemic control in adult patients with Type 1 or Type 2 diabetes mellitus. It is available as single-use cartridges of 4, 8, and 12 units, administered via oral inhalation at the beginning of a meal. Dosing must be individualized. Manual PA criteria were recommended to ensure appropriate use of the drug in Type 1 and Type 2 diabetic patients, including failure of or inability to tolerate an adequate trial (90 days) of a rapid or short-acting subcutaneous insulin product.

The P&T Committee recommended (**17 for, 0 opposed, 1 abstained, 0 absent**) manual PA criteria for Afrezza, consistent with the FDA-approved product labeling for use in Type 1 and Type 2 diabetic patients.

The full PA criteria are as follows: Manual PA criteria apply to all new and current users of Afrezza. Coverage is approved for non-smoking patients with either:

- **Type 1 Diabetes Mellitus (diagnosed)**

  - Failure to achieve hemoglobin A1C ≤ 7 % in 90 days of use of a rapid or short-acting subcutaneous (SC) insulin product or clinically significant adverse effects experienced with SC rapid or short-acting insulin unexpected to occur with inhaled insulin
  - Afrezza is used as adjunctive treatment to current basal insulin therapy
  - Spirometry testing [baseline forced expiratory volume in the first second
  - (FEV1) upon initiation with repeated FEV1 at 6 months after initiation and repeated annually thereafter] has been performed

- **Type 2 Diabetes Mellitus (diagnosed)**

  - Failure to achieve hemoglobin A1C ≤ 7 % in 90 days of use of a rapid or short-acting SC insulin product or clinically significant adverse effects experienced with SC rapid or short-acting insulin unexpected to occur with inhaled insulin
  - Failure of or clinically significant adverse effect to two oral anti-diabetic agents [i.e. sulfonylurea, thiazolidinedione, or dipeptidyl peptidase-4 inhibitor] if metformin is contraindicated
  - Spirometry testing (baseline FEV1 upon initiation with repeated FEV1 at 6 months after initiation and repeated annually thereafter) has been performed

    Contraindications to the use of Afrezza: hypoglycemia, chronic lung disease (asthma, COPD), hypersensitivity to regular human insulin, or any Afrezza excipients

B. BAP Comments

There were no more questions or comments from the Panel. The Chair called for the vote on PA Criteria for the Insulin: Inhaled Insulin (Afrezza).

1. Insulins: Inhaled Insulin (Afrezza) – PA Criteria

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

5. SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS

(Dr. Allerman)

A. SMBGS Test Strips: ACCU-CHEK Aviva Plus Test Strips – PA Criteria

The SMBGS test strips were evaluated at the November 2014 P&T Committee Meeting. Step therapy and MN criteria were recommended with an implementation date of August 5, 2015. PA and MN criteria allow for use of a non-preferred, NF test strip if the patient uses an insulin pump and requires a specific test strip that communicates wirelessly with a specific meter.

The ACCU-CHEK Aviva Plus test strips are designated non-preferred and NF. However, the ACCU-CHEK Aviva Plus test strips are used in the ACCU-CHEK Combo meter, which communicates wirelessly with the ACCU-CHEK Spirit Combo insulin pump.

The P&T Committee recommended (**17 for, 0 opposed, 1 abstain, 0 absent**) adding the ACCU-CHEK Aviva Plus test strips to the SMBGS Test Strips PA criteria for patients using the ACCU-CHEK Aviva Combo meter with the ACCU-CHEK Spirit Combo pump.

The PA criteria are as follows: New and current users of the NF test strips are required to try FreeStyle Lite or Precision Xtra.

Manual PA Criteria—Non-preferred test strip allowed if: patient uses an insulin pump and requires a specific test strip that communicates wirelessly with a specific meter

- CONTOUR NEXT strip with CONTOUR NEXT Link meter for Medtronic pump
- Nova Max strip with Nova Max Link meter for Medtronic pump
- ACCU-CHEK Aviva Plus test strip with the ACCU-CHEK Combo meter for the ACCU-CHEK Spirit Combo pump

B. BAP Comments

There were no more questions or comments from the Panel. The Chair called for the vote on PA Criteria the SMBGS Test Strips: ACCU-CHEK Aviva Plus Test Strips

1. **SMBGS Test Strips: ACCU-CHEK Aviva Plus Test Strips – PA Criteria**

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

Mr. Tackitt thanked the Panel for their participation.

CAPT Norton thanked panel and adjourned the meeting.

Mr. Robert Duane Tackitt

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 uses 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.

- BAP – Beneficiary Advisory Panel
- DFO – Designated Federal Officer
- A1C – hemoglobin
- AASLD – American Association for the Study of Liver Diseases
- BCF – Basic Core Formula
- BIA – Budget Impact Analysis
- CEA – Cost-Effectiveness Analysis
- CF – Cystic Fibrosis
- CFR – Code of Federal Regulations
- CFTR – Cystic Fibrosis Transmembrane Conductance Regulator
- CMA – Cost Minimization Analysis
- COPD – Chronic Obstructive Pulmonary Disease
- DAA – Direct Acting Antiviral
- DHA – Defense Health Agency
- DoD – Department of Defense
- FACA – Federal Advisory Committee Act
- FEV1 – Forced Expiratory Volume in the First Second
- FDA – Food & Drug Administration
- G1244E - Cystic Fibrosis Mutation
- G1339D - Cystic Fibrosis Mutation
- G178R 0 Cystic Fibrosis Mutation
- G55ID – Cystic Fibrosis Mutation
- G551S - Cystic Fibrosis Mutation
- GI – Gastrointestinal
- HCT – Hematocrit
- HCTZ – Diuretic
- HCV – Hepatitis C Virus
- HIV – Human Immunodeficiency Virus
- IDSA – Infectious Diseases Society of America
- IM – Intramuscular
- LMWH – Low-Molecular Weight Heparin
- MS – Multiple Sclerosis
- NDAA – National Defense Authorization Act

- NF – Non-Formulary
- NVAF – Non-Valvular Atrial Fibrillation
- NVP – Nausea and Vomiting during Pregnancy
- OTC – Over-the-Counter
- PE – Pulmonary Embolism
- P&T – Pharmacy & Therapeutic
- R117H - Cystic Fibrosis Mutation
- S1251N - Cystic Fibrosis Mutation
- S1255P - Cystic Fibrosis Mutation
- S549N - Cystic Fibrosis Mutation
- S549R - Cystic Fibrosis Mutation
- SC – Subcutaneous
- SED-1s – Sedative Hypnotic Agents
- SMBGS – Self-Monitoring Blood Glucose Systems
- SVR12 – Sustained Virologic Response at 12 weeks
- TRICARE – Military Health Care System
- TSOACs – Targeted-Specific Oral Anticoagulants
- UF – Uniform Formulary
- USC – United States Code
- VTE – Venous Thromboembolism