EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel (BAP)
July 12, 2018

UNIFORM FORUMULARY DRUG CLASS REVIEWS

I. UF CLASS REVIEWS

A. PANCREATIC ENZYME REPLACEMENT THERAPY

1. PERT—UF Recommendation

The P&T Committee recommended (15 for, 1 opposed, 0 abstained, 0 absent) the following, based on clinical and cost effectiveness:

UF and step-preferred
Creon

UF and non-step-preferred
Viokace tablet

NF and non-step-preferred
Pancreaze
Pertzye
Ultresa
Zenpep

This recommendation includes step therapy, which requires a trial of Creon prior to use of Viokace and the NF non-step-preferred PERT drugs in all new and current users.

2. PERT—Manual PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for the non-step-preferred products, requiring a trial of Creon first in all new and current users. Note that PA is not needed for Creon, and the step-therapy requirements will be included in the manual PA.

Manual PA Criteria: Pancreaze, Pertzye, Ultresa, Viokace, and Zenpep are approved if any of the following criteria are met:

The patient has failed an adequate trial of Creon, defined as at least two dose adjustments done over a period of at least four weeks OR

The patient is ≤ 2 years old and a sufficient trial of Creon was unsuccessful OR

For Viokace: the patient requires an uncoated tablet due to actual or suspected dissolution issues with enteric coating of Creon

PA does not expire.

3. PERT—Tier 1 Cost Share

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) lowering the current tier 2 cost share for Creon to the generic tier 1 cost share.

The authority for this recommendation is codified in 32 CFR 199.21(j)(3), which states that "when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the Pharmacy and Therapeutics Committee may also designate that the drug be cost-shared at the generic rate." The objective is to maximize use of Creon in the TRICARE Mail Order pharmacy and Retail Network, given its significantly lower cost relative to the other PERT products. Lowering the cost-share for Creon will provide a greater incentive for beneficiaries to use the most cost-effective PERT formulation in the purchased care points of service.

4. PERT—UF, PA, and Tier 1 Cost Share Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following: 1) an effective date of the first Wednesday after a 90-day implementation period in all points of service and 2) DHA send letters to beneficiaries who are affected by the UF decision.

Summary of Physician's Perspective:

This is the 3rd time that the pancreatic enzymes have been reviewed for formulary status. There are no new products in the class, and one product, Ultressa, appears to have been discontinued.

The PERT drugs can be used for either cystic fibrosis or pancreatitis. For DoD, the majority of the use was in older patients (ages 60-80 years), which supports that the PERT drugs are primarily used for pancreatitis.

When we surveyed MHS providers, Creon was most frequently mentioned as the preferred products. When providers were asked which product should be on the formulary, they requested having one PERT drug that was available in multiple strengths.

Creon is a good candidate for the step preferred PERT drug, since it has been on the formulary for several years; it is available in multiple strengths, including the dosages

needed for young children with cystic fibrosis; and it currently has the highest market share in the DoD at 75%.

Viokace is the other product selected for uniform formulary status, however, it will be after the step. Having Viokace allows for a different formulation – it is available in uncoated tablets, which was mentioned by some GI providers as an alternative to the Creon coated capsules.

Historically, all agents are highly therapeutically interchangeable based on clinical and safety factors, plus the fact that they all contain the same active ingredients, just in varying amounts.

There will be minimal disruption to patients, since 4,500 out of the 5,700 patients in the class are already on Creon. About 1,200 patients will be affected by the formulary recommendation.

When we look at DoD utilization, we found some other usage patterns that also support that the change to Creon as a step preferred product will have minimal impact to patients. There are a large number of new users per quarter, there is a low rate of patients increasing (or up-titrating their dose), and there is a relatively low persistence rate in the class (only about 30% of patients remain on therapy at one year). This shows us that many patients do not remain on therapy for long periods.

The one opposing vote was that the member felt there was not enough cost savings to make anything non-formulary, to avoid patient disruption. However, that concern was allayed when the tier one copay was proposed for Creon. Also, for Creon, there won't be a requirement for Prior Authorization, which is another incentive for patients to switch from the non-preferred products.

Summary of Panel Questions and Comments:

Mr. Hostettler asks how many of the patients have cystic fibrosis.

Dr. Allerman responds that out of 6000 patients, a little less than 1000 are diagnosed with cystic fibrosis. She doesn't have the breakdown of patients who are on non-preferred products.

Mr. Hostettler understands the interchangeability of the pancreatitis products. I have problems/concerns with the patients who have parents that provide care to the cystic fibrosis patients that are consider stable. I also understand the adjustments in dosage but they are, at least, familiar with the drug they are using. Adjusting is what they are familiar with and changing their process does not seem to be worth the potential cost savings. Let them make the decision once they are notified of a change and potential $17 savings. It becomes a patient-driven decision rather than a your-driven decision.

Dr. Allerman answers this is one of the reasons we didn't have a PA requirement for Creon. Currently, it has the highest utilization in DoD.

Ms. Buchanan raises an objection. She asks if we could grandfather the patients with cystic fibrosis.

Dr. Allerman replies that they can check on that.

Mr. Hostettler says a longer implementation period is needed if the grandfathering is not an option for the cystic fibrosis patients

Dr. Allerman asks if he means longer than 90 days.

Mr. Hostettler responds yes. This allows time to schedule appointments with their physicians and become comfortable with the adjustments/change to their normal routine.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, Tier 1 Cost Share and UF PA, and Tier 1 Cost Share Implementation Plan for the PERTs.

- **PERT – UF Recommendation**

  Concur: 2 Non-Concur: 3 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **PERT – Manual PA Criteria**

  Concur: 0 Non-Concur: 5 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **PERT – Tier 1 Cost Share**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **PERT – UF, PA, and Tier 1 Cost Share Implementation Plan**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

   These comments were taken under consideration prior to my final decision

  Recommendations and Comments from the Panel:

  The Panel members (Mr. Ostrowski, Ms. Buchanan, Mr. Hostettler, Dr. Bertin and Ms. Walker) asks the P&T Committee to consider grandfathering the cystic fibrosis patients. They further state that if the Committee had grandfathered the patients, all would have concurred with the recommendation of the P&T Committee.

B. GROWTH STIMULATING AGENTS

1. GSAs—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) the following, based on clinical and cost effectiveness:

- UF and step-preferred
  - Norditropin FlexPro
- UF and non-step-preferred
  - Omnitrope
  - Zomacton
- NF and non-step-preferred
  - Genotropin and Genotropin MiniQuick
  - Humatrope
  - Nutropin AQ Nuspin
  - Saizen
  - Serostim
- This recommendation includes step therapy, which requires a trial of Norditropin FlexPro prior to use of the non-step-preferred GSAs in all new and current users.

2. GSAs—Manual PA Criteria

PA criteria currently apply to the GSAs. The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) updating the current PA criteria for the class to include the updated safety warning for use of a GSA in patients with Prader-Willi

syndrome and obstructive sleep apnea and to require the prescription to be written by the appropriate subspecialist. Additionally the step therapy requirements for trial of Norditropin FlexPro in all new and current users will be included in the manual PA. Use of the non-step-preferred products is allowed if the patient has a contraindication or has experienced an adverse reaction to Norditropin FlexPro, and then Omnitrope and Zomacton, before moving to NF agents.

Manual PA Criteria: Norditropin FlexPro, Genotropin, Humatrope, Nutropin AQ Nuspin, Omnitrope, Saizen, Serostim, and Zomacton are approved if:

- The patient is younger than 18 years of age and has the following indications:

  Growth hormone deficiency
  Small for Gestational Age
  Chronic Renal Insufficiency **associated with growth failure**
  Prader-Willi Syndrome **(in patients with negative sleep study for obstructive sleep apnea)**
  Turner Syndrome
  Noonan's Syndrome
  Short stature homeobox (ShoX) gene mutation

- For patients younger than 18 years of age who do not have one of the indications above, the diagnosis must be documented

- For patients younger than 18 years of age, the prescription is written by or in consultation with a pediatric endocrinologist or nephrologist who recommends therapeutic intervention and will manage treatment

  OR

- The patient is older than 18 years of age and has the following indications:

  Growth hormone deficiency as a result of pituitary disease, hypothalamic disease, trauma, surgery, or radiation therapy, acquired as an adult or diagnosed during childhood
  Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS) wasting/cachexia
  Short Bowel Syndrome

- For patients older than 18 years of age, the prescription is written by or **in consultation with an appropriate specialist (endocrinologist, infectious disease specialist, general surgeon, or gastroenterologist).**

  AND

For Omnitrope and Zomacton: In addition to the above criteria, the following criteria applies to current users of Omnitrope and Zomacton:

- The patient has a contraindication to Norditropin FlexPro OR
- The patient has experienced an adverse reaction to Norditropin FlexPro that is not expected with Omnitrope or Zomacton (e.g., because of different preservative)

  OR

- For Zomacton: the patient prefers a needle-free device (Zomacton)

  AND

For Genotropin, Humatrope, Nutropin AQ Nuspin, Saizen, and Serostim: In addition to the above criteria, the following criteria applies to new and current users of Genotropin, Humatrope, Nutropin AQ Nuspin, Saizen, and Serostim:

- The patient has a contraindication to Norditropin FlexPro AND Omnitrope AND Zomacton OR

- The patient has experienced an adverse reaction to Norditropin FlexPro AND Omnitrope AND Zomacton that is not expected with the non-step-preferred product (e.g., because of different preservative)

  Note that all possible preservative formulations are available between Norditropin FlexPro, Omnitrope, and Zomacton.
  Note that patient preference for a particular device is insufficient grounds for approval of Genotropin, Humatrope, Nutropin AQ Nuspin, Saizen, or Serostim.

- Use of a GSA is not approved for idiopathic short stature, the normal ageing process, obesity, or depression

- Use of a GSA is not approved for other non-FDA-approved uses (e.g., non-alcoholic fatty liver disease, cirrhosis, mild cognitive impairment)

- Concomitant use of multiple GSAs is not approved

PA expires in one year.

5. GSAs—Tier 1 Cost Share

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) lowering the current tier 2 cost share for Norditropin FlexPro to the generic tier 1 cost share, under the authority previously discussed.

6. GSAs—UF, PA, and Tier 1 Cost Share Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) the following: 1) an effective date of the first Wednesday after a 90-day implementation period in all points of service and 2) DHA send letters to beneficiaries who are affected by the UF decision.

Summary of Physician's Perspective:

We last reviewed this growth hormone products over 10 years ago, and since the last review, some factors that previously showed differences between the products no longer apply, including the fact that now most of the products have the same FDA-approved indications.

Our MHS providers and several organizations, including the Pediatric Endocrine Society, the American Association of Clinical Endocrinologist, and the UK National Institute for Health and Care Excellence, consider these drugs as highly therapeutically interchangeable and do not prefer or recommend one product over another.

Norditropin Flex Pro has been the current market leader in the MHS since 2007. There are several advantages to Norditropin, as were outlined previously. Therefore, selecting it as the step preferred product impacts the fewest number of patients. Currently in the MHS, 72% of the Growth Hormone market share is for Norditropin. About 465 patients will be affected by formulary recommendation. However, the manufacturer has multiple mechanisms for patient and provider education on the Norditropin device, and we will work with them to ensure patients can receive training on the Norditropin. Additionally, the Norditropin prefilled syringe is the same device used for various insulin products, and has a long history of being on the market. MHS providers and patients are familiar with using the Norditropin device.

When we talked to providers, they felt that having one device in a prefilled syringe was adequate for all MHS patients. Providers felt that the growth hormone products were interchangeable.

Zomacton and Omnitope are the other two products recommended for uniform formulary status but after the step. They provide alternatives to Norditropin in terms of differences in preservatives for tolerability issues, plus Zomacton is a needle free device.

The Committee did recognize that there are some differences in the preservatives which may cause hypersensitivity reactions in some patients. The PA will take into account these types of contraindications and adverse effects

Other civilian health plans commonly only have 1-2 products on their formulary, so the formulary recommendation for the MHS is consistent with the civilian world.

We are also recommending a tier one co-pay for Norditropin, which is another benefit to patients and results in lower out-of-pocket costs, plus provides an incentive to switch to the step-preferred product.

Summary of Panel Questions and Comments:

Mr. Hostettler asks what Prader-Willi syndrome is.

LT COL Khoury replies I believe it's a genetic condition.

Mr. Hostettler asks if the beneficiary population affected are all sleep apnea patients.

LT COL Khoury answers no. The reference regarding Prader Willi is to ensure patients have negative sleep studies for obstructive sleep apnea. It is identified because it is a safety concern. It is not for all obstructive sleep apnea patients.

Mr. Hostettler states the total population affected by the recommendation is 1830. How many of those patients are on Zomacton?

Dr. Allerman says there is an error for number of affected users. Dr. Kugler is correct that there are 465 patients total who will be affected by the recommendation.

Mr. Hostettler asked if the majority are in mail.

Dr. Allerman responds the majority are in mail.

Mr. Hostettler asks how extensive is the training for each device and is there a significant difference in the training.

LT COL Khoury says each device is slightly different and requires some education. All of the devices have patient support programs to include nurse educators that will engage patients by phone and I believe, in person as well, as appropriate. They are available geographically to address any of the patient's questions.

Mr. Hostettler says 465 patients, a very small number in the MHS, will need time to scheduled appointment with their physicians for reassessment, get trained, a new prescription, and start on the new medication. His is concerned because that is a lot of activity to take place in 90 days. The patients currently on Zomacton have made that choice because it is a needle-free device. The recommendation requires them to potentially try a product that requires an injection to meet the manual PA requirements for Zomacton. For the small number of patients, it seems like a lot of impact for the small number of beneficiaries.

LT COL Khoury says please keep in mind all patients go through an annual PA for this agent.

Mr. Hostettler asks why there is an annual PA. Why does it expire?

LT COL Khoury responds that's the way it's always been and part of the disease process to ensure continued monitoring and assessment of the patients. It is part of the protocols for the patient to continue on the product.

Mr. Hostettler asks how many patients need the drug after a year. What the percentage is for re-order or re-start of the product.

LT COL Khoury says it depends on the age breakdown. There is a significant drop off at the age of 18. There are drop-offs between the age breakdowns of young child to 18.

Mr. Hostettler asks if those are drop-offs or disruptions.

LT COL Khoury states that we see discontinuations due to the reason for the need for replacement no longer being needed and those patients are continually monitored every year. Further, patients should be seeing their provider on a regular basis.

Mr. Ostrowski states we are here on behalf of the beneficiary. Can the patients continue on the drug until their next annual evaluation instead of switching within the 90 day timeframe? There is an annual PA for this product and the patient will be evaluated at the time anyway.

Mr. Hostettler says allowing the patients to switch at the annual review may have less impact overall.

LT COL Khoury says they will take that back for consideration.

NOTE: To accurately track the vote and minimize confusion. Col Hoerner asks the Panel to vote on the recommendation as the vote is written then comment.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, Tier 1 Cost Share, and UF, PA and Tier 1 Cost Share Implementation Plan for the GSAs.

- **GSAs – UF Recommendation**

  Concur: 0 Non-Concur: 5 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **GSAs – Manual PA Criteria**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **GSAs – Tier 1 Cost Share**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **GSAs – UF, PA, and Tier 1 Cost Share Implementation Plan**

  Concur: 0 Non-Concur: 5 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

Recommendation and comments from the Panel:

The Panel asks for a new implementation date. Rather than 90 days, they ask if the patients affected by the recommendation can switch during their annual review. The Panel believes switching at the annual review would cause less disruption to the patient therapy.

C. GASTROINTESTINAL-2 AGENTS: OPIOID-INDUCED CONSTIPATION SUBCLASS

1. GI-2 Agents: OIC Subclass—UF Recommendation

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

- UF
  Symproic
  Movantik

- NF
  Relistor tablets and injection

2. GI-2 Agents: OIC Subclass—Manual PA Criteria

PA criteria currently apply to Relistor and Movantik, which requires a trial of two traditional laxatives and a trial of lubiprostone (Amitiza) prior to use of an OIC drug. For new users of Symproic and Movantik, the P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) maintaining the requirement for a trial of over-the-counter (OTC) laxatives, and removing the requirement for a trial of Amitiza, based on the treatment guidelines from the American Gastroenterological Association where PAMORAs are recommended specifically for laxative-refractory patients.

The Committee also recommended updating the existing manual PA criteria for Relistor tablets to require a trial of Amitiza and both Symproic and Movantik, due to the relatively limited amount and low quality evidence available. The PA criteria for Relistor tablets will apply to new and current users. PA is not required for Relistor injection, as this product is limited to the palliative care setting.

<u>Manual PA criteria</u>

a. Movantik and **Symproic**

- The patient is 18 years of age or older with a diagnosis of OIC AND
- The patient is currently taking an opioid agonist AND
- The patient is not on other opioid antagonists (naloxone not including rescue agents, naltrexone, etc.) AND
- The patient has either failed or not tolerated two or more of the following:
  - At least one stimulant laxative (sennosides or bisacodyl) AND
  - At least one osmotic laxative (Miralax, lactulose, or magnesium citrate) AND

- The patient does not have a known or suspected gastrointestinal obstruction or is not at increased risk of recurrent obstruction AND

- The patient is not currently on strong CYP3A4 inducers inhibitors (e.g., clarithromycin, ketoconazole)

Non-FDA-approved uses are not approved.

PA expires in one year.

Renewal PA criteria: Coverage will be approved for an additional year if all of the following apply:

- The patient continues to take opioids AND

- The patient continues lifestyle modifications including regular use of a stimulant laxative (e.g., bisacodyl, senna), a high fiber diet, increased fluid intake, moderate exercise, and opioid dose de-escalation to minimum effective dose

- The patient is responding in a meaningful manner (e.g., improvement of at least one additional spontaneous bowel movement per week over baseline)

b. Movantik and **Symproic**

Manual PA criteria apply to new and current users of Relistor tablets.

Manual PA criteria: Approved if all criteria are met:

- The patient is 18 years of age or older with a diagnosis of OIC AND

- The patient is currently taking an opioid agonist AND

- The patient is not on other opioid antagonists (naloxone not including rescue agents, naltrexone, etc.) AND

- The patient has either failed or not tolerated two or more of the following:
  - At least one stimulant laxative (sennosides or bisacodyl) AND
  - At least one osmotic laxative (Miralax, lactulose, or magnesium citrate) AND

- The patient has tried and failed Movantik AND

- The patient has tried and failed Symproic AND

- The patient has tried and failed Amitiza AND

- The patient does not have a known or suspected gastrointestinal obstruction or is not at increased risk of recurrent obstruction AND

- The patient is not currently on strong CYP3A4 inducers inhibitors (e.g., clarithromycin, ketoconazole)

Non-FDA-approved uses are not approved.
PA expires in one year.

Renewal PA criteria: Coverage will be approved for an additional year if all of the following apply:

- The patient continues to take opioids AND

- The patient continues lifestyle modifications including regular use of a stimulant laxative (e.g., bisacodyl, senna), a high fiber diet, increased fluid intake, moderate exercise, and opioid dose de-escalation to minimum effective dose

- The patient is responding in a meaningful manner (e.g., improvement of at least one additional spontaneous bowel movement per week over baseline)

3. GI-2 Agents: OIC Subclass—UF and PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following:

1) an effective date of the first Wednesday after a 60-day implementation period in all points of service and 2) DHA send letters to beneficiaries who are affected by the UF decision.

Summary of Physician's Perspective:

This is a new class of drugs for treating OIC, however, they are not a first-line treatment. Professional guidelines recommend using traditional laxatives first, before using a PAMORA. A survey of MHS providers also agreed with this recommendation, that these drugs should only be used after laxatives have failed. Other approaches to reduce constipation are to decrease the dose of the opioid.

The reasons for the prior authorization are to ensure that the patient has tried the traditional laxatives first, and also due to the lack of long-term safety data with the PAMORAs.

For Relistor, the PA will also require at trial of either Movantik or Symproic, or Amitiza (which is also approved for OIC, but has a different mechanism of action). The Committee did recognize that Relistor injection is indicated only for patients in

the palliative care setting. Because of this the recommendation is that the Relistor injection will not have the requirement for a PA, just non-formulary status.

When we looked at current utilization, it does not appear that patients are on these drug long-term. We found that only 43% of patients had their prescription filled more than one time. We will continue to monitor usage patterns for this class, along with any new clinical information for efficacy or safety updates.

Summary of Panel Questions and Comments:

Mr. Hostettler asks of the 315 patients affected, how many are on Relistor?

Dr. Allerman replied they are all on Relistor because the PA changed for Symproic and Movatik which only applies to new patients.

Hostettler asks why did you take the PA out of one drug and put it back in the other.

Allerman replied it was based on cost effectiveness, evidence quantity, and evidence quality. There was not enough evidence/data for Relistor.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, and UF and PA Implementation Plan for the GI-2 agents.

- **GI2 Agents: OIC Subclass – UF Recommendation**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **GI2 Agents: OIC Subclass – Manual PA Criteria**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **GI2 Agents: OIC Subclass – UF and PA Implementation**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

   These comments were taken under consideration prior to my final decision

Additional Panel Questions and Comments:

Mr. Hostettler asks when letters go out to beneficiaries.

Dr. Allerman answered they go out about a month before the formulary decision on implementation

Mr. Hostettler said that would give the beneficiary approximately 90 days to switch. You said 60 days?

Dr. Allerman said it is 60 days because there are approximately 300 patients affected by the recommendation.

Mr. Hostettler asked if they would receive letters 30 days before the clock starts.

Dr. Allerman said some patients may have gotten their refill the day before they get the letter which allows additional time switch to the new drug.

Mr. Hostettler asks if those patient would be notified of a pending change which allows them to see their provider to get a new prescription before the change. I am just trying to see if a 60 day implementation period is enough time.

Dr. Allerman states that these patients are on opioids. They are probably getting their opioid prescriptions every month.

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

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

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following:

- UF:
  - apalutamide (Erleada) – Oral Oncologic Agent for Prostate Cancer
  - bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy) – Antiretrovirals for HIV
  - efavirenz/lamivudine/tenofovir disoproxil fumarate (Symfi) – HIV

- efavirenz/lamivudine/tenofovir disoproxil fumarate (Symfi Lo) – HIV
- ibrutinib tablets (Imbruvica) – Oral Oncologic Agent for mantle cell lymphoma and chronic lymphocytic leukemia, new formulation (note that Imbruvica capsules were already designated as uniform formulary prior to the Innovator Rule established in August 2015)
- insulin lispro (Admelog) – Short-Acting Insulin for Diabetes Mellitus
- lamivudine/tenofovir disoproxil fumarate (Cimduo) – Antiretrovirals for HIV
- netarsudil 0.02% ophthalmic solution (Rhopressa) – Glaucoma Agents
- tezacaftor/ivacaftor (Symdeko) – Cystic Fibrosis Agents
- vancomycin oral solution (Firvanq) – Gastrointestinal-2 agents: Miscellaneous for *Clostridium difficile* associated diarrhea or enterocolitis

- NF:
  - clobetasol propionate 0.025% cream (Impoyz) – High Potency Corticosteroids-Immune Modulators for Moderate to Severe Plaque Psoriasis
  - desmopressin nasal spray (Noctiva) – Miscellaneous Endocrine Agent for nocturia due to nocturnal polyuria
  - doxylamine succinate/pyridoxine ER tablets (Bonjesta) – Antiemetic-Antivertigo Agents
  - ertugliflozin (Steglatro) – Non-Insulin Diabetes Drugs – Sodium Glucose Co-Transporter-2 (SGLT2) Inhibitor
  - ertugliflozin/sitagliptin (Steglujan) – Non-Insulin Diabetes Drugs –SGLT2 Inhibitor
  - ertugliflozin (metformin) (Segluromet)
  - glycopyrrolate inhalation solution (Lonhala Magnair) – Pulmonary-2: Long-Acting Muscarinic Agents (LAMAs) for Chronic Obstructive Pulmonary Disease
  - pitavastatin magnesium (Zypitamag) – Antilipidemic-Is (LIP-Is)
  - secnidazole (Solosec) – Miscellaneous Anti-Infective for bacterial vaginosis in adult women

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

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following:

Applying the same manual PA criteria for Steglatro, Segluromet, and Steglujan in new and current users as is currently in place for the other non-step-preferred SGLT2 inhibitors. Patients must first try the step-preferred SGLT2 inhibitor empagliflozin (Jardiance, Glyxambi, Synjardy or Synjardy XR).

Applying the same step therapy and manual PA criteria to new and current users of Zypitamag as is currently in place for pitavastatin (Livalo). Step therapy for the Antilipidemic I's drug class requires a trial of a generic statin at comparable low-density lipoprotein (LDL) lowering capability.

Applying manual PA criteria to new and current users of Impoyz cream, Lonhala Magnair inhalation solution, Noctiva nasal spray, and Rhopressa ophthalmic solution.

Applying manual PA criteria to new users of Bonjesta, Erleada, and Symdeko.

Applying manual PA criteria to new users of Imbruvica tablets and capsules.

INTERIM P&T COMMITTEE MEETING—Following the May 2018 P&T Committee meeting, the Committee became aware that Imbruvica capsules would remain on the market. The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) to revise the PA for Imbruvica to require a trial of Imbruvica capsules first in new users, prior to use of the tablets; as shifting patients to the tablet formulation unnecessarily reduces dosage titration options..

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

a. Erleada

if all criteria are met:

- The patient has a diagnosis of non-metastatic castration-resistant prostate cancer (as shown by a negative CT scan of abdomen/pelvis and/or negative bone scan) AND
- Patients should be co-prescribed gonadotropin-releasing hormone analog therapy concurrently OR patients should have had bilateral orchiectomy AND
- Erleada is prescribed by or in consultation with an oncologist or urologist

Non-FDA-approved uses are not approved.

PA expires in one year.

Renewal criteria: Erleada will be continued for another year if:

- The patient continues to be free of metastases
- No toxicities have developed
- The patient has not had disease progression requiring subsequent therapy (such as abiraterone [Zytiga])

b. Impoyz

Manual PA applies to all new and current users of Impoyz.

Manual PA criteria: Coverage will be approved if all criteria are met:

- Patient has moderate to severe plaque psoriasis AND
- Patient is ≥ 18 years old AND
- Patient is not a candidate for or has failed phototherapy AND
- Contraindications exist to all formulary high-potency topical steroids OR
- Patient has had an inadequate response to all formulary high-potency topical steroids OR
- Patient has had an adverse effect to each of the formulary high-potency topical steroids

Non-FDA-approved uses are not approved.

PA expires in 30 days.

Renewal Criteria: Renewal of therapy is not allowed.

c. Noctiva

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

Manual PA criteria: Coverage will be approved if all criteria are met:

- The patient ≥ 50 years old (only the low dose is allowed for patients > 65 years old)
- Causes of nocturia have been evaluated, nocturnal polyuria is confirmed with a 24-hour urine collection, and the patient has experienced at least two nocturia episodes per night for ≥ 6 months
- The patient is not currently taking any of the following medications:
  loop diuretics, thiazide diuretics, systemic or inhaled corticosteroids, lithium, alpha1-adrenoceptor antagonists, 5-alpha reductase inhibitors (5-ARIs), anticholinergics, antispasmodics, sedative/hypnotic agents, NSAIDs, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), antidepressants, anti-epileptics, opioids, or SGLT2s

- The patient has normal sodium level (135-145 meq/L) prior to the initiation of therapy, the sodium level is rechecked after one week of therapy, and another sodium level is rechecked after one month of therapy

- The patient does not have the following conditions:
  - acute or chronic rhinitis
  - atrophy of nasal mucosa
  - renal impairment (eGFR < 50 mL/min)
  - hyponatremia or history of hyponatremia
  - polydipsia
  - nocturnal enuresis
  - syndrome of inappropriate antidiuretic hormone (SIADH)
  - congestive heart failure (New York Heart Association II-IV)
  - uncontrolled hypertension or uncontrolled diabetes mellitus

Non-FDA-approved uses are not approved.

PA expires in six months.

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

- Patient has not developed any of the above conditions

- Patient is not taking any of the above medications

- Patient has shown a reduction in nocturia episodes

d. Bonjesta

Manual PA criteria apply to all new users of Bonjesta.

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

- The patient has a diagnosis of nausea and vomiting associated with pregnancy

- The patient has tried at least one non-pharmacologic treatment (for example, ginger, acupressure, high protein bedtime snack) and failed to obtain relief of symptoms

- The patient has tried OTC doxylamine and pyridoxine and failed to obtain relief of symptoms

- The provider has considered a change to an alternate anti-emetic (e.g., ondansetron) prior to prescribing Bonjesta

Non-FDA-approved uses are not approved.

PA will expire after nine months.

e. Steglatro, Segluromet, and Steglujan

Manual PA criteria apply to all new and current users of Steglatro, Segluromet, and Steglujan.

Manual PA criteria: Coverage will be approved if all criteria are met:

- For Steglatro and Steglujan: The patient must have had an inadequate response or experienced significant adverse events, or have a contraindication to metformin AND

- For Steglatro, Segluromet, and Steglujan: The patient must have tried one of the preferred SGLT2 inhibitors (Jardiance, Glyxambi, Synjardy, and Synjardy XR) and had an inadequate response or experienced significant adverse events, or have a contraindication to empagliflozin OR

- For Steglujan: The patient must have had an inadequate response to sitagliptin alone

Non-FDA-approved uses are not approved.

PA does not expire.

f. Lonhala Magnair

Manual PA is required for all new and current users of Lonhala Magnair inhalation solution (starter kit and refill kit).

Lonhala Magnair is approved if all criteria are met:

- The patient has a diagnosis of Chronic Obstructive Pulmonary Disease (COPD) AND

- The patient has tried and failed an adequate course of a nebulized Short-Acting Muscarinic Antagonist (e.g., ipratropium) AND

- The patient has tried and failed an adequate course of Spiriva Respimat AND

- The patient has tried and failed an adequate course of therapy of at least one of the following dry powder inhalers: Tudorza Pressair, Incruse Ellipta, Spiriva Handihaler, or Seebri Neohaler OR

- The patient cannot generate the peak inspiratory flow needed to activate at least one of the following dry powder inhalers: Tudorza Pressair, Incruse Ellipta, Spiriva Handihaler, or Seebri Neohaler

Non-FDA-approved uses are not approved.

PA does not expire.

g. Imbruvica tablets and capsules

Manual PA criteria apply to all new users of Imbruvica tablets and capsules.

Manual PA criteria: Coverage will be approved if all criteria are met:

- Imbruvica capsules are the DoD-preferred formulation for Imbruvica.
    - **If the prescription is for Imbruvica capsules, please continue to the criteria below.**
    - **If the prescription is for Imbruvica tablets, provide documentation as to why the capsule formulation cannot be used, and then continue with the criteria below.**
- The patient is $\geq$ 18 years old
- The patient has laboratory evidence of and pathologic confirmation of one of the following:
    - Mantle Cell Lymphoma
    - Marginal Zone Lymphoma
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia ± 17p deletion
    - Waldenström's macroglobulinemia
    - Chronic Graft versus Host Disease
- Imbruvica is prescribed by or in consultation with a hematologist/oncologist

Non-FDA-approved uses are not approved.

PA does not expire.

h. Rhopressa

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

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

- The patient has a diagnosis of ocular hypertension or open-angle glaucoma

- The prescription is written by an ophthalmologist or an optometrist

- The patient has had a trial of appropriate duration of two different formulary options from different glaucoma drug classes, in combination or separately, and has not reached intraocular pressure target goals as defined by the provider. The drug classes include:

  - prostaglandin analogs (latanoprost or bimatoprost)
  - beta blockers (Betoptic, Betoptic-S, Ocupress, Betagan, Optipranolol)
  - alpha2-adrenergic agonists (brimonidine, apraclonidine)
  - topical carbonic anhydrase inhibitors [dorzolamide (Trusopt)]

Non-FDA-approved uses are not approved.

PA does not expire.

i. Zypitamag

All new and current users of Zypitamag must try a preferred statin at appropriate LDL lowering first.

Automated PA Criteria:

- The patient has received a prescription for a preferred agent (generic atorvastatin, simvastatin, pravastatin, fluvastatin, lovastatin, pravastatin or rosuvastatin) targeting similar LDL reduction (LDL lowering between 30% to 50%, LDL lowering < 30%) at any 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, Zypitamag is approved (e.g., trial of generic statin is NOT required) if:

- The patient has tried a preferred statin with similar LDL reduction (moderate or low intensity) and was unable to tolerate it due to adverse effects

- The patient is taking a drug that is metabolized by CYP3A4 is unable to take pravastatin or rosuvastatin

PA does not expire.

j. Symdeko

Manual PA criteria apply to all new users of Symdeko.

Manual PA Criteria: Symdeko is approved if ALL of the following criteria are met:

- Symdeko is prescribed for the treatment of cystic fibrosis in patient ages 12 years and older.

- The patient meets one of the following criteria:

  - The patient is homozygous for the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene as detected by an FDA-approved CF mutation test.
  - The patient has at least one specific gene mutation in the CFTR gene that is responsive to Symdeko as detected by an FDA-approved CF mutation test.

  - The CF-related gene mutation, based on FDA-approved testing, must be documented.

- Symdeko is not approved for use in combination with other CFTR modulators (e.g., Orkambi, Kalydeko).

Non-FDA-approved uses are not approved.

PA does not expire.

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

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) an effective date upon the first Wednesday two weeks after the signing of the minutes in all points of service.

Summary of Physicians Perspective:

We reviewed 19 new drugs at this meeting; with 10 recommended for UF status, and 9 recommended for non-formulary placement. For the drugs recommended for non-formulary status, several of them fall into classes that have already been reviewed by the P&T Committee, where there are cost effective products already available in the class.

For this review, for the 12 drugs where a PA was recommended, 7 of them fall into classes where there are already PA requirements (the three SGLT2 diabetes drugs, the statins, oncology drugs, the nausea and vomiting drug, and the cystic fibrosis drugs).

For 3 of the drugs with a PA requirement, grandfathering was recommended, so the PA will only apply to new users (the oncology drug, Erleada, the nausea and vomiting drug Bonjesta, and the Cystic Fibrosis drug Symdeko).

"No grandfathering", where the PA will apply to both new and current users, was recommended for 5 drugs: the new glaucoma drug Rhopressa, the topical steroid Impoyz, the nasal spray for nocturia Noctiva, the statin Zypitamag, and the nebulized drug for COPD.

There were a couple of comments made at the meeting for some of the drugs recommended for non-formulary status with Prior Authorization:

- Zypitamag (Statin): In the FDA briefing materials, there was a comment that there is "no pressing health need for an alternative formulation for pitavastatin, which is one of 7 statins marketed"

- Noctiva (nasal spray for nocturia) – very significant safety concerns with this drug were expressed by the P&T Committee, especially in regards to its use in the elderly population.

- Impoyz (topical steroids) – the Committee did not feel that this product would be effective, as it contains a smaller concentration of clobetasol than included in other high potency steroids.

Imbruvica – INTERIM P&T MEETING

- For Imbruvica, there is a new tablet formulation, as the capsule formulation has been available for many years. At the time of the meeting, the available information was that the capsules were being discontinued from the market. The interim meeting was held when the Committee became aware that the capsules would remain on the market.

- The updated recommendation was to revise the Imbruvica manual PA criteria to give preference to the capsules. The Imbruvica tabs and caps will both remain on the Uniform Formulary.

Summary of Panel Questions and Comments:

Mr. Hostettler asks how many patients are affected by the recommendation for Impoyz?

LT COL Khoury says there are 47 patients as of May 2018.

Mr. Hostettler asks if he can assume that all those new and current users of the drug have similar numbers.

LT COL Khoury asks for all the others?

Mr. Hostettler repeats for all the ones you had in the category of new and current users. Some of them were just new users. I am not concerned with the new users. It is the current users I am concerned with.

LT COL Khoury says if there is a specific drug he can provide the number to help guide your decision.

Mr. Hostettler says Noctiva.

Khoury says Noctiva has 99 users.

Hostettler asks about Steglartro, Segluromet, and Steglujan.

LT COL Khoury said those have a preordained process due to the fact they have been previously reviewed and have step preferred scenario

Mr. Hostettler asks about Imbruvica.

LT COL Khoury says Imbruvica has 780 patients.

Mr., Hostettler asks about Rhopressa.

LT COL Khoury says Rhopressa has 368 as of May.

Mr. Hostettler asks about the implementation timeframe on 300 patients.

LT COL Khoury replies this recommendation impacts formulary status. Implementation is 2 weeks after the signing of the minutes to move it from current non-formulary pending review to formulary.

Mr. Hostettler asks if the manual PA will apply to current users of Rhopressa (368 patients) 2-weeks after the signing of the minutes. On their next refill, they will be faced with the new criteria? That seems aggressive.

LT COL Khoury says he'll have to get back to you on the numbers. According to the process, the PA is in place pending the meeting of the UF BAP and is adjusted after the meeting. I am not positive that Rhopressa has a PA in place. It may have already gone through a PA but I need to verify.

Mr. Hostettler says if it wasn't already reviewed and put into a process that answer doesn't make sense.

LT COL Khoury says drugs like Imbruvica already have a PA in place. I'm not positive Rhopressa has a PA in place.

Mr. Hostettler says he doesn't think there should be one in place since it's never been reviewed prior to this meeting? The 2-week timeframe is aggressive to ensure 300 patients complete the process for a PA, not knowing whether the patients are at the MTF, Retail or mail.

LT COL Khoury says I want to ensure we are discussing the drugs with a PA in place. That is what I am referring to. There is a PA in place, some of these patients have to complete the PA process. Again, I want to ensure we are discussing the same thing and

not something different. There is a process for every patient that has a PA. I want to make sure we're saying the same thing.

Mr. Hostettler says they went through a class in the first place for Rhopressa.

LT COL Khoury repeats that he did not have that information on Rhopressa. I don't believe there is a PA so it would be likely that all 368 patients are required to complete the PA process.

Mr. Hostettler says this is why I am concerned. You will answer that question before the 2 week implementation date?

LT COL Khoury says there are two scenarios. (1) If the patient doesn't have a PA and they are faced with a PA. The policy requires that the provider consider the agents that they could potentially be on via the recommendation listed. If the patient meets those conditions, they fulfill the criteria for the PA and will continue on that prescription. (2) If they don't have a PA, the recommendation would be that they have not achieved the PA to get to that agent. The patient will be required to complete the PA process.

Mr. Hostettler believes completing the PA process for both of those prescriptions for 300 patients will be challenging.

LT COL Khoury repeats, these are new agents that are recently approved since the last meeting. If the provider prescribed these agents, they should be following up with the patients to see how they are doing. If there are problems the provider is probably not assessing the patient to ensure that are responding to the drug appropriately.

Mr. Hostettler asks if the affected population will receive a letter notifying them of the change 30 days prior to the 2 week implementation date.

LT COL Khoury says there is an awareness because the patient is currently in the non-formulary status. They will receive a letter notifying them of a change to formulary status.

Mr. Hostettler repeats his concerns regarding the short implementation period. The information about the PA is still confusing because this is a new product. It will be challenging for the patient to complete the PA process in 2-weeks.

Ms. Buchanan says if a patient uses drops, they don't run out of them overnight. There is a period of time where it would be actually longer depending on when the patient got a refill on the prescription.

Mr. Hostettler says when they get a refill, they will have to complete the PA process.

LT COL Khoury says that's what happens with all new drugs when the PA is placed for all the new drugs we have seen. If they have received the agent before the PA is in place, similar to a class review, those patients will be impacted.

Mr. Hostettler understands the issues you are dealing with but I am dealing with it from the beneficiary perspective. I didn't create the process but now you are making your problem my problem and giving me 2-weeks to solve it. I believe it is a short-timeframe. To comply with the PA criteria, the patient needs the provider to make the change or interact with a health plan, ESI, or someone to clear the use of the product is required.

LT COL Khoury says keep in mind that the reverse applies. Delaying the length of time for implementation forces the patient to potentially pay the non-formulary co-pay longer.

Mr. Hostettler asks if the letter will explain their options.

LT COL says, I am referring to the co-pays.

Mr. Hostettler asks if it will explain the co-pay change, as well.

LT COL Khoury says I am saying all that there is an impact to the patient the longer the implementation period is delayed. There are 10 drugs going non-formulary. As long as they are in the non-formulary status the patient will pay the higher (non-formulary) co-pay.

Mr. Hostettler asks if the implementation period for "this one" drug (Rhopressa) could be more 2-weeks. Why do all of the Newly Approved drugs need the same implementation period? Why can't they separate this drug?

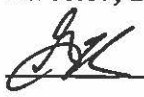
LT COL Khoury said I will take your comments back to the P&T committee.

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

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

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

   These comments were taken under consideration prior to my final decision

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

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

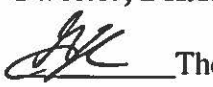
Director, DHA:

 These comments were taken under consideration prior to my final decision

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

Concur: 2 Non-Concur: 3 Abstain: 0 Absent: 2

Director, DHA:

 These comments were taken under consideration prior to my final decision

Recommendation and Comments from the Panel.

The Panel asked if Rhopressa can be separated and have a longer implementation period. Potentially 60 days.

Mr. Ostrowski said I hope in the future when the P&T Committee reviews drugs with similar problems, we could potentially resolve the issue by separating those anomalies and it will make the process smoother.

E. UTILIZATION MANAGEMENT

1. PA Criteria and Step Therapy

The P&T Committee recommended updates to the step therapy and manual PA criteria for several drugs due to a variety of reasons, including expanded FDA indications and feedback from the field. The updated manual PAs outlined below will apply to new users.

a. **Antiemetic-Antivertigo Agents: doxylamine succinate and pyridoxine hydrochloride ER (Diclegis)**—Diclegis PA criteria were first recommended at the August 2014 DoD P&T Committee Meeting. PA criteria were reviewed and updated to require a trial of both OTC doxylamine and pyridoxine before use of Diclegis.

b. **Targeted Immunomodulatory Biologics (TIBs): abatacept (Orencia)**—The TIBs were most recently reviewed in August 2014, with step therapy requiring a trial of adalimumab (Humira) first. Orencia was recently approved by the FDA for treatment of polyarticular Juvenile Idiopathic Arthritis (JIA) in patients two year or older. PA criteria were updated to add the additional indication JIA in pediatric patients.

c. **Targeted Immunomodulatory Biologics (TIBs): secukinumab (Cosentyx)**—Cosentyx was approved by the FDA in January 2015 for treatment of moderate to

severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. Since then, three additional indications were approved by the FDA: psoriatic arthritis, psoriasis of the scalp, and most recently ankylosing spondylitis in January 2018. The PA criteria were updated to add the additional FDA indications.

d. **Oncological Agents: abiraterone acetate (Zytiga)**—In April 2011, the FDA approved Zytiga for use in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer in patients who have received prior chemotherapy containing docetaxel. PA criteria for Zytiga were recommended at the November 2012 meeting, consistent with the FDA labeling. The FDA has subsequently updated the approved labeling for patients with metastatic high-risk castration-sensitive prostate cancer receiving concomitant prednisone. The PA criteria were updated to add the additional FDA indication and to require that the patient receive concomitant therapy with a gonadotropin-releasing hormone (GnRH) analog or have had bilateral orchiectomy.

e. **Non-Insulin Diabetes Drugs: Glucagon-Like Peptide-1 Receptor Agonists/Insulin Combination: insulin glargine/lixisenatide (Xultophy) and insulin degludec/liraglutide (Soliqua)**—Xultophy and Soliqua were reviewed in May 2017, and step therapy and manual PA criteria applied. Insulin glargine (Lantus) is the preferred basal insulin. The Glucagon-Like Peptide-1 Receptor Agonist (GLP1RA) class was reviewed in February 2018, and exenatide weekly (Bydureon/BCise) and dulaglutide (Trulicity) were designated as the preferred products. The PA criteria for Xultophy and Soliqua were updated to include provider acknowledgement of the preferred basal insulin and GLP1RAs.

f. **Parkinson's Disease Drugs: amantadine hydrochloride extended release (Gocovri)**—Gocovri was reviewed as a new drug during the November 2017 P&T Committee meeting, and PA criteria were recommended requiring the patient to have failed and tried amantadine immediate release (IR) 200 mg BID. Since this recommendation, feedback was received from neurologists that patients are not always able to tolerate a 400 mg daily dose of amantadine immediate release (IR). The PA criteria for Gocovri were updated to allow a trial of a lower dose of amantadine IR (300 mg daily in divided doses) to qualify for Gocovri.

g. **Oncological Agents: abemaciclib (Verzenio)**—Verzenio was first reviewed at the November 2017 P&T Committee meeting, and PA criteria were recommended for treatment of metastatic breast cancer. The PA criteria were updated to add the new FDA indication for use in postmenopausal women when used in combination with an aromatase inhibitor (i.e., anastrozole/letrozole) as initial endocrine-based therapy.

h. **Targeted Immunomodulatory Biologics (TIBs): apremilast (Otezla)**—The current PA criteria for the TIBs does not allow combination therapy with other TIBs, due to overlapping mechanisms of action and risk of enhanced toxicity. Otezla has a mechanism of action unique to the TIBs; it is a phosphodiesterase-4 (PDE4) inhibitor, which is an enzyme that breaks down cyclic adenosine monophosphate (cAMP). FDA

labeling for Otezla does not specify that it cannot be utilized in combination with other TIB agents, and it has a low risk of immunosuppression. The PA criteria for Otezla were updated to allow use in combination with the other TIBs (e.g., in a patient requiring Humira for treatment of RA and Otezla for treatment of plaque psoriasis), if the provider provides documented evidence as to why combination therapy is required.

2. Updated Manual PA Criteria

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) updates to the manual PA criteria for Diclegis, Orencia, Cosentyx, Zytiga, Xultophy, Soliqua, Gocovri, Verzenio, and Otezla. All updated PA criteria apply to new users.

3. Updated Manual PA Criteria an PA Renewal – PA Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) updates to the current PAs for Diclegis, Orencia, Cosentyx, Zytiga, Xultophy, Soliqua, Gocovri, Verzenio, and Otezla become effective on the first Wednesday two weeks after the signing of the minutes in all points of service.

Summary of Physician's Perspective:

Updated PA Criteria for the following drugs

1. Anti-emetic-Antivertigo Agent: - Diclegis
2. Targeted Immunomodulatory Biologics (TIBs): Orencia, Cosentyz, Otezla
3. Oncological Agents: Zytiga and Verzenio
4. Non-Insulin Diabetes Drugs: Xultophy and Soliqua
5. Parkinson's Disease Drugs: Gocovri

- We did not have any new PA's recommended at this meeting, just updates on existing Pas.
- For most of the drugs, the updates were due to new FDA-indications that needed to be added to the PA. (Orencia, Cosentyx; Zytiga, and Verzenio)
- We also updated the PAs for the GLP-1RA drugs to align the criteria with some recent P&T Committee decisions (for Xultophy and Soliqua).
- For two of the drugs, we updated the PA criteria based on feedback that we received from MHS providers. This was the case for the Parkinson's disease drug Gocovri, where we are allowing for a lower dose. The other case is for Otezla, where we will now allow combination use with another TIB.

Summary of Panel Questions and Comments:

There were no questions or comment from the Panel. The Chair called for a vote on the Updated Manual PA Criteria and PA Renewal Criteria and the Updated Manual PA Criteria and PA Renewal Criteria Implementation Plan for the Newly Approved Drugs.

- **Updated Manual PA Criteria and PA Renewal Criteria**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

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

- **Updated Manual PA Criteria and PA Renewal Criteria – PA Implementation Plan**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

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

F. SECTION 703, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR (FY) 2018

The P&T Committee reviewed four drugs from pharmaceutical manufacturers that were not included on a DoD Retail Refund Pricing Agreement; these drugs were not in compliance with FY08 NDAA, Section 703. The law stipulates that if a drug is not compliant with Section 703, it will be designated NF on the UF and will be restricted to the TRICARE Mail Order Pharmacy, requiring pre-authorization prior to use in the retail POS and medical necessity at MTFs. These NF drugs will remain available in the Mail Order POS without pre-authorization.

1. Drugs Designated as NF

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) the following products be designated NF on the UF:

- Aurobindo Pharma: armodafinil (*New Drug Application-authorized generic*) 200 mg tablet

- Quinn Pharmaceuticals: mercaptopurine (*NDA-authorized generic*) 50 mg tablet
- Noden Pharma: aliskiren (Tekturna) 150 mg tablet; 300 mg tablet

- Noden Pharma: aliskiren-hydrochlorothiazide (Tekturna HCT) 150-12.5 mg tablet, 150-25 mg tablet, 300-12.5 mg tablet, 300-25 mg tablet

2. Preauthorization Criteria

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) the following pre-authorization criteria for the Section 703 non-compliant NDCs of armodafinil, mercaptopurine, Tekturna, and Tekturna HCT:

a. Obtaining the product by home delivery would be detrimental to the patient; and,

b. For branded products with products with AB-rated generic availability, use of the generic product would be detrimental to the patient.

These pre-authorization criteria do not apply to any other POS other than retail network pharmacies.

NOTE: Should the mail order requirement impact availability of a drug, the P&T Committee will allow an exception to the Section 703 rule.

3. Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) the following: 1) an effective date of the first Wednesday after a 90-day implementation period for the Section 703 non-compliant NDCs of armodafinil, mercaptopurine, Tekturna, and Tekturna HCT and 2) DHA send letters to beneficiaries affected by this decision.

Summary of Physician's Perspective:

For two of the products recommended for NF status (generic armodafinil and mercaptopurine), only the generic formulations from one manufacturer are affected; there are other several cost-effective generic formulations and therapeutic alternatives are available on the UF.

For the other two drugs (Tekturna and Tekturna HCT), there are several generic therapeutic alternatives available, including ACE inhibitors and ARBs, plus their combinations with HCTZ.

The Pharmacy Operations Division does follow up with the affected manufacturers, to try to ensure compliance with the Section 703 requirements.

Summary of Panel Questions and Comments:

Mr. Hostettler asks about the section 703 rule. Regarding the notes that states should the mail order requirement impact availability of ta drug, the P&T Committee will allow an

exception to the section 703 rule. I am not sure what that means. How would the availability be impacted by mail order?

LT COL Khoury says if the drug is not available at mail. For instance, if the beneficiary can only get the medication through some other point of service other than mail.

There were no more questions or comments from the Panel. The Chair called for a vote on the Drugs Designated NF, Pre-Authorization Criteria and Implementation Period for the Section 703 products.

- **Drugs Designated NF**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **Pre-Authorization Criteria**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

- **Implementation Period**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

  Director, DHA:

  _____These comments were taken under consideration prior to my final decision

Mr. Ostrowski concludes the meeting. He asks the P&T Committee to review the notes and comment from today's meeting. In my instances, the Panel would have concurred with the P&T Committee recommendations. For instance, if the Committee could consider recommending implementation plans that coincide with annual PA requirements, it would have less impact on the beneficiary population. The Panel is here on behalf of the beneficiary. So we are constantly looking at how they are going to be affected by the Committee recommendations. Although some of the populations impacted were approximately 300-400 patients, we will do anything we can to minimize the impact their lives. I know that we can't please everybody all the time. He thanks the P&T Committee for their work and all those attending the meeting.

APPENDIX A

Table of Implementation Status of UF Recommendations/Decisions Summary

Date	DoD PEC Drug Class	Type of Action	UF Medications	Nonformulary Medications	Imple-ment Date	Notes and Unique Users Affected
May 2018	**Pancreatic Enzyme Replacement Therapy**	UF Class Review Class previously reviewed Feb 2011, Feb 2014	UF Step-Preferred ▪ Creon UF Non-Step-Preferred ▪ Viokace	NF Non-Step-Preferred ▪ Pancreaze ▪ Pertzye ▪ Ultresa ▪ Zenpep	90 days	▪ A trial of Creon is required first in all new and current users of the non-step-preferred product ▪ No PA required for Creon Unique Users Affected Mail 558 MTF 237 Retail 487 Total 1,282
May 2018	**Growth Stimulating Agents**	UF Class review Class previously reviewed in Aug 2007	UF Step-Preferred ▪ Norditropin FlexPro UF Non-Step-Preferred ▪ Omnitrope ▪ Zomacton	NF Non-Step-Preferred ▪ Genotropin ▪ Humatrope ▪ Nutropin ▪ Saizen ▪ Serostim	90 days	▪ Must try Norditropin FlexPro first in all new and current users. Then must use Omnitrope and Zomacton (either order) before moving to NF agents (Genotropin, Humatrope, Nutropin, Saizen, and Serostim) Unique Users Affected Mail 351 MTF 84 Retail 30 Total 465
May 2018	**GI-2 Agents: Opioid Induced Constipation (OIC) Subclass**	UF Class Review Subclass not reviewed; Class reviewed Nov 2015	UF ▪ naldemedine (Symproic) ▪ naloxegol (Movantik)	NF ▪ methylnaltrexone (Relistor) tablet and injection	60 days	▪ Manual PAs and QLs apply ▪ PA applies: must try two OTC laxatives before use of an OIC drug. ▪ Must try Movantik, Symproic and Amitiza before use of the nonformulary product Relistor Unique Users Affected: Mail 114 MTF 38 Retail 163 Total 315

Brief Listing of Acronyms Used in this Summary

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

- AIDS – Acquired Immunodeficiency Syndrome
- ARI – Alpha Reductase Inhibitor
- BAP – Beneficiary Advisory Panel
- BIA – Budget Impact Analysis
- cAMP – Cyclic Adenosine Monophosphate
- CFR – Code of Federal Regulations
- CFTR – Cystic Fibrosis Transmembrane Conductance Regulator
- CMA – Cost Minimization Analysis
- COPD – Chronic Obstructive Pulmonary Disease
- CT – Cognitive Therapy
- CVOTs – Cardiovascular Outcome Trials
- CYP3A4 – Cytochrome P450 isoforms
- DoD – Department of Defense
- eGFR – Estimated Glomerular Filtration Rate
- EPI – Exocrine Pancreatic Insufficiency
- ER – Extended Release
- FDA – Food and Drug Administration
- G-Tube – Gastronomy-Tube
- GI-2 – Gastrointestinal-2
- GSA – Growth Stimulating Agents
- HCT- Hematrocrit
- HIV – Human Immunodeficiency Virus
- IR – Immediate Release
- JIA – Juvenile Idiopoathic Arthritis
- L – liter
- LDL – Low Density Lipoprotein
- Mg – Milligram
- MTF – Military Treatment Facility
- NDAA – National Defense Authorization Act
- NDC – National Drug Code
- NF – Non Formulary
- NSAIDs – Nonsteroidal Anti-Inflammatory Drugs
- ODE4 – Phosphodiesterase-4
- OIC – Opioid-Induced Constipation
- OTC – Over the Counter
- P&T – Pharmacy and Therapeutics Committee
- PA – Prior Authorization

- PAMORAs – Peripherally Acting Mu Opioid Receptor Antagonists
- PERT – Pancreatic Enzyme Replacement Therapy
- POS – Point of Sale
- rhGH – Recombinant Human Growth Hormone
- SGLT2s – Sodiun Glucose Co-Transporter
- ShoX – Short Stature Homeobox
- SIADH – Syndrome Inappropriate Antidiuretic Hormone
- SNRI – Serotonin Norepinephrine Reuptake Inhibitor
- SSRI – Selective Reuptake Inhibitor
- TIBs – Targeted Immunomodulatory Agents
- TRICARE – Healthcare Network
- UF -0 Uniform Formulary
- XR – Extended Release

DOD Zenpep Formulary Change Response Letter

July 5, 2018

Col. Paul J. Hoerner
U.S. Air Force
Beneficiary Advisory Panel Chair
7700 Arlington Boulevard, Suite 5101,
Falls Church, VA 22042–5101
Email: dha.ncr.health-it.mbx.bapequests@mail.mil

Re: Pancreatic enzyme replacement therapy formulary recommendations, Uniform Formulary Beneficiary Advisory Panel meeting July 12, 2018

Dear Col. Hoerner,

The Allergan Chief Medical Office is aware that changes to the Uniform Formulary regarding pancreatic enzyme replacement therapy (PERT) will be discussed at the meeting on July 12, 2018. Allergan is the maker of Zenpep (pancrelipase), a combination of porcine-derived lipases, proteases, and amylases indicated for the treatment of exocrine pancreatic insufficiency (EPI) due to cystic fibrosis or other conditions. The P&T Committee is recommending that Zenpep be designated as non-formulary and non-step preferred.

This formulary change could lead to changes in therapy for Department of Defense patients currently treated with Zenpep, which could impact their health status. Patients needing PERT require individualized dose titration in order to achieve maximum therapeutic benefit. As stated in the FDA-approved labeling for Zenpep and other PERT products, "there is great inter-individual variation in response to enzymes; thus, a range of doses is recommended." As noted in the P&T Committee recommendations, Zenpep has the largest number of dosage strengths available of any of the PERT products.

Furthermore, FDA-approved labeling indicates that pancrelipase products (e.g. Zenpep) are not interchangeable. Should the formulary change be approved, there could be many patients forced to switch products, possibly impacting patient safety and outcomes. In the interest of patient safety and in consideration of the disruption in therapy patients may experience, Allergan respectfully requests that, regardless of any formulary changes in the PERT category, patients currently receiving Zenpep be allowed to continue this therapy. This option creates a pathway for patients with EPI who are currently well managed on Zenpep to avoid the need for titration onto a new product, which may subsequently impact symptoms and outcomes.

If I can provide any additional information or if you or the committee have any questions, please do not hesitate to contact me at phillip.jennings@allergan.com.

Respectfully Yours,

Phillip Jennings, PharmD
Managed Care Scientific Director
Allergan Chief Medical Office

Appendix D **07/12/2018 BAP Meeting**

Avadel Public Comments

At some point this morning you will consider the utilization management recommendation of the DoD P&T Committee with regard to Noctivan. (desmopressin acetate nasal spray .83mcg and 1.66mcg doses) for the treatment of nocturia due to nocturnal polyuria.

There are several DoD P&T Committee recommendations that are inconsistent with Noctiva's approved label. I will reserve addressing those for any presentation related to class review.

I am asking today that you consider seriously a few practical points in recommending to the Secretary of Defense NOT adopting the recommendations of the DoD P& T Committee with regard to its initial assessment of Noctiva ™. This is specifically with the safety of our troops and other beneficiaries at heart. Trusting the TRICARE provider to manage with diligence to the Noctiva™ label.

In its Summary Review for Regulatory Action, FDA comments regarding Noctiva TM: "A Boxed Warning is appropriate because severe hyponatremia can be life-threatening and is very serious in proportion to the potential benefit of the drug, and because hyponatremia can be mitigated with interventions (e.g., periodic monitoring of serum sodium)."

This warning is common to all market-approved forms and brands of desmopressin. The risk of severe hyponatremia is, in fact, the sole safety concern in the use of any brand or form of desmopressin. The safety of Noctiva TM has been studied with greater rigor, over a longer period of time, than any other desmopressin product.

First

- FDA approved labeling recommends, for patients 65 years and older, with concern for the risk of hyponatremia, initiating therapy at .83mcg and allowing an increase to 1.66mcg, if needed, provided the serum sodium has remained normal"
- Possibly an oversight, the DoD P&T Committee recommendation limits to patients 65 years and older the .83mcg dose, exposing them to potential of risk without the potential benefit of titration to an efficacious dose.

Neither HealthNet, Express Scripts nor Humana nor, the Criteria of any other insurer to date, impose this limit, likely with that logic in mind.

Second

The limitation of use, "not studied in patients younger than 50 years of age", is a negotiated feature of the pivotal trial design, a limitation of THE STUDY, requested by FDA, to ensure the evaluation of safety in an age group more at risk of hyponatremia. This is confirmed repeatedly in writing by FDA not to preclude clinical use in patients under the age of 50 but to ensure adequate study in patients who are at greater risk.

HealthNet Commercial criteria recognizes the safety-enhancing purpose of this study limitation and imposes no such limit (no >/= 50) in its clinical criteria. Neither Express Scripts nor Humana criteria are published.

Finally

> The TRICARE formulary includes all other forms and brands of desmopressin without governing criteria for use. There is no limitation on what these products might be prescribed for. There is no limitation on whom they might be prescribed to. The intranasal forms of these products are delivered in minimum doses that range from 6 to 90 times that of the highest dose of Noctiva TM.

There is no comparative safety data and I hope that none would be necessary for your understanding that the risk of hyponatremia -the sole safety concern with these products -would not diminish with the TRICARE provider prescribing one of the unrestricted desmopressin products in place of Noctiva ™ in treating a beneficiary's nocturia due to nocturnal polyuria.

I am asking your unanimous recommendation to the Secretary of Defense, in the interest of the safety of the beneficiary, for the rejection of the Noctiva ™ PA criteria you will consider today.

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
July 12, 2018
Washington, D.C.

Present Panel Members

- Mr. Jon Ostrowski, Non Commissioned Officers Association, Chairperson
- Ms. Theresa Buchanan, National Military Family Association
- Mr. Charles Hostettler, AMSUS, The Society of Federal Health Professionals
- Mr. Richard Bertin, Commissioned Officer Association (COA) of the United States Public Health Service, Inc.
- Ms. Suzanne Walker, Military Officers Association of America

Absent Panel Members

- Mr. John Du Teil, US Army Warrant Officers Association
- Dr. Sarika Joshi, HealthNet Federal Services

The meeting was held at Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington D.C., and COL Paul Hoerner called the meeting to order at 9:20 a.m.

Agenda

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

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

1. Drug Class Reviews

    a) Pancreatic Enzyme Replacement Therapy (PERT)
    b) Growth Stimulating Agents (GSAs)
    c) Gastrointestinal-2 (GI-2) Agents: Opioid-Induced Constipation (OIS) Subclass

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

    a) apalutamide (Erleada) – Oral Oncologic Agent for Prostate Cancer
    b) bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy) – Antiretrovirals for Human Immunodeficiency Virus (HIV)
    c) clobetasol propionate 0.025% cream (Impoyz) – High Potency Corticosteroids Immune Modulators for Moderate to Severe Plaque Psoriasis
    d) desmopressin nasal spray (Noctiva) – Miscellaneous Endocrine Agent for nocturia due to nocturnal polyuria

e) doxylamine succinate/pyridoxine ER tablets (Bonjesta) – Antiemetic-Antivertigo Agents
f) efavirenz/lamivudine/tenofovir disoproxil fumarate (Symfi) – HIV
g) efavirenz/lamivudine/tenofovir disoproxil fumarate (Symfi Lo) – HIV
h) ertugliflozin (Steglatro) – Non-Insulin Diabetes Drugs – Sodium Glucose Co-Transporter-2 (SGLT2) Inhibitor
i) ertugliflozin/sitagliptin (Steglujan) – Non-Insulin Diabetes Drugs –SGLT2 Inhibitor
j) glycopyrrolate inhalation solution (Lonhala Magnair) – Pulmonary-2: Long-Acting Muscarinic Agents (LAMAs) for Chronic Obstructive Pulmonary Disease (COPD)
k) ibrutinib tablets (Imbruvica) – Oral Oncologic Agent for mantle cell lymphoma and chronic lymphocytic leukemia, new formulation (note that Imbruvica capsules were already designated as UF prior to the Innovator Rule established in August 2015)
l) insulin lispro (Admelog) – Short-Acting Insulin for Diabetes Mellitus
m) lamivudine/tenofovir disoproxil fumarate (Cimduo) – Antiretrovirals for HIV
n) netarsudil 0.02% ophthalmic solution (Rhopressa) – Glaucoma Agents
o) pitavastatin magnesium (Zypitamag) – Antilipidemic-Is (LIP-Is)
p) secnidazole (Solosec) – Miscellaneous Anti-Infective for bacterial vaginosis in adult women
q) tezacaftor/ivacaftor (Symdeko) – Cystic Fibrosis Agents
r) vancomycin oral solution (Firvanq) – Gastrointestinal-2 agents: Miscellaneous for Clostridium difficile associated diarrhea or enterocolitis

3. Utilization Management Issues

a) Prior Authorization Criteria – Updated Criteria

- Antiemetic-Antivertigo Agents: doxylamine succinate and pyridoxine hydrochloride ER (Diclegis)
- Targeted Immunomodulatory Biologics (TIBs): abatacept (Orencia), secukinumab (Cosentyx), and apremilast (Otezla)
  Oncological Agents: abiraterone acetate (Zytiga) and abemaciclib
- (Verzenio)
- Non-Insulin Diabetes Drugs: Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)/Insulin Combination: insulin glargine/lixisenatide (Xultophy) and insulin degludec/liraglutide (Soliqua)
- Parkinson's Disease Drugs: amantadine hydrochloride extended release (Gocovri)

4. National Defense Authorization Act (NDAA) 2008, Section 703 Actions

5. Panel Discussions

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

Opening Remarks

Col Paul Hoerner introduced himself as the Designated Federal Officer (DFO) for the Uniform Formulary (UF) Beneficiary Advisory Panel (BAP). The Panel has convened to comment on the recommendations of the DoD Pharmacy and Therapeutics (P&T) Committee meeting, which occurred on May 9-10, 2018.

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

In addition, 10 U.S.C. Section 1074g, subsection c, also requires the Secretary to establish a UF Beneficiary Advisory Panel (BAP) to review and comment on the development of the Uniform Formulary. The Panel includes members that represent 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 to the Director of the DHA regarding recommended formulary status, pre-authorizations and the effective dates for changing drugs from "formulary" to "non-formulary" status must be reviewed by the Director before making a final decision.

- To hold quarterly meetings in an open forum. The Panel may not hold meetings except at the call or with the advance approval of the DFO and in consultation with the chairperson of the Panel.

- To prepare minutes of the proceedings and prepared comments of the Secretary or his designee regarding the Uniform Formulary or changes to the Formulary. The minutes will be available on the website, and comments will be prepared for the Director of DHA. As guidance to the Panel regarding this meeting, Col Hoerner said the role of the BAP is to comment on the UF recommendations made by the P&T Committee at their last meeting. While the department appreciates that the BAP maybe interested in the drug class they

selected for review, drugs recommended for the basic core formula (BCF) or specific pricing data, these items do not fall under the purview of the BAP.

- The P&T Committee met for approximately 13 hours conducting this review of the drug class recommendation presented today. Since this meeting is considerably shorter, the Panel will not receive the same extensive information as presented to the P&T Committee members. However, the BAP will receive an abbreviated version of each presentation and its discussion. The materials provided to the Panel are available on the TRICARE website. Detailed minutes of this meeting are being prepared. The BAP minutes, the DoD P&T Committee minutes, and the Director's decisions will be available on the TRICARE website in approximately four to six weeks.

The DFO provided ground rules for conducting the meeting:

- All discussions take place in an open public forum. There is to be no committee discussion outside the room, during breaks, or at lunch.

- Audience participation is limited to private citizens who signed up to address the Panel.

- Members of the Formulary Management Branch and P&T Committee are available to answer questions related to the BAP's deliberations. Should a misstatement be made, these individuals may interrupt to ensure the minutes accurately reflect relevant facts, regulations, or policy.

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

Private citizen comments from Allergen and Avadel were forwarded to the Panel for review and consideration. SEE APPENDIX C and D.

Chairman's Opening Remarks

Mr. Ostrowski welcomes audience, welcomes Panel members, welcomes LT COL Khoury for presenting today’s Panel meeting notes, and thanks Ms. Armstead for preparation for this Panel.

DRUG CLASS REVIEW PRESENTATION

(POD Script – LT COL KHOURY)

GOOD MORNING. I am Lieutenant Colonel Ronald Khoury, Chief of the Pharmacy and Therapeutics section of the DHA Formulary Management Branch. Joining me is doctor and retired Army Colonel John Kugler, the Chairman of the Pharmacy and Therapeutics Committee, who will provide the physician perspective and comments on the recommendations made by the P&T Committee. Also joining us from the Formulary Management Branch today is Angela Allerman, a clinical pharmacist. I would also like to recognize Department General Council Bryan Wheeler.

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:

- A brief overview of the relative clinical effectiveness analyses considered by the DoD P&T Committee. All reviews include but are not limited to the sources of information listed in 32 CFR 199.21 (e)(1) and (g)(5). Also note that nonformulary medications are generally restricted to the mail order program according to amended section 199.21, revised paragraphs (h)(3)(i) and (ii), effective August 26, 2015.

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

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

  The Committee reviewed the following:

  1. The P&T Committee reviewed three Uniform Formulary Drug Classes:

a) the Pancreatic Enzyme Replacement Therapy (PERT) drug class;

b) the Growth Stimulating Agents (GSAs) drug class; and

c) the Gastrointestinal-2 (GI-2) Agents: Opioid-Induced Constipation (OIC) subclass

A summary table of the UF drug class recommendations and the numbers of affected utilizers is found on pages 29-30 of the background document.

2. The P&T Committee also evaluated 18 newly approved drugs per 32 CFR 199.21 (g)(5), which are currently in pending status and available under terms comparable to nonformulary drugs.

3. We also discussed prior authorizations (PAs) for **9** drugs in **5** drug classes.

a) Antiemetic-Antivertigo Agents
b) Targeted Immunomodulatory Biologics
c) Oncological Agents
d) Non-Insulin Diabetes Drugs
e) Parkinson's Disease Drugs

and

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

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

UNIFORM FORUMULARY DRUG CLASS REVIEWS

I. UF CLASS REVIEWS

A. PANCREATIC ENZYME REPLACEMENT THERAPY

(DR. ALLERMAN)

1. Pancreatic Enzyme Replacement Therapy—Relative Clinical Effectiveness Analysis and Conclusion

Background—The class was most recently reviewed for UF status in February 2014. Since the last review, the drug class name was changed from "Pancreatic Enzyme Products" to "Pancreatic Enzyme Replacement Therapy (PERT)" to align with accepted nomenclature in the clinical literature. The drugs in the class all contain various amounts of lipase, amylase, and protease and are available under the trade names of Creon, Pancreaze, Pertzye, Ultresa, Viokace, and Zenpep.

The products were reviewed for the U.S. Food and Drug Administration (FDA)-approved indication of exocrine pancreatic insufficiency (EPI) due to cystic fibrosis or other conditions; other uses (e.g., pain relief from pancreatitis) were not reviewed.

The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

Creon, Pancreaze, Ultresa, and Zenpep are formulated as capsules containing delayed release enteric-coated microspheres, while Pertzye capsules contain enteric-coated microspheres with a bicarbonate buffer.

Viokace is an uncoated tablet that is not approved for use in pediatrics; it requires administration with a proton pump inhibitor to prevent degradation in the stomach.

Based on a 2016 Cochrane Review in patients with cystic fibrosis, Creon, Pancreaze, Zenpep, Viokace, Ultresa, and Pertzye are effective at improving fat malabsorption in patients with EPI, when compared to placebo.

The 2016 Cochrane review found no difference between Creon and other enteric-coated microsphere products in the endpoints of change in weight, stool frequency, abdominal pain, or fecal fat excretion. Creon was superior to the tablet formulation (Viokace) in only one endpoint, decreasing stool frequency.

Zenpep has the largest number of dosage strengths available, but multiple capsules can be used to obtain individualized patient dosing. Creon and Zenpep both have higher strengths available. All the products except for Viokace provide dosing for infants.

Creon has the greatest number of FDA-approved indications and the highest Military Health System (MHS) utilization.

Although Pertzye is the only product with gastrostomy (G)-tube administration information contained in the package insert, instructions are available for G-tube administration with Creon, Viokace, and Zenpep.

There is a high degree of therapeutic interchangeability among the PERT products, and having one on the formulary is sufficient to meet the needs of MHS patients.

2. PERT—Relative Cost-Effectiveness Analysis and Conclusion

Cost-minimization analysis (CMA) and budget impact analysis (BIA) were performed to evaluate the PERT agents. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

CMA results showed that Creon was the most cost-effective agent in the PERT class. BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating Creon as formulary and step-preferred; Viokace as UF and non-step-preferred; and Pertzye, Pancreaze, Ultresa, and Zenpep as NF and non-step-preferred demonstrated significant cost avoidance for the MHS.

3. PERT—UF Recommendation

The P&T Committee recommended (15 for, 1 opposed, 0 abstained, 0 absent) the following, based on clinical and cost effectiveness:

UF and step-preferred
- Creon

UF and non-step-preferred
- Viokace tablet

NF and non-step-preferred
- Pancreaze
- Pertzye
- Ultresa
- Zenpep

This recommendation includes step therapy, which requires a trial of Creon prior to use of Viokace and the NF non-step-preferred PERT drugs in all new and current users.

4. PERT—Manual PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for the non-step-preferred products, requiring a trial of Creon first in all new and current users. Note that PA is not needed for Creon, and the step-therapy requirements will be included in the manual PA.

Manual PA Criteria: Pancreaze, Pertzye, Ultresa, Viokace, and Zenpep are approved if any of the following criteria are met:

The patient has failed an adequate trial of Creon, defined as at least two dose adjustments done over a period of at least four weeks OR

The patient is ≤ 2 years old and a sufficient trial of Creon was unsuccessful OR

For Viokace: the patient requires an uncoated tablet due to actual or suspected dissolution issues with enteric coating of Creon

PA does not expire.

5. PERT—Tier 1 Cost Share

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) lowering the current tier 2 cost share for Creon to the generic tier 1 cost share.

The authority for this recommendation is codified in 32 CFR 199.21(j)(3), which states that "when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the Pharmacy and Therapeutics Committee may also designate that the drug be cost-shared at the generic rate." The objective is to maximize use of Creon in the TRICARE Mail Order pharmacy and Retail Network, given its significantly lower cost relative to the other PERT products. Lowering the cost-share for Creon will provide a greater incentive for beneficiaries to use the most cost-effective PERT formulation in the purchased care points of service.

6. PERT—UF, PA, and Tier 1 Cost Share Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following: 1) an effective date of the first Wednesday after a 90-day implementation period in all points of service and 2) DHA send letters to beneficiaries who are affected by the UF decision.

7. Physician's Perspective

This is the 3rd time that the pancreatic enzymes have been reviewed for formulary status. There are no new products in the class, and one product, Ultressa, appears to have been discontinued.

The PERT drugs can be used for either cystic fibrosis or pancreatitis. For DoD, the majority of the use was in older patients (ages 60-80 years), which supports that the PERT drugs are primarily used for pancreatitis.

When we surveyed MHS providers, Creon was most frequently mentioned as the preferred products. When providers were asked which product should be on the formulary, they requested having one PERT drug that was available in multiple strengths.

Creon is a good candidate for the step preferred PERT drug, since it has been on the formulary for several years; it is available in multiple strengths, including the dosages needed for young children with cystic fibrosis; and it currently has the highest market share in the DoD at 75%.

Viokace is the other product selected for uniform formulary status, however, it will be after the step. Having Viokace allows for a different formulation – it is available in uncoated tablets, which was mentioned by some GI providers as an alternative to the Creon coated capsules.

Historically, all agents are highly therapeutically interchangeable based on clinical and safety factors, plus the fact that they all contain the same active ingredients, just in varying amounts.

There will be minimal disruption to patients, since 4,500 out of the 5,700 patients in the class are already on Creon. About 1,200 patients will be affected by the formulary recommendation.

When we look at DoD utilization, we found some other usage patterns that also support that the change to Creon as a step preferred product will have minimal impact to patients. There are a large number of new users per quarter, there is a low rate of patients increasing (or up-titrating their dose), and there is a relatively low persistence rate in the class (only about 30% of patients remain on therapy at one year). This shows us that many patients do not remain on therapy for long periods.

The one opposing vote was that the member felt there was not enough cost savings to make anything non-formulary, to avoid patient disruption. However, that concern was allayed when the tier one copay was proposed for Creon. Also, for Creon, there won't be a requirement for Prior Authorization, which is another incentive for patients to switch from the non-preferred products.

8. Panel Questions and Comments

Mr. Hostettler asks how many of the patients have cystic fibrosis.

Dr. Allerman responds that out of 6000 patients, a little less than 1000 are diagnosed with cystic fibrosis. She doesn't have the breakdown of patients who are on non-preferred products.

Mr. Hostettler understands the interchangeability of the pancreatitis products. I have problems/concerns with the patients who have parents that provide care to the cystic fibrosis patients that are consider stable. I also understand the adjustments in dosage but they are, at least, familiar with the drug they are using. Adjusting is what they are familiar with and changing their process does not seem to be worth the potential cost savings. Let them make the decision once they are notified of a change and potential $17 savings. It becomes a patient-driven decision rather than a your-driven decision.

Dr. Allerman answers this is one of the reasons we didn't have a PA requirement for Creon. Currently, it has the highest utilization in DoD.

Ms. Buchanan raises an objection. She asks if we could grandfather the patients with cystic fibrosis.

Dr. Allerman replies that they can check on that.

Mr. Hostettler says a longer implementation period is needed if the grandfathering is not an option for the cystic fibrosis patients

Dr. Allerman asks if he means longer than 90 days.

Mr. Hostettler responds yes. This allows time to schedule appointments with their physicians and become comfortable with the adjustments/change to their normal routine.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, Tier 1 Cost Share and UF PA, and Tier 1 Cost Share Implementation Plan for the PERTs.

- **PERT – UF Recommendation**

  Concur: 2 Non-Concur: 3 Abstain: 0 Absent: 2

- **PERT – Manual PA Criteria**

  Concur: 0 Non-Concur: 5 Abstain: 0 Absent: 2

- **PERT – Tier 1 Cost Share**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

- **PERT – UF, PA, and Tier 1 Cost Share Implementation Plan**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

Recommendations and Comments from the Panel.

The Panel members (Mr. Ostrowski, Ms. Buchanan, Mr. Hostettler, Dr. Bertin and Ms. Walker) asks the P&T Committee to consider grandfathering the cystic fibrosis patients. They further state that if the Committee had grandfathered the patients, all would have concurred with the recommendation of the P&T Committee.

B. GROWTH STIMULATING AGENTS

(LT COL KHOURY)

1. Growth Stimulating Agents—Relative Clinical Effectiveness Analysis and Conclusion

Background—The Growth Stimulating Agents (GSAs) were last reviewed at the August 2007 DoD P&T Committee meeting. All the products contain recombinant human growth hormone (rhGH), or somatropin. Since the 2007 review, two products (Zorbtive and Tev-Tropin) were discontinued, and one product, Zomacton, has entered the market. There are no generic products in the class.

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

- The products are all bioidentical and equally biopotent to each other.
- Head-to-head trials show equivalency in pharmacokinetic profiles, efficacy, and safety.
- The GSA products all offer 5 mg and 10 mg dosing options, pen devices, small needle gauges (29-, 30-, and 31-gauge), a needle-guard option, patient support programs, home nurse education, instructional websites, and an emergency hotline number.
- The GSA products differ in terms of their FDA-approved indications; storage requirements (refrigeration vs. room temperature); preservative (benzyl alcohol vs. metacresol vs. phenol); delivery devices, smallest available dosage increment; and reconstitution or device assembly steps required prior to administration. None of these differences impact patient outcomes.
- Advantages of Norditropin FlexPro include that it has the greatest number of FDA-approved indications (seven); it does not require refrigeration or mixing prior to administration; it contains phenol as a preservative; and it is administered in a pen device that is convenient and easy to use. It can also deliver small increments in dosage, down to 0.025 mg with the 5 mg pen.
- One advantage of Genotropin is the availability of the low-dose, single-use MiniQuick formulation that can deliver the lowest dosage options for children. However, all the products can deliver low dosages.
- Norditropin FlexPro, Nutropin, Omnitrope, and Saizen are pre-mixed formulations that are convenient for patients.
- Disadvantages of Saizen, Serostim, Zomacton, and Omnitrope include the benzoyl alcohol preservative, which is toxic to neonates and infants. However, alternate formulation options are available for these products.
- Zomacton is the only product available in a needle-free device.
- Overall, the GSA products have a high degree of therapeutic interchangeability, based on MHS provider opinion, systematic reviews, meta-analyses, and professional treatment guidelines.

2. GSAs—Relative Cost-Effectiveness Analysis and Conclusion

CMA and BIA were performed to evaluate the GSAs. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA showed that Zomacton, Omnitrope, and Norditropin FlexPro were the most cost-effective products in the GSA class.

- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating Norditropin FlexPro as formulary and step-preferred demonstrated the greatest cost avoidance for the MHS.

3. GSAs—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) the following, based on clinical and cost effectiveness:

- UF and step-preferred
  - Norditropin FlexPro

- UF and non-step-preferred
  - Omnitrope
  - Zomacton

- NF and non-step-preferred
  - Genotropin and Genotropin MiniQuick
  - Humatrope
  - Nutropin AQ Nuspin
  - Saizen
  - Serostim

- This recommendation includes step therapy, which requires a trial of Norditropin FlexPro prior to use of the non-step-preferred GSAs in all new and current users.

4. GSAs—Manual PA Criteria

PA criteria currently apply to the GSAs. The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) updating the current PA criteria for the class to include the updated safety warning for use of a GSA in patients with Prader-Willi syndrome and obstructive sleep apnea and to require the prescription to be written by the appropriate subspecialist. Additionally the step therapy requirements for trial of Norditropin FlexPro in all new and current users will be included in the manual PA. Use of the non-step-preferred products is allowed if the patient has a contraindication or has experienced an adverse reaction to Norditropin FlexPro, and then Omnitrope and Zomacton, before moving to NF agents.

Manual PA Criteria: Norditropin FlexPro, Genotropin, Humatrope, Nutropin AQ Nuspin, Omnitrope, Saizen, Serostim, and Zomacton are approved if:

- The patient is younger than 18 years of age and has the following indications:

  Growth hormone deficiency
  Small for Gestational Age
  Chronic Renal Insufficiency **associated with growth failure**
  Prader-Willi Syndrome **(in patients with negative sleep study for obstructive sleep apnea)**
  Turner Syndrome
  Noonan's Syndrome
  Short stature homeobox (ShoX) gene mutation

- For patients younger than 18 years of age who do not have one of the indications above, the diagnosis must be documented
- For patients younger than 18 years of age, the prescription is written by or in consultation with a pediatric endocrinologist or nephrologist who recommends therapeutic intervention and will manage treatment

  OR

- The patient is older than 18 years of age and has the following indications:

  Growth hormone deficiency as a result of pituitary disease, hypothalamic disease, trauma, surgery, or radiation therapy, acquired as an adult or diagnosed during childhood
  Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS) wasting/cachexia
  Short Bowel Syndrome

- For patients older than 18 years of age, the prescription is written by or **in consultation with an appropriate specialist (endocrinologist, infectious disease specialist, general surgeon, or gastroenterologist).**

  AND

<u>For Omnitrope and Zomacton</u>: In addition to the above criteria, the following criteria applies to current users of Omnitrope and Zomacton:

- The patient has a contraindication to Norditropin FlexPro OR
- The patient has experienced an adverse reaction to Norditropin FlexPro that is not expected with Omnitrope or Zomacton (e.g., because of different preservative)

  OR

- For Zomacton: the patient prefers a needle-free device (Zomacton)

  AND

For Genotropin, Humatrope, Nutropin AQ Nuspin, Saizen, and Serostim: In addition to the above criteria, the following criteria applies to new and current users of Genotropin, Humatrope, Nutropin AQ Nuspin, Saizen, and Serostim:

- The patient has a contraindication to Norditropin FlexPro AND Omnitrope AND Zomacton OR

- The patient has experienced an adverse reaction to Norditropin FlexPro AND Omnitrope AND Zomacton that is not expected with the non-step-preferred product (e.g., because of different preservative)

  Note that all possible preservative formulations are available between Norditropin FlexPro, Omnitrope, and Zomacton.
  Note that patient preference for a particular device is insufficient grounds for approval of Genotropin, Humatrope, Nutropin AQ Nuspin, Saizen, or Serostim.

- Use of a GSA is not approved for idiopathic short stature, the normal ageing process, obesity, or depression

- Use of a GSA is not approved for other non-FDA-approved uses (e.g., non-alcoholic fatty liver disease, cirrhosis, mild cognitive impairment)

- Concomitant use of multiple GSAs is not approved

PA expires in one year.

5. GSAs—Tier 1 Cost Share

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) lowering the current tier 2 cost share for Norditropin FlexPro to the generic tier 1 cost share, under the authority previously discussed.

6. GSAs—UF, PA, and Tier 1 Cost Share Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) the following: 1) an effective date of the first Wednesday after a 90-day implementation period in all points of service and 2) DHA send letters to beneficiaries who are affected by the UF decision.

7. Physician's Perspective

We last reviewed this growth hormone products over 10 years ago, and since the last review, some factors that previously showed differences between the products no longer apply, including the fact that now most of the products have the same FDA-approved indications.

Our MHS providers and several organizations, including the Pediatric Endocrine Society, the American Association of Clinical Endocrinologist, and the UK National Institute for Health and Care Excellence, consider these drugs as highly therapeutically interchangeable and do not prefer or recommend one product over another.

Norditropin Flex Pro has been the current market leader in the MHS since 2007. There are several advantages to Norditropin, as were outlined previously. Therefore, selecting it as the step preferred product impacts the fewest number of patients. Currently in the MHS, 72% of the Growth Hormone market share is for Norditropin. About 465 patients will be affected by formulary recommendation. However, the manufacturer has multiple mechanisms for patient and provider education on the Norditropin device, and we will work with them to ensure patients can receive training on the Norditropin. Additionally, the Norditropin prefilled syringe is the same device used for various insulin products, and has a long history of being on the market. MHS providers and patients are familiar with using the Norditropin device.

When we talked to providers, they felt that having one device in a prefilled syringe was adequate for all MHS patients. Providers felt that the growth hormone products were interchangeable.

Zomacton and Omnitope are the other two products recommended for uniform formulary status but after the step. They provide alternatives to Norditropin in terms of differences in preservatives for tolerability issues, plus Zomacton is a needle free device.

The Committee did recognize that there are some differences in the preservatives which may cause hypersensitivity reactions in some patients. The PA will take into account these types of contraindications and adverse effects

Other civilian health plans commonly only have 1-2 products on their formulary, so the formulary recommendation for the MHS is consistent with the civilian world.

We are also recommending a tier one co-pay for Norditropin, which is another benefit to patients and results in lower out-of-pocket costs, plus provides an incentive to switch to the step-preferred product.

8. Panel Questions and Comments

Mr. Hostettler asks what Prader-Willi syndrome is.

LT COL Khoury replies I believe it's a genetic condition.

Mr. Hostettler asks if the beneficiary population affected are all sleep apnea patients.

LT COL Khoury answers no. The reference regarding Prader Willi is to ensure patients have negative sleep studies for obstructive sleep apnea. It is identified because it is a safety concern. It is not for all obstructive sleep apnea patients.

Mr. Hostettler states the total population affected by the recommendation is 1830. How many of those patients are on Zomacton?

Dr. Allerman says there is an error for number of affected users. Dr. Kugler is correct that there are 465 patients total who will be affected by the recommendation.

Mr. Hostettler asked if the majority are in mail.

Dr. Allerman responds the majority are in mail.

Mr. Hostettler asks how extensive is the training for each device and is there a significant difference in the training.

LT COL Khoury says each device is slightly different and requires some education. All of the devices have patient support programs to include nurse educators that will engage patients by phone and I believe, in person as well, as appropriate. They are available geographically to address any of the patient's questions.

Mr. Hostettler says 465 patients, a very small number in the MHS, will need time to scheduled appointment with their physicians for reassessment, get trained, a new prescription, and start on the new medication. His is concerned because that is a lot of activity to take place in 90 days. The patients currently on Zomacton have made that choice because it is a needle-free device. The recommendation requires them to potentially try a product that requires an injection to meet the manual PA requirements for Zomacton. For the small number of patients, it seems like a lot of impact for the small number of beneficiaries.

LT COL Khoury says please keep in mind all patients go through an annual PA for this agent.

Mr. Hostettler asks why there is an annual PA. Why does it expire?

LT COL Khoury responds that's the way it's always been and part of the disease process to ensure continued monitoring and assessment of the patients. It is part of the protocols for the patient to continue on the product.

Mr. Hostettler asks how many patients need the drug after a year. What the percentage is for re-order or re-start of the product.

LT COL Khoury says it depends on the age breakdown. There is a significant drop off at the age of 18. There are drop-offs between the age breakdowns of young child to 18.

Mr. Hostettler asks if those are drop-offs or disruptions.

LT COL Khoury states that we see discontinuations due to the reason for the need for replacement no longer being needed and those patients are continually monitored every year. Further, patients should be seeing their provider on a regular basis.

Mr. Ostrowski states we are here on behalf of the beneficiary. Can the patients continue on the drug until their next annual evaluation instead of switching within the 90 day timeframe? There is an annual PA for this product and the patient will be evaluated at the time anyway.

Mr. Hostettler says allowing the patients to switch at the annual review may have less impact overall.

LT COL Khoury says they will take that back for consideration.

NOTE: To accurately track the vote and minimize confusion. Col Hoerner asks the Panel to vote on the recommendation as the vote is written then comment.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, Tier 1 Cost Share, and UF, PA and Tier 1 Cost Share Implementation Plan for the GSAs.

- **GSAs – UF Recommendation**

  Concur: 0 Non-Concur: 5 Abstain: 0 Absent: 2

- **GSAs – Manual PA Criteria**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

- **GSAs – Tier 1 Cost Share**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

- **GSAs – UF, PA, and Tier 1 Cost Share Implementation Plan**

  Concur: 0 Non-Concur: 5 Abstain: 0 Absent: 2

Recommendation and comments from the Panel:

The Panel asks for a new implementation date. Rather than 90 days, they ask if the patients affected by the recommendation can switch during their annual review. The Panel believes switching at the annual review would cause less disruption to the patient therapy.

C. GASTROINTESTINAL-2 AGENTS: OPIOID-INDUCED CONSTIPATION SUBCLASS

(DR. ALLERMAN)

1. Gastrointestinal-2 Agents: Opioid-Induced Constipation Subclass—Relative Clinical Effectiveness Analysis and Conclusion

Background—The P&T Committee evaluated the peripherally acting mu opioid receptor antagonists (PAMORAs) for opioid-induced constipation (OIC). The products are a subclass of the Gastrointestinal-2 (GI-2); the subclass has not been reviewed previously for formulary status. The drugs in the class include methylnaltrexone (Relistor), naldemedine (Symproic), and naloxegol (Movantik) and are all indicated for treating OIC. Relistor is also available in an injection for treatment of OIC in the palliative care setting.

The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

The PAMORAs inhibit the action of opioids in the GI tract, which decreases constipation, but still maintain the analgesic effects from the mu receptors in the central nervous system.

According to professional treatment guidelines, scheduled doses of a stimulant laxative, (e.g., bisacodyl/senna) with or without a stool-softener (e.g., docusate), a high fiber diet, increased fluid intake, moderate exercise and opioid dosage reduction to the minimum effective dose are recommended as first-line options for OIC. The reason these drugs are used is due to opioids. We know there is an opioid epidemic so therefore decreasing the dose of the opioid will solve the OIC issue.

Limitations to the evidence for efficacy of the OIC drugs include the lack of a validated minimally clinically important difference in study endpoints, the allowance of concomitant or "rescue" laxative doses, and the short duration of the trials (less than three months). Additionally, in the trials leading to FDA approval for the OIC drugs, there were differing inclusion and exclusion criteria, especially with regard to intensity of opioid dosing.

Given the varying efficacy endpoints and lack of head-to-head trials, there is insufficient evidence to conclude that one PAMORA is more effective than another or associated with fewer adverse events.

There is no long-term safety data available with the OIC drugs. The FDA is requiring cardiovascular outcomes trials (CVOTs) for the PAMORAs to evaluate CV mortality, non-fatal myocardial infarction, and stroke. Results from the CVOTs are pending.

Advantages of Symproic include once daily dosing and no need to adjust the dose in patients with renal dysfunction. Symproic is available in one tablet strength, so dose titration is not required. However, disadvantages include rare cases of rash and hypersensitivity reactions reported in the clinical trials leading to FDA approval and CYP3A4 drug interactions.

Movantik can be crushed and placed down a nasogastric tube and is also dosed once daily. Disadvantages include that the 12.5 mg dosage was not statistically significant in one trial; it requires renal and hepatic dosing adjustment; and it has CYP3A4 drug interactions.

Advantages of the methylnaltrexone (Relistor) tablets include the lack of CYP3A4 drug interactions. However, only one phase III trial is available for the oral tablet. MHS provider feedback supported use of traditional laxative therapy as first-line therapy for OIC.

2. GI-2 Agents: OIC Subclass—Relative Cost Effectiveness Analysis and Conclusion

CMA and BIA were performed. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

CMA results showed that Symproic was the most cost-effective OIC drug, followed by Movantik, and Relistor.

BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results found that designating Symproic and Movantik as formulary with Relistor as NF demonstrated significant cost avoidance for the MHS.

3. GI-2 Agents: OIC Subclass—UF Recommendation

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

- UF
  Symproic
  Movantik

- NF
  Relistor tablets and injection

4. GI-2 Agents: OIC Subclass—Manual PA Criteria

PA criteria currently apply to Relistor and Movantik, which requires a trial of two traditional laxatives and a trial of lubiprostone (Amitiza) prior to use of an OIC drug. For new users of Symproic and Movantik, the P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) maintaining the requirement for a trial of over-the-counter (OTC) laxatives, and removing the requirement for a trial of Amitiza, based on the treatment guidelines from the American Gastroenterological Association where PAMORAs are recommended specifically for laxative-refractory patients.

The Committee also recommended updating the existing manual PA criteria for Relistor tablets to require a trial of Amitiza and both Symproic and Movantik, due to the relatively limited amount and low quality evidence available. The PA criteria for Relistor tablets will apply to new and current users. PA is not required for Relistor injection, as this product is limited to the palliative care setting.

<u>Manual PA criteria</u>

a. Movantik and **Symproic**

- The patient is 18 years of age or older with a diagnosis of OIC AND

- The patient is currently taking an opioid agonist AND

- The patient is not on other opioid antagonists (naloxone not including rescue agents, naltrexone, etc.) AND

- The patient has either failed or not tolerated two or more of the following:

- At least one stimulant laxative (sennosides or bisacodyl) AND
- At least one osmotic laxative (Miralax, lactulose, or magnesium citrate) AND

- The patient does not have a known or suspected gastrointestinal obstruction or is not at increased risk of recurrent obstruction AND

- The patient is not currently on strong CYP3A4 inducers inhibitors (e.g., clarithromycin, ketoconazole)

Non-FDA-approved uses are not approved.

PA expires in one year.

Renewal PA criteria: Coverage will be approved for an additional year if all of the following apply:

- The patient continues to take opioids AND

- The patient continues lifestyle modifications including regular use of a stimulant laxative (e.g., bisacodyl, senna), a high fiber diet, increased fluid intake, moderate exercise, and opioid dose de-escalation to minimum effective dose

- The patient is responding in a meaningful manner (e.g., improvement of at least one additional spontaneous bowel movement per week over baseline)

b. Movantik and **Symproic**

Manual PA criteria apply to new and current users of Relistor tablets.

Manual PA criteria: Approved if all criteria are met:

- The patient is 18 years of age or older with a diagnosis of OIC AND

- The patient is currently taking an opioid agonist AND

- The patient is not on other opioid antagonists (naloxone not including rescue agents, naltrexone, etc.) AND

- The patient has either failed or not tolerated two or more of the following:
  - At least one stimulant laxative (sennosides or bisacodyl) AND
  - At least one osmotic laxative (Miralax, lactulose, or magnesium citrate) AND

- The patient has tried and failed Movantik AND

- The patient has tried and failed Symproic AND
- The patient has tried and failed Amitiza AND
- The patient does not have a known or suspected gastrointestinal obstruction or is not at increased risk of recurrent obstruction AND
- The patient is not currently on strong CYP3A4 inducers inhibitors (e.g., clarithromycin, ketoconazole)

Non-FDA-approved uses are not approved.
PA expires in one year.

Renewal PA criteria: Coverage will be approved for an additional year if all of the following apply:

- The patient continues to take opioids AND
- The patient continues lifestyle modifications including regular use of a stimulant laxative (e.g., bisacodyl, senna), a high fiber diet, increased fluid intake, moderate exercise, and opioid dose de-escalation to minimum effective dose
- The patient is responding in a meaningful manner (e.g., improvement of at least one additional spontaneous bowel movement per week over baseline)

5. GI-2 Agents: OIC Subclass—UF and PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following:

1) an effective date of the first Wednesday after a 60-day implementation period in all points of service and 2) DHA send letters to beneficiaries who are affected by the UF decision.

6. Physician's Perspective

This is a new class of drugs for treating OIC, however, they are not a first-line treatment. Professional guidelines recommend using traditional laxatives first, before using a PAMORA. A survey of MHS providers also agreed with this recommendation, that these drugs should only be used after laxatives have failed. Other approaches to reduce constipation are to decrease the dose of the opioid.

The reasons for the prior authorization are to ensure that the patient has tried the traditional laxatives first, and also due to the lack of long-term safety data with the PAMORAs.

For Relistor, the PA will also require at trial of either Movantik or Symproic, or Amitiza (which is also approved for OIC, but has a different mechanism of action). The Committee did recognize that Relistor injection is indicated only for patients in the palliative care setting. Because of this the recommendation is that the Relistor injection will not have the requirement for a PA, just non-formulary status.

When we looked at current utilization, it does not appear that patients are on these drug long-term. We found that only 43% of patients had their prescription filled more than one time. We will continue to monitor usage patterns for this class, along with any new clinical information for efficacy or safety updates.

7. Panel Questions and Comments

Mr. Hostettler asks of the 315 patients affected, how many are on Relistor?

Dr. Allerman replied they are all on Relistor because the PA changed for Symproic and Movatik which only applies to new patients.

Hostettler asks why did you take the PA out of one drug and put it back in the other.

Allerman replied it was based on cost effectiveness, evidence quantity, and evidence quality. There was not enough evidence/data for Relistor.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, and UF and PA Implementation Plan for the GI-2 agents.

- **GI2 Agents: OIC Subclass – UF Recommendation**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

- **GI2 Agents: OIC Subclass – Manual PA Criteria**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

- **GI2 Agents: OIC Subclass – UF and PA Implementation**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

Additional Panel Questions and Comments:

Mr. Hostettler asks when letters go out to beneficiaries.

Dr. Allerman answered they go out about a month before the formulary decision on implementation

Mr. Hostettler said that would give the beneficiary approximately 90 days to switch. You said 60 days?

Dr. Allerman said it is 60 days because there are approximately 300 patients affected by the recommendation.

Mr. Hostettler asked if they would receive letters 30 days before the clock starts.

Dr. Allerman said some patients may have gotten their refill the day before they get the letter which allows additional time switch to the new drug.

Mr. Hostettler asks if those patient would be notified of a pending change which allows them to see their provider to get a new prescription before the change. I am just trying to see if a 60 day implementation period is enough time.

Dr. Allerman states that these patients are on opioids. They are probably getting their opioid prescriptions every month.

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

(LT COL KHOURY)

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

The P&T Committee agreed (16 for, 0 opposed, 0 abstained, 0 absent) with the relative clinical and cost-effectiveness analyses presented for the newly approved drugs reviewed according to 32 CFR 199.21(g)(5).

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

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following:

- UF:
  - apalutamide (Erleada) – Oral Oncologic Agent for Prostate Cancer
  - bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy) – Antiretrovirals for HIV

- efavirenz/lamivudine/tenofovir disoproxil fumarate (Symfi) – HIV
- efavirenz/lamivudine/tenofovir disoproxil fumarate (Symfi Lo) – HIV
- ibrutinib tablets (Imbruvica) – Oral Oncologic Agent for mantle cell lymphoma and chronic lymphocytic leukemia, new formulation (note that Imbruvica capsules were already designated as uniform formulary prior to the Innovator Rule established in August 2015)
- insulin lispro (Admelog) – Short-Acting Insulin for Diabetes Mellitus
- lamivudine/tenofovir disoproxil fumarate (Cimduo) – Antiretrovirals for HIV
- netarsudil 0.02% ophthalmic solution (Rhopressa) – Glaucoma Agents
- tezacaftor/ivacaftor (Symdeko) – Cystic Fibrosis Agents
- vancomycin oral solution (Firvanq) – Gastrointestinal-2 agents: Miscellaneous for *Clostridium difficile* associated diarrhea or enterocolitis

- NF:
  - clobetasol propionate 0.025% cream (Impoyz) – High Potency Corticosteroids-Immune Modulators for Moderate to Severe Plaque Psoriasis
  - desmopressin nasal spray (Noctiva) – Miscellaneous Endocrine Agent for nocturia due to nocturnal polyuria
  - doxylamine succinate/pyridoxine ER tablets (Bonjesta) – Antiemetic-Antivertigo Agents
  - ertugliflozin (Steglatro) – Non-Insulin Diabetes Drugs – Sodium Glucose Co-Transporter-2 (SGLT2) Inhibitor
  - ertugliflozin/sitagliptin (Steglujan) – Non-Insulin Diabetes Drugs –SGLT2 Inhibitor
  - ertugliflozin (metformin) (Segluromet)
  - glycopyrrolate inhalation solution (Lonhala Magnair) – Pulmonary-2: Long-Acting Muscarinic Agents (LAMAs) for Chronic Obstructive Pulmonary Disease
  - pitavastatin magnesium (Zypitamag) – Antilipidemic-Is (LIP-Is)
  - secnidazole (Solosec) – Miscellaneous Anti-Infective for bacterial vaginosis in adult women

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

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following:

Applying the same manual PA criteria for Steglatro, Segluromet, and Steglujan in new and current users as is currently in place for the other non-step-preferred SGLT2 inhibitors. Patients must first try the step-preferred SGLT2 inhibitor empagliflozin (Jardiance, Glyxambi, Synjardy or Synjardy XR).

Applying the same step therapy and manual PA criteria to new and current users of Zypitamag as is currently in place for pitavastatin (Livalo). Step therapy for the Antilipidemic I's drug class requires a trial of a generic statin at comparable low-density lipoprotein (LDL) lowering capability.

Applying manual PA criteria to new and current users of Impoyz cream, Lonhala Magnair inhalation solution, Noctiva nasal spray, and Rhopressa ophthalmic solution.

Applying manual PA criteria to new users of Bonjesta, Erleada, and Symdeko.

Applying manual PA criteria to new users of Imbruvica tablets and capsules.

INTERIM P&T COMMITTEE MEETING—Following the May 2018 P&T Committee meeting, the Committee became aware that Imbruvica capsules would remain on the market. The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) to revise the PA for Imbruvica to require a trial of Imbruvica capsules first in new users, prior to use of the tablets; as shifting patients to the tablet formulation unnecessarily reduces dosage titration options..

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

a. Erleada

if all criteria are met:

- The patient has a diagnosis of non-metastatic castration-resistant prostate cancer (as shown by a negative CT scan of abdomen/pelvis and/or negative bone scan) AND
- Patients should be co-prescribed gonadotropin-releasing hormone analog therapy concurrently OR patients should have had bilateral orchiectomy AND
- Erleada is prescribed by or in consultation with an oncologist or urologist

Non-FDA-approved uses are not approved.

PA expires in one year.

Renewal criteria: Erleada will be continued for another year if:

- The patient continues to be free of metastases
- No toxicities have developed
- The patient has not had disease progression requiring subsequent therapy (such as abiraterone [Zytiga])

b. Impoyz

Manual PA applies to all new and current users of Impoyz.

Manual PA criteria: Coverage will be approved if all criteria are met:

- Patient has moderate to severe plaque psoriasis AND
- Patient is ≥ 18 years old AND
- Patient is not a candidate for or has failed phototherapy AND
- Contraindications exist to all formulary high-potency topical steroids OR
- Patient has had an inadequate response to all formulary high-potency topical steroids OR
- Patient has had an adverse effect to each of the formulary high-potency topical steroids

Non-FDA-approved uses are not approved.

PA expires in 30 days.

Renewal Criteria: Renewal of therapy is not allowed.

c. Noctiva

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

Manual PA criteria: Coverage will be approved if all criteria are met:

- The patient ≥ 50 years old (only the low dose is allowed for patients > 65 years old)
- Causes of nocturia have been evaluated, nocturnal polyuria is confirmed with a 24-hour urine collection, and the patient has experienced at least two nocturia episodes per night for ≥ 6 months
- The patient is not currently taking any of the following medications:
  loop diuretics, thiazide diuretics, systemic or inhaled corticosteroids, lithium, alpha1-adrenoceptor antagonists, 5-alpha reductase inhibitors (5-ARIs), anticholinergics, antispasmodics, sedative/hypnotic agents, NSAIDs, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), antidepressants, anti-epileptics, opioids, or SGLT2s

- The patient has normal sodium level (135-145 meq/L) prior to the initiation of therapy, the sodium level is rechecked after one week of therapy, and another sodium level is rechecked after one month of therapy

- The patient does not have the following conditions:
  - acute or chronic rhinitis
  - atrophy of nasal mucosa
  - renal impairment (eGFR < 50 mL/min)
  - hyponatremia or history of hyponatremia
  - polydipsia
  - nocturnal enuresis
  - syndrome of inappropriate antidiuretic hormone (SIADH)
  - congestive heart failure (New York Heart Association II-IV)
  - uncontrolled hypertension or uncontrolled diabetes mellitus

Non-FDA-approved uses are not approved.

PA expires in six months.

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

- Patient has not developed any of the above conditions

- Patient is not taking any of the above medications

- Patient has shown a reduction in nocturia episodes

d. Bonjesta

Manual PA criteria apply to all new users of Bonjesta.

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

- The patient has a diagnosis of nausea and vomiting associated with pregnancy

- The patient has tried at least one non-pharmacologic treatment (for example, ginger, acupressure, high protein bedtime snack) and failed to obtain relief of symptoms

- The patient has tried OTC doxylamine and pyridoxine and failed to obtain relief of symptoms

- The provider has considered a change to an alternate anti-emetic (e.g., ondansetron) prior to prescribing Bonjesta

Non-FDA-approved uses are not approved.

PA will expire after nine months.

e. Steglatro, Segluromet, and Steglujan

Manual PA criteria apply to all new and current users of Steglatro, Segluromet, and Steglujan.

Manual PA criteria: Coverage will be approved if all criteria are met:

- For Steglatro and Steglujan: The patient must have had an inadequate response or experienced significant adverse events, or have a contraindication to metformin AND

- For Steglatro, Segluromet, and Steglujan: The patient must have tried one of the preferred SGLT2 inhibitors (Jardiance, Glyxambi, Synjardy, and Synjardy XR) and had an inadequate response or experienced significant adverse events, or have a contraindication to empagliflozin OR

- For Steglujan: The patient must have had an inadequate response to sitagliptin alone

Non-FDA-approved uses are not approved.

PA does not expire.

f. Lonhala Magnair

Manual PA is required for all new and current users of Lonhala Magnair inhalation solution (starter kit and refill kit).

Lonhala Magnair is approved if all criteria are met:

- The patient has a diagnosis of Chronic Obstructive Pulmonary Disease (COPD) AND

- The patient has tried and failed an adequate course of a nebulized Short-Acting Muscarinic Antagonist (e.g., ipratropium) AND

- The patient has tried and failed an adequate course of Spiriva Respimat AND

- The patient has tried and failed an adequate course of therapy of at least one of the following dry powder inhalers: Tudorza Pressair, Incruse Ellipta, Spiriva Handihaler, or Seebri Neohaler OR

- The patient cannot generate the peak inspiratory flow needed to activate at least one of the following dry powder inhalers: Tudorza Pressair, Incruse Ellipta, Spiriva Handihaler, or Seebri Neohaler

Non-FDA-approved uses are not approved.

PA does not expire.

g. Imbruvica tablets and capsules

Manual PA criteria apply to all new users of Imbruvica tablets and capsules.

Manual PA criteria: Coverage will be approved if all criteria are met:

- Imbruvica capsules are the DoD-preferred formulation for Imbruvica.
    - **If the prescription is for Imbruvica capsules, please continue to the criteria below.**
    - **If the prescription is for Imbruvica tablets, provide documentation as to why the capsule formulation cannot be used, and then continue with the criteria below.**

- The patient is ≥ 18 years old

- The patient has laboratory evidence of and pathologic confirmation of one of the following:
    - Mantle Cell Lymphoma
    - Marginal Zone Lymphoma
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia ± 17p deletion
    - Waldenström's macroglobulinemia
    - Chronic Graft versus Host Disease

- Imbruvica is prescribed by or in consultation with a hematologist/oncologist

Non-FDA-approved uses are not approved.

PA does not expire.

h. Rhopressa

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

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

- The patient has a diagnosis of ocular hypertension or open-angle glaucoma

- The prescription is written by an ophthalmologist or an optometrist

- The patient has had a trial of appropriate duration of <u>two different formulary options</u> from different glaucoma drug classes, in combination or separately, and has not reached intraocular pressure target goals as defined by the provider. The drug classes include:

    - prostaglandin analogs (latanoprost or bimatoprost)
    - beta blockers (Betoptic, Betoptic-S, Ocupress, Betagan, Optipranolol)
    - alpha2-adrenergic agonists (brimonidine, apraclonidine)
    - topical carbonic anhydrase inhibitors [dorzolamide (Trusopt)]

Non-FDA-approved uses are not approved.

PA does not expire.

i. Zypitamag

All new and current users of Zypitamag must try a preferred statin at appropriate LDL lowering first.

<u>Automated PA Criteria</u>:

- The patient has received a prescription for a preferred agent (generic atorvastatin, simvastatin, pravastatin, fluvastatin, lovastatin, pravastatin or rosuvastatin) targeting similar LDL reduction (LDL lowering between 30% to 50%, LDL lowering < 30%) at any MHS pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days

AND

<u>Manual PA Criteria</u>: If automated criteria are not met, Zypitamag is approved (e.g., trial of generic statin is NOT required) if:

- The patient has tried a preferred statin with similar LDL reduction (moderate or low intensity) and was unable to tolerate it due to adverse effects

- The patient is taking a drug that is metabolized by CYP3A4 is unable to take pravastatin or rosuvastatin

PA does not expire.

j. Symdeko

Manual PA criteria apply to all new users of Symdeko.

<u>Manual PA Criteria</u>: Symdeko is approved if ALL of the following criteria are met:

- Symdeko is prescribed for the treatment of cystic fibrosis in patient ages 12 years and older.

- The patient meets one of the following criteria:

    - The patient is homozygous for the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene as detected by an FDA-approved CF mutation test.
    - The patient has at least one specific gene mutation in the CFTR gene that is responsive to Symdeko as detected by an FDA-approved CF mutation test.

    - The CF-related gene mutation, based on FDA-approved testing, must be documented.

- Symdeko is not approved for use in combination with other CFTR modulators (e.g., Orkambi, Kalydeko).

Non-FDA-approved uses are not approved.

PA does not expire.

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

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) an effective date upon the first Wednesday two weeks after the signing of the minutes in all points of service.

5. Physician's Perspective

We reviewed 19 new drugs at this meeting; with 10 recommended for UF status, and 9 recommended for non-formulary placement. For the drugs recommended for non-formulary status, several of them fall into classes that have already been reviewed by the P&T Committee, where there are cost effective products already available in the class.

For this review, for the 12 drugs where a PA was recommended, 7 of them fall into classes where there are already PA requirements (the three SGLT2 diabetes drugs, the statins, oncology drugs, the nausea and vomiting drug, and the cystic fibrosis drugs).

For 3 of the drugs with a PA requirement, grandfathering was recommended, so the PA will only apply to new users (the oncology drug, Erleada, the nausea and vomiting drug Bonjesta, and the Cystic Fibrosis drug Symdeko).

"No grandfathering", where the PA will apply to both new and current users, was recommended for 5 drugs: the new glaucoma drug Rhopressa, the topical steroid Impoyz,

the nasal spray for nocturia Noctiva, the statin Zypitamag, and the nebulized drug for COPD.

There were a couple of comments made at the meeting for some of the drugs recommended for non-formulary status with Prior Authorization:

- Zypitamag (Statin): In the FDA briefing materials, there was a comment that there is "no pressing health need for an alternative formulation for pitavastatin, which is one of 7 statins marketed"

- Noctiva (nasal spray for nocturia) – very significant safety concerns with this drug were expressed by the P&T Committee, especially in regards to its use in the elderly population.

- Impoyz (topical steroids) – the Committee did not feel that this product would be effective, as it contains a smaller concentration of clobetasol than included in other high potency steroids.

Imbruvica – INTERIM P&T MEETING

- For Imbruvica, there is a new tablet formulation, as the capsule formulation has been available for many years. At the time of the meeting, the available information was that the capsules were being discontinued from the market. The interim meeting was held when the Committee became aware that the capsules would remain on the market.

- The updated recommendation was to revise the Imbruvica manual PA criteria to give preference to the capsules. The Imbruvica tabs and caps will both remain on the Uniform Formulary.

6. Panel Comments and Questions

Mr. Hostettler asks how many patients are affected by the recommendation for Impoyz?

LT COL Khoury says there are 47 patients as of May 2018.

Mr. Hostettler asks if he can assume that all those new and current users of the drug have similar numbers.

LT COL Khoury asks for all the others?

Mr. Hostettler repeats for all the ones you had in the category of new and current users. Some of them were just new users. I am not concerned with the new users. It is the current users I am concerned with.

LT COL Khoury says if there is a specific drug he can provide the number to help guide your decision.

Mr. Hostettler says Noctiva.

Khoury says Noctiva has 99 users.

Hostettler asks about Steglartro, Segluromet, and Steglujan.

LT COL Khoury said those have a preordained process due to the fact they have been previously reviewed and have step preferred scenario

Mr. Hostettler asks about Imbruvica.

LT COL Khoury says Imbruvica has 780 patients.

Mr., Hostettler asks about Rhopressa.

LT COL Khoury says Rhopressa has 368 as of May.

Mr. Hostettler asks about the implementation timeframe on 300 patients.

LT COL Khoury replies this recommendation impacts formulary status. Implementation is 2 weeks after the signing of the minutes to move it from current non-formulary pending review to formulary.

Mr. Hostettler asks if the manual PA will apply to current users of Rhopressa (368 patients) 2-weeks after the signing of the minutes. On their next refill, they will be faced with the new criteria? That seems aggressive.

LT COL Khoury says he'll have to get back to you on the numbers. According to the process, the PA is in place pending the meeting of the UF BAP and is adjusted after the meeting. I am not positive that Rhopressa has a PA in place. It may have already gone through a PA but I need to verify.

Mr. Hostettler says if it wasn't already reviewed and put into a process that answer doesn't make sense.

LT COL Khoury says drugs like Imbruvica already have a PA in place. I'm not positive Rhopressa has a PA in place.

Mr. Hostettler says he doesn't think there should be one in place since it's never been reviewed prior to this meeting? The 2-week timeframe is aggressive to ensure 300 patients complete the process for a PA, not knowing whether the patients are at the MTF, Retail or mail.

LT COL Khoury says I want to ensure we are discussing the drugs with a PA in place. That is what I am referring to. There is a PA in place, some of these patients have to complete the PA process. Again, I want to ensure we are discussing the same thing and not something different. There is a process for every patient that has a PA. I want to make sure we're saying the same thing.

Mr. Hostettler says they went through a class in the first place for Rhopressa.

LT COL Khoury repeats that he did not have that information on Rhopressa. I don't believe there is a PA so it would be likely that all 368 patients are required to complete the PA process.

Mr. Hostettler says this is why I am concerned. You will answer that question before the 2 week implementation date?

LT COL Khoury says there are two scenarios. (1) If the patient doesn't have a PA and they are faced with a PA. The policy requires that the provider consider the agents that they could potentially be on via the recommendation listed. If the patient meets those conditions, they fulfill the criteria for the PA and will continue on that prescription. (2) If they don't have a PA, the recommendation would be that they have not achieved the PA to get to that agent. The patient will be required to complete the PA process.

Mr. Hostettler believes completing the PA process for both of those prescriptions for 300 patients will be challenging.

LT COL Khoury repeats, these are new agents that are recently approved since the last meeting. If the provider prescribed these agents, they should be following up with the patients to see how they are doing. If there are problems the provider is probably not assessing the patient to ensure that are responding to the drug appropriately.

Mr. Hostettler asks if the affected population will receive a letter notifying them of the change 30 days prior to the 2 week implementation date.

LT COL Khoury says there is an awareness because the patient is currently in the non-formulary status. They will receive a letter notifying them of a change to formulary status.

Mr. Hostettler repeats his concerns regarding the short implementation period. The information about the PA is still confusing because this is a new product. It will be challenging for the patient to complete the PA process in 2-weeks.

Ms. Buchanan says if a patient uses drops, they don't run out of them overnight. There is a period of time where it would be actually longer depending on when the patient got a refill on the prescription.

Mr. Hostettler says when they get a refill, they will have to complete the PA process.

LT COL Khoury says that's what happens with all new drugs when the PA is placed for all the new drugs we have seen. If they have received the agent before the PA is in place, similar to a class review, those patients will be impacted.

Mr. Hostettler understands the issues you are dealing with but I am dealing with it from the beneficiary perspective. I didn't create the process but now you are making your problem my problem and giving me 2-weeks to solve it. I believe it is a short-timeframe. To comply with the PA criteria, the patient needs the provider to make the change or interact with a health plan, ESI, or someone to clear the use of the product is required.

LT COL Khoury says keep in mind that the reverse applies. Delaying the length of time for implementation forces the patient to potentially pay the non-formulary co-pay longer.

Mr. Hostettler asks if the letter will explain their options.

LT COL says, I am referring to the co-pays.

Mr. Hostettler asks if it will explain the co-pay change, as well.

LT COL Khoury says I am saying all that there is an impact to the patient the longer the implementation period is delayed. There are 10 drugs going non-formulary. As long as they are in the non-formulary status the patient will pay the higher (non-formulary) co-pay.

Mr. Hostettler asks if the implementation period for "this one" drug (Rhopressa) could be more 2-weeks. Why do all of the Newly Approved drugs need the same implementation period? Why can't they separate this drug?

LT COL Khoury said I will take your comments back to the P&T committee.

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

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

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

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

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

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

  Concur: 2 Non-Concur: 3 Abstain: 0 Absent: 2

Recommendation and Comments from the Panel.

The Panel asked if Rhopressa can be separated and have a longer implementation period. Potentially 60 days.

Mr. Ostrowski said I hope in the future when the P&T Committee reviews drugs with similar problems, we could potentially resolve the issue by separating those anomalies and it will make the process smoother.

E. UTILIZATION MANAGEMENT

(DR. ALLERMAN)

1. PA Criteria and Step Therapy

The P&T Committee recommended updates to the step therapy and manual PA criteria for several drugs due to a variety of reasons, including expanded FDA indications and feedback from the field. The updated manual PAs outlined below will apply to new users.

a. Antiemetic-Antivertigo Agents: doxylamine succinate and pyridoxine hydrochloride ER (Diclegis)—Diclegis PA criteria were first recommended at the August 2014 DoD P&T Committee Meeting. PA criteria were reviewed and updated to require a trial of both OTC doxylamine and pyridoxine before use of Diclegis.

b. Targeted Immunomodulatory Biologics (TIBs): abatacept (Orencia)—The TIBs were most recently reviewed in August 2014, with step therapy requiring a trial of adalimumab (Humira) first. Orencia was recently approved by the FDA for treatment of polyarticular Juvenile Idiopathic Arthritis (JIA) in patients two year or older. PA criteria were updated to add the additional indication JIA in pediatric patients.

c. Targeted Immunomodulatory Biologics (TIBs): secukinumab (Cosentyx)— Cosentyx was approved by the FDA in January 2015 for treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. Since then, three additional indications were approved by the FDA: psoriatic arthritis, psoriasis of the scalp, and most recently ankylosing spondylitis in January 2018. The PA criteria were updated to add the additional FDA indications.

d. **Oncological Agents: abiraterone acetate (Zytiga)—**In April 2011, the FDA approved Zytiga for use in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer in patients who have received prior chemotherapy containing docetaxel. PA criteria for Zytiga were recommended at the November 2012 meeting, consistent with the FDA labeling. The FDA has subsequently updated the approved labeling for patients with metastatic high-risk castration-sensitive prostate cancer receiving concomitant prednisone. The PA criteria were updated to add the

additional FDA indication and to require that the patient receive concomitant therapy with a gonadotropin-releasing hormone (GnRH) analog or have had bilateral orchiectomy.

e. **Non-Insulin Diabetes Drugs: Glucagon-Like Peptide-1 Receptor Agonists/Insulin Combination: insulin glargine/lixisenatide (Xultophy) and insulin degludec/liraglutide (Soliqua)**—Xultophy and Soliqua were reviewed in May 2017, and step therapy and manual PA criteria applied. Insulin glargine (Lantus) is the preferred basal insulin. The Glucagon-Like Peptide-1 Receptor Agonist **(**GLP1RA) class was reviewed in February 2018, and exenatide weekly (Bydureon/BCise) and dulaglutide (Trulicity) were designated as the preferred products. The PA criteria for Xultophy and Soliqua were updated to include provider acknowledgement of the preferred basal insulin and GLP1RAs.

f. **Parkinson's Disease Drugs: amantadine hydrochloride extended release (Gocovri)**—Gocovri was reviewed as a new drug during the November 2017 P&T Committee meeting, and PA criteria were recommended requiring the patient to have failed and tried amantadine immediate release (IR) 200 mg BID. Since this recommendation, feedback was received from neurologists that patients are not always able to tolerate a 400 mg daily dose of amantadine immediate release (IR). The PA criteria for Gocovri were updated to allow a trial of a lower dose of amantadine IR (300 mg daily in divided doses) to qualify for Gocovri.

g. **Oncological Agents: abemaciclib (Verzenio)**—Verzenio was first reviewed at the November 2017 P&T Committee meeting, and PA criteria were recommended for treatment of metastatic breast cancer. The PA criteria were updated to add the new FDA indication for use in postmenopausal women when used in combination with an aromatase inhibitor (i.e., anastrozole/letrozole) as initial endocrine-based therapy.

h. **Targeted Immunomodulatory Biologics (TIBs): apremilast (Otezla)—**The current PA criteria for the TIBs does not allow combination therapy with other TIBs, due to overlapping mechanisms of action and risk of enhanced toxicity. Otezla has a mechanism of action unique to the TIBs; it is a phosphodiesterase-4 (PDE4) inhibitor, which is an enzyme that breaks down cyclic adenosine monophosphate (cAMP). FDA labeling for Otezla does not specify that it cannot be utilized in combination with other TIB agents, and it has a low risk of immunosuppression. The PA criteria for Otezla were updated to allow use in combination with the other TIBs (e.g., in a patient requiring Humira for treatment of RA and Otezla for treatment of plaque psoriasis), if the provider provides documented evidence as to why combination therapy is required.

2. Updated Manual PA Criteria

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) updates to the manual PA criteria for Diclegis, Orencia, Cosentyx, Zytiga, Xultophy, Soliqua, Gocovri, Verzenio, and Otezla. All updated PA criteria apply to new users.

3. Updated Manual PA Criteria an PA Renewal – PA Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) updates to the current PAs for Diclegis, Orencia, Cosentyx, Zytiga, Xultophy, Soliqua, Gocovri, Verzenio, and Otezla become effective on the first Wednesday two weeks after the signing of the minutes in all points of service.

4. Physician's Perspective

Updated PA Criteria for the following drugs

1. Anti-emetic-Antivertigo Agent: - Diclegis
2. Targeted Immunomodulatory Biologics (TIBs): Orencia, Cosentyz, Otezla
3. Oncological Agents: Zytiga and Verzenio
4. Non-Insulin Diabetes Drugs: Xultophy and Soliqua
5. Parkinson's Disease Drugs: Gocovri

- We did not have any new PA's recommended at this meeting, just updates on existing Pas.

- For most of the drugs, the updates were due to new FDA-indications that needed to be added to the PA. (Orencia, Cosentyx; Zytiga, and Verzenio)

- We also updated the PAs for the GLP-1RA drugs to align the criteria with some recent P&T Committee decisions (for Xultophy and Soliqua).

- For two of the drugs, we updated the PA criteria based on feedback that we received from MHS providers. This was the case for the Parkinson's disease drug Gocovri, where we are allowing for a lower dose. The other case is for Otezla, where we will now allow combination use with another TIB.

5. Panel Questions and Comments

There were no questions or comment from the Panel. The Chair called for a vote on the Updated Manual PA Criteria and PA Renewal Criteria and the Updated Manual PA Criteria and PA Renewal Criteria Implementation Plan for the Newly Approved Drugs.

- **Updated Manual PA Criteria and PA Renewal Criteria**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

- **Updated Manual PA Criteria and PA Renewal Criteria – PA Implementation Plan**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

F. SECTION 703, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR (FY) 2018

(LT COL KHOURY)

The P&T Committee reviewed four drugs from pharmaceutical manufacturers that were not included on a DoD Retail Refund Pricing Agreement; these drugs were not in compliance with FY08 NDAA, Section 703. The law stipulates that if a drug is not compliant with Section 703, it will be designated NF on the UF and will be restricted to the TRICARE Mail Order Pharmacy, requiring pre-authorization prior to use in the retail POS and medical necessity at MTFs. These NF drugs will remain available in the Mail Order POS without pre-authorization.

1. Drugs Designated as NF

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) the following products be designated NF on the UF:

- Aurobindo Pharma: armodafinil (*New Drug Application-authorized generic*) 200 mg tablet
- Quinn Pharmaceuticals: mercaptopurine (*NDA-authorized generic*) 50 mg tablet
- Noden Pharma: aliskiren (Tekturna) 150 mg tablet; 300 mg tablet
- Noden Pharma: aliskiren-hydrochlorothiazide (Tekturna HCT) 150-12.5 mg tablet, 150-25 mg tablet, 300-12.5 mg tablet, 300-25 mg tablet

2. Preauthorization Criteria

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) the following pre-authorization criteria for the Section 703 non-compliant NDCs of armodafinil, mercaptopurine, Tekturna, and Tekturna HCT:

a. Obtaining the product by home delivery would be detrimental to the patient; and,

b. For branded products with products with AB-rated generic availability, use of the generic product would be detrimental to the patient.

These pre-authorization criteria do not apply to any other POS other than retail network pharmacies.

NOTE: Should the mail order requirement impact availability of a drug, the P&T Committee will allow an exception to the Section 703 rule.

3. Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) the following: 1) an effective date of the first Wednesday after a 90-day implementation period for the Section 703 non-compliant NDCs of armodafinil, mercaptopurine, Tekturna, and Tekturna HCT and 2) DHA send letters to beneficiaries affected by this decision.

4. Physician's Perspective

For two of the products recommended for NF status (generic armodafinil and mercaptopurine), only the generic formulations from one manufacturer are affected; there are other several cost-effective generic formulations and therapeutic alternatives are available on the UF.

For the other two drugs (Tekturna and Tekturna HCT), there are several generic therapeutic alternatives available, including ACE inhibitors and ARBs, plus their combinations with HCTZ.

The Pharmacy Operations Division does follow up with the affected manufacturers, to try to ensure compliance with the Section 703 requirements.

5. Panel Questions and Comments

Mr. Hostettler asks about the section 703 rule. Regarding the notes that states should the mail order requirement impact availability of ta drug, the P&T Committee will allow an exception to the section 703 rule. I am not sure what that means. How would the availability be impacted by mail order?

LT COL Khoury says if the drug is not available at mail. For instance, if the beneficiary can only get the medication through some other point of service other than mail

There were no more questions or comments from the Panel. The Chair called for a vote on the Drugs Designated NF, Pre-Authorization Criteria and Implementation Period for the Section 703 products.

- **Drugs Designated NF**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

- **Pre-Authorization Criteria**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

- **Implementation Period**

  Concur: 5 Non-Concur: 0 Abstain: 0 Absent: 2

Mr. Ostrowski concludes the meeting. He asks the P&T Committee to review the notes and comment from today's meeting. In my instances, the Panel would have concurred with the P&T Committee recommendations. For instance, if the Committee could consider recommending implementation plans that coincide with annual PA requirements, it would have less impact on the beneficiary population. The Panel is here on behalf of the beneficiary. So we are constantly looking at how they are going to be affected by the Committee recommendations. Although some of the populations impacted were approximately 300-400 patients, we will do anything we can to minimize the impact their lives. I know that we can't please everybody all the time. He thanks the P&T Committee for their work and all those attending the meeting.

(Meeting Concludes)

Appendix A – Table of Implementation Status of UF Recommendations/Decisions Summary
Appendix B – Brief Listing of Acronyms Used in this Summary
Appendix C – Private Citizen Comments – Allergan
Appendix D – Private Citizen Comments – Avadel

Mr. Jon Ostrowski,
UF BAP Chairperson

APPENDIX A

Table of Implementation Status of UF Recommendations/Decisions Summary

Date	DoD PEC Drug Class	Type of Action	UF Medications	Nonformulary Medications	Imple-ment Date	Notes and Unique Users Affected
May 2018	**Pancreatic Enzyme Replacement Therapy**	UF Class Review Class previously reviewed Feb 2011, Feb 2014	UF Step-Preferred ▪ Creon UF Non-Step-Preferred ▪ Viokace	NF Non-Step-Preferred ▪ Pancreaze ▪ Pertzye ▪ Ultresa ▪ Zenpep	90 days	▪ A trial of Creon is required first in all new and current users of the non-step-preferred product ▪ No PA required for Creon Unique Users Affected Mail 558 MTF 237 Retail 487 Total 1,282
May 2018	**Growth Stimulating Agents**	UF Class review Class previously reviewed in Aug 2007	UF Step-Preferred ▪ Norditropin FlexPro UF Non-Step-Preferred ▪ Omnitrope ▪ Zomacton	NF Non-Step-Preferred ▪ Genotropin ▪ Humatrope ▪ Nutropin ▪ Saizen ▪ Serostim	90 days	▪ Must try Norditropin FlexPro first in all new and current users. Then must use Omnitrope and Zomacton (either order) before moving to NF agents (Genotropin, Humatrope, Nutropin, Saizen, and Serostim) Unique Users Affected Mail 351 MTF 84 Retail 30 Total 465
May 2018	**GI-2 Agents: Opioid Induced Constipation (OIC) Subclass**	UF Class Review Subclass not reviewed; Class reviewed Nov 2015	UF ▪ naldemedine (Symproic) ▪ naloxegol (Movantik)	NF ▪ methylnaltrexone (Relistor) tablet and injection	60 days	▪ Manual PAs and QLs apply ▪ PA applies: must try two OTC laxatives before use of an OIC drug. ▪ Must try Movantik, Symproic and Amitiza before use of the nonformulary product Relistor Unique Users Affected: Mail 114 MTF 38 Retail 163 Total 315

Appendix B **07/12/2018 BAP Meeting**

Brief Listing of Acronyms Used in this Summary

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

- AIDS – Acquired Immunodeficiency Syndrome
- ARI – Alpha Reductase Inhibitor
- BAP – Beneficiary Advisory Panel
- BIA – Budget Impact Analysis
- cAMP – Cyclic Adenosine Monophosphate
- CFR – Code of Federal Regulations
- CFTR – Cystic Fibrosis Transmembrane Conductance Regulator
- CMA – Cost Minimization Analysis
- COPD – Chronic Obstructive Pulmonary Disease
- CT – Cognitive Therapy
- CVOTs – Cardiovascular Outcome Trials
- CYP3A4 – Cytochrome P450 isoforms
- DoD – Department of Defense
- eGFR – Estimated Glomerular Filtration Rate
- EPI – Exocrine Pancreatic Insufficiency
- ER – Extended Release
- FDA – Food and Drug Administration
- G-Tube – Gastronomy-Tube
- GI-2 – Gastrointestinal-2
- GSA – Growth Stimulating Agents
- HCT- Hematrocrit
- HIV – Human Immunodeficiency Virus
- IR – Immediate Release
- JIA – Juvenile Idiopoathic Arthritis
- L – liter
- LDL – Low Density Lipoprotein
- Mg – Milligram
- MTF – Military Treatment Facility
- NDAA – National Defense Authorization Act
- NDC – National Drug Code
- NF – Non Formulary
- NSAIDs – Nonsteroidal Anti-Inflammatory Drugs
- ODE4 – Phosphodiesterase-4
- OIC – Opioid-Induced Constipation
- OTC – Over the Counter
- P&T – Pharmacy and Therapeutics Committee
- PA – Prior Authorization

- PAMORAs – Peripherally Acting Mu Opioid Receptor Antagonists
- PERT – Pancreatic Enzyme Replacement Therapy
- POS – Point of Sale
- rhGH – Recombinant Human Growth Hormone
- SGLT2s – Sodiun Glucose Co-Transporter
- ShoX – Short Stature Homeobox
- SIADH – Syndrome Inappropriate Antidiuretic Hormone
- SNRI – Serotonin Norepinephrine Reuptake Inhibitor
- SSRI – Selective Reuptake Inhibitor
- TIBs – Targeted Immunomodulatory Agents
- TRICARE – Healthcare Network
- UF -0 Uniform Formulary
- XR – Extended Release

Appendix C **07/12/2018 BAP Meeting**

DOD Zenpep Formulary Change Response Letter

July 5, 2018

Col. Paul J. Hoerner
U.S. Air Force
Beneficiary Advisory Panel Chair
7700 Arlington Boulevard, Suite 5101,
Falls Church, VA 22042–5101
Email: dha.ncr.health-it.mbx.baprequests@mail.mil

Re: Pancreatic enzyme replacement therapy formulary recommendations, Uniform Formulary Beneficiary Advisory Panel meeting July 12, 2018

Dear Col. Hoerner,

The Allergan Chief Medical Office is aware that changes to the Uniform Formulary regarding pancreatic enzyme replacement therapy (PERT) will be discussed at the meeting on July 12, 2018. Allergan is the maker of Zenpep (pancrelipase), a combination of porcine-derived lipases, proteases, and amylases indicated for the treatment of exocrine pancreatic insufficiency (EPI) due to cystic fibrosis or other conditions. The P&T Committee is recommending that Zenpep be designated as non-formulary and non-step preferred.

This formulary change could lead to changes in therapy for Department of Defense patients currently treated with Zenpep, which could impact their health status. Patients needing PERT require individualized dose titration in order to achieve maximum therapeutic benefit. As stated in the FDA-approved labeling for Zenpep and other PERT products, "there is great inter-individual variation in response to enzymes; thus, a range of doses is recommended." As noted in the P&T Committee recommendations, Zenpep has the largest number of dosage strengths available of any of the PERT products.

Furthermore, FDA-approved labeling indicates that pancrelipase products (e.g. Zenpep) are not interchangeable. Should the formulary change be approved, there could be many patients forced to switch products, possibly impacting patient safety and outcomes. In the interest of patient safety and in consideration of the disruption in therapy patients may experience, Allergan respectfully requests that, regardless of any formulary changes in the PERT category, patients currently receiving Zenpep be allowed to continue this therapy. This option creates a pathway for patients with EPI who are currently well managed on Zenpep to avoid the need for titration onto a new product, which may subsequently impact symptoms and outcomes.

If I can provide any additional information or if you or the committee have any questions, please do not hesitate to contact me at phillip.jennings@allergan.com.

Respectfully Yours,

Phillip Jennings, PharmD
Managed Care Scientific Director
Allergan Chief Medical Office

Appendix D **07/12/2018 BAP Meeting**

Avadel Public Comments

At some point this morning you will consider the utilization management recommendation of the DoD P&T Committee with regard to Noctivan. (desmopressin acetate nasal spray .83mcg and 1.66mcg doses) for the treatment of nocturia due to nocturnal polyuria.
There are several DoD P&T Committee recommendations that are inconsistent with Noctiva's approved label. I will reserve addressing those for any presentation related to class review.

I am asking today that you consider seriously a few practical points in recommending to the Secretary of Defense NOT adopting the recommendations of the DoD P& T Committee with regard to its initial assessment of Noctiva ™. This is specifically with the safety of our troops and other beneficiaries at heart. Trusting the TRICARE provider to manage with diligence to the Noctiva™ label.

In its Summary Review for Regulatory Action, FDA comments regarding Noctiva TM: "A Boxed Warning is appropriate because severe hyponatremia can be life-threatening and is very serious in proportion to the potential benefit of the drug, and because hyponatremia can be mitigated with interventions (e.g., periodic monitoring of serum sodium)."

This warning is common to all market-approved forms and brands of desmopressin. The risk of severe hyponatremia is, in fact, the sole safety concern in the use of any brand or form of desmopressin. The safety of Noctiva TM has been studied with greater rigor, over a longer period of time, than any other desmopressin product.

First

- FDA approved labeling recommends, for patients 65 years and older, with concern for the risk of hyponatremia, initiating therapy at .83mcg and allowing an increase to 1.66mcg, if needed, provided the serum sodium has remained normal"
- Possibly an oversight, the DoD P&T Committee recommendation limits to patients 65 years and older the .83mcg dose, exposing them to potential of risk without the potential benefit of titration to an efficacious dose.

Neither HealthNet, Express Scripts nor Humana nor, the Criteria of any other insurer to date, impose this limit, likely with that logic in mind.

Second

The limitation of use, "not studied in patients younger than 50 years of age", is a negotiated feature of the pivotal trial design, a limitation of THE STUDY, requested by FDA, to ensure the evaluation of safety in an age group more at risk of hyponatremia. This is confirmed repeatedly in writing by FDA not to preclude clinical use in patients under the age of 50 but to ensure adequate study in patients who are at greater risk.

HealthNet Commercial criteria recognizes the safety-enhancing purpose of this study limitation and imposes no such limit (no >/= 50) in its clinical criteria. Neither Express Scripts nor Humana criteria are published.

Finally

> The TRICARE formulary includes all other forms and brands of desmopressin without governing criteria for use. There is no limitation on what these products might be prescribed for. There is no limitation on whom they might be prescribed to. The intranasal forms of these products are delivered in minimum doses that range from 6 to 90 times that of the highest dose of Noctiva TM.

There is no comparative safety data and I hope that none would be necessary for your understanding that the risk of hyponatremia -the sole safety concern with these products -would not diminish with the TRICARE provider prescribing one of the unrestricted desmopressin products in place of Noctiva ™ in treating a beneficiary's nocturia due to nocturnal polyuria.

I am asking your unanimous recommendation to the Secretary of Defense, in the interest of the safety of the beneficiary, for the rejection of the Noctiva ™ PA criteria you will consider today.