EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel (BAP)
January 8, 2020

UNIFORM FORMULARY DRUG CLASS REVIEWS

I. UF CLASS REVIEWS

A. PHOSPHODIESTERASE-5 (PDE-5) INHIBITORS

- **PDE-5 Inhibitors – UF/Tier 4/Not Covered Recommendation**

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

  - UF and step-preferred
    - sildenafil (generic Viagra only)
  - UF and non-step-preferred
    - tadalafil (generic Cialis only)
  - NF – none
  - This recommendation includes step therapy in new users, which requires a trial of generic sildenafil before generic tadalafil.
  - Tier 4/Not Covered
    - avanafil (Stendra)
    - vardenafil ODT (Staxyn, generics)
    - vardenafil tablets (Levitra, generics)
    - Brand Viagra
    - Brand Cialis

  When considering the PDE-5 inhibitor candidates for Tier 4/Not Covered status, the P&T Committee considered the information outlined in the interim rule, Section 702(b)(10) of the NDAA 2018 published on December 11, 2018, and found at: https://www.federalregister.gov/documents/2018/12/11/2018-26562/tricare-pharmacy-benefits-program-reforms.

  For the five PDE-5 inhibitors recommended for Tier 4/Not Covered status, the P&T Committee concluded they provide very little to no additional clinical effectiveness relative to the other PDE-5 inhibitors. Overall, the P&T

Committee felt that the needs of TRICARE beneficiaries could be met by the formulary PDE-5 inhibitors, generic sildenafil, and generic tadalafil.

- **PDE-5 Inhibitors – Manual Prior Authorization (PA) Criteria**

Automated step therapy requirements currently apply to the class for ED, requiring a trial of sildenafil (Viagra) first. The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 0 absent) removing the automation, and requiring manual PA criteria for generic sildenafil and generic tadalafil. The manual PA will continue to require a trial of generic sildenafil prior to generic tadalafil for ED in new users. The age and gender edit for males 40 years and older will continue to apply. PA will continue to be required for ED in males younger than age 40 years and for the off-label uses.

The PA criteria are as follows in bold and strikethrough:

a) Generic sildenafil tablets

~~Automated and~~ Manual PA criteria apply to all new users of generic sildenafil. Note that brand Viagra is not covered by TRICARE.

Age and Gender edit: Coverage is approved for treatment of ED if the patient is a male aged 40 years or older.

Manual PA Criteria: Coverage is approved if the following criteria are met:
- Patient is older than 18 years of age AND
- Patient is less than 40 years of age and is being treated for ED of organic or mixed organic/psychogenic origin OR
- Patient is less than 40 years of age and is being treated for drug-induced ED where the causative drug cannot be altered or discontinued OR

Coverage is approved for the following non-ED uses requiring daily therapy:
- Use of generic sildenafil for preservation/restoration of erectile function after prostatectomy. PA expires after one year. OR
- Use of generic sildenafil for Raynaud's Phenomenon ~~OR~~
- ~~**Use of sildenafil for pulmonary arterial hypertension (PAH)**~~

Other non-FDA-approved uses are not approved, including use for females for the treatment of sexual dysfunction.
PA does not expire except as noted above following prostatectomy.

b) Generic tadalafil tablets

Manual PA criteria apply to all new users of generic tadalafil. Note that brand Cialis is not covered by TRICARE.

Note that the previous automation for the step therapy has been removed.

Manual PA criteria:

- Patient is older than 18 years of age AND
- Patient has tried generic sildenafil and has had an inadequate response or was unable to tolerate treatment due to adverse effects
  OR
- Treatment with generic sildenafil is contraindicated. OR
- Patient is less than 40 years of age and is being treated for ED of organic or mixed organic/psychogenic origin. The patient must try generic sildenafil first and is unable to use generic sildenafil due to reasons stated above (inadequate response or adverse events.) OR
- Patient is less than 40 years of age and is being treated for drug-induced ED where the causative drug cannot be altered or discontinued. The patient must try generic sildenafil first and is unable to use generic sildenafil due to reasons stated above (inadequate response or adverse events.) OR
- Use of generic tadalafil 2.5 mg or 5 mg for patients with BPH or BPH with ED meeting PA criteria requiring use of an alpha blocker [tamsulosin (Flomax) or alfuzosin (Uroxatral)] first unless there is a contraindication, inadequate response, or intolerable adverse effects with the alpha blocker

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

- Patient requires generic tadalafil for preservation/restoration of erectile function after prostatectomy. PA expires 1-year post-surgery.
- Use of generic tadalafil for Raynaud's Phenomenon ~~**OR**~~
- ~~**Use of tadalafil for pulmonary arterial hypertension (PAH)**~~

Other non-FDA-approved uses are not approved, including use for females for the treatment of sexual dysfunction.

PA does not expire except as noted above following prostatectomy.

- **PDE-5 Inhibitors – UF/Tier 4/Not Covered and PA Implementation Plan**

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 0 absent) 1) An effective date of the first Wednesday 120 days after signing of the P&T minutes at all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/Not Covered recommendations at 30 and 60 days prior to implementation.

Summary of Physician's Perspective:

One of the reasons for reviewing this drug class again is due to the entrance of generic products into the market.

With this recommendation, we will now have the two most popular PDE-5s available on the formulary, the generics for Viagra and Cialis. All the other products, including branded Viagra and Cialis will be Tier 4. Currently, only Viagra is on the formulary, with all the other products requiring a trial of Viagra first. For generic Viagra, men older than age 40 will not require a PA when used for ED, which we have had for several years. For generic Cialis, we will continue to require a trial of generic Viagra first.

The Tier 4 recommendation for this class includes the branded Viagra and Cialis products. The cost differences between the branded products and the generics is significant. Shortages of the generics are unlikely, as there are a large number of generics available from several manufacturers, including 9 generics available for Viagra, and 17 generics for Cialis. Currently, generic Viagra and Cialis together account for about 93% of the market share.

Five branded products (Viagra, Cialis, Stendra, Levitra and Staxyn) are recommended for Tier 4 status. However, in addition to moving generic Cialis from NF to UF status, we are also increasing the quantity limit from 6 tablets a month to 10 tablets a month.

Some additional reasons to have multiple candidates for Tier 4 status include the low persistence rates in the class. DoD data shows only 56% of patients remain on a PDE-5 after 4 months, which drops to 34% at 12 months and 17% at 24 months. This low persistence may partly reflect the fact that these products are used on an "as needed" basis, and not on a chronic basis.

The Tier 4 recommendation will affect about 7% of the patients on a PDE-5 inhibitor, or around 10,000 patients out of the total of over 144,000 patients. The implementation period will be 120 days, and we will send out letters at 60 days and 30 days before implementation. Overall the main goal here is to switch patients to generic Viagra and generic Cialis.

One last comment about all the Tier 4 drugs that have been reviewed so far since the February 2019 meeting, the P&T Committee will be re-evaluating Tier 4 status approximately one year after implementation, to look for any clinical or cost consideration that would warrant changing Tier 4 status.

Approximately 20000 patients who receive tadalafil may benefit from a reduced copay as this agent will move from NF to UF.

Summary of Panel's Questions and Comments:

Mr. DuTeil asks if current users are required to complete the step-preferred criteria. He believes the patient and provider should make the decision regarding which medication (tadalafil or silenafil) is best for the patient.

Dr. Allerman responds, the new prior authorization criteria only refers to generic tadalafil. The P&T committee recommended all others drugs move to Tier 4. If the patient has a current prior authorization in place and is currently receiving generic tadalafil, they are not required to complete the step. However, if the patient is currently on branded Cialis, which is moving to Tier 4, a trial of either generic sildenafil or generic tadalafil is required after fulfilling the prior authorization

Mr. DuTiel clarifies, if the patient is on one of the medications moving to Tier 4, the patient is required to repeat the step preferred process.

Dr. Allerman responds that is correct.

Mr. Hostettler asks if Viagra has a daily indication.

Dr. Allerman responds Viagra does not have a daily indication. She explains that Cialis, generic tadalafil, is moving from non-formulary to formulary status. The current prior authorization, which has been in effect since 2011, and the current prior authorization for once daily use, are a part of the prior authorization criteria. Because the data shows that other drugs for treating an enlarged prostate are equally or more effective than the PDE-5 inhibitors, the PA requires the use of an alpha blocker first.

Mr. Hostettler clarifies the PA criteria requires a trial of sildenafil first regardless of whether the patient is using Viagra daily which does not have a daily indication.

Dr. Allerman responds it is a part of the prior authorization criteria. The PA criteria for sildenafil is automated PA for males over 40 with ED. If the patient wants the once daily, for BPH, they have to fill out the manual prior authorization.

Ms. Hostettler asks and skip sildenafil?

Dr. Allerman responds, the trial of sildenafil is not required as long as the patient has tried an alpha blocker. This is not a change, the PA has been in place since 2011.

Dr. Peloquin asks if the patient is required to go through the step when transitioning from a brand name to the generic. More specifically, if the

patient is on brand name Cialis, is the patient required to complete the PA or go through the step to transition to the generic.

Dr. Allerman responds the system would recognize or consider the change from brand to generic as a new user. Yes, the patient would be required to complete the PA criteria for generic sildenafil. If the patient is already on the generic, tadalafil, the step is not required. The majority of the patients impacted by the decision are on generic tadalafil

Mr. Hostettler asks how many of the 10,000 patients are on branded medications

Dr. Allerman states approximately 2,500 are on branded Cialis.

Mr. Hostettler asks if the patients on branded Cialis are automatically placed on the generic. Are they required to repeat the process? He further states that grandfathering these patients will solve the problem for 25% of the population affected without any impact to the MHS.

Dr. Allerman responds we will follow-up and look at a process to operationalize or grandfather the patients on branded Cialis.

Mr. DuTeil expresses concerns about requiring the patient to repeat the PA process. If the patient is using one of the medications moving to Tier 4, why the patient and physician can't decide which of the UF products is best for the patient. Is there a difference between the two UF products?

Dr. Allerman responds if a male over 40 chooses the generic sildenafil there is no requirement to complete the PA. The patient will receive generic sildenafil. However, if the patient wants to try generic tadalafil, the PA requires a trial of generic sildenafil.

Mr. DuTeil asks if there is a difference between the two medications.

Dr. Allerman responds, generic sildenafil is a shorter half-life agent and generic tadalafil is a longer half-life agent. One provider (urologist) commented that both a longer and shorter acting agent be included on the formulary.

Mr. DuTeil asks if there are any similarities with all the medications on the formulary.

Dr. Allerman responds Viagra is a shorter acting agent and the preferred agent since 2005. The P&T Committee recommends moving generic tadalafil from non-formulary to formulary status. According to the clinical efficacy data,

the major guidelines and meta-analysis, they were all found to be therapeutically inter-changeable when treating the condition, ED.

Mr. Hostettler asks if the provider gave a rationale for placing both a longer and shorter acting agent on the formulary.

Dr. Allerman responds that it was their preference as a prescriber.

Dr. Khoury clarifies, if I am not mistaken, the provider did not provide a rationale beyond stating both a short and long acting were needed.

Mr. Hostettler asks the presenters to confirm that the provider definitely stated that both the shorter and longer acting agent was needed.

Dr. Khoury responds that one provider made the request to include a longer and shorter acting agent on the formulary and there were numerous comments.

Dr. McKeon interjects that the side-effects can be negative for air crews. So a shorter acting agent is better because the side effects do not impact the patient the following day. It has to do with readiness.

Dr. Allerman clarifies that we are discussing the generic Viagra which we have had available for years.

Dr. Khoury clarifies the disease state does not impact readiness specifically.

Dr. McKeon responds if treated correctly, the disease is taken care of, it is the side effect that cause an issue.

Mr. Hostettler states it appears there is a preference by one provider to place a longer and shorter acting agent on the Formulary but the recommendation requires all patients complete the step to get the shorter acting agent.

Dr. Allerman responds I don't believe they set a preference that the shorter acting is better than the longer acting.

Mr. Hostettler states, regardless, the step requires a trial of the shorter acting agent first. He further states that the longer and shorter acting agent should be UF and step preferred. The provider will make the decision about the best agent for the patient. Based on the clinical information presented, there does not appear to be a difference between the two medications. It was a provider decision to make the two medications available. I agree that both medications should be UF but I don't agree with the recommendation to require the trial of sildenafil to get tadalafil. Theoretically, there is no therapeutic difference.

Mr. DuTeil responds it does make sense because there are two different products that do two different things. In my opinion, that is a decision for a provider.

There were no more questions or comments. The Chair called for a vote on the UF/Tier 4/Not Covered Manual PA Criteria, and the UF /Tier 4/Not Covered and PA Implementation recommendations for the PDE-5 Inhibitors.

- **PDE-5 Inhibitors – UF/Tier 4/Not Covered Recommendation**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

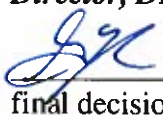
   These comments were taken under consideration prior to my final decision.

- **PDE-5 Inhibitors – Manual PA Criteria**

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

  **** The non-concurring Panel members believed that both agents should be step-preferred and provider decides which agent is best for the patient.**

  Director, DHA:

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

- **PDE-5 Inhibitors – UF/Tier 4/Not Covered and PA Implementation Plan**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

II. RAPID-ACTING INSULINS SUBCLASS

A. RAIs – UF/Tier 4/Not Covered Recommendation

1) The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) the following:

- UF and step-preferred
  - insulin aspart (Novolog)
  - insulin lispro (Humalog and authorized generic insulin lispro)

- NF and non-step-preferred:
  - insulin lispro (Admelog)
  - insulin glulisine (Apidra)
  - inhaled insulin (Afrezza)

- This recommendation includes step therapy (automated PA), which requires a trial of insulin aspart (Novolog) and insulin lispro (Humalog or authorized generic lispro) prior to use of the NF, non-step-preferred RAIs in all new and current users.

2) The P&T Committee recommended (9 for, 7 opposed, 0 abstained, 1 absent) the following:

- Tier 4/Not Covered
  - insulin aspart plus niacinamide (Fiasp)

The P&T Committee concluded that Fiasp provides very little to no additional clinical effectiveness relative to the other RAIs. Overall, the P&T Committee felt that the needs of TRICARE beneficiaries can be met by the other RAIs. The formulary alternatives include Novolog, Humalog, and authorized generic insulin lispro.

B. RAIs – Automated PA (Step Therapy) and Manual PA Criteria\

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) automated PA and manual PA criteria for all new and current users of the non-step-preferred RAIs, insulin lispro (Admelog) and insulin glulisine (Apidra). A trial of Novolog and either Humalog or authorized generic insulin lispro will be required first, unless the patient is using an insulin pump/CSII and is stabilized on Admelog or Apidra, or if they have tried and failed the step-preferred insulins.

Existing manual PA criteria apply to inhaled insulin (Afrezza). The P&T Committee recommend updating the manual PA criteria requiring the patient to have tried and failed Novolog and Humalog or authorized generic insulin lispro in all new and current users. Note that Afrezza will not be included in the automated step therapy criteria.

The PA criteria are as follows, with the changes highlighted in bold and strikethrough:

a. Inhaled insulin (Afrezza)

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

Coverage is approved if all the criteria are met for non-smoking patients with either:

Type 1 Diabetes Mellitus (diagnosed)

- **Patient has tried and failed (defined as a failure to achieve hemoglobin Alc < 7% in 90 days) with insulin aspart (Novolog)**
- **Patient has tried and failed (defined as a failure to achieve hemoglobin Alc ≤ 7 % in 90 days) with insulin lispro (Humalog or authorized generic insulin lispro**
- ~~Failure to achieve hemoglobin Alc ≤ 7 % in 90 days of use of a rapid or short acting subcutaneous (SC) insulin product or clinically significant adverse effects experience with SC rapid or short acting insulin unexpected to occur with inhaled insulin~~
- Afrezza is used as adjunctive treatment to current basal insulin therapy
- Spirometry testing [baseline forced expiratory volume in the first second (FEV_1)] has been performed upon initiation of therapy, with repeated FEV_1 at 6 months after initiation and repeated annually thereafter
- Patient does not have a contraindication to Afrezza (e.g. hypoglycemia, chronic lung disease [asthma, chronic obstructive pulmonary disease (COPD)], hypersensitivity to regular human insulin, or any Afrezza excipients)

Type 2 Diabetes Mellitus (diagnosed)

- **Patient has tried and failed (defined as a failure to achieve hemoglobin Alc < 7% in 90 days) with insulin aspart (Novolog)**
- **Patient has tried and failed (defined as a failure to achieve hemoglobin Alc ≤ 7 % in 90 days) with insulin lispro (Humalog or authorized generic insulin lispro**
- ~~Failure to achieve hemoglobin Alc ≤ 7 % in 90 days of use of a rapid or short acting subcutaneous (SC) insulin product or clinically significant adverse effects experience with SC rapid or short acting insulin unexpected to occur with inhaled insulin~~
- Patient has had failure of or clinically significant adverse effects to two oral anti-diabetic agents (i.e., sulfonylurea, TZD, DPP-4 inhibitor, or **SGLT2 inhibitor**) if metformin is contraindicated
- Spirometry testing [baseline forced expiratory volume in the first second (FEV1)] has been performed upon initiation of therapy, with repeated FEV1 at 6 months after initiation and repeated annually thereafter

- Patient does not have a contraindication to Afrezza (e.g. hypoglycemia, chronic lung disease [asthma, chronic obstructive pulmonary disease (COPD)], hypersensitivity to regular human insulin, or any Afrezza excipients)

Non-FDA-approved uses are not approved.

PA does not expire.

b. Insulin glulisine (Apidra) and insulin lispro (Admelog)

Step therapy and manual PA criteria apply to all new and current users of Apidra and Admelog.

Automated PA Criteria: The patient has filled a prescription for insulin aspart (Novolog) and insulin lispro (Humalog or authorized generic lispro) at any MHS pharmacy point of service [military treatment facility (MTFs), retail network pharmacies, or mail order] during the previous 720 days.

AND

Manual PA Criteria if automated criteria are not met:

Note: Novolog, Humalog, and the authorized generic insulin lispro are DoD's preferred RAIs. If the prescription is for Novolog, Humalog, or the authorized generic insulin lispro, PA is not required.

- If automated criteria are not met, Apidra or Admelog is approved if all criteria are met:
  - Patient has diabetes AND
    - Patient has tried and failed insulin aspart (Novolog) AND
    - Patient has tried and failed insulin lispro (Humalog or authorized generic insulin lispro)
      OR
    - Patient is using an insulin pump/continuous subcutaneous insulin infusion (CSII) and is stabilized on insulin glulisine (Apidra) or insulin lispro (Admelog)

Non-FDA-approved uses are not approved

PA does not expire

C. RAIs – Removal of Authorized Generic Insulin Lispro Manual PA Criteria

The authorized generic insulin lispro entered the market in April 2019, and manual PA criteria requiring a trial of Humalog first was implemented in May 2019. The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) removing the manual PA on authorized generic lispro, as it is no longer cost advantageous.

D. RAIs – UF/Tier 4/Not Covered and PA Implementation Plan

The P&T Committee recommended 1) an effective date of the first Wednesday after a 150-day implementation period, and no earlier than July 1, 2020 in all points of service and, 2) DHA send letters to beneficiaries who are affected by the UF/Tier 4 and PA. Patients affected by the Tier 4 recommendation will receive letters at 90, 60, and 30 days prior to implementation.

Summary of Physician's Perspective:

This is the first time we're reviewing the Rapid Acting Insulins. However, both Novolog and Humalog have been available in DoD dating back to 1999. We are now seeing new products enter the market, which was part of the reason for the class review.

The Committee was unanimous in recommending step therapy for the class. Novolog and Humalog will be on the formulary and step-preferred, with no Prior Authorization required. Admelog, Apidra and Afrezza will all be non-formulary and non-step preferred and will require a trial of both Novolog and Humalog first in all patients.

The inhaled insulin Afrezza will remain non-formulary. While the Committee did acknowledge the novel administration route, patients will still require injections of basal insulin (like Lantus), which significantly limits any perceived potential benefits of Afrezza. There are additional criteria in the Afrezza PA due to the risks in patients with underlying pulmonary disease.

The formulary decision to have Novolog and Humalog as the two preferred products is very similar to the current status, and these two insulins make up over 97% of the current market share. There is very little utilization of the non-preferred products, so the Committee felt there would be less patient and provider abrasion, while maximizing cost savings. Also, having two products as step-preferred decreases the risk if a shortage of one of the preferred insulins were to occur.

Since the PAs for Apidra, Admelog and Afrezza will now be "no grandfathering" scenarios where new and current users will be affected, we will be adding this to the "safety net" program managed by ESI, to help ensure that patients don't "fall through the cracks". This program will identify patients who have not received a prescription fill after an initial reject occurs and both the provider and patient will receive follow-up letters.

There was discussion on the Tier 4 status recommendation for Fiasp. The Committee members voting against the Tier 4 recommendation were due to the provider survey which found there was not unanimous agreement from endocrinologists that Fiasp should be Tier 4, and concerns that a patient could walk away from the pharmacy counter without receiving their insulin. However, the reasons for having this product designated as Tier 4 were due to the fact it has the same active ingredient as Novolog, with only Vitamin B3 added, and that it has not been shown to have a clinically significant difference in blood glucose values than Novolog, along with cost. Several commercial health plans also have Fiasp excluded from formulary coverage.

For the implementation period, the Committee recommended 150 days after signing, because of the Tier 4 recommendation for Fiasp. We will send letters to the patients affected by the UF to NF changes (Admelog and Apidra), the updated "no grandfathering" PAs (Admelog, Apidra and Afrezza), and to patients currently receiving Fiasp. The patients affected by the Tier 4 change for Fiasp will get three letters this time– one at 90 days prior to implementation, one at 60 days and then at 30 days, if they are still on Fiasp. As of late December, there were about 175 patients on Fiasp in the DoD.

Summary of Panel's Questions and Comments:

Mr. Hostettler states the Panel was assured that Tier 4 would be judiciously used and minimal products affected. I have been attending this meeting, in some manner, since its inception and I have never seen a 9-7 vote from the P&T Committee. Although there were seven dissenting votes, the P&T Committee proceeded with moving this product to Tier 4. As a beneficiary, I am very concerned. Why not place the medication on step therapy or require a prior authorization.

Mr. DuTeil concurs with Mr. Hostettler's comments regarding the P&T Committee vote. Although he has not served on the Panel as long, rarely is there more than one (1) person objecting to a change that has been approved by the P&T Committee. It is obvious, the current users will not be able to afford the drug once it moves to Tier 4 status. He asks for a rationale or an alternative that would satisfy the seven P&T Committee members that opposed the vote as far as combinations?

Dr. Khoury responds the P&T Committee vote was 9-7. The endocrinologist and seven committee members believed Fiasp should remain formulary and available. The Committee sees the full gamut of data provided regarding the clinical and cost effectiveness. The same data is not under the preview of or available to the Panel. In spite of the clinical concerns about this specific disease state, a majority of Committee members believed the clinical and cost effectiveness of Fiasp warranted the Tier 4 recommendation. The data showed no clinical differences, very little to no clinical advantage to the other drugs available and the cost effectiveness is of such a concern that a majority of the Committee recommended

placement on Tier 4. Your comments are valid and will be forwarded to the Director, DHA for consideration.

Ms. Buchanan also concurs with her colleagues. She asks if current beneficiaries can continue using Fiasp. There must have been some reason the providers prescribed the drug for the patients. Is there any data that shows they actually tried other medications prior to being placed on the drug? Recognizing that it is only 175 patients but we are talking about diabetes, this can be a life or death decision.

Mr. Hostettler states this decision impacts new and current users. This is a disease that has ramifications far beyond the drug cost. This recommendation requires beneficiaries, whose disease state is stable, to repeat the step. I don't understand why the Committee is taking such draconian steps. As stated, we aren't provided the same data briefed to the P&T Committee. If there is a compelling reason for the decision, please share it with the Panel rather than asking us to trust you. In my opinion, the current users should be grandfathered.

Dr. Dager asks about available tools such as step therapy or a prior authorization to make the medication available to patients.

Dr. Khoury responds he will address some of the sentiments and concerns raised. To clarify, the decision or recommendation to move a drug to Tier 4, cannot include step therapy or a prior authorization. Each is a separate tool and process. We can take your comments for consideration and potentially discuss other options. We did look at prior utilization tendencies of those patients that were prescribed Fiasp, the data showed that they hadn't tried all the formulary alternatives. Because this is a very small subset, I hesitate to arrive at any conclusions from the data. The data is not adequate enough to arrive at a valid conclusion.

Mr. Hostettler appreciates the utilization is low. If I am not mistaken, it was previously stated that the endocrinologists dissented on the vote. Those are the experts in this area and I can't understand why we are ignoring the experts' comments not to mention the seven dissenting votes.

Dr. Khoury clarifies the comments were from the endocrinologist and the P&T committee members provided the dissenting votes.

Dr. Piirainen asks if data is available on the number patients who were using Fiasp in a pump.

Dr. Allerman responds we did not look at that.

Dr. Piirainen asks if there was any consideration regarding members who may already be stable on an insulin pump with Fiasp as with other PAs for the other non-formulary RAIs.

Dr. Allerman responses we would have to conduct a higher level analysis to actually look at the patients that have Type 1 diabetes and then some type of claim for a pump.

Col Hoerner states I would share that the P&T committee had more information that you have and that was the vote that came out of it. Because it was a majority of committee members, the recommendation was accepted.

Dr. Bertin states he shares the comments of the other Panel members. He asks if the Panel members can concur with all aspects of the recommendation except for the Tier 4.

Col Hoerner responds no. The Panel must vote on the recommendation as written. Either the Panel agrees with the recommendation or they don't. As previously stated, your questions and comments will be presented to the Director, DHA for consideration.

Mr. DuTiel interjects that he understands the Chair's question. It appears that the Panel will non-concur with this recommendation and we don't want to delay the other changes.

Col Hoerner reiterates that the information is recorded into the record and presented to the Director, DHA for consideration.

Dr. Peloquin comments that the language regarding the automated step and the manual PA criteria is confusing. According to the recommendation, the automated PA and manual PA require new and current users to try the NF and non-step-preferred agents. Will they continue on therapy because they are on the product? Because it is a 720 day look-back starting at that point, will the patient be required to repeat the step? The patient has a history of the drug. If the look back is 720 they are essentially grandfathered.

Dr. Khoury responds they will not be grandfathered and they will have to try the one of the step-preferred agents.

Dr. Peloquin asks Dr. Khoury to address the automated PA and manual PA criteria with the Panel.

Dr. Khoury responds, we extended that typical look back to reflect this specific disease state. Typically we would do a 365 day look back. Because of this disease state, it was expanded to capture that the patient has tried the alternatives. If the

patient meets the criteria, they can pass through that 720 day look back in the automated PA.

Mr. Hostettler asks if there is a standard process to seamlessly transition a patient from a medication where the disease-state is stable and require the patient to repeat the process for a trial of Novolog or Humalog. Because this is a unique disease, I am concerned that the patent will be forced to make numerous trips to his/her physician, repeat labs/test in an effort to maintain a stable disease state. This incurs cost to the MHS outside of drug acquisition cost.

Dr. Khoury responds this is a unique disease state. Unlike the PDE-5, where someone can get one prescription and it potentially lasts a year, this one requires engagement with the provider on a regular basis. A Type 1 diabetic is in contact with the provider on a frequent and regular basis. I would also say that a Type II diabetic sees their provider every 3-6 months to manage all the chronic disease state issues that arise in that disease state. In response to your question regarding the frequency in which a Type I or Type II diabetic is likely engaging in care, there is a high likelihood they are seeing the provider on a regular basis. To prepare the patients impacted by the decision, we are sending out three letters at varying times during the implementation period. We are trying to increase awareness of the change as well as provide ample time and opportunity to ensure the patient can transition to the new medication without causing an issue with their disease state. We also believe that it will be easy to the patient to make the switch and in some cases preferable because: (1) the decision does not impact tens of thousands of patients; (2) Novolog and Humalog are clinically similar to the Admelog and (3) there is no clinical difference; and (4) alternate dosage forms are available in UF and step preferred products. Additionally, the pens, vials and cartridges are available in preferred products but not necessarily available in the alternative agents. Switching to the preferred medication may be a more preferable outcome for the patients who were prescribed the medication because their provider was not aware there was a better option available. As discussed, every benefit is different. The provider may prescribe a certain type of agent for any number of reasons. This recommendation might encourage a shift to something that is a better outcome for the patient to also include a lower copay.

Mr. Hostetler states that he understands. Regardless, a patient impacted by the decision may not agree with you. There were two comments regarding pumps that appear to have not been taken into account. In my opinion, changing the criteria to new users would ease my concerns.

Dr. Khoury responds, if the pumps are an issue, that the pumps were taken into consideration on the PA.

Mr. Hosteller replies the pumps were not taken into consideration for the Tier 4 products. In my opinion, this decision is putting patients at risk by forcing patients in a stable condition to change their therapy. In my opinion, changing the PA

criteria to new users is a better option. We can better manage a new patient, in an unstable condition within the system because there is no interruption to their therapy.

Dr. Peloquin asks how many patients meet the criteria in the automated step. For instance, if 175 patients are impacted by the decision and 100 meet the automated step criteria, the population impacted decreases.

Dr. Khoury responds I don't have the exact numbers but the data reviewed by the committee suggested that most hadn't met the step. The implementation period provides ample opportunity to shift to the formulary step-preferred agent. This benefits the patient because the lower co-pay applies. The patient may be paying a higher co-pay because the provider and patient is not aware that an alternative is available.

Dr. Peloquin asks for the number of beneficiaries using the non-formulary and non-step preferred.

Dr. Khoury responds that there are 1,000 beneficiaries on Apidra, 125 using Admelog 125, and 87 using Afrezza. This is the number of beneficiaries using each agent at the time of the review. This is out of a total of 56,000 patients that require these agents. The vast majority are on Novolog and Humalog.

Mr. Hostettler responds his concerns go away if the PA criteria is changes to new users. The unique user affected by the Tier 4 decision is low.

Ms. Buchanan raises an issue of concern regarding provider education. There was a reason the providers prescribed the drug. Are they new to the medical practice? Did a pharmaceutical drug salesman get to them? Bottom line the education needs to be in place.

Mr. Hostettler asks for a clarification regarding the PA criteria for Afrezza. It states that coverage is approved it all criteria are met for non-smoking patients. Why the differentiation?

Dr. Khoury responds the concern is the specific issues regarding the inhalation aspect of the drug.

Dr. Allerman states that inhaled insulin Afrezza causes pulmonary problems, which is why it should not be used by smokers.

Mr. Hostettler adds the significant risks involved to the patient is recognized in the implementation plan. That is why you are sending 3 letters over the 150 days. The criteria should only be new users!

There were no more questions and comments from the Panel. The Chair called for a vote on the UF/Tier 4/Not Covered Recommendation, Automated (Step Therapy) Manual PA Criteria, Removal of Authorized Generic Insulin Lispro Manual PA Criteria and UF/Tier 4/Not Covered recommendations for the RAI's.

- **RAI's – UF/Tier 4/Not Covered Recommendation**

  Concur: 0 Non-Concur: 8 Abstain: 0 Absent: 1

  ****The Panel agrees with the Specialist and the 7 dissenting votes on the P&T committee**

  Director, DHA:

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

- **RAI's – Automated (Step Therapy) Manual PA Criteria**

  Concur: 0 Non-Concur: 8 Abstain: 0 Absent: 1

  **** The Panel believes that the criteria should only be new users**

  Director, DHA:

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

- **RAI's – Removal of Authorized Generic Insulin Lispro Manual PA Criteria**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

- **RAI's - UF/Tier 4/Not Covered and PA Implementation Plan**

  Concur: 7 Non-Concur: 1 Abstain: 0 Absent: 1

  **** The non-concurring Panel member does not believe it should go forward as new and current users. No tier 4 and only new users.**

  Director, DHA:

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

III. NEWLY APPROVED DRUGS

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

1. Newly Approved Drugs per 32 CFR 199.21(g)(5) – UF/Tier 4/Not Covered Recommendation

The P&T Committee recommended for groups 1 and 2: (16 for, 0 opposed, 0 abstained, 1 absent); and group 3: (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- UF:
  - bremelanotide injection (Vyleesi) – Miscellaneous gynecological agent for Hypoactive Sexual Desire Disorder (HSDD)
  - darolutamide (Nubeqa) – Oral oncologic agent for non-metastatic castration-resistant prostate cancer (nmCRPC)
  - entrectinib (Rozlytrek) – Oral oncologic agent for lung cancer
  - fedratinib (Inrebic) – Oral oncologic agent for myelofibrosis
  - glucagon injection (Gvoke Hypopen and Pre-filled Syringe) – Binders-Chelators-Antidotes-Overdose Agent for severe hypoglycemia
  - glucagon nasal spray (Baqsimi) – Binders-Chelators-Antidotes-Overdose Agent for severe hypoglycemia
  - lamivudine/tenofovir disoproxil fumarate (Temixys) – Antiretroviral combination for human immunodeficiency virus (HIV)
  - midazolam nasal spray (Nayzilam) – Anticonvulsants-antimania agent for seizures
  - pexidartinib (Turalio) – Oral oncologic agent for tenosynovial giant cell tumors
  - segesterone acetate/ethinyl estradiol vaginal ring (Annovera) – Miscellaneous contraceptive agent
  - selinexor (Xpovio) – Oral oncologic agent for relapsing remitting multiple myeloma

- semaglutide oral tablet (Rybelsus) – Oral glucagon-like peptide-1 receptor agonist for type 2 diabetes mellitus in adults
- tiopronin extended release (Thiola EC) - Miscellaneous urinary agent for cystinuria

- NF:

  - amlodipine oral suspension (Katerzia) – Calcium channel blocking agent in an oral suspension for hypertension
  - duloxetine extended-release (Drizalma Sprinkle) – Antidepressants and non-opioid pain syndrome, serotonin-norepinephrine reuptake inhibitors (SNRIs)
  - istradefylline (Nourianz) – Parkinson's agent for off episodes
  - lefamulin (Xenleta) – Antibiotic for community acquired bacterial pneumonia (CABP)
  - pitolisant (Wakix) – Sleep disorders: wakefulness promoting agent for narcolepsy
  - upadacitinib (Rinvoq) – Targeted Immunomodulatory Biologic (TIB) for rheumatoid arthritis

- Tier 4 (Not Covered):

  - formoterol/aclidinium (Duaklir Pressair) inhaler– Pulmonary-2 Agent for Chronic Obstructive Pulmonary Disease (COPD)

    a. Duaklir Pressair was recommended for Tier 4 status as it has little to no additional clinical effectiveness relative to similar long-acting muscarinic antagonist/long-acting beta agonist (LAMA/LABA) combination drugs; and the needs of TRICARE beneficiaries are met by alternative agents.
       - Formulary LAMA/LABA alternatives to Duaklir Pressair are umeclidinium/vilanterol (Anoro Ellipta), tiotropium/olodaterol (Stiolto Respimat), glycopyrrolate/indacaterol (Utibron Neohaler), and glycopyrrolate/formoterol (Bevespi Aerosphere).

  - sumatriptan nasal (Tosymra) – Migraine agents, Triptans

    a. Tosymra was recommended for Tier 4 status as it has little to no additional clinical effectiveness relative to similar nasal triptan migraine agents; and the needs of TRICARE beneficiaries are met by alternative agents.
       - Formulary alternatives to sumatriptan nasal (Tosymra) are sumatriptan nasal spray (Imitrex, generics); zolmitriptan nasal spray (Zomig); and sumatriptan nasal powder (Onzetra Xsail).

- tegaserod (Zelnorm) – Gastrointestinal-2 agent for constipation-predominant irritable bowel syndrome (IBS-C)

    a. Zelnorm was recommended for Tier 4 status as it has no clinical benefit relative to other agents approved for IBS-C and has significant safety concerns relative to other IBS-C drugs including cardiovascular and suicidality risks; and the needs of TRICARE beneficiaries are met by alternative agents.
        - Formulary alternatives to Zelnorm include linaclotide (Linzess), plecanatide (Trulance), and lubiprostone (Amitiza).

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

The P&T Committee recommended for groups 1 and 2: (16 for, 0 opposed, 0 abstained, 1 absent); and group 3: (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Applying manual PA criteria to new and current users of Drizalma Sprinkle, Nourianz, Rybelsus, Vyleesi, and Wakix.
- Applying manual PA criteria to new users of Inrebic, Nubeqa, Rozlytrek, Thiola EC, Turalio, and Xpovio.
- Targeted Immunomodulatory Biologic (TIBs): Applying the same manual PA criteria in new users of Rinvoq that are currently in place for the other non-step-preferred TIBs. Patients must first try adalimumab (Humira). Additionally, for Rinvoq a trial of tofacitinib (Xeljanz) or baricitinib (Olumiant) is required if the patient cannot be treated with Humira.

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

a) bremelanotide injection (Vyleesi)

Manual PA criteria applies to all new and current users of Vyleesi.

Manual PA Criteria: Vyleesi is approved if all criteria are met:
- Patient is ≥ 18 years
- Patient is a premenopausal woman with a documented diagnosis of acquired, generalized hypoactive sexual desire disorder (HSDD) as characterized by low sexual desire that causes marked distress or interpersonal difficulty
- Decreased sexual desire is NOT caused by:
    - Co-existing medical or psychiatric condition
    - Problems with the relationship
    - Effects of a medication or drug substance

- Patient has been informed that other treatment options, such as cognitive-behavior therapy, sexual therapy, or couples therapy, may provide benefit without the risk of side effects
- Patient does not have uncontrolled hypertension or known cardiovascular disease
- Patient has been counseled on the risks of focal hyperpigmentation (skin discoloration) and severe nausea
- Patient agrees to use effective contraception while taking Vyleesi

Non-FDA-approved are not approved.

PA expires in 3 months.

Renewal PA criteria: Coverage will be approved indefinitely for continuation of therapy if the patient has had documented improvement in symptoms without serious side effects.

b) darolutamide (Nubeqa)

Manual PA is required for all new users of Nubeqa.

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

- Note that Xtandi is the Department of Defense's preferred 2nd-Generation Antiandrogen Agent. The patient is required to try Xtandi first. OR
- Patient has a contraindication or has had an inadequate response or adverse reaction to Xtandi that is not expected to occur with Nubeqa AND
- Patient is ≥ 18 years AND
- Drug is prescribed by or in consultation with an oncologist or urologist AND
- Patient has diagnosis of non-metastatic castration-resistant prostate cancer (nmCRPC) AND
- The patient has had a negative CT scan of abdomen/pelvis and/or negative bone scan AND
- Prostate-specific antigen doubling time (PSADT) is ≤ 10 months

OR

- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy

Other Non-FDA-approved uses are not approved.

PA expires in 1 year.

Renewal criteria: Nubeqa is approved for 1 year for continuation therapy if all criteria are met:

- The patient continues to be metastases-free
- The patient has not progressed onto subsequent therapy (such as abiraterone)

c) Duloxetine delayed-release capsules (Drizalma Sprinkle)

PA criteria applies to all new and current users of Drizalma Sprinkle except PA does not apply to patients 12 years of age and younger (age edit)

Manual PA Criteria: Drizalma Sprinkle is approved if the provider explains why the patient requires duloxetine sprinkle capsules and cannot take alternatives.

Non-FDA-approved uses are not approved.
PA expires in 1 year.

Renewal PA criteria: No renewal allowed. A new prescription will require submission of a new PA.

d) Entrectinib (Rozlytrek)

Manual PA criteria apply to all new users of Rozlytrek.

Manual PA Criteria: Rozlytrek will be approved if all criteria are met:

- Patient is ≥ 12 years
- Drug is prescribed by or in consultation with an oncologist
- Patient has a diagnosis of either:
- ROS1(+) Metastatic Non Small Cell Lung Cancer or
- The patient has a solid tumor that meets all three of the following criteria:
- Has a neurotrophic tropomyosin receptor kinase (NTRK) gene fusion without a known acquired resistance mutation, and
- Is metastatic OR where surgical resection is likely to result in severe morbidity, and
- Has no satisfactory alternative treatments OR that has progressed following such treatment(s)
- The patient has had a recent evaluation of his/her left ventricle including ejection fraction
- The patient does not have decompensated congestive heart failure (CHF)
- The patient has had a recent uric acid level

- The provider is aware and has informed the patient of the risk of CHF development and exacerbation, myocarditis, neurotoxicity, fracture risk, hepatotoxicity, hyperuricemia, QT-prolongation, permanent visual impairment, and embryo-fetal toxicity
- Female patients will not breastfeed during treatment and for 1 week after cessation of treatment
- All patients (females AND males) of reproductive potential will use highly effective contraception during treatment and for at least 5 weeks or 3 months after cessation of treatment for females and males, respectively.
- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.

Other non-FDA-approved uses are not approved.

PA does not expire.

e) fedratinib (Inrebic)

Manual PA is required for all new users of Inrebic.

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

- Patient is ≥ 18 years
- Drug is prescribed by or in consultation with a hematologist/oncologist
- Inrebic will be used for intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis
- Provider acknowledges that serious and fatal encephalopathy including Wernicke's encephalopathy has occurred in patients treated with Inrebic. If thiamine deficiency is expected or confirmed, Inrebic should be discontinued immediately and the patient should receive emergent parenteral thiamine.
- The patient does not have vitamin B1 deficiency.
- The following labs will be assessed prior to starting Inrebic and periodically while the patient is taking Inrebic: thiamine (Vitamin B1), complete blood count (CBC) with platelets, serum creatinine and blood, urea nitrogen (BUN), hepatic panel and amylase and lipase
- Nutritional status will be assessed prior to starting Inrebic and periodically while the patient is taking Inrebic
- If the patient is female, she is not pregnant or planning to become pregnant.

- Female patients will not breastfeed during treatment and for at least 1 month after discontinuation.
- Females of reproductive potential will use effective contraception during treatment and for at least 1 month after discontinuation.
- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.

Other non-FDA-approved uses are not approved.

PA does not expire.

f) istradefylline (Nourianz)

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

Manual PA Criteria: Nourianz approved if all criteria are met:

- Patient is ≥ 18 years
- Patient has a diagnosis of Parkinson's disease
- Drug is prescribed by or in consultation with a neurologist
- Patient continues to experience wearing off periods, despite optimizing (e.g., increasing dose and daily frequency) carbidopa/levodopa therapy
- Patient is currently taking and will continue taking carbidopa-levodopa therapy
- Patient must try and fail an adequate trial of at least two drugs from any of the three classes:
  - Dopamine Agonist: pramipexole (Mirapex), ropinirole (Requip), rotigotine (Neupro)
  - MAO-B: rasagiline (Azilect), selegiline (Eldepryl)
  - COMT: tolcapone (Tasmar), entacapone (Comtan)

Non-FDA-approved uses are NOT approved, including restless legs syndrome.

PA does not expire.

g) pexidartinib (Turalio)

Manual PA is required for all new users of Turalio.

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

- Patient is ≥ 18

- Drug is prescribed by or in consultation with an oncologist
- Patient has symptomatic tenosynovial giant cell tumor associated with severe morbidity or functional limitations, is not amenable to improvement with surgery, and has not progressed on Turalio.
- Patient will be monitored for hepatotoxicity
- Prescriber is certified with Risk Evaluation and Mitigation Strategy (REMS) program
- Patient is enrolled in REMS program
- If the patient is female, she is not pregnant or planning to become pregnant.
- Female patients will not breastfeed.
- All patients (females AND males) of reproductive potential will use effective contraception during treatment and for 1 month after discontinuation in females and 1 week after discontinuation in males with female partners.
- The diagnosis IS NOT listed above but IS cited in the NCCN guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.

Other non-FDA-approved uses are not approved.

PA does not expire.

h) pitolisant (Wakix)

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

Manual PA Criteria: Wakix is approved if ALL criteria are met:

- Patient is ≥ 18 years
- Patient has a documented diagnosis of excessive daytime sleepiness associated with narcolepsy
- Narcolepsy was diagnosed by polysomnography or mean sleep latency time (MSLT) objective testing
- Drug is prescribed by a neurologist, psychiatrist, or sleep medicine specialist
- Patient is not concurrently taking any of the following:
  - Modafinil, armodafinil, or stimulant-based therapy, such as amphetamine or methylphenidate
- Patient must have tried and failed and had an inadequate response to modafinil
- Patient must have tried and failed and had an inadequate response to armodafinil
- Patient must have tried and failed and had an inadequate response to stimulant-based therapy (amphetamine or methylphenidate)

- Patient does not have a history of severe hepatic impairment
- Other causes of sleepiness have been ruled out or treated, including but not limited to obstructive sleep apnea

Non-FDA-approved uses are not approved (including but not limited to fibromyalgia, insomnia, excessive sleepiness not associated with narcolepsy, cataplexy, obstructive sleep apnea, major depression, Attention Deficit Hyperactivity Disorder (ADHD), or shift work disorder).

Not approved for use in children, adolescents, or pregnant patients
PA expires in 1 year.

Renewal PA criteria: No renewal allowed. When the PA expires, the next fill will require submission of a new PA.

i) selinexor (Xpovio)

Manual PA applies to new users of Xpovio.

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

- Age ≥ 18
- Drug is prescribed by or in consultation with an oncologist
- Xpovio will be used in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody
- Patient will be monitored for cytopenias including anemia, neutropenia, and thrombocytopenia
- Patient will be monitored for electrolyte disturbances including hyponatremia and hypokalemia
- Patient will be monitored for infection including upper respiratory infection and pneumonia
- Patients will be monitored for dizziness and altered mental status
- If the patient is female, she is not pregnant or planning to become pregnant.
- Female patients will not breastfeed.
- All patients (females AND males) of reproductive potential will use effective contraception during treatment and for at least 1 week after discontinuation.
- The diagnosis IS NOT listed above but IS cited in the NCCN guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.

Other non-FDA-approved uses are not approved.

PA does not expire.

j) semaglutide oral tablet (Rybelsus)

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

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

- Patient is ≥ 18
- Patient has a documented diagnosis of type 2 diabetes
- Patient has tried and had an inadequate response to metformin, or has a contraindication to metformin
- Patient must be able to adhere to the administration requirements (take on an empty stomach with no more than 4 oz. of water at least 30 min before the first meal of the day)
- Patient does not have a history of pancreatitis
- Patient does not have a personal or family history of medullary thyroid carcinoma (MTC)
- Patient does not have multiple endocrine neoplasia syndrome type 2 (MEN2)
- Patient and provider acknowledge that Rybelsus has not been shown to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease

Not approved for use in children or pregnant patients.

Non-FDA approved uses are not approved including weight loss (obesity) or type 1 diabetes mellitus.

PA does not expire.

k) tiopronin immediate-release (Thiola)/tiopronin delayed-release tablets (Thiola EC)

Note that PA criteria were also recommended for the original Thiola immediate release preparation.

Manual PA Criteria: Thiola or Thiola EC is approved if all criteria are met:

- Patient is ≥ 9 years

- Drug is prescribed by or in consultation with a nephrologist or urologist
- Patient has a documented diagnosis of severe homozygous cystinuria
- Patient has elevated urinary cystine concentration (> 250 mg/L) as demonstrated by a 24-hour urine test
- Patient has tried and failed treatment with all of the following conservative treatment measures:
  - High fluid intake ≥ 3 L/day
  - Urinary alkalization with potassium citrate or potassium bicarbonate
  - Diet modification with restricted protein and sodium consumption

Non-FDA-approved uses are not approved.

PA does not expire.

l) **upadacitinib (Rinvoq)**

Note that Humira is the DoD's preferred targeted biologic agent for rheumatoid arthritis.

Manual PA criteria applies to all new users of Rinvoq

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

- Patient is ≥ 18
- Patient has diagnosis of active rheumatoid arthritis
- Patient has had an inadequate response or an intolerance to methotrexate or other disease-modifying anti-rheumatic drugs (DMARDs)
- Patient has had an inadequate response to Humira OR
- Patient has experienced an adverse reaction to Humira that is not expected to occur with the requested agent OR
- Patient has a contraindication to Humira AND
- Patient has had an inadequate response to Xeljanz or Olumiant OR
- Patient has experienced an adverse reaction to Xeljanz or Olumiant that is not expected to occur with the requested agent OR
- Patient has a contraindication to Xeljanz or Olumiant that does not apply to Rinvoq AND
- Patient has no evidence of active tuberculosis (TB) infection
- Patient has no history of venous thromboembolic (VTE) disease
- Patient has no evidence of neutropenia (ANC <1000)
- Patient has no evidence of lymphocytopenia (ALC <500)
- Patient has no evidence of anemia (Hgb < 8)

- Patient is not taking Rinvoq concomitantly with other TIBs agents except for Otezla and other potent immunosuppressants (e.g., azathioprine, cyclosporine).

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 groups 1 and 2: 16 for, 0 opposed, 0 abstained, 1 absent); and group 3: 17 for, 0 opposed, 0 abstained, 0 absent) the following:

- **New Drugs Recommended for UF or NF Status:** An effective date upon the first Wednesday two weeks after signing of the minutes in all points of service.
- **New Drugs Recommended for Tier 4 Status Duaklir Pressair, Tosymra, and Zelnorm:** 1) An effective date of the first Wednesday after a 120-day implementation period at all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/Not Covered recommendation at 30 days and 60 days prior to implementation.

Summary of Physician's Perspective:

The Committee reviewed 22 new drugs, of which 13 were recommended for UF status, with 6 recommended for NF status, and 3 Tier 4/Not Covered candidates. Prior authorization criteria will apply to 12 of the drugs. Several drugs were recommended for PAs since criteria already apply for the class, including the 5 oncology drugs, the TIB product (Rinvoq), and the diabetes drug (Rybelsus). For the new drugs, whenever a PA is recommended, we do reach out to providers for their comments on potential criteria.

"No grandfathering," where both new and current users will be affected by the PA, is recommended for 5 of the drugs, including the Parkinson's disease drug Nourianz because the FDA originally denied approval due to concerns of lack of efficacy and limited efficacy data and the female sexual desire disorder drug Vyleesi - due to safety concerns. For the narcolepsy drug Wakix, there are several low-cost generic alternatives available, which is also the case for the antidepressant drug Drizalma Sprinkle.

There were three Tier 4 candidates recommended at this meeting.

- formoterol/aclidinium (Duaklir Pressair inhaler)

1. This drug is used for COPD and contains two ingredients; formoterol which is found in other inhalers, and aclidinium, which is available under the trade name "Tudorza" and has very low usage in the DoD.
2. Duaklir is given twice daily, which could affect adherence. The single ingredient inhaler Spiriva has extensive utilization in the DoD and is dosed once daily.
3. Feedback from pulmonologists supported Tier 4 status, and confirmed that there are unlikely any clinically significant differences between the products in relieving symptoms of COPD.

- sumatriptan Nasal (Tosymra)

1. Tosymra is a nasal sumatriptan formulation that has the same active ingredient and uses the same delivery device as Imitrex nasal spray.
2. This product used the data from the Imitrex nasal spray to gain FDA approval, and did not conduct any new clinical trials. There are three other nasal triptan products available.
3. Neurology specialists also supported tier 4 status.

- tegaserod (Zelnorm) for IBS –C

1. Zelnorm was previously off the market for 12 years, but is now available again.
2. This drug has a very narrow indication - it is only approved for treating women younger than 65 with constipation-predominant irritable syndrome. The Committee was concerned that although the trials used to gain FDA-approval showed statistically significant results compared to placebo, the clinical significance of the results is unclear.
3. The majority of the GI specialists we reached out to supported Tier 4 status for Zelnorm, and stated that the risk of heart attacks and stroke, and also suicide outweighed the benefits. However some GI specialists said it should be available as they wanted options for this difficult to treat condition of IBS. When the drug class was first reviewed in 2012, there were few drugs available for treating irritable bowel syndrome. Now, there are several products approved, that have wider FDA indications.

The agents under review in the newly approved drug program had nearly 60 post marketing studies that were identified in the approval letter published by the FDA. These ranged from studies analyzing drug interactions, pharmacokinetics, animal studies, to things such final overall survival data.

Summary of Panel's Questions and Comments:

Mr. Hostettler asks if there is an alternative or calcium channel liquid product for Kateriza (Amlodipine).

Dr. Allerman responds, amlodipine is one where the recipes are widely available and there is stability data available to support putting it in a solution. It is commercially available as well as an oral suspension or oral solution. We are handling this product the way we have previously established for these types of cardiovascular drugs.

Mr. Hosteller comments it is difficult for some cancer and thyroid patients to swallow pills. Rather than moving it to non-formulary, I would recommend moving it to uniform formulary with a PA requiring similar criteria. I believe this would be a better option for the patient.

Dr. Allerman responds, historically, we handle the oral liquid preparations for cardiovascular conditions by moving them to non-formulary without a prior authorization requirement. These agents are low utilization but we have looked at the utilization of a couple of agents that are now available in liquids.

Mr. Hostettler asks if a patient who has problems swallowing pills qualifies for UF with the lower co-pay.

Dr. Allerman responds they can apply for medical necessity to request a reduction in the co-pay.

Dr. McKeon comments we are requiring a woman to meet all of these prerequisite. One of the prerequisites states, "Decreases sexual desire is not caused by a co-existing medical or psychiatric condition. The next bullet states, "the patient has been informed that other treatment options, such as cogitative behavior therapy, sexual therapy, or couples therapy, may provide benefit without the risk of side effects. Those two bullets seem mutually exclusive to me.

Dr. Allerman responds the TRICARE Policy Manual summarizes treatment coverage for ED. There are only two drugs on the market for female sexual dysfunction. The first was Addyi and the second is Vyleese. The prerequisites are listed, because the profile for female sexual dysfunction is characterized by some cardiovascular effects.

Dr. McKeon asks about females who want to become pregnant.

Dr. Allerman states the reasons for that is the problem have not been studied in patients who are pregnant. The side effect alone by themselves are a concern. We have no data for pregnancy.

Dr. Khoury: This agent, Vyleesi, had 3 post marketing study requirements.

Mr. Hostettler comments the PA criteria for Wakix states that the patient must try and fail at least 3 other products and it expires in a year. If the patient has

met the PA criteria, what is the justification for requiring the patient to repeat it after a year?

Dr. Allerman replies the data shows that the provider will know if a patient is responds to therapy within 6 months. Requiring the patient to repeat the PA after a year, provides the opportunity for the physician to make a determination about whether the drug is working; whether something else would work better and to have a reassessment of how the patient is doing.

Mr. Hostetler clarifies, the assumption is that the patient may know that it is not working but they will take it any way.

Dr. Allerman answers Believe it or not, we do see that.

Dr. Piirainen refers to the language in the PA criteria for Wakix. It requires an "inadequate response" to the three alternatives but it does not call for or require a contraindication. Normally in the PA you have to either try it or there is a contraindication.

Dr. Allerman replies that is an oversight. We can add the contraindications.

Dr. Peloquin responds the PA criteria for Wakix also states, "Drug is prescribed by a neurologist, psychiatrist or sleep medicine specialist. The language normally states in consultation with.

Dr. Allerman replies the omission of "in consultation with" was intentional. The manual PA criteria states, "The patient has a documented diagnosis of excessive daytime sleepiness associated with narcolepsy. Because there is a potential to list non-labeled drugs, we don't list all the non-FDA approved drugs. That is why we to limit to potential specialists who would be prescribing drugs for narcolepsy.

Dr. Peloquin asks if the ability to collect data or ensure the sleep medicine specialists follows-up with a patient.

Dr. Allerman replies we have no way to go back and check that. It will depend on the system whether we can check with a sleep medicine specialist or not. For instance, if a prescription is going to a provider at the MTF, the pharmacists at the MTF filling the prescription will know the specialty of the physician at the MTF.

Dr. Khoury clarifies the providers in these specialties are often well known to MTF pharmacies and likely external points of service. This is more in general, there are not many in this sub-set of specialists. The pharmacists and pharmacies filling these prescriptions may know the provider. In the end the form relies on trust.

Mr. Hostettler comments rather than requiring a patient to use a formula to extemporaneously compound a tablet into a liquid, the FDA has an approved product and it should be used. In my opinion, we should support a product manufactured under Good Manufacturing standards allow patients access to the FDA-approved drug.

Dr. Piirainen asks if the PA criteria for Rinvoq will require evidence of a negative TB test within the last year as the other TIBs require a negative TB test within the past 12 months, for consistency, however prefer the current proposed language.

Dr. Allerman replies we discussed standardizing all the TIBS for those types of things in the label. We will take that back because we did try to standardize for all the cytopenias and the labels.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF/Tier 4/Not Covered, Manual PA Criteria, and UF and PA Implementation Plan recommendations for the Newly Approved Drugs per 32 CFR 199.21(g)(5)

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

  Concur: 7 Non-Concur: 1 Abstain: 0 Absent: 1

  ****The non-concurring Panel member suggests UF vs. NF for Katerzia an FDA approved product vs. an extemporaneously compounded one.**

  Director, DHA:

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

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

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

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

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

IV. UTILIZATION MANAGEMENT

I. UTILIZATION MANAGEMENT – NEW MANUAL PA CRITERIA

A. New PA Criteria – Newly Approved Drugs Not Subject to 32 CFR 199.21(g)(5)

New manual PA criteria were recommended by the P&T Committee due to a variety of reasons. The new manual PAs outlined below will apply to new users for the Parkinson's drug Neupro and the oncology drugs Venclexta and Zydelig, and to new and current users for the skeletal muscle relaxant chlorzoxazone, and the topical anesthetic cream.

1) Skeletal Muscle Relaxants and Combinations – Chlorozoxazone 375 mg and 750 mg (Lorzone, generics)

Chlorzoxazone 375 mg and 750 mg are new strengths approved via the Abbreviated New Drug Application (ANDA) pathway and thus do not qualify for review by the DoD P&T Committee under the innovator program. Chlorzoxazone 500 mg is a scored tablet and produced by several manufacturers. Skeletal muscle relaxants are not considered first-line therapy for musculoskeletal conditions. Cost-effective generic formulations of chlorzoxazone 500 mg and multiple comparable muscle relaxants (e.g., cyclobenzaprine, methocarbamol) are available on the UF without PA being required. PA criteria also apply to the chlorzoxazone 250 mg strength, from the November 2018 meeting.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for chlorzoxazone 375 mg and 750 mg (Lorzone, generics) in new and current users, due to significant cost differences compared with splitting the 500 mg tablets or using other generic muscle relaxants.

Manual PA Criteria: Coverage for chlorzoxazone 375 mg and 750 will be approved if all criteria are met:

- The provider explains why the patient requires chlorzoxazone 375 mg or 750 mg and why the patient cannot take chlorzoxazone 500 mg tablet.

Non-FDA-approved uses are NOT approved.

PA does not expire.

2) **Anesthetic Agents: Local—Lidocaine-Tetracaine 7%-7% topical cream (Pliaglis, generics)**

This combination topical anesthetic cream is an authorized generic of Pliaglis and is approved for use prior to superficial dermatological procedures, including dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal. Prior to 2018, this product was restricted to use in the clinic setting by health care professionals. However, the "Not for Home Use" restriction was removed, as the manufacturer submitted a study supporting patient self-use. Numerous cost-effective topical anesthetics (e.g., lidocaine 4% cream, lidocaine 5% cream/ointment, and lidocaine-prilocaine 2.5%-2.5% cream [Emla]) are available that a patient could apply prior to a procedure.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for new users and current users over the age of 12 years, due to the availability of several cost-effective alternatives.

Manual PA Criteria: Coverage for lidocaine-tetracaine 7%-7% topical cream is approved if all criteria are met:

- The provider acknowledges that there are multiple formulary topical local anesthetics available for DoD beneficiaries without a PA including lidocaine 4% cream, lidocaine 5% cream or ointment, and lidocaine-prilocaine 2.5%-2.5% cream
- Drug is prescribed by or in consultation with a dermatologist or surgeon
- Not approved for use in back or joint pain
- Not approved for use in compounding
- Not approved for use as local anesthetic associated with cosmetic procedures including but not limited to dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal
- The provider must document the clinical rationale of why patient cannot take any of the formulary topical local anesthetics

Non-FDA-approved uses are NOT approved.

New PA required per prescription fill.

3) **Parkinson's Agents: rotigotine (Neupro) patch**

The P&T Committee has not previously reviewed the Parkinson's disease drug class. Rotigotine (Neupro) patch was marketed in 2012, and was designated as UF prior to the establishment of the Innovator Rule in August 2015. Although rotigotine is the only non-oral dopamine agonist, Parkinson's disease guidelines do not give a preference for any one agent over another. Cost effective generic formulations of oral pramipexole and ropinirole are available.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for new users, requiring use of an oral dopamine agonist first, unless the patient has swallowing difficulties.

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

- Age ≥ 18 years
- Patient has a diagnosis of:
  1. Parkinson's disease OR
  2. Moderate to severe primary restless legs syndrome
- Patient cannot swallow tablets due to a documented medical condition (i.e. dysphagia, oral candidiasis, systemic sclerosis, etc.) and not due to convenience OR
- Patient has tried and failed or has a contraindication to other dopamine agonist oral therapy:
  1. pramipexole (Mirapex) OR ropinirole (Requip)

Non-FDA-approved uses are NOT approved.

Prior authorization does not expire.

4) **Oral Oncologic Agents: venetoclax (Venclexta) and idelalisib (Zydelig)**

PA criteria have not previously been required for the chronic lymphocytic leukemia (CLL) drugs, Venclexta and Zydelig. However, PA criteria is in place for several other oncological drugs used to treat CLL.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for these two products in new users in order to ensure prescribing in accordance with FDA-approved indications or National Comprehensive Cancer Network (NCCN) Guideline-endorsed off-label indications.

a) Venetoclax (Venclexta)

- Age ≥ 18 years

- Drug is prescribed by or in consultation with a hematologist or oncologist
- Venclexta will be used in one of the following contexts:

    1. Frontline therapy for chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) without del(17p)/TP53 mutation
        - Patient fits one of the following categories:
            - Frail patient with significant comorbidity (not able to tolerate purine analogues)
            - Patient ≥ 65 years old with significant comorbidity
            - Patient < 65 years old
        - Will be combined with obinutuzumab (Gazyva) infusion

    2. Relapsed/refractory therapy for CLL/SLL without del(17p)/TP53 mutation
        - Patient fits one of the following categories:
            - Frail patient with significant comorbidity (not able to tolerate purine analogues)
            - Patient ≥ 65 years old with significant comorbidity
            - Patient < 65 years old
    3. Frontline or relapsed/refractory therapy for CLL/SLL with del(17p)/TP53 mutation
    4. Patient has newly diagnosed acute myeloid leukemia (AML) and is a candidate for intensive remission induction therapy and meets the following criteria:
        - Age ≥ 60 years old
        - Unfavorable-risk cytogenetics (exclusive of AML with myelodysplasia-related changes)
    5. Patient is ≥ 60 years old and has newly diagnosed AML and is not a candidate for intensive remission induction therapy
    6. Patient is ≥ 60 years old and completed lower-intensity induction therapy for AML with a response
    7. Patient has relapsed refractory AML

- Will titrate to therapeutic dose in consideration of tumor lysis syndrome (TLS)
- Will not be concomitantly used at initiation or during ramp-up with a strong CYP3A inhibitor
- Will prophylax and monitor for tumor lysis syndrome (TLS) (based on tumor burden-defined risk)
- Will monitor for neutropenia
- Will monitor for signs and symptoms of infection
- Will not administer live attenuated vaccines prior to, during, or after treatment with Venclexta until B-cell recovery occurs.
- If the patient is female, she is not pregnant or planning to become pregnant

- Female patients will not breastfeed
- Male patients have been informed of risk of infertility
- Female patients of reproductive potential will use effective contraception during treatment and for at least 30 days after discontinuation
- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis:

  _____

Non-FDA approved uses are NOT approved.

Prior Authorization does not expire.

b) Idelalisib (Zydelig)

- Age ≥ 18 years
- Drug is prescribed by or in consultation with a hematologist or oncologist
- Zydelig will be used in one of the following indications:
  1. Relapsed/refractory therapy for CLL/SLL without del(17p)/TP53 mutation
     - Patient fits one of the following categories:
       - Frail patient with significant comorbidity (not able to tolerate purine analogues)
       - Patient ≥ 65 years old with significant comorbidity
       - Patient < 65 years old
  2. Relapsed/refractory therapy for CLL/SLL with del(17p)/TP53 mutation
  3. Relapsed/refractory follicular lymphoma AND:
     - Patient has completed ≥ 2 prior therapies OR
     - Patient has completed 1 prior therapy and relapsed ≤ 2 years
  4. Relapsed/refractory marginal zone lymphoma after 2 prior therapies
- Provider has reviewed the REMS program including the letter to healthcare providers and the fact sheet and has shared the medication guide and patient safety information card with the patient
- Will monitor for hepatotoxicity, colitis, intestinal perforation, pneumonitis, infection, neutropenia, and Steven Johnson Syndrome/toxic epidermal necrolysis
- Will monitor for cytomegalovirus reactivation
- Will prophylax for *pneumocystis jiroveci* pneumonia
- If the patient is female, she is not pregnant or planning to become pregnant
- Female patients will not breastfeed
- Female patients of reproductive potential will use effective contraception during treatment and for at least 30 days after discontinuation

- Male patients of reproductive potential will use effective contraception during treatment and for at least 3 months after discontinuation
- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____

Non-FDA approved uses are NOT approved.

Prior Authorization does not expire.

B. New PA Criteria – PA Implementation

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) the new PAs for chlorzoxazone 375 mg and 750 mg (Lorzone, generics), lidocaine-tetracaine 7%-7%, Neupro patch, Venclexta, and Zydelig become effective the first Wednesday 90-days after the signing of the minutes. DHA will send letters to beneficiaries affected by the new PA requirements for chlorzoxazone and lidocaine-tetracaine 7%-7%, topical cream as new and current users will be subject to the PA.

Summary of Physician's Perspective:

There were 5 drugs from four classes where new PA criteria were recommended.

- **Lidocaine- tetracaine cream** – The Committee was concerned about the cost of this product, compared to other widely used topical anesthetics creams. However, the PA will apply only to patients older than age 12 years, as there is the potential for this drug to be used in children receiving pulsed laser therapy for port wine stain birthmarks, which would be an appropriate use. We will send letters to the patients, since both new and current users will be required to go through the PA process.

- **Chlorzoxazone 375 mg and 750 mg tablets** – These are new dosage strengths that are significantly less cost effective than generic formulations of the 500 mg tablets. The Committee felt that there is no clinical need for these new in-between dosage strengths, and since the 500 mg tablets are scored, they are easy to break. The 400 patients currently on these products will be receiving letters notifying them of the new PA requirement.

- **Rotigotine (Neupro Patch) for Parkinson's disease**–The PA criteria require use of the generic oral dopamine agonists first, which is consistent with professional treatment guidelines. PA was also recommended due to the high amount of current off-label use for restless leg disorder. Existing patients will be grandfathered, so only new patients will be affected by the PA requirements.

- **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma drugs (Venclexta and Zydelig)**: This is part of our ongoing process of reviewing the oncology drugs to determine which ones do not have PAs in place where one is warranted. PA was recommended for these two drugs to ensure the appropriate patients receive the drugs, based on FDA indications and safety information. These new PA's allow off-label uses that are included in the NCCN guidelines be considered as part of the PA review, before having the provider file an appeal. Only new patients will be have to undergo the PA process.

Summary of Panel's Questions and Comments:

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

- **New PA Criteria**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

- **New PA Criteria – PA Implementation Plan**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

II. UTILIZATION MANAGEMENT – UPDATED MANUAL PA CRITERIA

A. Updated PA Criteria

Updates to the manual PA criteria and step therapy criteria for several drugs were recommended due to a variety of reasons, including expanded FDA indications, new NCCN guideline recommendations, clinical trial data, and standardization with existing PAs for the drug class, changes due to FDA safety announcements and boxed warnings, and age indications. The updated PAs and step therapy criteria outlined below will apply to new users.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) to implement the PA criteria for Cimzia originally recommended at the May 2019 P&T Committee meeting (the Humira step requirement). The Committee also recommended the updates to the manual PA criteria for Symbicort and Dulera, Xeljanz, Xeljanz XR, Olumiant, Zytiga, and Doptelet.

The updates are as follows:

Updated Criteria for reasons other than new FDA indications, NCCN Guideline Updates, or Age Ranges

a) **Pulmonary-1 Agent: Combinations: budesonide/formoterol Symbicort AND mometasone/formoterol (Dulera)**—Manual PA criteria for Symbicort and Dulera were originally recommended in February 2014, requiring a trial of fluticasone/salmeterol (Advair) first. Recently the Global Initiative for Asthma (GINA) 2019 evidence-based strategy was updated, and states that combination low-dose inhaled corticosteroid (ICS)-formoterol used as needed is now the preferred reliever ("rescue use") for asthma control and reducing exacerbations in adults and adolescents 12 years and older with mild asthma. Short-acting beta agonists (SABAs) are now listed as an "other reliever option" and are no longer the preferred rescue treatment in adults and adolescents with mild asthma. This new approach was based on two studies that used a combination budesonide-formoterol inhaler (SYGMA 1 and SYGMA2, New England Journal of Medicine May 2018).

   Limitations to this recommendation include that the two supporting studies were industry funded, and used an active comparator (terbutaline Turbuhaler) that is not available in the U.S. Additionally, the budesonide-formoterol inhaler evaluated in the trials was a dry powder inhaler, while the commercially available U.S. product is a pressurized metered-dose inhaler (Symbicort), and the study design was changed from a superiority trial to a non-inferiority trial. The study results also show that this method is not as effective at decreasing asthma symptoms.

   Provider feedback was mixed and not overwhelmingly supportive of the consensus statement guidelines given the available data. Manual PA criteria for both Symbicort and Dulera were updated to allow use in patients with mild asthma who require rescue therapy with an ICS-formoterol combination, without requiring a trial of Advair first.

b) **Target Immunomodulatory Biologics (TIBs): certolizumab (Cimzia))**—Manual PA criteria for Cimzia were most recently reviewed at the May 2019 P&T Committee meeting after Cimzia was granted FDA-approval for adults with non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation. The Cimzia and Humira PA criteria were updated to allow for the indication of nr-axSpA but still require the use of adalimumab (Humira) prior to use of Cimzia. This recommendation was based on the Assessment of Spondylo Arthritis International Society (ASAS)/European League against Rheumatism (EULAR) guidelines and clinical trial data.

   The implementation of the Humira step requirement was delayed in light of new information that was not available at the May 2019 P&T meeting. The fact that the manufacturer for Humira sought FDA-approval for this indication and was denied in 2009-2013 had not been presented to the Committee in May 2019. The new information presented at this meeting included the FDA's review of both Cimzia and Humira for nr-axSpA, the high degree of difficulty of actually diagnosing this disease, and provider feedback. The P&T Committee recommended maintaining the requirement for Humira prior to Cimzia for nr-axSpA after evaluating this

additional information. The Cimzia PA criteria from the May 2019 P&T Committee meeting requiring use of Humira first in patients with nr-axSpA will now be implemented.

c) **TIBs: Janus Kinase (JAK) inhibitors tofacitinib (Xeljanz, Xeljanz XR) and baricitinib (Olumiant)**—The FDA has issued several safety alerts for Xeljanz and Xeljanz XR for pulmonary embolism and death with certain doses, most recently in July 2019. The Xeljanz/Xeljanz XR PA criteria were updated to ensure the provider is aware of the July 2019 FDA safety announcement and boxed warning, and to ensure patients do not have a history of thromboembolic disease.

   Olumiant PA criteria were recommended in August 2018, and suggested using Xeljanz prior to Olumiant, since at that time Xeljanz did not contain a boxed warning for thrombosis. This comment will be removed from the Olumiant PA, as Xeljanz/Xeljanz XR now have the warning mentioned above.

   For Xeljanz/Xeljanz XR and Olumiant, additional requirements for absolute neutrophil count (ANC) and absolute lymphocyte count (ALC) monitoring were also added, consistent with the package inserts. The PAs will also allow concomitant use with Otezla, if the provider includes supporting literature for combination use.

d) **Oncological Agents: Prostate Cancer CYP-17 Inhibitors: abiraterone acetate (Zytiga, generics)**—Manual PA criteria for Zytiga were recommended when the CYP-17 Inhibitor subclass was reviewed at the February 2019 P&T Committee meeting. Step therapy requiring a trial of abiraterone acetate micronized (Yonsa) first was required. Furthermore, an additional step required Zytiga generic 250 mg prior to Zytiga brand 500 mg, as the 500 mg branded formulation did not have generic equivalents and provided no clinical benefit at a significantly higher cost.

   As of October 2019, the blended monthly cost of generic abiraterone acetate 250 mg is now comparable to the step-preferred Yonsa formulation. The step requiring Yonsa before Zytiga generic 250 mg will be removed. The abiraterone acetate (Zytiga) brand 500 mg PA form will still require use of Yonsa or the 250 mg generics first.

e) **Hematological Agents: Platelets: avatrombopag (Doptelet)**—Manual PA criteria for Doptelet were first recommended in August 2018 for thrombocytopenia associated with chronic liver disease in patients who are scheduled to undergo a procedure with at least a moderate bleeding risk. Manual PA criteria were later updated in February 2019 to require a trial of Mulpleta first. Mulpleta has the same indication as Doptelet for pre-procedure use, has less complex dosing and was less expensive. There has been a significant price reduction in Doptelet, and manual PA criteria were updated to remove the requirement that Mulpleta be used ahead of Doptelet in thrombocytopenia associated with chronic liver disease

New FDA-Approved Indications, NCCN Guideline Updates, or Age Ranges

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) updates to the manual PA criteria for Taltz, Stelara, Erleada, Xtandi, Corlanor, Harvoni, Sovaldi, Ofev, Esbriet, Calquence, Copiktra, Imbruvica, Vitrakvi, and Revlimid.

a) **TIBs: ixekizumab (Taltz)**—For plaque psoriasis, Taltz currently requires a trial of adalimumab (Humira), secukinumab (Cosentyx) and ustekinumab (Stelara). Taltz is now approved for treating active ankylosing spondylitis (AS) in adult patients, and the new indication was added to the criteria. Note that for AS, a trial of adalimumab (Humira) and secukinumab (Cosentyx) are required first; however a trial of ustekinumab (Stelara) is not required as it is not FDA-approved for use in AS.

b) **TIBs: ustekinumab (Stelara)**—Manual PA criteria were updated to reflect a new FDA-approved indication for adults with moderately to severely active ulcerative colitis (UC). The requirement to try Humira prior to Stelara for this indication still applies.

c) **Cardiovascular Agents Miscellaneous—ivabradine (Corlanor)**—Manual PA criteria for Corlanor were updated to reflect a new pediatric indication for treating stable symptomatic heart failure due to dilated cardiomyopathy in pediatric patients ≥ 6 months and older, who are in sinus rhythm with an elevated heart rate.

d) **Hepatitis C Agents: Direct Acting Agents: ledipasvir/sofosbuvir (Harvoni) AND sofosbuvir (Sovaldi)**—Updates were made to the PA criteria for Harvoni and authorized generics of Harvoni to allow use for adult and pediatric patients ≥ 3 years of age with chronic hepatitis C virus (HCV) genotype 1, 4, 5, or 6 infection, without cirrhosis or with compensated cirrhosis. Other recent indications were also added to the form, including genotype 1 infection with decompensated cirrhosis, in combination with ribavirin; and genotype 1 or 4 infection in liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin. Manual PA criteria for Sovaldi were updated to reflect a new FDA-approved indication for adults and pediatric patients 3 years of age or older for treatment of chronic HCV genotype 2 or 3 infection, without cirrhosis or with compensated cirrhosis.

e) **Pulmonary-1 Agents: Idiopathic Pulmonary Fibrosis (IPF): nintedanib (Ofev) and pirfenidone (Esbriet)**—The IPF drugs were reviewed for formulary status in May 2017 and step therapy requires a trial of pirfenidone (Esbriet) prior to Ofev. Ofev recently gained an indication to slow the rate of decline in pulmonary function for a rare condition, systemic sclerosis-associated interstitial lung disease (SSc-ILD). Esbriet lacks the indication for SSc-ILD, so it is not required before Ofev in this condition. The new SSc-ILD indication

was added to the Ofev PA. The renewal criteria from the May 2017 class review were also updated for clarification for both Ofev and Esbriet.

f) **Oncological Agents: Prostate Cancer 2nd-Generation Antiandrogens: apalutamide (Erleada) and enzalutamide (Xtandi)**—Manual PA criteria were updated to reflect the new FDA-approved indication and NCCN guideline update for treatment of metastatic, castration-sensitive prostate cancer. For Erleada, renewal criteria were removed since it is now indicated for use in metastatic disease.

g) **Oncologic Agents: acalabrutinib (Calquence), duvelisib (Copiktra), ibrutinib (Imbruvica), larotrectinib (Vitrakvi) capsules and oral solution, lenalidomide (Revlimid)**—Updates to the manual PA criteria for these oncologic agents reflects more detailed safety information, including standardized embryo-fetal toxicity information. New FDA-approved indications or NCCN guideline-supported indications were also updated as summarized below. A synopsis of the changes submitted are summarized below:
   - acalabrutinib (Calquence)—Allow use for NCCN CLL and small lymphocytic lymphoma (SLL) guideline updates for relapsed or refractory disease
   - duvelisib (Copiktra)—Allow use in refractory marginal zone lymphoma
   - ibrutinib (Imbruvica)—Allow use for mantle cell lymphoma maintenance therapy
   - larotrectinib (Vitrakvi)—Allow first-line use for neurotropic tropomyosin receptor kinase (NTRK) gene fusion positive non-small cell lung cancer (NSCLC)
   - lenalidomide (Revlimid)—Allow use for marginal zone lymphoma

B. Updated PA Criteria – Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) the following implementation periods:

- Updates to the current PA criteria for Cimzia in new users will become effective the first Wednesday upon signing of the minutes.
- Updates to the current PA criteria for abiraterone acetate 250 mg in new users will become effective the first Wednesday 30-days after the signing of the minutes.
- Updates to the current PA criteria for Xeljanz, Xeljanz XR, Olumiant, Taltz, Stelara, Erleada, Xtandi, Vitrakvi capsule and solution, Calquence, Copiktra, Imbruvica, Revlimid, Doptelet, Ofev, Esbriet, Symbicort, Dulera, Harvoni, Sovaldi, and Corlanor in new users become effective the first Wednesday 60-days after the signing of the minutes.

Summary Physician's Perspective:

There were 22 drugs discussed here, so only a few drugs will have comments.

- **Symbicort and Dulera for asthma**

  Currently Advair has been the step-preferred combination inhaler since 2014, with Symbicort and Dulera made non-preferred and non-formulary. Symbicort and Dulera contain formoterol which has a faster onset of action than the salmeterol component of Advair. Because of this, for rescue use, patients won't be required to try Advair first.

  There is some controversy about this new consensus statement, the PA update will remove a barrier, so that providers who want to follow this guideline can do so.

- **Cimzia - TIB for non-radiographic axial spondyloarthritis**: The original recommendation from the May 2019 meeting was on hold, until the data could be re-examined. Based on the review of the evidence, and feedback from rheumatologists, we will now implement the original recommendation for Humira to be tried first before Cimzia for this indication.

- **Generic Zytiga 250 mg for prostate cancer**: Because of a price reduction for the generic 250 mg product, we are removing the requirement to try Yonsa first. This is a good example of where pricing is monitored, and where step therapy is discontinued when there is not significant cost benefit

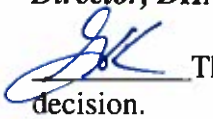
Summary of Panel's Questions and Comments:

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

- **Updated Manual PA Criteria**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

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

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

Closing Remarks:

Mr. Hostettler states that we had several issues today that recur each meeting. The Panel is told that the information will be taken back for research but I don't recall ever receiving any feedback. We want to add the requested updates from this meeting to the requests for updates from the previous meetings. I usually go back and review the minutes and documentation after it is signed by the Director, DHA. During the discussions at the last meeting, PA criteria was omitted from a new drug and the Panel was told that the information would be added to the existing criteria. Feedback would be provided to the Panel. The new criteria requires patients to have surgery. In my opinion, that seems drastic. Can someone provide a justification? The update states that the patient has a past surgical history or endoscopic surgical intervention. My interpretation of this criteria is that a patient has to have surgery before they can use this drug. This significant information should have been presented to the Panel.
In the future, I would have like to have a chance to review the evidence and comment.

Additionally I am requesting feedback on issues that the presenter states they will "take back".

Dr. Khoury states that he does not recall the discussion regarding the criteria referenced but if information was omitted it was not intentional and he apologizes.

Dr. Khoury asks which product is being referred to.

Mr. Hostettler replies Dupilumab (Dupixent)

Dr. Bertin thanks the Panel for their attention to detail. A good and productive meeting. He expressed appreciation to the super staff for their presentations.

Meeting adjourned at 11:50am.

Informational Item—SUMMARY OF RECOMMENDATIONS AND BENEFICIARY IMPACT November 2019

Table of Implementation Status of UF Recommendations/Decisions Summary

DoD PEC Drug Class	UF Drugs	NF Drugs	Tier 4/Not Covered Drugs	Implement Date	Notes and Unique Users Affected
Phosphodiesterase-5 Inhibitors	*UF and Step-preferred* ▪ sildenafil generic only *UF and non-step-preferred* ▪ tadalafil generic only	▪ None	▪ avanafil (Stendra) ▪ vardenafil ODT (Staxyn and generics) ▪ vardenafil tablet (Levitra and generics) ▪ brand Viagra ▪ brand Cialis	Pending signing of the minutes / 120 days	▪ Manual PA criteria applies to both sildenafil and generic tadalafil ▪ Trial of sildenafil still required before tadalafil ▪ Men over 40 years do not require a PA Unique Users Affected (Tier 4 candidates) Mail – 6,016 MTF – 3,744 Retail – 433 Total – 10,193
Rapid-Acting Insulins	*UF and step-preferred* ▪ insulin aspart (Novolog) ▪ insulin lispro (Humalog and authorized generic insulin lispro)	*NF and non-step-preferred* ▪ insulin glulisine (Apidra) ▪ insulin lispro (Admelog) ▪ inhaled insulin (Afrezza)	▪ insulin aspart plus niacinamide (Fiasp)	Pending signing of the minutes / 150 days and no earlier than July 1 2020	▪ All new and current users of Admelog and Apidra must try Novolog and Humalog ▪ Changes also made to the Afrezza PA Unique Users Affected (Tier 4 candidate Fiasp) Mail: 122 MTF: 44 Retail: 17 Total: 183

Drugs with New Prior Authorization Criteria—Unique Utilizers Affected

Drug	MTF	Mail Order	Retail	Total
Chlorzoxazone 375 mg (Lorzone, generics)	2	21	61	84
Chlorzoxazone 750 mg (Lorzone, generics)	24	86	233	340
Anesthetic Agents: Local—Lidocaine-Tetracaine 7%-7% topical cream (Pliaglis, generics)	0	0	1,616	1,616

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 "BAP" in this summary refers to the "Uniform Formulary Beneficiary Panel," the group who's meeting in the subject of this report.

- ADHD – Attention Deficit Hyperactivity Disorder
- AML – Acute Myeloid Leukemia
- ANC – Absolute Neutrophil Count
- ANDA – Abbreviated New Drug Application
- ASAS – Assessment of Spodylo Arthritis International Society
- AUS – American Urological Association
- BIA – Budget Impact Analysis
- BPH – Benign Prostatic Hyperplasia
- BUN – Blood, Urea Nitrogen
- CABP – Community Acquired Bacterial Pneumonia
- CBC – Complete Blood Count
- CFR – Code of Federal Regulation
- CHF – Congestive Heart Failure
- CLL – Chronic Lymphocytic Leukemia
- CMA – Cost-Minimization Analysis
- COPD – Chronic Obstructive Pulmonary Disease
- DHA – Defense Health Agency
- DKA – Diabetic Ketoacidosis
- DMARDs – Disease-Modifying Anti-Rheumatic Drugs
- DoD – Department of Defense
- ED – Erectile Dysfunction
- EULAR – European League Against Rheumatism
- FDA – Federal Drug Administration
- GnRH – Gonadotropin-Releasing Hormone
- HCV – Hepatitis C Virus
- HSDD – Hypoactive Sexual Desire Disorder
- IBS-C – Irritable Bowel Syndrome – Constipation
- IPF – Idiopathic Pulmonary Fibrosis
- JAK Inhibitors – Janus Kinase Inhibitors
- L – Liter
- LAMA/LABA – Long-acting Muscarinic Antagonists/Long-acting Beta Agonist
- MEN2 – Multiple Endocrine Neoplasia Syndrome Type
- ml – Milliliter
- MSLT – Mean Sleep Latency Time
- MTC – Medullary Thyroid Carcinoma
- MTF – Military Treatment Facility
- NCCN – National Comprehensive Cancer Network

- NDAA – National Defense Authorization Act
- NF – Non-Formulary
- NSCLS – Non-Small Cell Lung Cancer
- NTRK – Neurotrophic Tropomyosin Receptor Kinase
- ODT – Oral Disintegrating Tablet
- P&T – Pharmacy & Therapeutic
- PA – Prior Authorization
- PDE-5 – Phosphodiesterase-5
- PSADT – Prostate-Specific Antigen Doubling Time
- RAI – Rapid-Acting Insulins
- REMS – Risk Evaluation Mitigation Strategy
- RRMM – Relapsed or Refractory Multiple Myeloma
- SLL – Small Lymphocytic Lymphoma
- SSc-ILD – Systemic Sclerosis-Associated Interstitial Lung Disease
- TB – Tuberculosis
- TIB – Targeted Immunomodulatory Biologic
- TLS – Tumor Lysis Syndrome
- UC - Ulcerative Colitis
- UF – Uniform Formulary
- VTE – Venous Thromboembolic
- XR – Extended Release

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
January 8, 2020
Washington D.C.

Present Panel Members

- Dr. Richard Bertin, Commissioned Officers Association (COA) of the United States Public Health Service, Inc., Alternate Chairperson
- Ms. Theresa Buchanan, National Military Family Association
- Dr. Karen Dager, Health Net Federal Services
- Mr. John R. Du Teil, United States Army Warrant Officers Association
- Mr. Charles Hostettler, AMSUS
- Dr. Jay Peloquin, Express Scripts, Inc.
- Dr. Lindsey Piirainen, USFHP Martin's Point Healthcare

New Member

- Dr. Joseph McKeon, Humana

Absent

- Mr. Jon R. Ostrowski, Non-Commissioned Officers Association, Chairperson

The meeting was held at the Naval Heritage Center Theater, 702 Pennsylvania Ave., N.W., Washington D.C. and Col Paul Hoerner called the meeting to order at 9:15 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) Phosphodiesterase-5 (PDE-5) Inhibitors
        b) Insulins: Rapid-Acting Insulins (RAIs) Subclass

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

        a) amlodipine oral suspension (Katerzia) – Calcium channel blocking agent in an oral suspension for hypertension

b) bremelanotide injection (Vyleesi) – Miscellaneous gynecological agent for Hypoactive Sexual Desire Disorder (HSDD)
c) darolutamide (Nubeqa) – Oral oncologic agent for non-metastatic castration-resistant prostate cancer (nmCRPC)
d) duloxetine extended-release (Drizalma Sprinkle) – Another formulation of duloxetine with similar indications to Cymbalta
e) entrectinib (Rozlytrek) – Oral oncologic agent for lung cancer
f) fedratinib (Inrebic) – Oral oncologic agent for myelofibrosis
g) formoterol/aclidinium inhaler (Duaklir Pressair) – Pulmonary-2 Agent for Chronic Obstructive Pulmonary Disease (COPD)
h) glucagon injection (Gvoke Hypopen and Prefilled Syringe [PFS]) – Binders-Chelators-Antidotes-Overdose Agent for severe hypoglycemia
i) glucagon nasal spray (Baqsimi) – Binders-Chelators-Antidotes-Overdose Agent for severe hypoglycemia
j) istradefylline (Nourianz) – Parkinson's agent for off episodes
k) lamivudine/tenofovir disoproxil fumarate (TDF) (Temixys) – Antiretroviral combination for human immunodeficiency virus (HIV)
l) lefamulin (Xenleta) – Antibiotic for community acquired bacterial pneumonia (CABP)
m) midazolam nasal spray (Nayzilam) – Anticonvulsants-antimania agent for seizures
n) pexidartinib (Turalio) – Oral oncologic agent for tenosynovial giant cell tumors
o) pitolisant (Wakix) – Sleep disorders: wakefulness promoting agent for narcolepsy
p) segesterone acetate/ethinyl estradiol (Annovera) – Vaginal ring for contraception
q) selinexor (Xpovio) – Oral oncologic agent for relapsing remitting multiple myeloma
r) semaglutide oral tablet (Rybelsus) – Oral glucagon-like peptide-1 receptor agonist for type 2 diabetes mellitus in adults
s) sumatriptan nasal spray (Tosymra) – Another formulation of sumatriptan
t) tegaserod (Zelnorm) – Gastrointestinal-2 agent for constipation-predominant irritable bowel syndrome (IBS-C)
u) tiopronin ER (Thiola EC) – Miscellaneous urinary agent for cystinuria
v) upadacitinib (Rinvoq) – Targeted Immunomodulatory Biologic (TIB) for rheumatoid arthritis

3. Utilization Management Issues

a) Prior Authorization Criteria – New Criteria

- Skeletal muscle Relaxants and Combinations – chlorzoxazone 375 mg and 750 mg (Lorzone, generics)
- Anesthetic Agents: Local – lidocaine tetracaine 7%-7% topical cream (Pliaglis, generics)
- Parkinson's Agents: rotigotine (Neupro) patch
- Oral Oncologic Agents: venetoclax (Venclexta) and idelalisib (Zydelig)

b) Prior Authorization Criteria – Updated Criteria

- Pulmonary-1 Agents: combinations: budesonide/formoterol (Symbicort) AND mometasone/formoterol (Dulera)
- Targeted Immunomodulatory Biologics: certolizumab (Cimzia)
- Targeted Immunomodulatory Biologics: baricitinib (Olumiant, generics), tofacitinib (Xeljanz, Xeljanz XR), ixekizumab (Taltz), ustekinumab (Stelara)
- Oncological Agents: Prostate Cancer CYP-17 Inhibitors: abiraterone acetate (Zytiga, generics)
- Oncological Agents: Prostate Cancer 2nd Generation Antiandrogens: apalutamide (Erleada) and enzalutamide (Xtandi)
- Thrombopoietin Agents: Platelets: avatrombopag (Doptelet)
- Cardiovascular Agents: Miscellaneous: ivabradine (Corlanor)
- Hepatitis C Agents: Direct Acting Agents: ledipasvir/sofosbuvir (Harvoni) AND sofosbuvir (Sovaldi)
- Pulmonary-1 Agents: Idiopathic Pulmonary Fibrosis (IPF): pirfenidone (Esbriet) and nintedanib (Ofev)
- Oncological Agents: acalabrutinib (Calquence), duvelisib (Copiktra), ibrutinib (Imbruvica), larotrectinib (Vitrakvi), lenalidomide (Revlimid)

4. Panel Discussions

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

Opening Remarks

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

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

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

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

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

- To review and comment on the recommendations of the P&T Committee concerning the establishment of the UF and subsequently recommending changes. Comments to the Director of the DHA regarding recommended formulary status, pre-authorizations and the effective dates for changing drugs from "formulary" to "non-formulary" status must be reviewed by the Director before making a final decision.
- To hold quarterly meetings in an open forum. The panel may not hold meetings except at the call or with the advance approval of the DFO and in consultation with the chairperson of the Panel.
- To prepare minutes of the proceedings and prepared comments of the Secretary or his designee regarding the Uniform Formulary or changes to the Formulary. The minutes will be available on the website, and comments will be prepared for the Director of DHA. As guidance to the Panel regarding this meeting, Col Hoerner said the role of the BAP is to comment on the UF recommendations made by the P&T Committee at their last meeting. While the department appreciates that the BAP maybe interested in the drug class they selected for review, drugs recommended for the basic core formula (BCF) or specific pricing data, these items do not fall under the purview of the BAP.
- The P&T Committee met for approximately 16 hours conducting this review of the drug class recommendation presented today. Since this meeting is considerably shorter, the Panel will not receive the same extensive information as presented to the P&T Committee members. However, the BAP will receive an abbreviated version of each presentation and its discussion. The materials provided to the Panel are available on the TRICARE website.

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

- All discussions take place in an open public forum. There is to be no committee discussion outside the room, during breaks, or at lunch.
- Audience participation is limited to private citizens who signed up to address the Panel.
- Members of the Formulary Management Branch and P&T Committee are available to answer questions related to the BAP's deliberations. Should a misstatement be made, these individuals may interrupt to ensure the minutes accurately reflect relevant facts, regulations, or policy.

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

Private Citizen Comments

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

Chairman's Opening Remarks

Dr. Bertin welcomes the Panel and audience then calls for the presentations to begin.

DRUG CLASS REVIEW PRESENTATION

(POD Script – LT COL KHOURY)

GOOD MORNING. I am Lieutenant Colonel Ronald Khoury, Chief of the Formulary Management Branch of the DHA Pharmacy Operations Division. Absent is doctor and retired Army Colonel John Kugler, the Chairman of the Pharmacy and Therapeutics Committee, who provided the physician perspective and comments on the recommendations made by the P&T Committee. Also joining us one of the clinical pharmacists from the Formulary Management Branch today is Dr. Angela Allerman. I would also like to recognize Mr. Bryan Wheeler, Deputy General Counsel.

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

We are here to present an overview of the analyses presented to the P&T Committee. 32 Code of Federal Regulations (CFR) establishes procedures for inclusion of pharmaceutical agents on the Uniform Formulary based upon both relative clinical effectiveness and relative cost effectiveness. Additionally, all TRICARE Tier 4/not covered drugs were reviewed for clinical and cost-effectiveness in accordance with amended 32 CFR 199.21(e)(3) effective December 11, 2018.

The goal of this presentation is not to provide you with the same in-depth analyses presented to the DoD P&T Committee but a summary of the processes and analyses presented to the DoD P&T Committee. These include:

- A brief overview of the relative clinical effectiveness analyses considered by the DoD P&T Committee. All reviews include but are not limited to the sources of information listed in 32 CFR 199.21 (e)(1) and (g)(5). Also note that Nonformulary medications are generally restricted to the mail order program according to amended section 199.21, revised paragraphs (h)(3)(i) and (ii), effective August 26, 2015.
- A brief general overview of the relative cost effectiveness analyses. This overview will be general in nature since we are unable to disclose the actual costs used in the economic models. This overview will include the factors used to evaluate the costs of the agents in relation to the safety, effectiveness, and clinical outcomes.
- The DoD P&T Committee's Uniform Formulary recommendation is based upon the Committee's collective professional judgment when considering the analyses from both the relative clinical and relative cost effectiveness evaluations.
  The Committee reviewed the following:

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

     a) Phosphodiesterase-5 (PDE-5) Inhibitors and

b) Insulins: Rapid Acting Insulins subclass

A summary table of the UF drug class recommendations and the numbers of affected utilizers is found on page 37 of the background document.

2. The P&T Committee also evaluated 22 newly approved drugs per 32 CFR 199.21 (g)(5), which are currently in pending status and available under terms comparable to Nonformulary drugs.

   And

3. We also discussed prior authorizations (PAs) for **27** drugs in **10** drug classes.

   a) Skeletal Muscle Relaxants and Combinations
   b) Local Anesthetic Agents
   c) Parkinson's Agents
   d) Oncological Agents – a total of 10 drugs
   e) Pulmonary-1 Agents: Combinations
   f) TIB – 6 drugs
   g) Hematologic Agents: Platelets
   h) Cardiovascular Agents Miscellaneous: Miscellaneous
   i) Hepatitis C Agents: Direct Acting Agents
   j) Pulmonary-1 Agents: Idiopathic Pulmonary Fibrosis (IPF)

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 or for Tier 4/Not Covered status. Based on 32 CFR 199.21, such change will not be longer than 180 days from the final decision date but may be less.

UNIFORM FORMULARY DRUG CLASS REVIEWS

I. UF CLASS REVIEWS

(DR. ALLERMAN)

A. PHOSPHODIESTERASE-5 (PDE-5) INHIBITORS

1. PDE-5 Inhibitors – Relative Clinical Effectiveness Conclusion

Background—The P&T Committee evaluated the relative clinical effectiveness of the PDE-5 inhibitors, which include avanafil (Stendra), sildenafil (Viagra), tadalafil (Cialis), vardenafil oral disintegrating tablet (ODT) (Staxyn), and vardenafil tablets (Levitra). Generic formulations are marketed for all the products, except for Stendra. All the PDE-5 inhibitors are indicated to treat erectile dysfunction (ED) on an as needed basis. Tadalafil is the only PDE-5 inhibitor approved for daily use in addition to as needed use for ED, and is approved for treating benign prostatic hyperplasia (BPH).

The class was most recently reviewed in November 2011. Sildenafil is currently UF and step-preferred, with the remaining PDE-5 inhibitors designated as NF and non-step-preferred, requiring a trial of Viagra first. Prior Authorization (PA) is not required for men over the age of 40 years for ED; however PA is required in men younger than 40 years for ED, for men of all ages for the Food and Drug Administration (FDA) approved indication of BPH, and for off-label uses (post-prostatectomy and Raynaud's phenomena).

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

- There were no major updates to the November 2011 conclusion that there is a high degree of therapeutic interchangeability for the PDE-5 inhibitors for treating ED.
- The 2018 American Urological Association (AUA) guidelines support PDE-5 inhibitors as first-line therapy for ED and state there are no major differences in efficacy between the drugs.
- Two recent network meta-analyses also support that there are no significant differences in efficacy between the PDE-5 inhibitors for ED. Sildenafil (Viagra) was associated with the highest efficacy compared to placebo, but head-to-head comparisons between the individual PDE-5 inhibitors have not been studied. (Chen 2015, Corona 2016).
- Based on meta-analysis findings, vardenafil (Levitra) is associated with the highest reporting of adverse events followed by sildenafil (Viagra) and tadalafil (Cialis). (Chen 2015)

BPH

- A 2018 Cochrane review evaluated the effects of the PDE-5 inhibitors compared to placebo, and the alpha-blockers and 5-alpha reductase inhibitors on urinary symptoms of BPH. When compared to the alpha-blockers, the PDE-5 inhibitors were found to probably provide similar improvement in urinary symptoms, based on moderate-quality evidence.

Off-label uses

- Post-prostatectomy: A Cochrane review in 2018 supports PDE-5 inhibitor use to preserve erectile function following -prostatectomy surgery, but did not provide conclusive evidence of a preferred agent or dosing regimen (i.e., daily vs. on-demand). The authors acknowledge that tadalafil (Cialis) is the only PDE-5 inhibitor indicated for daily use and the most studied agent for daily dosing.
- Raynaud's phenomenon: There are no guidelines for treating this condition. According to the 2017 European Society of Vascular Medicine consensus statement, no specific agent is recommended, but sildenafil (Viagra) and tadalafil (Cialis) are the most studied PDE-5 inhibitors.

Individual PDE-5 characteristics

- Sildenafil (Viagra) was the first PDE-5 inhibitor marketed and has a long history of use. It has the highest Military Health System (MHS) utilization of all the PDE-5 inhibitors. Generic formulations of sildenafil were launched in December 2017, and there are at least nine generic manufacturers available as of November 2019.
- Tadalafil (Cialis) advantages include its indication for BPH in addition to ED, approval for daily dosing and on-demand dosing, and a long half-life of 17 hours. Multiple generic formulations of tadalafil are marketed (17 as of November 2019).
- Vardenafil is available in both a film-coated tablet (under the trade name Levitra) and orally dissolving tablet (ODT), (Staxyn). The ODT theoretically provides a convenience to the patient, but there are no studies supporting this. Disadvantages of vardenafil include low MHS utilization, and limited generic availability.
- Avanafil (Stendra) was the fourth PDE-5 to enter the market. Although it has the fastest onset of action of 15 minutes, this has not translated into increased efficacy over the other PDE-5 inhibitors. There is limited published data with avanafil, compared to the other products. One meta-analysis reported a statistically significant lower number of adverse events compared to the other PDE-5 inhibitors (Corona 2016); however, this has not correlated with increased efficacy or a lower discontinuation rate. Generic formulations are not expected before 2023.

- Input from MHS providers support Tier 4 status for multiple PDE-5 inhibitors, as long as both a short-acting and long-acting product is available.

2. PDE-5 Inhibitors – Relative Cost-Effectiveness Analysis and Conclusion

Cost-minimization analysis (CMA) and budget impact analysis (BIA) were performed to evaluate the PDE-5s. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA results showed that generic sildenafil and generic tadalafil were the most cost effective PDE-5 inhibitors, followed by vardenafil tablet (Levitra, generics), vardenafil ODT (Staxyn, generics), and avanafil (Stendra), which were substantially less cost effective.
- BIA was performed to evaluate the potential impact of designating selected PDE-5 inhibitors as formulary, NF, or Tier 4 on the UF. The BIA results showed that designating generic sildenafil as UF and step-preferred, generic tadalafil as UF and non-step-preferred, with vardenafil ODT (Staxyn, generics), vardenafil tablet (Levitra, generics), avanafil (Stendra), and branded Viagra and branded Cialis as Tier 4 demonstrated significant cost avoidance for the MHS.

3. PDE-5 Inhibitors – UF/Tier 4/Not Covered Recommendation

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

- UF and step-preferred
  - sildenafil (generic Viagra only)

- UF and non-step-preferred
  - tadalafil (generic Cialis only)

- NF – none

- This recommendation includes step therapy in new users, which requires a trial of generic sildenafil before generic tadalafil.

- Tier 4/Not Covered
  - avanafil (Stendra)
  - vardenafil ODT (Staxyn, generics)
  - vardenafil tablets (Levitra, generics)
  - Brand Viagra
  - Brand Cialis

When considering the PDE-5 inhibitor candidates for Tier 4/Not Covered status, the P&T Committee considered the information outlined in the interim rule, Section 702(b)(10) of the NDAA 2018 published on December 11, 2018,

and found at: https://www.federalregister.gov/documents/2018/12/11/2018-26562/tricare-pharmacy-benefits-program-reforms.

For the five PDE-5 inhibitors recommended for Tier 4/Not Covered status, the P&T Committee concluded they provide very little to no additional clinical effectiveness relative to the other PDE-5 inhibitors. Overall, the P&T Committee felt that the needs of TRICARE beneficiaries could be met by the formulary PDE-5 inhibitors, generic sildenafil, and generic tadalafil.

4. PDE-5 Inhibitors – Manual Prior Authorization (PA) Criteria

Automated step therapy requirements currently apply to the class for ED, requiring a trial of sildenafil (Viagra) first. The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 0 absent) removing the automation, and requiring manual PA criteria for generic sildenafil and generic tadalafil. The manual PA will continue to require a trial of generic sildenafil prior to generic tadalafil for ED in new users. The age and gender edit for males 40 years and older will continue to apply. PA will continue to be required for ED in males younger than age 40 years and for the off-label uses.

The PA criteria are as follows in bold and strikethrough:

a) Generic sildenafil tablets

~~Automated and~~ Manual PA criteria apply to all new users of generic sildenafil. Note that brand Viagra is not covered by TRICARE.

Age and Gender edit: Coverage is approved for treatment of ED if the patient is a male aged 40 years or older.

Manual PA Criteria: Coverage is approved if the following criteria are met:
- Patient is older than 18 years of age AND
- Patient is less than 40 years of age and is being treated for ED of organic or mixed organic/psychogenic origin OR
- Patient is less than 40 years of age and is being treated for drug-induced ED where the causative drug cannot be altered or discontinued OR

Coverage is approved for the following non-ED uses requiring daily therapy:
- Use of generic sildenafil for preservation/restoration of erectile function after prostatectomy. PA expires after one year. OR
- Use of generic sildenafil for Raynaud's Phenomenon ~~OR~~
- ~~**Use of sildenafil for pulmonary arterial hypertension (PAH)**~~

Other non-FDA-approved uses are not approved, including use for females for the treatment of sexual dysfunction.

PA does not expire except as noted above following prostatectomy.

b) Generic tadalafil tablets

Manual PA criteria apply to all new users of generic tadalafil. Note that brand Cialis is not covered by TRICARE.

Note that the previous automation for the step therapy has been removed.

Manual PA criteria:

- Patient is older than 18 years of age AND
- Patient has tried generic sildenafil and has had an inadequate response or was unable to tolerate treatment due to adverse effects
  OR
- Treatment with generic sildenafil is contraindicated. OR
- Patient is less than 40 years of age and is being treated for ED of organic or mixed organic/psychogenic origin. The patient must try generic sildenafil first and is unable to use generic sildenafil due to reasons stated above (inadequate response or adverse events.) OR
- Patient is less than 40 years of age and is being treated for drug-induced ED where the causative drug cannot be altered or discontinued. The patient must try generic sildenafil first and is unable to use generic sildenafil due to reasons stated above (inadequate response or adverse events.) OR
- Use of generic tadalafil 2.5 mg or 5 mg for patients with BPH or BPH with ED meeting PA criteria requiring use of an alpha blocker [tamsulosin (Flomax) or alfuzosin (Uroxatral)] first unless there is a contraindication, inadequate response, or intolerable adverse effects with the alpha blocker

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

- Patient requires generic tadalafil for preservation/restoration of erectile function after prostatectomy. PA expires 1-year post-surgery.
- Use of generic tadalafil for Raynaud's Phenomenon ~~**OR**~~
- ~~**Use of tadalafil for pulmonary arterial hypertension (PAH)**~~

Other non-FDA-approved uses are not approved, including use for females for the treatment of sexual dysfunction.

PA does not expire except as noted above following prostatectomy.

5. PDE-5 Inhibitors – UF/Tier 4/Not Covered and PA Implementation Plan

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 0 absent) 1) An effective date of the first Wednesday 120 days after signing of the P&T

minutes at all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/Not Covered recommendations at 30 and 60 days prior to implementation.

6. Physician's Perspective

One of the reasons for reviewing this drug class again is due to the entrance of generic products into the market.

With this recommendation, we will now have the two most popular PDE-5s available on the formulary, the generics for Viagra and Cialis. All the other products, including branded Viagra and Cialis will be Tier 4. Currently, only Viagra is on the formulary, with all the other products requiring a trial of Viagra first. For generic Viagra, men older than age 40 will not require a PA when used for ED, which we have had for several years. For generic Cialis, we will continue to require a trial of generic Viagra first.

The Tier 4 recommendation for this class includes the branded Viagra and Cialis products. The cost differences between the branded products and the generics is significant. Shortages of the generics are unlikely, as there are a large number of generics available from several manufacturers, including 9 generics available for Viagra, and 17 generics for Cialis. Currently, generic Viagra and Cialis together account for about 93% of the market share.

Five branded products (Viagra, Cialis, Stendra, Levitra and Staxyn) are recommended for Tier 4 status. However, in addition to moving generic Cialis from NF to UF status, we are also increasing the quantity limit from 6 tablets a month to 10 tablets a month.

Some additional reasons to have multiple candidates for Tier 4 status include the low persistence rates in the class. DoD data shows only 56% of patients remain on a PDE-5 after 4 months, which drops to 34% at 12 months and 17% at 24 months. This low persistence may partly reflect the fact that these products are used on an "as needed" basis, and not on a chronic basis.

The Tier 4 recommendation will affect about 7% of the patients on a PDE-5 inhibitor, or around 10,000 patients out of the total of over 144,000 patients. The implementation period will be 120 days, and we will send out letters at 60 days and 30 days before implementation. Overall the main goal here is to switch patients to generic Viagra and generic Cialis.

One last comment about all the Tier 4 drugs that have been reviewed so far since the February 2019 meeting, the P&T Committee will be re-evaluating Tier 4 status approximately one year after implementation, to look for any clinical or cost consideration that would warrant changing Tier 4 status.

Approximately 20000 patients who receive tadalafil may benefit from a reduced copay as this agent will move from NF to UF.

7. Panel's Questions and Comments

Mr. DuTeil asks if current users are required to complete the step-preferred criteria. He believes the patient and provider should make the decision regarding which medication (tadalafil or silenafil) is best for the patient.

Dr. Allerman responds, the new prior authorization criteria only refers to generic tadalafil. The P&T committee recommended all others drugs move to Tier 4. If the patient has a current prior authorization in place and is currently receiving generic tadalafil, they are not required to complete the step. However, if the patient is currently on branded Cialis, which is moving to Tier 4, a trial of either generic sildenafil or generic tadalafil is required after fulfilling the prior authorization

Mr. DuTiel clarifies, if the patient is on one of the medications moving to Tier 4, the patient is required to repeat the step preferred process.

Dr. Allerman responds that is correct.

Mr. Hostettler asks if Viagra has a daily indication.

Dr. Allerman responds Viagra does not have a daily indication. She explains that Cialis, generic tadalafil, is moving from non-formulary to formulary status. The current prior authorization, which has been in effect since 2011, and the current prior authorization for once daily use, are a part of the prior authorization criteria. Because the data shows that other drugs for treating an enlarged prostate are equally or more effective than the PDE-5 inhibitors, the PA requires the use of an alpha blocker first.

Mr. Hostettler clarifies the PA criteria requires a trial of sildenafil first regardless of whether the patient is using Viagra daily which does not have a daily indication.

Dr. Allerman responds it is a part of the prior authorization criteria. The PA criteria for sildenafil is automated PA for males over 40 with ED. If the patient wants the once daily, for BPH, they have to fill out the manual prior authorization.

Ms. Hostettler asks and skip sildenafil?

Dr. Allerman responds, the trial of sildenafil is not required as long as the patient has tried an alpha blocker. This is not a change, the PA has been in place since 2011.

Dr. Peloquin asks if the patient is required to go through the step when transitioning from a brand name to the generic. More specifically, if the patient is on brand name Cialis, is the patient required to complete the PA or go through the step to transition to the generic.

Dr. Allerman responds the system would recognize or consider the change from brand to generic as a new user. Yes, the patient would be required to complete the PA criteria for generic sildenafil. If the patient is already on the generic, tadalafil, the step is not required. The majority of the patients impacted by the decision are on generic tadalafil

Mr. Hostettler asks how many of the 10,000 patients are on branded medications

Dr. Allerman states approximately 2,500 are on branded Cialis.

Mr. Hostettler asks if the patients on branded Cialis are automatically placed on the generic. Are they required to repeat the process? He further states that grandfathering these patients will solve the problem for 25% of the population affected without any impact to the MHS.

Dr. Allerman responds we will follow-up and look at a process to operationalize or grandfather the patients on branded Cialis.

Mr. DuTeil expresses concerns about requiring the patient to repeat the PA process. If the patient is using one of the medications moving to Tier 4, why the patient and physician can't decide which of the UF products is best for the patient. Is there a difference between the two UF products?

Dr. Allerman responds if a male over 40 chooses the generic sildenafil there is no requirement to complete the PA. The patient will receive generic sildenafil. However, if the patient wants to try generic tadalafil, the PA requires a trial of generic sildenafil.

Mr. DuTeil asks if there is a difference between the two medications.

Dr. Allerman responds, generic sildenafil is a shorter half-life agent and generic tadalafil is a longer half-life agent. One provider (urologist) commented that both a longer and shorter acting agent be included on the formulary.

Mr. DuTeil asks if there are any similarities with all the medications on the formulary.

Dr. Allerman responds Viagra is a shorter acting agent and the preferred agent since 2005. The P&T Committee recommends moving generic tadalafil from non-formulary to formulary status. According to the clinical efficacy data, the major guidelines and meta-analysis, they were all found to be therapeutically inter-changeable when treating the condition, ED.

Mr. Hostettler asks if the provider gave a rationale for placing both a longer and shorter acting agent on the formulary.

Dr. Allerman responds that it was their preference as a prescriber.

Dr. Khoury clarifies, if I am not mistaken, the provider did not provide a rationale beyond stating both a short and long acting were needed.

Mr. Hostettler asks the presenters to confirm that the provider definitely stated that both the shorter and longer acting agent was needed.

Dr. Khoury responds that one provider made the request to include a longer and shorter acting agent on the formulary and there were numerous comments.

Dr. McKeon interjects that the side-effects can be negative for air crews. So a shorter acting agent is better because the side effects do not impact the patient the following day. It has to do with readiness.

Dr. Allerman clarifies that we are discussing the generic Viagra which we have had available for years.

Dr. Khoury clarifies the disease state does not impact readiness specifically.

Dr. McKeon responds if treated correctly, the disease is taken care of, it is the side effect that cause an issue.

Mr. Hostettler states it appears there is a preference by one provider to place a longer and shorter acting agent on the Formulary but the recommendation requires all patients complete the step to get the shorter acting agent.

Dr. Allerman responds I don't believe they set a preference that the shorter acting is better than the longer acting.

Mr. Hostettler states, regardless, the step requires a trial of the shorter acting agent first. He further states that the longer and shorter acting agent should be UF and step preferred. The provider will make the decision about the best agent for the patient. Based on the clinical information presented, there does not appear to be a difference between the two medications. It was a provider decision to make the two medications available. I agree that both medications should be UF but I don't agree with the recommendation to

require the trial of sildenafil to get tadalafil. Theoretically, there is no therapeutic difference.

Mr. DuTeil responds it does make sense because there are two different products that do two different things. In my opinion, that is a decision for a provider.

There were no more questions or comments. The Chair called for a vote on the UF/Tier 4/Not Covered Manual PA Criteria, and the UF /Tier 4/Not Covered and PA Implementation recommendations for the PDE-5 Inhibitors.

- **PDE-5 Inhibitors – UF/Tier 4/Not Covered Recommendation**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

- **PDE-5 Inhibitors – Manual PA Criteria**

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

  **** The non-concurring Panel members believed that both agents should be step-preferred and provider decides which agent is best for the patient.**

- **PDE-5 Inhibitors – UF/Tier 4/Not Covered and PA Implementation Plan**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

B. RAPID-ACTING INSULINS SUBCLASS

(LTC KHOURY)

1. Rapid-Acting Insulins (RAIs) – Relative Clinical Effectiveness Analysis and Conclusion

Background—The RAIs have not been previously reviewed for formulary status. Insulin aspart (Novolog) has been BCF since 2003, prior to implementation of the UF Rule in 2005. Insulin lispro (Humalog) and insulin glulisine (Apidra) have not been previously reviewed and have been UF "by default" since their approval. Two products were reviewed as innovators: insulin aspart plus niacinamide (Fiasp) was made NF in November 2017 and inhaled insulin (Afrezza) was made NF in February 2016; both Fiasp and Afrezza require a PA.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 2 absent) the following:

- There were no major updates to the P&T clinical conclusions from 2003 that showed there are no clinically relevant differences between insulin aspart (Novolog) and lispro (Humalog) in lowering hemoglobin A1c.
- Numerous clinical practice guidelines are available (e.g., American Diabetes Association, American Association of Clinical Endocrinologists, American College of Endocrinology) and none give preference to one RAI over another.
- Although there are subtle differences between RAIs with regard to pharmacokinetic profiles in terms of onset and duration of action, clinical efficacy appears similar between the products.
- Insulin aspart (Novolog) is the current Basic Core Formulary RAI and is approved for use in insulin pumps and in children as young as 2 years of age. Other advantages include that it is available in all dosage forms (pen, vials, and cartridges), and has the majority of the market share in the MHS (>60%).
- Insulin lispro (Humalog) advantages include a long history of use in the MHS, approval for insulin pumps and in pediatric patients down to age 3 years, and availability in all dosage forms (pen, vials, and cartridges). Humalog is second in utilization in the MHS (30%).
- Insulin glulisine (Apidra) was the third FDA-approved RAI. It may be used in insulin pumps and in pediatric patients down to 4 years. Disadvantages of Apidra compared to insulin aspart or lispro include a greater susceptibility to precipitation and catheter occlusions during continuous subcutaneous insulin infusion (CSII), and the association with significantly elevated hypoglycemia rates. It has very low utilization in the MHS (<1%).
- Fiasp is a new formulation of insulin aspart that contains niacinamide, a form of vitamin B3. Although Fiasp has a faster onset of action, the change in pharmacokinetic profile did not show a clinically significant difference in A1c or post-prandial blood glucose compared to Novolog. Fiasp recently gained FDA approval for use in pumps, but was not approved in pediatrics at the time of the P&T Committee review. It has similar adverse effects to Novolog with slightly higher rates of hypoglycemia, upper respiratory infections, and nasopharyngitis.
- Admelog is a new formulation of insulin lispro that did not show a clinically significant difference in A1c or post-prandial blood glucose versus the active comparator Humalog. It is approved for use in pumps and in pediatrics down to age 3 years.
- Afrezza is the only inhaled insulin. Although it is approved for use in adults, it lacks pediatric labeling, has very low utilization in the MHS, and is the only RAI with a black box warning regarding bronchospasm in patients with asthma or chronic obstructive pulmonary disease (COPD). Despite the unique drug delivery system, Afrezza has numerous limitations including contraindications and warnings. As with all the RAIs, Afrezza requires concomitant basal insulin injections, which negates a potential advantage in patients with needle phobia. Overall, Afrezza offers no clinically compelling advantage over other RAIs.

- With regard to adverse events, there was no new data to change the 2003 conclusion that there is no evidence of a difference in the number, type, or severity of adverse reactions between insulin aspart (Novolog) or lispro (Humalog).
- In a retrospective claims analysis comparing insulin aspart and lispro, there were no significant differences in the percentage of patients experiencing a hypoglycemic event or new or worsening diabetes complications. Additionally, there were no significant differences in emergency department visits between any of the products or device (e.g., vial, pen, and cartridge) comparisons.
- With regard to special populations, two systematic reviews found that RAIs were safe in pregnancy, pediatric patients, and in patients with diabetic ketoacidosis (DKA). No preferences were given regarding use of one RAI over another.
- With regard to devices, the RAI pens are the most widely used dosage form in the MHS, followed by vials, then cartridges.
- Overall, with the exception of inhaled insulin (Afrezza), there is a high degree of interchangeability among the RAIs.

2. RAIs – Relative Cost-Effectiveness Analysis and Conclusion

CMA and BIA were performed to evaluate the RAIs. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA results for the RAIs showed the following products ranked from most cost effective to least cost effective as follows: insulin aspart (Novolog), insulin lispro (Humalog and authorized generic insulin lispro), insulin lispro (Admelog), insulin glulisine (Apidra), insulin aspart with niacinamide (Fiasp), and inhaled insulin (Afrezza), respectively.

- BIA was performed to evaluate the potential impact of designating selected insulins as formulary, NF or Tier 4 on the UF. BIA results showed that designating insulin aspart (Novolog) and insulin lispro (Humalog and authorized generic insulin lispro) as UF and step-preferred, and insulin lispro (Admelog), insulin glulisine (Apidra), insulin aspart with niacinamide (Fiasp), and inhaled insulin (Afrezza) as NF and non-step-preferred demonstrated the most cost avoidance for the MHS.

3. RAIs – UF/Tier 4/Not Covered Recommendation

a) The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) the following:

- UF and step-preferred
  - insulin aspart (Novolog)
  - insulin lispro (Humalog and authorized generic insulin lispro)

- NF and non-step-preferred:
  - insulin lispro (Admelog)
  - insulin glulisine (Apidra)
  - inhaled insulin (Afrezza)

- This recommendation includes step therapy (automated PA), which requires a trial of insulin aspart (Novolog) and insulin lispro (Humalog or authorized generic lispro) prior to use of the NF, non-step-preferred RAIs in all new and current users.

b) The P&T Committee recommended (9 for, 7 opposed, 0 abstained, 1 absent) the following:

- Tier 4/Not Covered
  - insulin aspart plus niacinamide (Fiasp)

The P&T Committee concluded that Fiasp provides very little to no additional clinical effectiveness relative to the other RAIs. Overall, the P&T Committee felt that the needs of TRICARE beneficiaries can be met by the other RAIs. The formulary alternatives include Novolog, Humalog, and authorized generic insulin lispro.

4. RAIs – Automated PA (Step Therapy) and Manual PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) automated PA and manual PA criteria for all new and current users of the non-step-preferred RAIs, insulin lispro (Admelog) and insulin glulisine (Apidra). A trial of Novolog and either Humalog or authorized generic insulin lispro will be required first, unless the patient is using an insulin pump/CSII and is stabilized on Admelog or Apidra, or if they have tried and failed the step-preferred insulins.

Existing manual PA criteria apply to inhaled insulin (Afrezza). The P&T Committee recommend updating the manual PA criteria requiring the patient to have tried and failed Novolog and Humalog or authorized generic insulin lispro in all new and current users. Note that Afrezza will not be included in the automated step therapy criteria.

The PA criteria are as follows, with the changes highlighted in bold and strikethrough:

a. Inhaled insulin (Afrezza)

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

Coverage is approved if all the criteria are met for non-smoking patients with either:

Type 1 Diabetes Mellitus (diagnosed)

- **Patient has tried and failed (defined as a failure to achieve hemoglobin Alc < 7% in 90 days) with insulin aspart (Novolog)**
- **Patient has tried and failed (defined as a failure to achieve hemoglobin Alc ≤ 7 % in 90 days) with insulin lispro (Humalog or authorized generic insulin lispro**
- ~~Failure to achieve hemoglobin Alc ≤ 7 % in 90 days of use of a rapid or short acting subcutaneous (SC) insulin product or clinically significant adverse effects experience with SC rapid or short acting insulin unexpected to occur with inhaled insulin~~
- Afrezza is used as adjunctive treatment to current basal insulin therapy
- Spirometry testing [baseline forced expiratory volume in the first second (FEV_1)] has been performed upon initiation of therapy, with repeated FEV_1 at 6 months after initiation and repeated annually thereafter
- Patient does not have a contraindication to Afrezza (e.g. hypoglycemia, chronic lung disease [asthma, chronic obstructive pulmonary disease (COPD)], hypersensitivity to regular human insulin, or any Afrezza excipients)

Type 2 Diabetes Mellitus (diagnosed)

- **Patient has tried and failed (defined as a failure to achieve hemoglobin Alc < 7% in 90 days) with insulin aspart (Novolog)**
- **Patient has tried and failed (defined as a failure to achieve hemoglobin Alc ≤ 7 % in 90 days) with insulin lispro (Humalog or authorized generic insulin lispro**
- ~~Failure to achieve hemoglobin Alc ≤ 7 % in 90 days of use of a rapid or short acting subcutaneous (SC) insulin product or clinically significant adverse effects experience with SC rapid or short acting insulin unexpected to occur with inhaled insulin~~
- Patient has had failure of or clinically significant adverse effects to two oral anti-diabetic agents (i.e., sulfonylurea, TZD, DPP-4 inhibitor, or **SGLT2 inhibitor**) if metformin is contraindicated
- Spirometry testing [baseline forced expiratory volume in the first second (FEV1)] has been performed upon initiation of therapy, with repeated FEV1 at 6 months after initiation and repeated annually thereafter
- Patient does not have a contraindication to Afrezza (e.g. hypoglycemia, chronic lung disease [asthma, chronic obstructive

pulmonary disease (COPD)], hypersensitivity to regular human insulin, or any Afrezza excipients)

Non-FDA-approved uses are not approved.
PA does not expire.

b. Insulin glulisine (Apidra) and insulin lispro (Admelog)

Step therapy and manual PA criteria apply to all new and current users of Apidra and Admelog.

Automated PA Criteria: The patient has filled a prescription for insulin aspart (Novolog) and insulin lispro (Humalog or authorized generic lispro) at any MHS pharmacy point of service [military treatment facility (MTFs), retail network pharmacies, or mail order] during the previous 720 days.

AND

Manual PA Criteria if automated criteria are not met:

Note: Novolog, Humalog, and the authorized generic insulin lispro are DoD's preferred RAIs. If the prescription is for Novolog, Humalog, or the authorized generic insulin lispro, PA is not required.

- If automated criteria are not met, Apidra or Admelog is approved if all criteria are met:
  - Patient has diabetes AND
    - Patient has tried and failed insulin aspart (Novolog) AND
    - Patient has tried and failed insulin lispro (Humalog or authorized generic insulin lispro)
      OR
    - Patient is using an insulin pump/continuous subcutaneous insulin infusion (CSII) and is stabilized on insulin glulisine (Apidra) or insulin lispro (Admelog)

Non-FDA-approved uses are not approved

PA does not expire

5. RAIs – Removal of Authorized Generic Insulin Lispro Manual PA Criteria

The authorized generic insulin lispro entered the market in April 2019, and manual PA criteria requiring a trial of Humalog first was implemented in May 2019. The

P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) removing the manual PA on authorized generic lispro, as it is no longer cost advantageous.

6. RAIs – UF/Tier 4/Not Covered and PA Implementation Plan

The P&T Committee recommended 1) an effective date of the first Wednesday after a 150-day implementation period, and no earlier than July 1, 2020 in all points of service and, 2) DHA send letters to beneficiaries who are affected by the UF/Tier 4 and PA. Patients affected by the Tier 4 recommendation will receive letters at 90, 60, and 30 days prior to implementation.

7. Physician's Perspective

This is the first time we're reviewing the Rapid Acting Insulins. However, both Novolog and Humalog have been available in DoD dating back to 1999. We are now seeing new products enter the market, which was part of the reason for the class review.

The Committee was unanimous in recommending step therapy for the class. Novolog and Humalog will be on the formulary and step-preferred, with no Prior Authorization required. Admelog, Apidra and Afrezza will all be non-formulary and non-step preferred and will require a trial of both Novolog and Humalog first in all patients.

The inhaled insulin Afrezza will remain non-formulary. While the Committee did acknowledge the novel administration route, patients will still require injections of basal insulin (like Lantus), which significantly limits any perceived potential benefits of Afrezza. There are additional criteria in the Afrezza PA due to the risks in patients with underlying pulmonary disease.

The formulary decision to have Novolog and Humalog as the two preferred products is very similar to the current status, and these two insulins make up over 97% of the current market share. There is very little utilization of the non-preferred products, so the Committee felt there would be less patient and provider abrasion, while maximizing cost savings. Also, having two products as step-preferred decreases the risk if a shortage of one of the preferred insulins were to occur.

Since the PAs for Apidra, Admelog and Afrezza will now be "no grandfathering" scenarios where new and current users will be affected, we will be adding this to the "safety net" program managed by ESI, to help ensure that patients don't "fall through the cracks". This program will identify patients who have not received a prescription fill after an initial reject occurs and both the provider and patient will receive follow-up letters.

There was discussion on the Tier 4 status recommendation for Fiasp. The Committee members voting against the Tier 4 recommendation were due to the provider survey which found there was not unanimous agreement from endocrinologists that Fiasp should be Tier 4, and concerns that a patient could walk away from the pharmacy counter without receiving their insulin. However, the reasons for having this product designated as Tier 4 were due to the fact it has the same active ingredient as Novolog, with only Vitamin B3 added, and that it has not been shown to have a clinically significant difference in blood glucose values than Novolog, along with cost. Several commercial health plans also have Fiasp excluded from formulary coverage.

For the implementation period, the Committee recommended 150 days after signing, because of the Tier 4 recommendation for Fiasp. We will send letters to the patients affected by the UF to NF changes (Admelog and Apidra), the updated "no grandfathering" PAs (Admelog, Apidra and Afrezza), and to patients currently receiving Fiasp. The patients affected by the Tier 4 change for Fiasp will get three letters this time– one at 90 days prior to implementation, one at 60 days and then at 30 days, if they are still on Fiasp. As of late December, there were about 175 patients on Fiasp in the DoD.

8. Panel's Questions and Comments

Mr. Hostettler states the Panel was assured that Tier 4 would be judiciously used and minimal products affected. I have been attending this meeting, in some manner, since its inception and I have never seen a 9-7 vote from the P&T Committee. Although there were seven dissenting votes, the P&T Committee proceeded with moving this product to Tier 4. As a beneficiary, I am very concerned. Why not place the medication on step therapy or require a prior authorization.

Mr. DuTeil concurs with Mr. Hostettler's comments regarding the P&T Committee vote. Although he has not served on the Panel as long, rarely is there more than one (1) person objecting to a change that has been approved by the P&T Committee. It is obvious, the current users will not be able to afford the drug once it moves to Tier 4 status. He asks for a rationale or an alternative that would satisfy the seven P&T Committee members that opposed the vote as far as combinations?

Dr. Khoury responds the P&T Committee vote was 9-7. The endocrinologist and seven committee members believed Fiasp should remain formulary and available. The Committee sees the full gamut of data provided regarding the clinical and cost effectiveness. The same data is not under the preview of or available to the Panel. In spite of the clinical concerns about this specific disease state, a majority of Committee members believed the clinical and cost effectiveness of Fiasp warranted the Tier 4 recommendation. The data showed no clinical differences, very little to no clinical advantage to the other

drugs available and the cost effectiveness is of such a concern that a majority of the Committee recommended placement on Tier 4. Your comments are valid and will be forwarded to the Director, DHA for consideration.

Ms. Buchanan also concurs with her colleagues. She asks if current beneficiaries can continue using Fiasp. There must have been some reason the providers prescribed the drug for the patients. Is there any data that shows they actually tried other medications prior to being placed on the drug? Recognizing that it is only 175 patients but we are talking about diabetes, this can be a life or death decision.

Mr. Hostettler states this decision impacts new and current users. This is a disease that has ramifications far beyond the drug cost. This recommendation requires beneficiaries, whose disease state is stable, to repeat the step. I don't understand why the Committee is taking such draconian steps. As stated, we aren't provided the same data briefed to the P&T Committee. If there is a compelling reason for the decision, please share it with the Panel rather than asking us to trust you. In my opinion, the current users should be grandfathered.

Dr. Dager asks about available tools such as step therapy or a prior authorization to make the medication available to patients.

Dr. Khoury responds he will address some of the sentiments and concerns raised. To clarify, the decision or recommendation to move a drug to Tier 4, cannot include step therapy or a prior authorization. Each is a separate tool and process. We can take your comments for consideration and potentially discuss other options. We did look at prior utilization tendencies of those patients that were prescribed Fiasp, the data showed that they hadn't tried all the formulary alternatives. Because this is a very small subset, I hesitate to arrive at any conclusions from the data. The data is not adequate enough to arrive at a valid conclusion.

Mr. Hostettler appreciates the utilization is low. If I am not mistaken, it was previously stated that the endocrinologists dissented on the vote. Those are the experts in this area and I can't understand why we are ignoring the experts' comments not to mention the seven dissenting votes.

Dr. Khoury clarifies the comments were from the endocrinologist and the P&T committee members provided the dissenting votes.

Dr. Piirainen asks if data is available on the number patients who were using Fiasp in a pump.

Dr. Allerman responds we did not look at that.

Dr. Piirainen asks if there was any consideration regarding members who may already be stable on an insulin pump with Fiasp as with other PAs for the other non-formulary RAIs.

Dr. Allerman responds we would have to conduct a higher level analysis to actually look at the patients that have Type 1 diabetes and then some type of claim for a pump.

Col Hoerner states I would share that the P&T committee had more information that you have and that was the vote that came out of it. Because it was a majority of committee members, the recommendation was accepted.

Dr. Bertin states he shares the comments of the other Panel members. He asks if the Panel members can concur with all aspects of the recommendation except for the Tier 4.

Col Hoerner responds no. The Panel must vote on the recommendation as written. Either the Panel agrees with the recommendation or they don't. As previously stated, your questions and comments will be presented to the Director, DHA for consideration.

Mr. DuTiel interjects that he understands the Chair's question. It appears that the Panel will non-concur with this recommendation and we don't want to delay the other changes.

Col Hoerner reiterates that the information is recorded into the record and presented to the Director, DHA for consideration.

Dr. Peloquin comments that the language regarding the automated step and the manual PA criteria is confusing. According to the recommendation, the automated PA and manual PA require new and current users to try the NF and non-step-preferred agents. Will they continue on therapy because they are on the product? Because it is a 720 day look-back starting at that point, will the patient be required to repeat the step? The patient has a history of the drug. If the look back is 720 they are essentially grandfathered.

Dr. Khoury responds they will not be grandfathered and they will have to try the one of the step-preferred agents.

Dr. Peloquin asks Dr. Khoury to address the automated PA and manual PA criteria with the Panel.

Dr. Khoury responds, we extended that typical look back to reflect this specific disease state. Typically we would do a 365 day look back. Because of this disease state, it was expanded to capture that the patient has tried the

alternatives. If the patient meets the criteria, they can pass through that 720 day look back in the automated PA.

Mr. Hostettler asks if there is a standard process to seamlessly transition a patient from a medication where the disease-state is stable and require the patient to repeat the process for a trial of Novolog or Humalog. Because this is a unique disease, I am concerned that the patent will be forced to make numerous trips to his/her physician, repeat labs/test in an effort to maintain a stable disease state. This incurs cost to the MHS outside of drug acquisition cost.

Dr. Khoury responds this is a unique disease state. Unlike the PDE-5, where someone can get one prescription and it potentially lasts a year, this one requires engagement with the provider on a regular basis. A Type 1 diabetic is in contact with the provider on a frequent and regular basis. I would also say that a Type II diabetic sees their provider every 3-6 months to manage all the chronic disease state issues that arise in that disease state. In response to your question regarding the frequency in which a Type I or Type II diabetic is likely engaging in care, there is a high likelihood they are seeing the provider on a regular basis. To prepare the patients impacted by the decision, we are sending out three letters at varying times during the implementation period. We are trying to increase awareness of the change as well as provide ample time and opportunity to ensure the patient can transition to the new medication without causing an issue with their disease state. We also believe that it will be easy to the patient to make the switch and in some cases preferable because: (1) the decision does not impact tens of thousands of patients; (2) Novolog and Humalog are clinically similar to the Admelog and (3) there is no clinical difference; and (4) alternate dosage forms are available in UF and step preferred products. Additionally, the pens, vials and cartridges are available in preferred products but not necessarily available in the alternative agents. Switching to the preferred medication may be a more preferable outcome for the patients who were prescribed the medication because their provider was not aware there was a better option available. As discussed, every benefit is different. The provider may prescribe a certain type of agent for any number of reasons. This recommendation might encourage a shift to something that is a better outcome for the patient to also include a lower copay.

Mr. Hostetler states that he understands. Regardless, a patient impacted by the decision may not agree with you. There were two comments regarding pumps that appear to have not been taken into account. In my opinion, changing the criteria to new users would ease my concerns.

Dr. Khoury responds, if the pumps are an issue, that the pumps were taken into consideration on the PA.

Mr. Hosteller replies the pumps were not taken into consideration for the Tier 4 products. In my opinion, this decision is putting patients at risk by forcing patients in a stable condition to change their therapy. In my opinion, changing the PA criteria to new users is a better option. We can better manage a new patient, in an unstable condition within the system because there is no interruption to their therapy.

Dr. Peloquin asks how many patients meet the criteria in the automated step. For instance, if 175 patients are impacted by the decision and 100 meet the automated step criteria, the population impacted decreases.

Dr. Khoury responds I don't have the exact numbers but the data reviewed by the committee suggested that most hadn't met the step. The implementation period provides ample opportunity to shift to the formulary step-preferred agent. This benefits the patient because the lower co-pay applies. The patient may be paying a higher co-pay because the provider and patient is not aware that an alternative is available.

Dr. Peloquin asks for the number of beneficiaries using the non-formulary and non-step preferred.

Dr. Khoury responds that there are 1,000 beneficiaries on Apidra, 125 using Admelog 125, and 87 using Afrezza. This is the number of beneficiaries using each agent at the time of the review. This is out of a total of 56,000 patients that require these agents. The vast majority are on Novolog and Humalog.

Mr. Hostettler responds his concerns go away if the PA criteria is changes to new users. The unique user affected by the Tier 4 decision is low.

Ms. Buchanan raises an issue of concern regarding provider education. There was a reason the providers prescribed the drug. Are they new to the medical practice? Did a pharmaceutical drug salesman get to them? Bottom line the education needs to be in place.

Mr. Hostettler asks for a clarification regarding the PA criteria for Afrezza. It states that coverage is approved it all criteria are met for non-smoking patients. Why the differentiation?

Dr. Khoury responds the concern is the specific issues regarding the inhalation aspect of the drug.

Dr. Allerman states that inhaled insulin Afrezza causes pulmonary problems, which is why it should not be used by smokers.

Mr. Hostettler adds the significant risks involved to the patient is recognized in the implementation plan. That is why you are sending 3 letters over the 150 days. The criteria should only be new users**!**

There were no more questions and comments from the Panel. The Chair called for a vote on the UF/Tier 4/Not Covered Recommendation, Automated (Step Therapy) Manual PA Criteria, Removal of Authorized Generic Insulin Lispro Manual PA Criteria and UF/Tier 4/Not Covered recommendations for the RAI's.

- **RAI's – UF/Tier 4/Not Covered Recommendation**

  Concur: 0 Non-Concur: 8 Abstain: 0 Absent: 1

  ****The Panel agrees with the Specialist and the 7 dissenting votes on the P&T committee**

- **RAI's – Automated (Step Therapy) Manual PA Criteria**

  Concur: 0 Non-Concur: 8 Abstain: 0 Absent: 1

  **** The Panel believes that the criteria should only be new users**

- **RAI's – Removal of Authorized Generic Insulin Lispro Manual PA Criteria**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

- **RAI's - UF/Tier 4/Not Covered and PA Implementation Plan**

  Concur: 7 Non-Concur: 1 Abstain: 0 Absent: 1

  **** The non-concurring Panel member does not believe it should go forward as new and current users. No tier 4 and only new users.**

II. NEWLY APPROVED DRUGS

(LTC KHOURY)

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

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

The P&T Committee agreed for groups 1 and 2: (16 for, 0 opposed, 0 abstained, 1 absent) and group 3: (17 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/Tier 4/Not Covered Recommendation

The P&T Committee recommended for groups 1 and 2: (16 for, 0 opposed, 0 abstained, 1 absent); and group 3: (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- UF:
    - bremelanotide injection (Vyleesi) – Miscellaneous gynecological agent for Hypoactive Sexual Desire Disorder (HSDD)
    - darolutamide (Nubeqa) – Oral oncologic agent for non-metastatic castration-resistant prostate cancer (nmCRPC)
    - entrectinib (Rozlytrek) – Oral oncologic agent for lung cancer
    - fedratinib (Inrebic) – Oral oncologic agent for myelofibrosis
    - glucagon injection (Gvoke Hypopen and Pre-filled Syringe) – Binders-Chelators-Antidotes-Overdose Agent for severe hypoglycemia
    - glucagon nasal spray (Baqsimi) – Binders-Chelators-Antidotes-Overdose Agent for severe hypoglycemia
    - lamivudine/tenofovir disoproxil fumarate (Temixys) – Antiretroviral combination for human immunodeficiency virus (HIV)
    - midazolam nasal spray (Nayzilam) – Anticonvulsants-antimania agent for seizures
    - pexidartinib (Turalio) – Oral oncologic agent for tenosynovial giant cell tumors
    - segesterone acetate/ethinyl estradiol vaginal ring (Annovera) – Miscellaneous contraceptive agent
    - selinexor (Xpovio) – Oral oncologic agent for relapsing remitting multiple myeloma
    - semaglutide oral tablet (Rybelsus) – Oral glucagon-like peptide-1 receptor agonist for type 2 diabetes mellitus in adults
    - tiopronin extended release (Thiola EC) - Miscellaneous urinary agent for cystinuria
- NF:
    - amlodipine oral suspension (Katerzia) – Calcium channel blocking agent in an oral suspension for hypertension
    - duloxetine extended-release (Drizalma Sprinkle) – Antidepressants and non-opioid pain syndrome, serotonin-norepinephrine reuptake inhibitors (SNRIs)

- istradefylline (Nourianz) – Parkinson's agent for off episodes
- lefamulin (Xenleta) – Antibiotic for community acquired bacterial pneumonia (CABP)
- pitolisant (Wakix) – Sleep disorders: wakefulness promoting agent for narcolepsy
- upadacitinib (Rinvoq) – Targeted Immunomodulatory Biologic (TIB) for rheumatoid arthritis

- Tier 4 (Not Covered):

  - formoterol/aclidinium (Duaklir Pressair) inhaler– Pulmonary-2 Agent for Chronic Obstructive Pulmonary Disease (COPD)

    a. Duaklir Pressair was recommended for Tier 4 status as it has little to no additional clinical effectiveness relative to similar long-acting muscarinic antagonist/long-acting beta agonist (LAMA/LABA) combination drugs; and the needs of TRICARE beneficiaries are met by alternative agents.
       - Formulary LAMA/LABA alternatives to Duaklir Pressair are umeclidinium/vilanterol (Anoro Ellipta), tiotropium/olodaterol (Stiolto Respimat), glycopyrrolate/indacaterol (Utibron Neohaler), and glycopyrrolate/formoterol (Bevespi Aerosphere).

  - sumatriptan nasal (Tosymra) – Migraine agents, Triptans

    a. Tosymra was recommended for Tier 4 status as it has little to no additional clinical effectiveness relative to similar nasal triptan migraine agents; and the needs of TRICARE beneficiaries are met by alternative agents.
       - Formulary alternatives to sumatriptan nasal (Tosymra) are sumatriptan nasal spray (Imitrex, generics); zolmitriptan nasal spray (Zomig); and sumatriptan nasal powder (Onzetra Xsail).

  - tegaserod (Zelnorm) – Gastrointestinal-2 agent for constipation-predominant irritable bowel syndrome (IBS-C)

    a. Zelnorm was recommended for Tier 4 status as it has no clinical benefit relative to other agents approved for IBS-C and has significant safety concerns relative to other IBS-C drugs including cardiovascular and suicidality risks; and the needs of TRICARE beneficiaries are met by alternative agents.
       - Formulary alternatives to Zelnorm include linaclotide (Linzess), plecanatide (Trulance), and lubiprostone (Amitiza).

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

The P&T Committee recommended for groups 1 and 2: (16 for, 0 opposed, 0 abstained, 1 absent); and group 3: (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Applying manual PA criteria to new and current users of Drizalma Sprinkle, Nourianz, Rybelsus, Vyleesi, and Wakix.
- Applying manual PA criteria to new users of Inrebic, Nubeqa, Rozlytrek, Thiola EC, Turalio, and Xpovio.
- Targeted Immunomodulatory Biologic (TIBs): Applying the same manual PA criteria in new users of Rinvoq that are currently in place for the other non-step-preferred TIBs. Patients must first try adalimumab (Humira). Additionally, for Rinvoq a trial of tofacitinib (Xeljanz) or baricitinib (Olumiant) is required if the patient cannot be treated with Humira.

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

a) bremelanotide injection (Vyleesi)

Manual PA criteria applies to all new and current users of Vyleesi.

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

- Patient is ≥ 18 years
- Patient is a premenopausal woman with a documented diagnosis of acquired, generalized hypoactive sexual desire disorder (HSDD) as characterized by low sexual desire that causes marked distress or interpersonal difficulty
- Decreased sexual desire is NOT caused by:
  - Co-existing medical or psychiatric condition
  - Problems with the relationship
  - Effects of a medication or drug substance
- Patient has been informed that other treatment options, such as cognitive-behavior therapy, sexual therapy, or couples therapy, may provide benefit without the risk of side effects
- Patient does not have uncontrolled hypertension or known cardiovascular disease
- Patient has been counseled on the risks of focal hyperpigmentation (skin discoloration) and severe nausea
- Patient agrees to use effective contraception while taking Vyleesi

Non-FDA-approved are not approved.

PA expires in 3 months.

Renewal PA criteria: Coverage will be approved indefinitely for continuation of therapy if the patient has had documented improvement in symptoms without serious side effects.

b) darolutamide (Nubeqa)

Manual PA is required for all new users of Nubeqa.

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

- Note that Xtandi is the Department of Defense's preferred 2nd-Generation Antiandrogen Agent. The patient is required to try Xtandi first. OR
- Patient has a contraindication or has had an inadequate response or adverse reaction to Xtandi that is not expected to occur with Nubeqa AND
- Patient is ≥ 18 years AND
- Drug is prescribed by or in consultation with an oncologist or urologist AND
- Patient has diagnosis of non-metastatic castration-resistant prostate cancer (nmCRPC) AND
- The patient has had a negative CT scan of abdomen/pelvis and/or negative bone scan AND
- Prostate-specific antigen doubling time (PSADT) is ≤ 10 months

OR

- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.
- Patient must be receiving a gonadotropin-releasing hormone (GnRH) analog concomitantly OR have had a bilateral orchiectomy

Other Non-FDA-approved uses are not approved.
PA expires in 1 year.

Renewal criteria: Nubeqa is approved for 1 year for continuation therapy if all criteria are met:

- The patient continues to be metastases-free
- The patient has not progressed onto subsequent therapy (such as abiraterone)

c) Duloxetine delayed-release capsules (Drizalma Sprinkle)

PA criteria applies to all new and current users of Drizalma Sprinkle except PA does not apply to patients 12 years of age and younger (age edit)

Manual PA Criteria: Drizalma Sprinkle is approved if the provider explains why the patient requires duloxetine sprinkle capsules and cannot take alternatives.

Non-FDA-approved uses are not approved.
PA expires in 1 year.

Renewal PA criteria: No renewal allowed. A new prescription will require submission of a new PA.

d) Entrectinib (Rozlytrek)

Manual PA criteria apply to all new users of Rozlytrek.

Manual PA Criteria: Rozlytrek will be approved if all criteria are met:

- Patient is ≥ 12 years
- Drug is prescribed by or in consultation with an oncologist
- Patient has a diagnosis of either:
  - ROS1(+) Metastatic Non Small Cell Lung Cancer or
  - The patient has a solid tumor that meets all three of the following criteria:
- Has a neurotrophic tropomyosin receptor kinase (NTRK) gene fusion without a known acquired resistance mutation, and
- Is metastatic OR where surgical resection is likely to result in severe morbidity, and
- Has no satisfactory alternative treatments OR that has progressed following such treatment(s)
- The patient has had a recent evaluation of his/her left ventricle including ejection fraction
- The patient does not have decompensated congestive heart failure (CHF)
- The patient has had a recent uric acid level
- The provider is aware and has informed the patient of the risk of CHF development and exacerbation, myocarditis, neurotoxicity, fracture risk, hepatotoxicity, hyperuricemia, QT-prolongation, permanent visual impairment, and embryo-fetal toxicity
- Female patients will not breastfeed during treatment and for 1 week after cessation of treatment
- All patients (females AND males) of reproductive potential will use highly effective contraception during treatment and for at least 5 weeks or 3 months after cessation of treatment for females and males, respectively.
- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1,

2A, or 2B recommendation. If so, please list the diagnosis: _____.

Other non-FDA-approved uses are not approved.

PA does not expire.

e) fedratinib (Inrebic)

Manual PA is required for all new users of Inrebic.

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

- Patient is ≥ 18 years
- Drug is prescribed by or in consultation with a hematologist/oncologist
- Inrebic will be used for intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis
- Provider acknowledges that serious and fatal encephalopathy including Wernicke's encephalopathy has occurred in patients treated with Inrebic. If thiamine deficiency is expected or confirmed, Inrebic should be discontinued immediately and the patient should receive emergent parenteral thiamine.
- The patient does not have vitamin B1 deficiency.
- The following labs will be assessed prior to starting Inrebic and periodically while the patient is taking Inrebic: thiamine (Vitamin B1), complete blood count (CBC) with platelets, serum creatinine and blood, urea nitrogen (BUN), hepatic panel and amylase and lipase
- Nutritional status will be assessed prior to starting Inrebic and periodically while the patient is taking Inrebic
- If the patient is female, she is not pregnant or planning to become pregnant.
- Female patients will not breastfeed during treatment and for at least 1 month after discontinuation.
- Females of reproductive potential will use effective contraception during treatment and for at least 1 month after discontinuation.
- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.

Other non-FDA-approved uses are not approved.

PA does not expire.

f) istradefylline (Nourianz)

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

Manual PA Criteria: Nourianz approved if all criteria are met:

- Patient is ≥ 18 years
- Patient has a diagnosis of Parkinson's disease
- Drug is prescribed by or in consultation with a neurologist
- Patient continues to experience wearing off periods, despite optimizing (e.g., increasing dose and daily frequency) carbidopa/levodopa therapy
- Patient is currently taking and will continue taking carbidopa-levodopa therapy
- Patient must try and fail an adequate trial of at least two drugs from any of the three classes:
  - Dopamine Agonist: pramipexole (Mirapex), ropinirole (Requip), rotigotine (Neupro)
  - MAO-B: rasagiline (Azilect), selegiline (Eldepryl)
  - COMT: tolcapone (Tasmar), entacapone (Comtan)

Non-FDA-approved uses are NOT approved, including restless legs syndrome.

PA does not expire.

g) pexidartinib (Turalio)

Manual PA is required for all new users of Turalio.

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

- Patient is ≥ 18
- Drug is prescribed by or in consultation with an oncologist
- Patient has symptomatic tenosynovial giant cell tumor associated with severe morbidity or functional limitations, is not amenable to improvement with surgery, and has not progressed on Turalio.
- Patient will be monitored for hepatotoxicity
- Prescriber is certified with Risk Evaluation and Mitigation Strategy (REMS) program
- Patient is enrolled in REMS program
- If the patient is female, she is not pregnant or planning to become pregnant.
- Female patients will not breastfeed.
- All patients (females AND males) of reproductive potential will use effective contraception during treatment and for 1 month after

discontinuation in females and 1 week after discontinuation in males with female partners.
- The diagnosis IS NOT listed above but IS cited in the NCCN guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.

Other non-FDA-approved uses are not approved.

PA does not expire.

h) pitolisant (Wakix)

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

Manual PA Criteria: Wakix is approved if ALL criteria are met:

- Patient is ≥ 18 years
- Patient has a documented diagnosis of excessive daytime sleepiness associated with narcolepsy
- Narcolepsy was diagnosed by polysomnography or mean sleep latency time (MSLT) objective testing
- Drug is prescribed by a neurologist, psychiatrist, or sleep medicine specialist
- Patient is not concurrently taking any of the following:
  - Modafinil, armodafinil, or stimulant-based therapy, such as amphetamine or methylphenidate
- Patient must have tried and failed and had an inadequate response to modafinil
- Patient must have tried and failed and had an inadequate response to armodafinil
- Patient must have tried and failed and had an inadequate response to stimulant-based therapy (amphetamine or methylphenidate)
- Patient does not have a history of severe hepatic impairment
- Other causes of sleepiness have been ruled out or treated, including but not limited to obstructive sleep apnea

Non-FDA-approved uses are not approved (including but not limited to fibromyalgia, insomnia, excessive sleepiness not associated with narcolepsy, cataplexy, obstructive sleep apnea, major depression, Attention Deficit Hyperactivity Disorder (ADHD), or shift work disorder).

Not approved for use in children, adolescents, or pregnant patients
PA expires in 1 year.

Renewal PA criteria: No renewal allowed. When the PA expires, the next fill will require submission of a new PA.

i) selinexor (Xpovio)

Manual PA applies to new users of Xpovio.

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

- Age ≥ 18
- Drug is prescribed by or in consultation with an oncologist
- Xpovio will be used in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody
- Patient will be monitored for cytopenias including anemia, neutropenia, and thrombocytopenia
- Patient will be monitored for electrolyte disturbances including hyponatremia and hypokalemia
- Patient will be monitored for infection including upper respiratory infection and pneumonia
- Patients will be monitored for dizziness and altered mental status
- If the patient is female, she is not pregnant or planning to become pregnant.
- Female patients will not breastfeed.
- All patients (females AND males) of reproductive potential will use effective contraception during treatment and for at least 1 week after discontinuation.
- The diagnosis IS NOT listed above but IS cited in the NCCN guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.

Other non-FDA-approved uses are not approved.

PA does not expire.

j) semaglutide oral tablet (Rybelsus)

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

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

- Patient is ≥ 18
- Patient has a documented diagnosis of type 2 diabetes

- Patient has tried and had an inadequate response to metformin, or has a contraindication to metformin
- Patient must be able to adhere to the administration requirements (take on an empty stomach with no more than 4 oz. of water at least 30 min before the first meal of the day)
- Patient does not have a history of pancreatitis
- Patient does not have a personal or family history of medullary thyroid carcinoma (MTC)
- Patient does not have multiple endocrine neoplasia syndrome type 2 (MEN2)
- Patient and provider acknowledge that Rybelsus has not been shown to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease

Not approved for use in children or pregnant patients.

Non-FDA approved uses are not approved including weight loss (obesity) or type 1 diabetes mellitus.

PA does not expire.

k) tiopronin immediate-release (Thiola)/tiopronin delayed-release tablets (Thiola EC)

Note that PA criteria were also recommended for the original Thiola immediate release preparation.

Manual PA Criteria: Thiola or Thiola EC is approved if all criteria are met:

- Patient is ≥ 9 years
- Drug is prescribed by or in consultation with a nephrologist or urologist
- Patient has a documented diagnosis of severe homozygous cystinuria
- Patient has elevated urinary cystine concentration (> 250 mg/L) as demonstrated by a 24-hour urine test
- Patient has tried and failed treatment with all of the following conservative treatment measures:
  - High fluid intake ≥ 3 L/day
  - Urinary alkalization with potassium citrate or potassium bicarbonate
  - Diet modification with restricted protein and sodium consumption

Non-FDA-approved uses are not approved.

PA does not expire.

l) upadacitinib (Rinvoq)

Note that Humira is the DoD's preferred targeted biologic agent for rheumatoid arthritis.

Manual PA criteria applies to all new users of Rinvoq

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

- Patient is ≥ 18
- Patient has diagnosis of active rheumatoid arthritis
- Patient has had an inadequate response or an intolerance to methotrexate or other disease-modifying anti-rheumatic drugs (DMARDs)
- Patient has had an inadequate response to Humira OR
- Patient has experienced an adverse reaction to Humira that is not expected to occur with the requested agent OR
- Patient has a contraindication to Humira AND
- Patient has had an inadequate response to Xeljanz or Olumiant OR
- Patient has experienced an adverse reaction to Xeljanz or Olumiant that is not expected to occur with the requested agent OR
- Patient has a contraindication to Xeljanz or Olumiant that does not apply to Rinvoq AND
- Patient has no evidence of active tuberculosis (TB) infection
- Patient has no history of venous thromboembolic (VTE) disease
- Patient has no evidence of neutropenia (ANC <1000)
- Patient has no evidence of lymphocytopenia (ALC <500)
- Patient has no evidence of anemia (Hgb < 8)
- Patient is not taking Rinvoq concomitantly with other TIBs agents except for Otezla and other potent immunosuppressants (e.g., azathioprine, cyclosporine).

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 groups 1 and 2: 16 for, 0 opposed, 0 abstained, 1 absent); and group 3: 17 for, 0 opposed, 0 abstained, 0 absent) the following:

- **New Drugs Recommended for UF or NF Status:** An effective date upon the first Wednesday two weeks after signing of the minutes in all points of service.
- **New Drugs Recommended for Tier 4 Status Duaklir Pressair, Tosymra, and Zelnorm:** 1) An effective date of the first Wednesday after a 120-day implementation period at all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/Not Covered recommendation at 30 days and 60 days prior to implementation.

5. Physician's Perspective

The Committee reviewed 22 new drugs, of which 13 were recommended for UF status, with 6 recommended for NF status, and 3 Tier 4/Not Covered candidates. Prior authorization criteria will apply to 12 of the drugs. Several drugs were recommended for PAs since criteria already apply for the class, including the 5 oncology drugs, the TIB product (Rinvoq), and the diabetes drug (Rybelsus). For the new drugs, whenever a PA is recommended, we do reach out to providers for their comments on potential criteria.

"No grandfathering," where both new and current users will be affected by the PA, is recommended for 5 of the drugs, including the Parkinson's disease drug Nourianz because the FDA originally denied approval due to concerns of lack of efficacy and limited efficacy data and the female sexual desire disorder drug Vyleesi - due to safety concerns. For the narcolepsy drug Wakix, there are several low-cost generic alternatives available, which is also the case for the antidepressant drug Drizalma Sprinkle.

There were three Tier 4 candidates recommended at this meeting.

- formoterol/aclidinium (Duaklir Pressair inhaler)

    1. This drug is used for COPD and contains two ingredients; formoterol which is found in other inhalers, and aclidinium, which is available under the trade name "Tudorza" and has very low usage in the DoD.
    2. Duaklir is given twice daily, which could affect adherence. The single ingredient inhaler Spiriva has extensive utilization in the DoD and is dosed once daily.
    3. Feedback from pulmonologists supported Tier 4 status, and confirmed that there are unlikely any clinically significant differences between the products in relieving symptoms of COPD.

- sumatriptan Nasal (Tosymra)

    1. Tosymra is a nasal sumatriptan formulation that has the same active ingredient and uses the same delivery device as Imitrex nasal spray.

2. This product used the data from the Imitrex nasal spray to gain FDA approval, and did not conduct any new clinical trials. There are three other nasal triptan products available.
3. Neurology specialists also supported tier 4 status.

- tegaserod (Zelnorm) for IBS –C

1. Zelnorm was previously off the market for 12 years, but is now available again.
2. This drug has a very narrow indication - it is only approved for treating women younger than 65 with constipation-predominant irritable syndrome. The Committee was concerned that although the trials used to gain FDA-approval showed statistically significant results compared to placebo, the clinical significance of the results is unclear.
3. The majority of the GI specialists we reached out to supported Tier 4 status for Zelnorm, and stated that the risk of heart attacks and stroke, and also suicide outweighed the benefits. However some GI specialists said it should be available as they wanted options for this difficult to treat condition of IBS. When the drug class was first reviewed in 2012, there were few drugs available for treating irritable bowel syndrome. Now, there are several products approved, that have wider FDA indications.

The agents under review in the newly approved drug program had nearly 60 post marketing studies that were identified in the approval letter published by the FDA. These ranged from studies analyzing drug interactions, pharmacokinetics, animal studies, to things such final overall survival data.

6. Panel's Questions and Comments

Mr. Hostettler asks if there is an alternative or calcium channel liquid product for Kateriza (Amlodipine).

Dr. Allerman responds, amlodipine is one where the recipes are widely available and there is stability data available to support putting it in a solution. It is commercially available as well as an oral suspension or oral solution. We are handling this product the way we have previously established for these types of cardiovascular drugs.

Mr. Hosteller comments it is difficult for some cancer and thyroid patients to swallow pills. Rather than moving it to non-formulary, I would recommend moving it to uniform formulary with a PA requiring similar criteria. I believe this would be a better option for the patient.

Dr. Allerman responds, historically, we handle the oral liquid preparations for cardiovascular conditions by moving them to non-formulary without a prior

authorization requirement. These agents are low utilization but we have looked at the utilization of a couple of agents that are now available in liquids.

Mr. Hostettler asks if a patient who has problems swallowing pills qualifies for UF with the lower co-pay.

Dr. Allerman responds they can apply for medical necessity to request a reduction in the co-pay.

Dr. McKeon comments we are requiring a woman to meet all of these prerequisite. One of the prerequisites states, "Decreases sexual desire is not caused by a co-existing medical or psychiatric condition. The next bullet states, "the patient has been informed that other treatment options, such as cogitative behavior therapy, sexual therapy, or couples therapy, may provide benefit without the risk of side effects. Those two bullets seem mutually exclusive to me.

Dr. Allerman responds the TRICARE Policy Manual summarizes treatment coverage for ED. There are only two drugs on the market for female sexual dysfunction. The first was Addyi and the second is Vyleese. The prerequisites are listed, because the profile for female sexual dysfunction is characterized by some cardiovascular effects.

Dr. McKeon asks about females who want to become pregnant.

Dr. Allerman states the reasons for that is the problem have not been studied in patients who are pregnant. The side effect alone by themselves are a concern. We have no data for pregnancy.

Dr. Khoury: This agent, Vyleesi, had 3 post marketing study requirements.

Mr. Hostettler comments the PA criteria for Wakix states that the patient must try and fail at least 3 other products and it expires in a year. If the patient has met the PA criteria, what is the justification for requiring the patient to repeat it after a year?

Dr. Allerman replies the data shows that the provider will know if a patient is responds to therapy within 6 months. Requiring the patient to repeat the PA after a year, provides the opportunity for the physician to make a determination about whether the drug is working; whether something else would work better and to have a reassessment of how the patient is doing.

Mr. Hostetler clarifies, the assumption is that the patient may know that it is not working but they will take it any way.

Dr. Allerman answers Believe it or not, we do see that.

Dr. Piirainen refers to the language in the PA criteria for Wakix. It requires an "inadequate response" to the three alternatives but it does not call for or require a contraindication. Normally in the PA you have to either try it or there is a contraindication.

Dr. Allerman replies that is an oversight. We can add the contraindications.

Dr. Peloquin responds the PA criteria for Wakix also states, "Drug is prescribed by a neurologist, psychiatrist or sleep medicine specialist. The language normally states in consultation with.

Dr. Allerman replies the omission of "in consultation with" was intentional. The manual PA criteria states, "The patient has a documented diagnosis of excessive daytime sleepiness associated with narcolepsy. Because there is a potential to list non-labeled drugs, we don't list all the non-FDA approved drugs. That is why we to limit to potential specialists who would be prescribing drugs for narcolepsy.

Dr. Peloquin asks if the ability to collect data or ensure the sleep medicine specialists follows-up with a patient.

Dr. Allerman replies we have no way to go back and check that. It will depend on the system whether we can check with a sleep medicine specialist or not. For instance, if a prescription is going to a provider at the MTF, the pharmacists at the MTF filling the prescription will know the specialty of the physician at the MTF.

Dr. Khoury clarifies the providers in these specialties are often well known to MTF pharmacies and likely external points of service. This is more in general, there are not many in this sub-set of specialists. The pharmacists and pharmacies filling these prescriptions may know the provider. In the end the form relies on trust.

Mr. Hostettler comments rather than requiring a patient to use a formula to extemporaneously compound a tablet into a liquid, the FDA has an approved product and it should be used. In my opinion, we should support a product manufactured under Good Manufacturing standards allow patients access to the FDA-approved drug.

Dr. Piirainen asks if the PA criteria for Rinvoq will require evidence of a negative TB test within the last year as the other TIBs require a negative TB test within the past 12 months, for consistency, however prefer the current proposed language.

Dr. Allerman replies we discussed standardizing all the TIBS for those types of things in the label. We will take that back because we did try to standardize for all the cytopenias and the labels.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF/Tier 4/Not Covered, Manual PA Criteria, and UF and PA Implementation Plan recommendations for the Newly Approved Drugs per 32 CFR 199.21(g)(5)

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

  Concur: 7 Non-Concur: 1 Abstain: 0 Absent: 1

  ****The non-concurring Panel member suggest UF vs. NF for Katerzia an FDA approved product vs. an extemporaneously compounded one.**

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

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

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

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

III. UTILIZATION MANAGEMENT

(LT KHOURY)

A. UTILIZATION MANAGEMENT – NEW MANUAL PA CRITERIA

1. New PA Criteria – Newly Approved Drugs Not Subject to 32 CFR 199.21(g)(5)

New manual PA criteria were recommended by the P&T Committee due to a variety of reasons. The new manual PAs outlined below will apply to new users for the Parkinson's drug Neupro and the oncology drugs Venclexta and Zydelig, and to new and current users for the skeletal muscle relaxant chlorzoxazone, and the topical anesthetic cream.

a) Skeletal Muscle Relaxants and Combinations – Chlorozoxazone 375 mg and 750 mg (Lorzone, generics)

Chlorzoxazone 375 mg and 750 mg are new strengths approved via the Abbreviated New Drug Application (ANDA) pathway and thus do not qualify

for review by the DoD P&T Committee under the innovator program. Chlorzoxazone 500 mg is a scored tablet and produced by several manufacturers. Skeletal muscle relaxants are not considered first-line therapy for musculoskeletal conditions. Cost-effective generic formulations of chlorzoxazone 500 mg and multiple comparable muscle relaxants (e.g., cyclobenzaprine, methocarbamol) are available on the UF without PA being required. PA criteria also apply to the chlorzoxazone 250 mg strength, from the November 2018 meeting.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for chlorzoxazone 375 mg and 750 mg (Lorzone, generics) in new and current users, due to significant cost differences compared with splitting the 500 mg tablets or using other generic muscle relaxants.

Manual PA Criteria: Coverage for chlorzoxazone 375 mg and 750 will be approved if all criteria are met:

- The provider explains why the patient requires chlorzoxazone 375 mg or 750 mg and why the patient cannot take chlorzoxazone 500 mg tablet.

Non-FDA-approved uses are NOT approved.

PA does not expire.

b) Anesthetic Agents: Local—Lidocaine-Tetracaine 7%-7% topical cream (Pliaglis, generics)

This combination topical anesthetic cream is an authorized generic of Pliaglis and is approved for use prior to superficial dermatological procedures, including dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal. Prior to 2018, this product was restricted to use in the clinic setting by health care professionals. However, the "Not for Home Use" restriction was removed, as the manufacturer submitted a study supporting patient self-use. Numerous cost-effective topical anesthetics (e.g., lidocaine 4% cream, lidocaine 5% cream/ointment, and lidocaine-prilocaine 2.5%-2.5% cream [Emla]) are available that a patient could apply prior to a procedure.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for new users and current users over the age of 12 years, due to the availability of several cost-effective alternatives.

Manual PA Criteria: Coverage for lidocaine-tetracaine 7%-7% topical cream is approved if all criteria are met:

- The provider acknowledges that there are multiple formulary topical local anesthetics available for DoD beneficiaries without a PA including lidocaine

4% cream, lidocaine 5% cream or ointment, and lidocaine-prilocaine 2.5%-2.5% cream
- Drug is prescribed by or in consultation with a dermatologist or surgeon
- Not approved for use in back or joint pain
- Not approved for use in compounding
- Not approved for use as local anesthetic associated with cosmetic procedures including but not limited to dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal
- The provider must document the clinical rationale of why patient cannot take any of the formulary topical local anesthetics

Non-FDA-approved uses are NOT approved.

New PA required per prescription fill.

c) Parkinson's Agents: rotigotine (Neupro) patch

The P&T Committee has not previously reviewed the Parkinson's disease drug class. Rotigotine (Neupro) patch was marketed in 2012, and was designated as UF prior to the establishment of the Innovator Rule in August 2015. Although rotigotine is the only non-oral dopamine agonist, Parkinson's disease guidelines do not give a preference for any one agent over another. Cost effective generic formulations of oral pramipexole and ropinirole are available.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for new users, requiring use of an oral dopamine agonist first, unless the patient has swallowing difficulties.

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

- Age ≥ 18 years
- Patient has a diagnosis of:
  a. Parkinson's disease OR
  b. Moderate to severe primary restless legs syndrome
- Patient cannot swallow tablets due to a documented medical condition (i.e. dysphagia, oral candidiasis, systemic sclerosis, etc.) and not due to convenience OR
- Patient has tried and failed or has a contraindication to other dopamine agonist oral therapy:
  a. pramipexole (Mirapex) OR ropinirole (Requip)

Non-FDA-approved uses are NOT approved.

Prior authorization does not expire.

d. Oral Oncologic Agents: venetoclax (Venclexta) and idelalisib (Zydelig)

PA criteria have not previously been required for the chronic lymphocytic leukemia (CLL) drugs, Venclexta and Zydelig. However, PA criteria is in place for several other oncological drugs used to treat CLL.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for these two products in new users in order to ensure prescribing in accordance with FDA-approved indications or National Comprehensive Cancer Network (NCCN) Guideline-endorsed off-label indications.

1) Venetoclax (Venclexta)

- Age ≥ 18 years
- Drug is prescribed by or in consultation with a hematologist or oncologist
- Venclexta will be used in one of the following contexts:
  a. Frontline therapy for chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) without del(17p)/TP53 mutation
     - Patient fits one of the following categories:
       - Frail patient with significant comorbidity (not able to tolerate purine analogues)
       - Patient ≥ 65 years old with significant comorbidity
       - Patient < 65 years old
     - Will be combined with obinutuzumab (Gazyva) infusion

  b. Relapsed/refractory therapy for CLL/SLL without del(17p)/TP53 mutation
     - Patient fits one of the following categories:
       - Frail patient with significant comorbidity (not able to tolerate purine analogues)
       - Patient ≥ 65 years old with significant comorbidity
       - Patient < 65 years old
  c. Frontline or relapsed/refractory therapy for CLL/SLL with del(17p)/TP53 mutation
  d. Patient has newly diagnosed acute myeloid leukemia (AML) and is a candidate for intensive remission induction therapy and meets the following criteria:
     - Age ≥ 60 years old
     - Unfavorable-risk cytogenetics (exclusive of AML with myelodysplasia-related changes)
  e. Patient is ≥ 60 years old and has newly diagnosed AML and is not a candidate for intensive remission induction therapy
  f. Patient is ≥ 60 years old and completed lower-intensity induction therapy for AML with a response

g. Patient has relapsed refractory AML

- Will titrate to therapeutic dose in consideration of tumor lysis syndrome (TLS)
- Will not be concomitantly used at initiation or during ramp-up with a strong CYP3A inhibitor
- Will prophylax and monitor for tumor lysis syndrome (TLS) (based on tumor burden-defined risk)
- Will monitor for neutropenia
- Will monitor for signs and symptoms of infection
- Will not administer live attenuated vaccines prior to, during, or after treatment with Venclexta until B-cell recovery occurs.
- If the patient is female, she is not pregnant or planning to become pregnant
- Female patients will not breastfeed
- Male patients have been informed of risk of infertility
- Female patients of reproductive potential will use effective contraception during treatment and for at least 30 days after discontinuation
- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis:

  _____

Non-FDA approved uses are NOT approved.

Prior Authorization does not expire.

2) Idelalisib (Zydelig)

- Age ≥ 18 years
- Drug is prescribed by or in consultation with a hematologist or oncologist
- Zydelig will be used in one of the following indications:
  a. Relapsed/refractory therapy for CLL/SLL without del(17p)/TP53 mutation
     - Patient fits one of the following categories:
       - Frail patient with significant comorbidity (not able to tolerate purine analogues)
       - Patient ≥ 65 years old with significant comorbidity
       - Patient < 65 years old
  b. Relapsed/refractory therapy for CLL/SLL with del(17p)/TP53 mutation
  c. Relapsed/refractory follicular lymphoma AND:
     - Patient has completed ≥ 2 prior therapies OR
     - Patient has completed 1 prior therapy and relapsed ≤ 2 years
  d. Relapsed/refractory marginal zone lymphoma after 2 prior therapies

- Provider has reviewed the REMS program including the letter to healthcare providers and the fact sheet and has shared the medication guide and patient safety information card with the patient
- Will monitor for hepatotoxicity, colitis, intestinal perforation, pneumonitis, infection, neutropenia, and Steven Johnson Syndrome/toxic epidermal necrolysis
- Will monitor for cytomegalovirus reactivation
- Will prophylax for *pneumocystis jiroveci* pneumonia
- If the patient is female, she is not pregnant or planning to become pregnant
- Female patients will not breastfeed
- Female patients of reproductive potential will use effective contraception during treatment and for at least 30 days after discontinuation
- Male patients of reproductive potential will use effective contraception during treatment and for at least 3 months after discontinuation
- The diagnosis IS NOT listed above but IS cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis:
  _____

Non-FDA approved uses are NOT approved.

Prior Authorization does not expire.

2. New PA Criteria – PA Implementation

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) the new PAs for chlorzoxazone 375 mg and 750 mg (Lorzone, generics), lidocaine-tetracaine 7%-7%, Neupro patch, Venclexta, and Zydelig become effective the first Wednesday 90-days after the signing of the minutes. DHA will send letters to beneficiaries affected by the new PA requirements for chlorzoxazone and lidocaine-tetracaine 7%-7%, topical cream as new and current users will be subject to the PA.

3. **Physician's Perspective**

There were 5 drugs from four classes where new PA criteria were recommended.

- **Lidocaine- tetracaine cream** – The Committee was concerned about the cost of this product, compared to other widely used topical anesthetics creams. However, the PA will apply only to patients older than age 12 years, as there is the potential for this drug to be used in children receiving pulsed laser therapy for port wine stain birthmarks, which would be an appropriate use. We will send letters to the patients, since both new and current users will be required to go through the PA process.

- **Chlorzoxazone 375 mg and 750 mg tablets** – These are new dosage strengths that are significantly less cost effective than generic formulations of the 500 mg tablets. The Committee felt that there is no clinical need for these new in-between dosage strengths, and since the 500 mg tablets are scored, they are easy to break. The 400 patients currently on these products will be receiving letters notifying them of the new PA requirement.

- **Rotigotine (Neupro Patch) for Parkinson's disease**–The PA criteria require use of the generic oral dopamine agonists first, which is consistent with professional treatment guidelines. PA was also recommended due to the high amount of current off-label use for restless leg disorder. Existing patients will be grandfathered, so only new patients will be affected by the PA requirements.

- **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma drugs (Venclexta and Zydelig)**: This is part of our ongoing process of reviewing the oncology drugs to determine which ones do not have PAs in place where one is warranted. PA was recommended for these two drugs to ensure the appropriate patients receive the drugs, based on FDA indications and safety information. These new PA's allow off-label uses that are included in the NCCN guidelines be considered as part of the PA review, before having the provider file an appeal. Only new patients will be have to undergo the PA process.

4. Panel's Questions and Comments

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

- **New PA Criteria**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

- **New PA Criteria – PA Implementation Plan**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

B. UTILIZATION MANAGEMENT – UPDATED MANUAL PA CRITERIA

(LT KHOURY)

1. Updated PA Criteria

Updates to the manual PA criteria and step therapy criteria for several drugs were recommended due to a variety of reasons, including expanded FDA

indications, new NCCN guideline recommendations, clinical trial data, and standardization with existing PAs for the drug class, changes due to FDA safety announcements and boxed warnings, and age indications. The updated PAs and step therapy criteria outlined below will apply to new users.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) to implement the PA criteria for Cimzia originally recommended at the May 2019 P&T Committee meeting (the Humira step requirement). The Committee also recommended the updates to the manual PA criteria for Symbicort and Dulera, Xeljanz, Xeljanz XR, Olumiant, Zytiga, and Doptelet.

The updates are as follows:

Updated Criteria for reasons other than new FDA indications, NCCN Guideline Updates, or Age Ranges

a) **Pulmonary-1 Agent: Combinations: budesonide/formoterol Symbicort AND mometasone/formoterol (Dulera)**—Manual PA criteria for Symbicort and Dulera were originally recommended in February 2014, requiring a trial of fluticasone/salmeterol (Advair) first. Recently the Global Initiative for Asthma (GINA) 2019 evidence-based strategy was updated, and states that combination low-dose inhaled corticosteroid (ICS)-formoterol used as needed is now the preferred reliever ("rescue use") for asthma control and reducing exacerbations in adults and adolescents 12 years and older with mild asthma. Short-acting beta agonists (SABAs) are now listed as an "other reliever option" and are no longer the preferred rescue treatment in adults and adolescents with mild asthma. This new approach was based on two studies that used a combination budesonide-formoterol inhaler (SYGMA 1 and SYGMA2, New England Journal of Medicine May 2018).

   Limitations to this recommendation include that the two supporting studies were industry funded, and used an active comparator (terbutaline Turbuhaler) that is not available in the U.S. Additionally, the budesonide-formoterol inhaler evaluated in the trials was a dry powder inhaler, while the commercially available U.S. product is a pressurized metered-dose inhaler (Symbicort), and the study design was changed from a superiority trial to a non-inferiority trial. The study results also show that this method is not as effective at decreasing asthma symptoms.

   Provider feedback was mixed and not overwhelmingly supportive of the consensus statement guidelines given the available data. Manual PA criteria for both Symbicort and Dulera were updated to allow use in patients with mild asthma who require rescue therapy with an ICS-formoterol combination, without requiring a trial of Advair first.

b) Target Immunomodulatory Biologics (TIBs): certolizumab (Cimzia))— Manual PA criteria for Cimzia were most recently reviewed at the May 2019 P&T Committee meeting after Cimzia was granted FDA-approval for adults with non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation. The Cimzia and Humira PA criteria were updated to allow for the indication of nr-axSpA but still require the use of adalimumab (Humira) prior to use of Cimzia. This recommendation was based on the Assessment of Spondylo Arthritis International Society (ASAS)/European League against Rheumatism (EULAR) guidelines and clinical trial data.

The implementation of the Humira step requirement was delayed in light of new information that was not available at the May 2019 P&T meeting. The fact that the manufacturer for Humira sought FDA-approval for this indication and was denied in 2009-2013 had not been presented to the Committee in May 2019. The new information presented at this meeting included the FDA's review of both Cimzia and Humira for nr-axSpA, the high degree of difficulty of actually diagnosing this disease, and provider feedback. The P&T Committee recommended maintaining the requirement for Humira prior to Cimzia for nr-axSpA after evaluating this additional information. The Cimzia PA criteria from the May 2019 P&T Committee meeting requiring use of Humira first in patients with nr-axSpA will now be implemented.

c) TIBs: Janus Kinase (JAK) inhibitors tofacitinib (Xeljanz, Xeljanz XR) and baricitinib (Olumiant)—The FDA has issued several safety alerts for Xeljanz and Xeljanz XR for pulmonary embolism and death with certain doses, most recently in July 2019. The Xeljanz/Xeljanz XR PA criteria were updated to ensure the provider is aware of the July 2019 FDA safety announcement and boxed warning, and to ensure patients do not have a history of thromboembolic disease.

Olumiant PA criteria were recommended in August 2018, and suggested using Xeljanz prior to Olumiant, since at that time Xeljanz did not contain a boxed warning for thrombosis. This comment will be removed from the Olumiant PA, as Xeljanz/Xeljanz XR now have the warning mentioned above.

For Xeljanz/Xeljanz XR and Olumiant, additional requirements for absolute neutrophil count (ANC) and absolute lymphocyte count (ALC) monitoring were also added, consistent with the package inserts. The PAs will also allow concomitant use with Otezla, if the provider includes supporting literature for combination use.

d) Oncological Agents: Prostate Cancer CYP-17 Inhibitors: abiraterone acetate (Zytiga, generics)—Manual PA criteria for Zytiga were recommended when the CYP-17 Inhibitor subclass was reviewed at the February 2019 P&T Committee meeting. Step therapy requiring a trial of abiraterone acetate micronized (Yonsa) first was required. Furthermore, an additional step required

Zytiga generic 250 mg prior to Zytiga brand 500 mg, as the 500 mg branded formulation did not have generic equivalents and provided no clinical benefit at a significantly higher cost.

As of October 2019, the blended monthly cost of generic abiraterone acetate 250 mg is now comparable to the step-preferred Yonsa formulation. The step requiring Yonsa before Zytiga generic 250 mg will be removed. The abiraterone acetate (Zytiga) brand 500 mg PA form will still require use of Yonsa or the 250 mg generics first.

e) **Hematological Agents: Platelets: avatrombopag (Doptelet)—**Manual PA criteria for Doptelet were first recommended in August 2018 for thrombocytopenia associated with chronic liver disease in patients who are scheduled to undergo a procedure with at least a moderate bleeding risk. Manual PA criteria were later updated in February 2019 to require a trial of Mulpleta first. Mulpleta has the same indication as Doptelet for pre-procedure use, has less complex dosing and was less expensive. There has been a significant price reduction in Doptelet, and manual PA criteria were updated to remove the requirement that Mulpleta be used ahead of Doptelet in thrombocytopenia associated with chronic liver disease

New FDA-Approved Indications, NCCN Guideline Updates, or Age Ranges

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) updates to the manual PA criteria for Taltz, Stelara, Erleada, Xtandi, Corlanor, Harvoni, Sovaldi, Ofev, Esbriet, Calquence, Copiktra, Imbruvica, Vitrakvi, and Revlimid.

a) **TIBs: ixekizumab (Taltz)—**For plaque psoriasis, Taltz currently requires a trial of adalimumab (Humira), secukinumab (Cosentyx) and ustekinumab (Stelara). Taltz is now approved for treating active ankylosing spondylitis (AS) in adult patients, and the new indication was added to the criteria. Note that for AS, a trial of adalimumab (Humira) and secukinumab (Cosentyx) are required first; however a trial of ustekinumab (Stelara) is not required as it is not FDA-approved for use in AS.

b) **TIBs: ustekinumab (Stelara)—**Manual PA criteria were updated to reflect a new FDA-approved indication for adults with moderately to severely active ulcerative colitis (UC). The requirement to try Humira prior to Stelara for this indication still applies.

c) **Cardiovascular Agents Miscellaneous—ivabradine (Corlanor)—**Manual PA criteria for Corlanor were updated to reflect a new pediatric indication for treating stable symptomatic heart failure due to dilated cardiomyopathy in

pediatric patients ≥ 6 months and older, who are in sinus rhythm with an elevated heart rate.

d) **Hepatitis C Agents: Direct Acting Agents: ledipasvir/sofosbuvir (Harvoni) AND sofosbuvir (Sovaldi)—**Updates were made to the PA criteria for Harvoni and authorized generics of Harvoni to allow use for adult and pediatric patients ≥ 3 years of age with chronic hepatitis C virus (HCV) genotype 1, 4, 5, or 6 infection, without cirrhosis or with compensated cirrhosis. Other recent indications were also added to the form, including genotype 1 infection with decompensated cirrhosis, in combination with ribavirin; and genotype 1 or 4 infection in liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin. Manual PA criteria for Sovaldi were updated to reflect a new FDA-approved indication for adults and pediatric patients 3 years of age or older for treatment of chronic HCV genotype 2 or 3 infection, without cirrhosis or with compensated cirrhosis.

e) **Pulmonary-1 Agents: Idiopathic Pulmonary Fibrosis (IPF): nintedanib (Ofev) and pirfenidone (Esbriet)—**The IPF drugs were reviewed for formulary status in May 2017 and step therapy requires a trial of pirfenidone (Esbriet) prior to Ofev. Ofev recently gained an indication to slow the rate of decline in pulmonary function for a rare condition, systemic sclerosis-associated interstitial lung disease (SSc-ILD). Esbriet lacks the indication for SSc-ILD, so it is not required before Ofev in this condition. The new SSc-ILD indication was added to the Ofev PA. The renewal criteria from the May 2017 class review were also updated for clarification for both Ofev and Esbriet.

f) **Oncological Agents: Prostate Cancer 2nd-Generation Antiandrogens: apalutamide (Erleada) and enzalutamide (Xtandi)—**Manual PA criteria were updated to reflect the new FDA-approved indication and NCCN guideline update for treatment of metastatic, castration-sensitive prostate cancer. For Erleada, renewal criteria were removed since it is now indicated for use in metastatic disease.

g) **Oncologic Agents: acalabrutinib (Calquence), duvelisib (Copiktra), ibrutinib (Imbruvica), larotrectinib (Vitrakvi) capsules and oral solution, lenalidomide (Revlimid)—**Updates to the manual PA criteria for these oncologic agents reflects more detailed safety information, including standardized embryo-fetal toxicity information. New FDA-approved indications or NCCN guideline-supported indications were also updated as summarized below. A synopsis of the changes submitted are summarized below:
   - acalabrutinib (Calquence)—Allow use for NCCN CLL and small lymphocytic lymphoma (SLL) guideline updates for relapsed or refractory disease
   - duvelisib (Copiktra)—Allow use in refractory marginal zone lymphoma

- ibrutinib (Imbruvica)—Allow use for mantle cell lymphoma maintenance therapy
- larotrectinib (Vitrakvi)—Allow first-line use for neurotropic tropomyosin receptor kinase (NTRK) gene fusion positive non-small cell lung cancer (NSCLC)
- lenalidomide (Revlimid)—Allow use for marginal zone lymphoma

2. Updated PA Criteria – Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 1 absent) the following implementation periods:

- Updates to the current PA criteria for Cimzia in new users will become effective the first Wednesday upon signing of the minutes.
- Updates to the current PA criteria for abiraterone acetate 250 mg in new users will become effective the first Wednesday 30-days after the signing of the minutes.
- Updates to the current PA criteria for Xeljanz, Xeljanz XR, Olumiant, Taltz, Stelara,
- Erleada, Xtandi, Vitrakvi capsule and solution, Calquence, Copiktra, Imbruvica, Revlimid, Doptelet, Ofev, Esbriet, Symbicort, Dulera, Harvoni, Sovaldi, and Corlanor in new users become effective the first Wednesday 60-days after the signing of the minutes.

3. Physician's Perspective

There were 22 drugs discussed here, so only a few drugs will have comments.

- **Symbicort and Dulera for asthma**

  Currently Advair has been the step-preferred combination inhaler since 2014, with Symbicort and Dulera made non-preferred and non-formulary. Symbicort and Dulera contain formoterol which has a faster onset of action than the salmeterol component of Advair. Because of this, for rescue use, patients won't be required to try Advair first.

  There is some controversy about this new consensus statement, the PA update will remove a barrier, so that providers who want to follow this guideline can do so.

- **Cimzia - TIB for non-radiographic axial spondyloarthritis**: The original recommendation from the May 2019 meeting was on hold, until the data could be re-examined. Based on the review of the evidence, and feedback from rheumatologists, we will now implement the original recommendation for Humira to be tried first before Cimzia for this indication.

- **Generic Zytiga 250 mg for prostate cancer**: Because of a price reduction for the generic 250 mg product, we are removing the requirement to try Yonsa first. This is a good example of where pricing is monitored, and where step therapy is discontinued when there is not significant cost benefit

3. Panel's Questions and Comments

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

- **Updated Manual PA Criteria**

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

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

  Concur: 8 Non-Concur: 0 Abstain: 0 Absent: 1

Closing Remarks:

Mr. Hostettler states that we had several issues today that recur each meeting. The Panel is told that the information will be taken back for research but I don't recall ever receiving any feedback. We want to add the requested updates from this meeting to the requests for updates from the previous meetings. I usually go back and review the minutes and documentation after it is signed by the Director, DHA. During the discussions at the last meeting, PA criteria was omitted from a new drug and the Panel was told that the information would be added to the existing criteria. Feedback would be provided to the Panel. The new criteria requires patients to have surgery. In my opinion, that seems drastic. Can someone provide a justification? The update states that the patient has a past surgical history or endoscopic surgical intervention. My interpretation of this criteria is that a patient has to have surgery before they can use this drug. This significant information should have been presented to the Panel.
In the future, I would have like to have a chance to review the evidence and comment.

Additionally I am requesting feedback on issues that the presenter states they will "take back".

Dr. Khoury states that he does not recall the discussion regarding the criteria referenced but if information was omitted it was not intentional and he apologizes.

Dr. Khoury asks which product is being referred to.

Mr. Hostettler replies Dupilumab (Dupixent)

Dr. Bertin thanks the Panel for their attention to detail. A good and productive meeting. He expressed appreciation to the super staff for their presentations.

Meeting adjourned at 11:50am.

Dr. Richard Bertin
UF BAP Co-Chairperson

Appendix 1 **01/08/2020 BAP Meeting**

Informational Item—SUMMARY OF RECOMMENDATIONS AND BENEFICIARY IMPACT November 2019

Table of Implementation Status of UF Recommendations/Decisions Summary

DoD PEC Drug Class	UF Drugs	NF Drugs	Tier 4/Not Covered Drugs	Implement Date	Notes and Unique Users Affected
Phosphodiesterase-5 Inhibitors	*UF and Step-preferred* ▪ sildenafil generic only *UF and non-step-preferred* ▪ tadalafil generic only	▪ None	▪ avanafil (Stendra) ▪ vardenafil ODT (Staxyn and generics) ▪ vardenafil tablet (Levitra and generics) ▪ brand Viagra ▪ brand Cialis	Pending signing of the minutes / 120 days	▪ Manual PA criteria applies to both sildenafil and generic tadalafil ▪ Trial of sildenafil still required before tadalafil ▪ Men over 40 years do not require a PA Unique Users Affected (Tier 4 candidates) Mail – 6,016 MTF – 3,744 Retail – 433 Total – 10,193
Rapid-Acting Insulins	*UF and step-preferred* ▪ insulin aspart (Novolog) ▪ insulin lispro (Humalog and authorized generic insulin lispro)	*NF and non-step-preferred* ▪ insulin glulisine (Apidra) ▪ insulin lispro (Admelog) ▪ inhaled insulin (Afrezza)	▪ insulin aspart plus niacinamide (Fiasp)	Pending signing of the minutes / 150 days and no earlier than July 1 2020	▪ All new and current users of Admelog and Apidra must try Novolog and Humalog ▪ Changes also made to the Afrezza PA Unique Users Affected (Tier 4 candidate Fiasp) Mail: 122 MTF: 44 Retail: 17 Total: 183

Drugs with New Prior Authorization Criteria—Unique Utilizers Affected

Drug	MTF	Mail Order	Retail	Total
Chlorzoxazone 375 mg (Lorzone, generics)	2	21	61	84
Chlorzoxazone 750 mg (Lorzone, generics)	24	86	233	340
Anesthetic Agents: Local—Lidocaine-Tetracaine 7%-7% topical cream (Pliaglis, generics)	0	0	1,616	1,616

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 "BAP" in this summary refers to the "Uniform Formulary Beneficiary Panel," the group who's meeting in the subject of this report.

- ADHD – Attention Deficit Hyperactivity Disorder
- AML – Acute Myeloid Leukemia
- ANC – Absolute Neutrophil Count
- ANDA – Abbreviated New Drug Application
- ASAS – Assessment of Spodylo Arthritis International Society
- AUS – American Urological Association
- BIA – Budget Impact Analysis
- BPH – Benign Prostatic Hyperplasia
- BUN – Blood, Urea Nitrogen
- CABP – Community Acquired Bacterial Pneumonia
- CBC – Complete Blood Count
- CFR – Code of Federal Regulation
- CHF – Congestive Heart Failure
- CLL – Chronic Lymphocytic Leukemia
- CMA – Cost-Minimization Analysis
- COPD – Chronic Obstructive Pulmonary Disease
- DHA – Defense Health Agency
- DKA – Diabetic Ketoacidosis
- DMARDs – Disease-Modifying Anti-Rheumatic Drugs
- DoD – Department of Defense
- ED – Erectile Dysfunction
- EULAR – European League Against Rheumatism
- FDA – Federal Drug Administration
- GnRH – Gonadotropin-Releasing Hormone
- HCV – Hepatitis C Virus
- HSDD – Hypoactive Sexual Desire Disorder
- IBS-C – Irritable Bowel Syndrome – Constipation
- IPF – Idiopathic Pulmonary Fibrosis
- JAK Inhibitors – Janus Kinase Inhibitors
- L – Liter
- LAMA/LABA – Long-acting Muscarinic Antagonists/Long-acting Beta Agonist
- MEN2 – Multiple Endocrine Neoplasia Syndrome Type
- ml – Milliliter
- MSLT – Mean Sleep Latency Time
- MTC – Medullary Thyroid Carcinoma

- MTF – Military Treatment Facility
- NCCN – National Comprehensive Cancer Network
- NDAA – National Defense Authorization Act
- NF – Non-Formulary
- NSCLS – Non-Small Cell Lung Cancer
- NTRK – Neurotrophic Tropomyosin Receptor Kinase
- ODT – Oral Disintegrating Tablet
- P&T – Pharmacy & Therapeutic
- PA – Prior Authorization
- PDE-5 – Phosphodiesterase-5
- PSADT – Prostate-Specific Antigen Doubling Time
- RAI – Rapid-Acting Insulins
- REMS – Risk Evaluation Mitigation Strategy
- RRMM – Relapsed or Refractory Multiple Myeloma
- SLL – Small Lymphocytic Lymphoma
- SSc-ILD – Systemic Sclerosis-Associated Interstitial Lung Disease
- TB – Tuberculosis
- TIB – Targeted Immunomodulatory Biologic
- TLS – Tumor Lysis Syndrome
- UC - Ulcerative Colitis
- UF – Uniform Formulary
- VTE – Venous Thromboembolic
- XR – Extended Release