EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel Meeting June 28, 2023

For the May 2023 DoD Pharmacy and Therapeutics Committee Meeting

The Uniform Formulary Beneficiary Advisory Panel (UFBAP) convened at 10:00 A.M. EDT on June 28, 2023 via teleconference. The current meeting took place over 1 hour and 45 minutes. The information presented included the recommendations from the May 2023 DoD Pharmacy and Therapeutics Committee (P&T) meeting.

The detailed meeting information is found starting on page 9.

UNIFORM FORMULARY (UF) DRUG CLASS REVIEWS

I. UF CLASS REVIEWS— Antilipidemics-1—Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors Subclass

A. PCSK9 Inhibitors—UF Recommendations

- UF and step-preferred
  - evolocumab (Repatha)
- UF and non-step-preferred
  - alirocumab (Praluent)
  - Note that as part of the formulary recommendation for Praluent, a trial of Repatha is required first.
- NF
  - None
- Complete exclusion
  - None

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

B. PCSK9 Inhibitors —Manual PA Criteria

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

C. PCSK9 Inhibitors —UF, PA, and Implementation Plan of an effective date of 30 days

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

II. UF CLASS REVIEWS—Ophthalmic—Dry Eye Agents

A. Ophthalmic—Dry Eye Agents—UF Recommendations

- **UF**
  - Restasis unit-dose, generics
  - Restasis Multidose
  - Cequa – *moves from NF to UF*
  - Xiidra
- **NF**
  - Verkazia
  - Tyrvaya
- **Complete exclusion**
  - Eysuvis – *moves from NF to complete exclusion*

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

B. Ophthalmic—Dry Eye Agents —Prior Authorization Criteria

The P&T Committee recommended Manual PA criteria for the ophthalmic dry eye agents.

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

C. Ophthalmic—Dry Eye Agents —UF, PA, and Implementation Plan of 60 days

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

III. NEWLY APPROVED DRUGS PER 32 CFR 199.21(g)(5)

A. Newly Approved Drugs Per 32 CFR 199.21(g)(5)—UF/NF/Complete Exclusion Recommendation

- **UF**
  - adagrasib (Krazati)
  - antihemophilic factor (recombinant), Fc-VWF-XTEN fusion protein-ehtl vial (Altuviiio)
  - elacestrant (Orserdu)
  - omeprazole and sodium bicarbonate 2 mg/mL oral suspension (Konvomep)
  - pegfilgrastim-fpgk injection (Stimufend)
  - pirtobrutinib (Jaypirca)
  - sparsentan (Filspari)
  - tezepelumab-ekko autoinjector (Tezspire)

- trofinetide 200 mg/mL oral solution (Daybue)

- **NF**
  - adalimumab-atto injection (Amjevita)
  - atorvastatin 20 mg/5 mL oral suspension (Atorvaliq)
  - dabigatran oral pellet packets (Pradaxa pellets)
  - insulin glargine KwikPen (Rezvoglar)

- **Complete exclusion**
  - None

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

B. Newly Approved Drugs Per 32 CFR 199.21(g)(5)—PA Criteria for Krazati, Amjevita, Atorvaliq, Pradaxa Pellets, Orserdu, Rezvoglar, Konvomep, Stimufend, Jaypirca, Filspari, Tezspire, Daybue

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

C. Newly Approved Drugs Per 32 CFR 199.21(g)(5)—UF, NF, Complete Exclusion and PA Implementation Plan of 2 weeks

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

IV. UTILIZATION MANAGEMENT—NEW MANUAL PA CRITERIA AND IMPLEMENTATION PLAN

A. New Manual PA Criteria for Tirosint, Sucraid and Humira

Summary of Panel Questions and Comments

Dr. McKeon applauded the DoD P&T Committee for allowing rheumatology specialists to prescribe Humira without having to go through the PA process.

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

B. New Manual PA Criteria for Tirosint, Sucraid and Humira Implementation Plan

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

V. UTILIZATION MANAGEMENT—UPDATED PA CRITERIA FOR NEW FDA- APPROVED INDICATIONS AND IMPLEMENTATION PLAN

A. Updated PA Criteria for New FDA-Approved Indications

The P&T Committee evaluated updates to the PA criteria for Cibinqo, Verzenio, Takhzyro, Brukinsa, Odactra, Tukysa, and FreeStyle Libre 2 and FreeStyle Libre 3 due to new FDA-approved indications,

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

B. Updated PA Criteria for New FDA-Approved Indications Implementation Plan of 60 days

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

VI. UTILIZATION MANAGEMENT—UPDATED PA CRITERIA FOR REASONS OTHER THAN NEW INDICATIONS ND IMPLEMENTATION PLAN

A. Updated PA Criteria for Reasons other than New Indications for Lybalvi, Bydureon BCise, Victoza and Lumakras

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

B. Updated PA Criteria for Reasons other than New Indications Implementation Plan of 60 Days

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

VII. UTILIZATION MANAGEMENT—REMOVAL OF PA CRITERIA AND IMPLEMENTATION PLAN

A. Removal of PA criteria for the step-preferred TZDs (pioglitazone) and DPP-4 inhibitors (sitagliptin and their combinations)

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

B. Removal of PA Criteria Implementation Period of two weeks

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

VIII. BRAND OVER GENERIC AUTHORIZATION AND TIER 1 COPAY AND IMPLEMENTATION PLAN

A. Brand over generic authorization and Tier 1 Copay for Advair HFA, Revlimid and Trokendi XR

Summary of Panel Questions and Comments

Mr. Ostrowski stated he appreciated having the brand product available for beneficiaries.

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

B. Brand over generic authorization and Tier 1 Copay for Advair HFA, Revlimid and Trokendi XR and Implementation Plan of 60 days

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

IX. OVER-THE-COUNTER (OTC) DRUG BENEFIT—NALOXONE NASAL SPRAY—UF RECOMMENDATION, COPAY, PRESCRIPTION REQUIREMENT, AND IMPLEMENTATION PLAN

A. OTC Naloxone UF Recommendation, Copay, Prescription requirement and implementation plan of 2 weeks of market launch

Summary of Panel Questions and Comments

There were no questions or comments from the Panel.

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

Director, DHA:

_____ The comments outlined above were taken under consideration prior to my final decision.

Uniform Formulary Beneficiary Advisory Panel
Virtual Meeting Summary Minutes
June 28, 2023

Panel Members Present

- Mr. Jon Ostrowski, Non-Commissioned Officer Association, Chair
- Dr. Karen Dager, PharmD, Health Net Federal Services
- Ms. Holly Dailey, the Association of the United States Army
- Dr. Joseph McKeon, MD, Humana Military
- Dr. Betsaida Guzman, PharmD, Veterans of Foreign Wars
- Ms. Amanda Meyers, Military Officers Association of America (MOAA)
- Dr. Jay Peloquin, Pharm D, Express Scripts
- Dr. Jennifer Soucy, PharmD, U.S. Family Health Plan, Martins Point Services

Acting Designated Federal Officer (Non-Voting): CDR Phung Nguyen, USPHS

DHA HQ and Pharmacy Operations Division Participants (Non-Voting)

- Dr. John Kugler, Division Chief, J-6; DoD P&T Committee Chair
- Edward VonBerg, PharmD, BCPS, Chief, Pharmacy Operations Division Formulary Management Branch (POD FMB)
- CDR Scott Raisor, Chief, P&T Section POD FMB
- Maj Angelina Escano, MC POD FMB
- LCDR Elizabeth Hall POD FMB
- LCDR Giao Phung, POD FMB
- LT Stephani Klimes, POD FMB
- Angela Allerman, PharmD, BCPS, POD FMB
- Ms. Megan Gemunder Office of General Counsel

Agenda is found starting on page 17.

- Panel Discussion

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 concur or non-concur on the recommendations of the P&T Committee concerning the establishment of the UF and subsequent recommended changes. The Panel will provide comments on their vote as directed by the Panel Chairman. Comments to the Director, DHA, or their designee will be considered before making a final UF decision.

Opening Remarks

CDR Nguyen introduced herself as the Designated Federal Officer (DFO) for the Uniform Formulary (UF) Beneficiary Advisory Panel (BAP). The Panel has convened to comment on the recommendations of the DoD Pharmacy and Therapeutics (P&T) Committee meeting, which occurred on May 3-4, 2023.

CDR Nguyen then 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 pharmaceutical agents and establishes the P&T committee to review the formulary on a periodic basis to make additional recommendations regarding the formulary as the committee determines necessary and appropriate.

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

CDR Nguyen then outlined 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 to subsequently recommend changes. Comments to the Director, DHA, regarding recommended formulary status, 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 of or with the advance approval of the DFO in consultation with the Chairperson of the Panel.

- To prepare minutes of the proceeding and prepare comments for 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 by the Director, DHA.

The DFO provided guidance regarding this meeting.

- 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 of Defense appreciates that the BAP may be interested in the drug classes selected for review, drugs recommended for the basic core formulary (BCF) or specific pricing date, these topics do not fall under the purview of the BAP.

- The P&T Committee met for approximately 16 hours conducting its reviews of the drug class recommendations that will be presented today. Since this meeting is considerably shorter, the Panel will not receive the same extensive information that is 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 meeting minutes, the DoD P&T Committee meeting minutes, and the Director's decisions will be available on the TRICARE website in approximately four to six weeks.

The DFO provided a few ground rules for conduct during the virtual meeting:

- Audience participation is limited to private citizen comments received in writing prior to the meeting.

- Participants will be joined in a LISTEN MODE only.

- To ensure that there are not disruptions to discussion and as a precaution, please mute your phones.

Panel and Presenter Guidance

- When asking or responding to questions:
  - Panel members are asked to state their name prior to asking your questions.
  - Presenters or anyone responding to a question are asked to state their name prior to responding.
  - The meeting is being recorded. Please speak clearly.
- Members of the Formulary Management Branch and the 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.

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

Private Citizen Comments: Written comments were forwarded to the Panel for their review and consideration for the following.

1. Axsome Pharma for bupropion/dextromethorphan (Auvelity) – April 4, 2023 meeting
2. Calliditas Pharma for budesonide delayed release (Tarpeyo) – April 4, 2023 meeting and current meeting (June 28, 2023)
3. IQVIA for budesonide delayed release (Tarpeyo) – April 4, 2023 meeting

There were no questions from the Panel members regarding the private citizen submissions.

The meeting was handed over to the Panel Chair Mr. Ostrowski for his opening remarks.

Chairman's Opening Remarks

Mr. Ostrowski welcomed all panel members and attendees participating today.

Dr. VonBerg's Opening Remarks

The meeting then proceeded with comments from Dr. VonBerg, a pharmacist and retired Navy Captain who thanked the panel for the involvement today and stated that the Panels' voices were critical today. He then introduced the team speaking *(see list above).*

Dr. VonBerg then continued with his opening remarks, stating that 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.

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.

The full presentations then started. Following some of the sections the DoD P&T Committee physician perspective was provided by Dr. John Kugler, and is included starting on page 15. The information starting on page 20 includes the full meeting information.

Closing Remarks

Mr. Ostrowski thanked everyone participating for the fantastic work by the Committee and the POD, along with the members today. He also wished everyone a safe summer and is looking forward to seeing everyone in the fall.

Dr. VonBerg thanked the P&T Committee and BAP members for the continuing reviews and updates to the benefit, especially in streamlining coverage for multiple medications.

CDR Nguyen closed the meeting by thanking the Panel members for their time, involvement, and stated that she expresses warmest appreciation for continued commitment to the TRICARE pharmacy benefit.

The Meeting Adjourned at 10:45 AM EDT.

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

Jon R. Ostrowski
Chairperson, UFBAP

DoD P&T Committee Physician Perspective

Dr. John Kugler's comments on the formulary recommendations followed selected individual sections and are outlined below:

Drug Class Reviews

Antilipidemics-1—Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors

- This is the second time we've evaluated the class. After reviewing the new cardiovascular outcomes studies, the Committee agreed that the two drugs remain highly therapeutically interchangeable.
- There was no change to the current formulary recommendation - both drugs remain on the formulary, and Repatha is required first, before Praluent. Patients currently taking Praluent will be able to stay on the drug.
- For the PA criteria updates, the Committee reviewed provider input and new information, including the recent ACC Consensus Pathway. Most of the discussion from the Committee centered around removing the requirement for specialist prescribing, and also ensuring that an appropriate statin trial and failure are addressed in the PA criteria. Overall, as a result, the PCSK9 PA criteria will improve access by, allowing generalist prescribing and through elimination of renewal criteria for these drugs with long history of experience in the market.

Ophthalmic—Dry Eye Agents

- For this class, several of the drugs contain the same active ingredient, cyclosporine, but at different concentrations. The 0.05% cyclosporine generic Restasis formulation has now entered the market, and it is the highest utilized prescription dry eye disease product in DoD. The PA updates will allow easier access to the 0.05% cyclosporine with the elimination of renewal criteria. The PA updates also require that the other branded products will require a trial of the generic first.
- The two agents that were recommended for nonformulary placement, Verkazia and the one nasal spray (Tyrvaya), are currently nonformulary, and will remain nonformulary. Provider input felt that the current formulary status and PA criteria were appropriate.
- One drug was recommended to be completely excluded from the benefit- Eysuvis. The active ingredient is already available in multiple concentrations, which although they do not have formal FDA approval for dry eye disease, they are commonly used off-label. There are currently less than 100 patients on Eysuvis.

Utilization Management

Removal of PA Criteria for the Step-Preferred TZDs and DPP4-Inhibitors and Implementation plan

- This is another example today of the Committee reducing the PA burden for providers. PAs have been removed for the step-preferred drugs from other diabetes drug classes, including the SGLTs inhibitors, and this was the recommendation for the TZDs and DPP4.
- The most recent American Diabetes Association guidelines have now moved the SGLT2 inhibitors and GLP1 agents higher up in the algorithm as first line therapies. However, older drug classes like the TZDs and DPP4s still play a role in treating diabetes.
- The Committee will continue to look for cases where PA criteria can either be streamlined or removed altogether, when appropriate.

OTC Naloxone Nasal

- We do have the authority to add OTC drugs to the pharmacy benefit, and the Committee did consider the clinical and cost effectiveness of this lifesaving opioid reversal agent.
- This product has not launched yet, it is expected to be available on the market in late summer. The Committee wanted to have this recommendation ready to go prior to launch.

AGENDA

Uniform Formulary Beneficiary Advisory Panel (BAP)
For the May 2023 DoD Pharmacy and Therapeutics Committee Meetings June 28, 2023 at 10:00 AM Eastern Daylight Saving Time

Virtual Meeting

- **Administrative Meeting: 8:00 AM – 9:45 AM Eastern Daylight Saving Time (General session starts at 10:00 AM Eastern Daylight Saving Time)**
- **Roll Call**
- **Therapeutic Class Reviews**

  Members of the DHA Pharmacy Operations Division (POD) Formulary Management Branch (FMB) will present relative clinical and cost-effective analyses along with the DoD Pharmacy & Therapeutics Committee (P&T) recommendations for the Uniform Formulary (UF) and any recommended complete exclusion candidates.

  The P&T Committee made recommendations for the following drugs/drug classes during the May 2023 meeting:

  - **Drug Class Reviews**
    - *Antilipidemics-1 – Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors Subclass*
    - *Ophthalmic – Dry Eye Agents Subclass*
  - **Newly Approved Drugs per 32 CFR 199.21(g)(5)**
    - *adagrasib (Krazati) – Oncological agent for advanced or metastatic non-small cell lung cancer*
    - *adalimumab-atto injection (Amjevita) – Targeted Immunomodulatory Biologics (TIBS); Humira biosimilar*
    - *antihemophilic factor (recombinant), Fc-VWF-XTEN fusion protein-ehtl vial (Altuviiio) – Antihemophilic Factors*
    - *atorvastatin 20 mg/5 mL oral suspension (Atorvaliq) – Antilipidemics-1 agents*
    - *dabigatran oral pellet packets (Pradaxa pellets) – Direct Acting Oral Anticoagulant; treatment of venous thromboembolism in pediatric patients aged 3 months to less than 12 years*
    - *elacestrant (Orserdu) – Oncological agent for breast cancer*
    - *insulin glargine KwikPen (Rezvoglar) – Basal Insulins; Lantus biosimilar*
    - *omeprazole and sodium bicarbonate 2 mg/mL oral suspension(Konvomep) – Proton Pump Inhibitors*

- *pegfilgrastim-fpgk injection (Stimufend) – White Blood Cell Stimulants: pegfilgrastims*
- *pirtobrutinib (Jaypirca) – Oncological agent for relapsed or refractory mantle cell lymphoma*
- *sparsentan (Filspari) – Nephrology Miscellaneous Agent for immunoglobulin A nephropathy*
- *tezepelumab-ekko autoinjector (Tezspire) – Atopy Agent for add on maintenance severe asthma treatment*
- *trofinetide 200 mg/mL oral solution (Daybue) – Neurological Miscellaneous Agent for treatment of Rett syndrome*

➢ **Utilization Management Issues**

- **Prior Authorization Criteria—New Manual PA Criteria**
  - *Gastrointestinal-2 Agents—sacrosidase oral solution (Sucraid)*
  - *Targeted Immunomodulatory Biologics—adalimumab (Humira)*
  - *Thyroid Agents—levothyroxine sodium capsule (Tirosint)*
- **Prior Authorization Criteria—Updated PA Criteria for New FDA-Approved Indications**
  - *Atopy Agents: Oral Janus Kinase Inhibitor (JAK-1)—abrocitinib (Cibinqo)*
  - *Breast Cancer Agents: Cyclin-Dependent Kinase (CDK) Inhibitors—abemaciclib (Verzenio)*
  - *Corticosteroid-Immune Modulators for Hereditary Angioedema Prophylaxis (HAE) —lanadelumab (Takhzyro)*
  - *Immunological Agents Miscellaneous: Oral Agents—house dust mite allergen extract (Odactra)*
  - *Leukemia and Lymphoma Agents: Bruton Tyrosine Kinase (BTK) Inhibitors—zanubrutinib (Brukinsa)*
  - *Oncological Agents—tucatinib (Tukysa)*
  - *Therapeutic Continuous Glucose Monitoring Systems (CGMs) —Freestyle Libre 2 and Freestyle Libre 3*
- **Prior Authorization Criteria—Updated PA Criteria for Reasons Other Than New Indications**
  - *Antipsychotic Agents*: *Atypical—olanzapine/samidorphan* (*Lybalvi)*
  - *Non-Insulin Diabetes Drugs: Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)*

        - *exenatide once weekly (Bydureon BCise)*
        - *liraglutide (Victoza)*
    - *Oncological Agents: Lung Cancer—sotorasib (Lumakras)*
- **Prior Authorization Criteria Removals**
    - *Diabetes Non-Insulin: Dipeptidyl Peptidase-4 (DPP-4s) Inhibitors*
    - *Diabetes Non-Insulin: Thiazolidinediones (TZDs)*

➢ **Brand Over Generic PA Authorization and Tier 1 copay**

- *Pulmonary Is: Inhaled Corticosteroid/Long Acting Beta Agonist Inhalers—fluticasone/salmeterol HFA inhaler (Advair HFA)*
- *Oncological Agents: Multiple Myeloma—lenalidomide (Revlimid)*
- *Anticonvulsant-Anti Mania Agents—topiramate ER (Trokendi XR)*

➢ **Over-the-Counter (OTC) Formulary Addition**

- *OTC naloxone nasal 4 mg (OTC Narcan Nasal)*

➢ **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 concur or non-concur on the recommendations of the P&T Committee concerning the establishment of the UF and subsequent recommended changes. The Panel will provide comments on their vote as directed by the Panel Chairman. Comments to the Director, DHA, or their designee will be considered

DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS FROM THE MAY 2023 MEETING

INFORMATION FOR THE UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL MEETING JUNE 28, 2023

I. UNIFORM FORMULARY REVIEW PROCESS

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

II. UF DRUG CLASS REVIEWS—ANTILIPIDEMICS-1—PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) INHIBITORS

P&T Comments

A. Antilipidemics-1—PCSK9 Inhibitors—Relative Clinical Effectiveness Conclusion

Background—The P&T Committee evaluated the relative clinical effectiveness of the PCSK9 inhibitors, which reduce low density lipoprotein cholesterol (LDL-C). The two drugs in the class include alirocumab (Praluent) and evolocumab (Repatha). The PCSK9 inhibitors were previously reviewed for formulary status in November 2016 based on trials demonstrating reduction in LDL-C. Since then, two large cardiovascular outcomes studies have been published.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

Efficacy

- Both alirocumab (Praluent) and evolocumab (Repatha) are injectable nonstatin therapies that provide significant reductions in LDL-C, ranging from 45% to 65%.
- In addition to lowering LDL-C, both PCSK9 inhibitors reduce major adverse cardiovascular events when used as secondary prevention, based on data from the ODYSSEY OUTCOMES trial with alirocumab, and the FOURIER trial with evolocumab.

- The drugs are FDA-approved for patients with established cardiovascular disease (CVD) to reduce the risk of myocardial infarction (MI), stroke and coronary revascularization (for Repatha) or to reduce the risk of MI, stroke and unstable angina requiring hospitalization (for Praluent).
- There is conflicting data between the FOURIER and ODYSSEY OUTCOMES trials with regard to effects on risk of cardiovascular (CV) death and all-cause death.
- The full mortality benefits of PCSK9s inhibitors are unknown due to early study termination.

Guidelines

- Recent updated guidance for nonstatins from the 2022 American College of Cardiology Expert Consensus Decision Pathway continue to support use of high intensity statins first-line for adults with atherosclerotic cardiovascular disease (ASCVD). The high intensity statins include atorvastatin 40 mg and 80 mg, and rosuvastatin 20 mg and 40 mg.
- PCSK9 inhibitors either alone or with ezetimibe can be considered in patients receiving maximally tolerated statin therapy who require a greater than 50% reduction in LDL-C.
- PCSK9 inhibitors may be considered for patients with clinical ASCVD at very high risk for future ASCVD events and who require a greater than 25% additional LDL lowering. Patients at very high risk for future ASCVD events include those with a history of major ASCVD events (i.e., recent acute coronary syndrome within the past 12 months, prior MI, prior ischemic stroke or symptomatic peripheral arterial disease), or those with one major ASCVD event and who have multiple high-risk conditions (e.g., age older than 65 years, heterozygous familial hypercholesterolemia, prior coronary revascularization, diabetes mellitus, hypertension, chronic kidney disease, current smoking, LDL-C > 100 mg/dL despite maximal statin therapy and history of chronic heart failure).
- The decision pathway now recommends lower LDL-C thresholds for starting nonstatin therapy, based on clinical status.
    - For patients with ASCVD at very high risk of future ASCVD events, the threshold for starting a nonstatin is an LDL-C > 55 mg/dL.
    - For patients with ASCVD not at very high risk of future ASCDV events, the threshold for starting a nonstatin is an LDL-C of > 70 mg/dL.

Safety

- Overall, the PCSK9 inhibitors are well tolerated, with injection site reactions reported most commonly. Alirocumab is associated with significantly more

injection site reactions than evolocumab, based on systematic review and network meta-analysis.

- No major differences are seen between the PCSK9 inhibitors with regard to discontinuations due to adverse effects.

Other Factors

- *Other nonstatins:* The results of a CV outcomes trial (CLEAR OUTCOMES) with bempedoic acid (Nexletol, Nexlizet) were recently published. CV outcomes trials are currently ongoing with inclisiran (Leqvio injection), which is available under the TRICARE medical benefit.
- Both PCSK9 inhibitors are indicated for treating homozygous familial hypercholesterolemia (HoFH) and heterozygous familiar hypercholesterolemia (HeFH), which are rare genetic conditions causing highly elevated LDL-C levels. Repatha is indicated for patients as young as 10 years of age with HoFH or HeFH, while Praluent is only labeled for use in adults.
- Repatha is available in a prefilled syringe, autoinjector, and an on-body infusor (Pushtronex), while Praluent is solely available in an autoinjector.

Overall Clinical Effectiveness Conclusion

- Although head-to-head trials are not available, the two PCSK9 inhibitors are highly therapeutically interchangeable, based on systematic reviews and network meta-analyses.
- At least one PCSK9 inhibitor is required on the formulary to meet the needs of MHS beneficiaries.

B. Antilipidemics-1—PCSK9 Inhibitors—Relative Cost Effectiveness Conclusion

Relative Cost Effectiveness Analysis and Conclusion—A cost minimization analysis (CMA), budget impact analysis (BIA) and sensitivity analysis were performed. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA results showed that evolocumab (Repatha) is more cost effective than alirocumab (Praluent).
- BIA was performed to evaluate the potential impact of designating the PCSK9 inhibitors as UF, NF, or completely excluded from the formulary. BIA results showed that designating evolocumab (Repatha) as UF and step-preferred and alirocumab (Praluent) as UF and non-step-preferred demonstrated significant cost avoidance to the MHS.

C. Antilipidemics-1—PCSK9 Inhibitors—UF Recommendation

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) maintaining the current formulary status for the PCSK9 inhibitors.

- UF and step-preferred
  - evolocumab (Repatha)
- UF and non-step-preferred
  - alirocumab (Praluent)
  - Note that as part of the formulary recommendation for Praluent, a trial of Repatha is required first.
- NF
  - None
- Complete exclusion
  - None

D. Antilipidemics-1—PCSK9 Inhibitors—Manual PA Criteria

PA criteria have been in place for the PCSK9 inhibitors since market entrance in 2015. In general, the following are currently required: specialist prescribing by a cardiologist; a trial of both high intensity atorvastatin and rosuvastatin, or if the patient is not on a high-intensity statin, they must be on ezetimibe plus a lower intensity statin, unless statin intolerance is documented; and renewal criteria are required after one year. Additionally, a trial of Repatha is required before Praluent.

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following changes to the criteria for new users. Reducing the requirement to try both high intensity atorvastatin and rosuvastatin to a trial of one high intensity statin and removing the requirement for specialist prescribing. Updates to the threshold LDL-C for patients with ASCVD were made, based on the ACC Expert Consensus Decision Pathway. Lastly, the requirement for renewal criteria was removed, and the PA will not expire.

The Manual PA criteria is as follows:

1. evolocumab (Repatha)

Changes from May 2023 meeting are in BOLD and strikethrough

PA applies to new patients

Manual PA Criteria: evolocumab (Repatha) is approved if all criteria are met:

- ~~The initial prescription is written by a cardiologist, lipidologist, or endocrinologist.~~

For HoFH and HeFH

- For HeFH and HoFH, the patient is 10 years of age or older
- The patient has HoFH and is receiving other LDL-lowering therapies (e.g., statin, ezetimibe, LDL apheresis), and requires additional lowering of LDL cholesterol
- The patient has HeFH and is on concurrent statin therapy at maximal tolerated doses

For ASCVD

- The patient is at least 18 years of age for clinical atherosclerotic cardiovascular disease (ASCVD)
- ~~The patient has established atherosclerotic cardiovascular disease (ASCVD) with an LDL >70 mg/dL despite statin therapy at maximally-tolerated doses, according to the criteria below:~~
- **The patient has established ASCVD with the following LDLs, despite maximally tolerated statin doses:**
  - **Very high risk of events: LDL > 55 mg/dL (very high risk of events includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high risk conditions. *Refer to the 2022 ACC Expert Consensus Decision Pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of ASCVD for more information*)**
    OR
  - **Not at very high risk of events: LDL > 70 mg/dL**

    AND
    - The patient must have tried **either** ~~both~~ atorvastatin 40-80 mg **or** ~~and~~ rosuvastatin 20-40 mg, OR
    - The patient must have tried any maximally-tolerated statin in combination with ezetimibe, OR
    - If the patient is statin-intolerant, they must have tried at least ezetimibe monotherapy ~~with or without other lipid-lowering therapy (e.g., fenofibrate, niacin, bile acid sequestrants)~~, AND
    - The patient must have had a trial of at least 4-6 weeks of maximally-tolerated therapy
- For both HeFH and ASCVD: If the patient is not on concurrent statin therapy, the patient is either intolerant of statins or has a contraindication to statins as defined below:
  - Intolerance

- The patient has experienced intolerable and persistent (for longer than 2 weeks) muscle symptoms (muscle pain, weakness, cramps), AND
- The patient has undergone at least 2 trials of statin re-challenges with reappearance of muscle symptoms, OR
- The patient has had a creatine kinase (CK) level >10x upper limit of normal (ULN)and/or rhabdomyolysis with CK > 10,000 IU/L that is unrelated to statin use.

- Contraindication to statin
  - The contraindication must be defined (active liver disease, hypersensitivity, pregnancy, breastfeeding)

For all indications

- Repatha is not approved for any indication other than HoFH, HeFH, or clinical ASCVD
- Repatha is not approved for patients who are pregnant or lactating
- The dosage must be documented on the PA Form as either:
  - 140 mg every 2 weeks, or
  - 420 mg every 4 weeks. Note that only patients with HoFH will be allowed to use 3 of the 140 mg syringes to make the 420 mg dose

PA does not expire ~~PA expires in one year.~~

- ~~PA criteria for renewal: After one year, PA must be resubmitted. The renewal request may be submitted by a primary care provider in consultation with the initial prescribing cardiologist, endocrinologist, and lipidologist. Continued use of Repatha will be approved for the following:~~
  - ~~The patient has a documented positive response to therapy with LDL < 70 mg/dL (or LDL ↓ >30% from baseline), AND~~

~~The patient has documented adherence~~

2. alirocumab (Praluent)

Changes from May 2023 meeting are in BOLD and strikethrough

Manual PA criteria apply to all new users of alirocumab (Praluent).

Manual PA criteria: Praluent is approved if:

For HoFH and HeFH

- ~~The initial prescription is written by a cardiologist, lipidologist, or endocrinologist.~~
- For HeFH and HoFH, patient is at least 18 years of age and older

- The patient has homozygous familial hypercholesterolemia (HoFH) and is receiving other LDL-lowering therapies (e.g., statin, ezetimibe, LDL apheresis), and requires additional lowering of LDL cholesterol
- The patient has heterozygous familial hypercholesterolemia (HeFH) and is on concurrent statin therapy at maximal tolerated doses

For ASCVD

- The patient is at least 18 years of age for clinical ASCVD
- ~~The patient has established atherosclerotic cardiovascular disease (ASCVD) with an LDL >100 mg/dL despite statin therapy at maximally-tolerated doses, according to the criteria below:~~
- **The patient has established atherosclerotic cardiovascular disease (ASCVD) with the following LDLs, despite maximally tolerated statin doses:**
  - **Very high risk of events: LDL > 55 mg/dL (very high risk of events includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high risk conditions. *Refer to the 2022 ACC Expert Consensus Decision Pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of ASCVD for more information*)**
    OR
  - **Not at very high risk of events: LDL > 70 mg/dL**
    AND
  - The patient must have tried **either** ~~both~~ atorvastatin 40-80 mg **or** ~~and~~ rosuvastatin 20-40 mg, OR
  - The patient must have tried any maximally-tolerated statin in combination with ezetimibe, OR
  - If the patient is statin-intolerant, they must have tried at least ezetimibe monotherapy ~~with or without other lipid-lowering therapy (e.g., fenofibrate, niacin, bile acid sequestrants)~~, AND
  - The patient must have had a trial of at least 4-6 weeks of maximally-tolerated therapy
- For both HeFH and ASCVD: If the patient is not on concurrent statin therapy, the patient is either intolerant of statins or has a contraindication to statins as defined below:
  - Intolerance
    - The patient has experienced intolerable and persistent (for longer than 2 weeks) muscle symptoms (muscle pain, weakness, cramps), AND

- The patient has undergone at least 2 trials of statin re-challenges with reappearance of muscle symptoms, OR
- The patient has had a creatine kinase (CK) level >10x ULN and/or rhabdomyolysis with CK > 10,000 IU/L that is unrelated to statin use

- Contraindication to statin
  - The contraindication must be defined (active liver disease, hypersensitivity, pregnancy, breastfeeding)

For all indications

- Praluent is not approved for any indication other than HoFH, HeFH, or clinical ASCVD
- The patient has tried and failed therapy with evolocumab (Repatha) OR
- The patient has experienced a significant adverse reaction to evolocumab (Repatha) that is not expected to occur with alirocumab (Praluent)
- Praluent is not approved for patients who are pregnant or lactating
- The dosage must be documented on the PA Form as either:
  - 75 mg every 2 weeks, or
  - 150 mg every 2 weeks.

PA does not expire ~~PA expires in one year.~~

- ~~PA criteria for renewal: After one year, PA must be resubmitted. The renewal request may be submitted by a primary care provider in consultation with the initial prescribing cardiologist, endocrinologist, and lipidologist. Continued use of Repatha will be approved for the following:~~
  - ~~The patient has a documented positive response to therapy with LDL < 70 mg/dL (or LDL ↓ >30% from baseline), AND~~

~~The patient has documented adherence~~

E. Antilipidemics-1—PCSK9 Inhibitors—UF, PA, and Implementation Period

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) an effective date of the first Wednesday 30 days after signing of the minutes in all points of service.

III. UF DRUG CLASS REVIEWS—ANTILIPIDEMICS-1—PCSK9 INHIBITORS

BAP Comments

A. Antilipidemics-1—PCSK9 Inhibitors—UF Recommendation

The P&T Committee recommended maintaining the current formulary status for the PCSK9 inhibitors as discussed above.

- UF and step-preferred
  - Repatha
- UF and non-step-preferred
  - Praluent
  - Note that as part of the formulary recommendation for Praluent, a trial of Repatha is required first.
- NF
  - None
- Complete exclusion
  - None

BAP Comments

Concur: Non-Concur: Abstain: Absent:

B. Antilipidemics-1—PCSK9 Inhibitors—Manual Criteria

The P&T Committee recommended manual PA criteria as outlined above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

C. Antilipidemics-1—PCSK9 Inhibitors—UF, PA, and Implementation Plan

The P&T Committee recommended an effective date of the first Wednesday 30 days after signing of the minutes in all points of service.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

IV. UF DRUG CLASS REVIEWS—OPHTHALMIC—DRY EYE AGENTS

P&T Comments

A. Ophthalmic—Dry Eye Agents—Relative Clinical Effectiveness Analysis and Conclusion

Background—The P&T Committee evaluated the relative clinical effectiveness of the Ophthalmic Dry Eye Agents, which are used to treat keratoconjunctivitis sicca (dry eye disease) and vernal keratoconjunctivitis. The class is comprised of 4 formulations containing differing concentrations of cyclosporine [0.05% ophthalmic emulsion unit dose and multidose (Restasis, Restasis Multidose), 0.09% ophthalmic solution (Cequa), and 0.1% ophthalmic emulsion (Verkazia)], lifitegrast 5% ophthalmic solution (Xiidra), loteprednol 0.25% ophthalmic suspension (Eysuvis), and varenicline nasal solution (Tyrvaya). Restasis and Xiidra were previously reviewed for formulary status in February 2018, while the remaining drugs were reviewed individually as new drugs.

All the drugs are indicated for dry eye disease, except for Verkazia, which is only indicated for vernal keratoconjunctivitis.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

Clinical Practice Guidelines

Dry Eye Disease

- The 2018 American Academy of Ophthalmology Preferred Practice Pattern (AAO PPP), and the 2017 Tear Film and Ocular Surface Society International Dry Eye Workshop II (TFOS DEWS II) recommend a stepwise treatment approach based on disease severity, and do not favor one product over another.
    - Ocular lubricants (e.g., artificial tears) are recommended as first-line (Step 1) treatments for dry eye disease, along with education, environmental changes, and eyelid hygiene.
    - Second-line (Step 2) treatments include cyclosporine, lifitegrast, or short course low-dose ophthalmic steroids (e.g., prednisolone, loteprednol).
    - The guidelines have not yet been updated to include the newer agents Cequa, Tyrvaya, or Eysuvis.

Vernal Keratoconjunctivitis (VKC)

- VKC is a rare disease causing severe ocular inflammation which can lead to corneal scarring and vision loss. It most commonly occurs in pediatric males living in warm, dry subtropical climates.
- The 2018 AAO PPP guidelines for VKC recommend a stepwise treatment approach based on disease severity, along with cool compresses and ocular lubricants.

- Mild disease can be treated with ocular mast cell stabilizers (e.g., azelastine, olopatadine) and antihistamines, followed by topical corticosteroids for moderate disease severity, with severe disease requiring treatment with the immunomodulatory therapies (cyclosporine and tacrolimus).

Efficacy

- There are no direct comparative studies between Restasis, Xiidra, Cequa, Tyrvaya, and Eysuvis for treatment of dry eye disease.
- *Dry Eye Disease:* A 2022 abstract from the Association for the Research in Vision and Ophthalmology (ARVO) Annual Meeting indirectly compared Cequa, Restasis, and Xiidra. There were no significant differences between the products with regard to patient subjective improvement, objective tests (Schirmer's tear test and tear osmolarity) and side effects. Limitations to this analysis include the retrospective study design and small sample size.
- *VKC*: No direct comparative data is available between Verkazia and lower dose cyclosporine agents for VKC treatment; however, the 2018 AAO PPP guidelines state that cyclosporine 0.05% is an appropriate option for treatment and has been effective in preventing seasonal recurrences.

Safety

- Ocular stinging and burning are common adverse effects with all the products. Unique safety features include the following:
  - Xiidra can cause dysgeusia.
  - Eysuvis carries warnings of delayed healing, intraocular pressure increase, cataracts, and risk of bacterial, viral, and fungal infections.
  - Tyrvaya as a nasal spray has unique nasal symptoms including nasal irritation, coughing, and sneezing.

Individual Product Characteristics

- **cyclosporine 0.05% (Restasis)** has a well-established efficacy and safety profile. Full clinical response may take 3 to 6 months to occur. The unit-dose formulation is now available as a generic product, while the multi-dose formulation is still branded. Ocular burning and stinging are the most commonly reported adverse effects. MHS providers agreed that generic Restasis can be trialed before other dry eye agents.
- **cyclosporine 0.09% (Cequa)** provides a higher strength of cyclosporine but does not show compelling clinical benefits over Restasis or Xiidra.
- **cyclosporine 0.1% (Verkazia)** is a higher strength cyclosporine formulation specifically indicated to treat VKC.
  - Clinical trial data and guidelines (2018 AAO PPP) support efficacy of lower-strength cyclosporine formulations for treatment of severe VKC.

- MHS providers agreed that a trial with other cyclosporine strengths is appropriate, and Verkazia should be reserved for severe VKC cases.

- **lifitegrast (Xiidra)** offers a different mechanism of action and potentially a faster onset of action compared to Restasis (as early as 2 weeks, with peak effect at 12 weeks vs. 6 months with cyclosporine), but there are no significantly compelling clinical benefits of Xiidra over Restasis.
- **loteprednol 0.25% (Eysuvis)** is currently the only loteprednol formulation to carry the FDA indication for short-term treatment of dry eye disease. However, guidelines (2018 AAO PPP and 2017 TFOS DEWS II) and MHS providers support the use of alternative loteprednol formulations, as well as other low-dose steroids for effective treatment. Ophthalmic steroids should only be used for short-term periods due to the risk of corneal perforation and increased ocular pressure. Eysuvis provides little-to-no clinical benefit over other ophthalmic steroid products. Note that loteprednol 0.2% (Alrex) and loteprednol 0.5% (Lotemax) and several other ophthalmic steroids are on the UF.
- **varenicline nasal spray (Tyrvaya)** has a unique mechanism of action using the parasympathetic pathway to increase tear production and does not cause ocular burning. However, Tyrvaya does not correct the underlying ocular inflammation. Sneezing, coughing and throat irritation can occur. MHS providers recommend a trial OTC artificial tears and generic cyclosporine or Xiidra first, before Tyrvaya. Its place in therapy remains unclear, and long-term benefit has not been determined.

Overall Clinical Conclusion

- In order to meet the needs of MHS patients, at least one ophthalmic immunomodulatory agent is needed to treat the majority of patients with dry eye disease and VKC.

B. Ophthalmic—Dry Eye Agents—Relative Cost Effectiveness Analysis and Conclusion

The Committee reviewed the solicited bids from manufacturers and conducted a CMA, BIA, and sensitivity analysis. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA results showed that cyclosporine 0.05% (Restasis and Restasis MultiDose), lifitegrast 5% (Xiidra), cyclosporine 0.09% (Cequa), varenicline nasal spray (Tyrvaya), and cyclosporine 0.1% (Verkazia) were cost effective, and that loteprednol 0.25% (Eysuvis) was not cost effective.
- A BIA and a sensitivity analysis were performed to evaluate the potential impact of designating selected agents as formulary, NF, or completely excluded on the UF. BIA results showed that designating cyclosporine 0.05% (Restasis and Restasis MultiDose), lifitegrast 5% (Xiidra), and cyclosporine

0.09% (Cequa) as UF, with varenicline nasal spray (Tyrvaya) and cyclosporine 0.1% (Verkazia) as NF, and loteprednol 0.25% (Eysuvis) as completely excluded, demonstrated the greatest cost avoidance for the MHS.

C. Ophthalmic—Dry Eye Agents—UF Recommendation

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

- UF
  - cyclosporine 0.05% ophthalmic solution unit dose (Restasis unit-dose, generics)
  - cyclosporine 0.05% ophthalmic solution multidose (Restasis Multidose)
  - cyclosporine 0.09% ophthalmic solution (Cequa) – *moves from NF to UF*
  - lifitegrast 5% ophthalmic solution (Xiidra)
- NF
  - cyclosporine 0.1% ophthalmic solution (Verkazia)
  - varenicline nasal solution (Tyrvaya)
- Complete exclusion
  - loteprednol etabonate 0.25% ophthalmic solution (Eysuvis) – *moves from NF to complete exclusion*

D. Ophthalmic—Dry Eye Agents—Manual PA Criteria

PA criteria has applied to all the products in the class since they were first reviewed individually for formulary status. In general, the following are required: specialist prescribing, a trial of two OTC lubricants (including preservative-free products), objective testing to confirm the diagnosis of dry eye disease or VKC, and renewal criteria, as the PAs expire in one year. Off-label use of Restasis is allowed for several conditions, including VKC.

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following changes to the PAs for new patients. For generic Restasis unit dose, Restasis Multidose, Cequa and Xiidra, the current 18 year age restriction and renewal criteria will be removed. For Restasis Multidose, Cequa and Xiidra, a 3-month trial of generic Restasis multidose will now be required for dry eye disease. Cequa will also be authorized for patients with VKC without requiring a trial of Restasis first.

There were no changes to the current PA criteria for Tyrvaya, which requires trial of Restasis or Xiidra first.

The Manual PA criteria is as follows: Updates from the May 2023 meeting are in Bold and strikethrough

1. **cyclosporine 0.05% ophthalmic emulsion unit dose (Restasis, generic unit dose)**

   Manual PA criteria apply to all new users of cyclosporine 0.05% ophthalmic emulsion unit-dose (Restasis unit-dose, generic)

   ~~Automated PA: If there is no Restasis, Cequa, or Xiidra prescription in the past 120 days, a manual PA is required.~~

   Manual PA criteria: Coverage is approved if all the criteria are met:

   - The drug is prescribed by an ophthalmologist or optometrist
   - ~~The patient is 18 years of age or older~~
   - A diagnosis of moderate to severe dry eye disease is supported by both of the criteria below:
     - Positive symptomology screening for moderate to severe dry eye disease from an appropriate measure
     - At least one positive diagnostic test (e.g., Tear Film Breakup Time, Osmolarity, Ocular Surface Staining, Schirmer Tear Test)
   - Patient must try and fail the following:
     - At least 1 month of one ocular lubricant used at optimal dosing and frequency (e.g., carboxymethylcellulose [Refresh, Celluvisc, Thera Tears, Genteal, etc.], polyvinyl alcohol [Liquitears, Refresh Classic, etc.], or wetting agents [Systame, Lacrilube])
     - Followed by at least 1 month of a different ocular lubricant that is non-preserved at optimal dosing and frequency (e.g., carboxymethylcellulose, polyvinyl alcohol)
   - Concomitant use of Restasis, Cequa, or Xiidra is NOT allowed.
   - Restasis unit-dose is also approved for the following conditions: graft rejection/graft versus host disease (GvHD), corneal transplant, atopic keratoconjunctivitis (AKC) / VKC, and LASIK associated dry eye (limited to 3 months of therapy)

   Other Non-FDA-approved uses are not approved
   ~~PA expires in one year.~~ **PA does not expire**

   ~~Renewal Criteria: Note that initial TRICARE PA approval is required for renewal. Coverage will be approved indefinitely if all criteria are met:~~

   - ~~The drug is prescribed by an ophthalmologist or optometrist.~~
   - ~~The patient must have documented improvement in ocular discomfort.~~

   ~~The patient must have documented improvement in signs of dry eye disease.~~

2. cyclosporine 0.05% ophthalmic multi dose (Restasis Multidose), cyclosporine 0.09% ophthalmic (Cequa), and lifitegrast 5% ophthalmic solution (Xiidra)

Updates from May 2023 are in BOLD and strikethrough

Manual PA criteria apply to all new users of Restasis Multidose, Cequa and Xiidra

~~PA criteria apply to all new and current users. A new user is defined as a patient who has not filled a prescription for Cequa in the past 120 days.~~

- ~~If there is no Restasis, Cequa, or Xiidra prescription in the past 120 days, a manual PA is required.~~

Manual PA Criteria: Coverage is approved if all the criteria are met:

- The drug is prescribed by an ophthalmologist or optometrist
- ~~For Cequa: the patient is 18 years of age or older~~
- A diagnosis of moderate to severe dry eye disease is supported by both of the criteria below:
  - Positive symptomatology screening for moderate to severe dry eye disease from an appropriate measure
  - At least one positive diagnostic test (e.g., Tear Film Breakup Time, Osmolarity, Ocular Surface Staining, Schirmer Tear Test)
- Patient must try and fail the following:
  - At least 1 month of one ocular lubricant used at optimal dosing and frequency (e.g., carboxymethylcellulose [Refresh, Celluvisc, Thera Tears, Genteal, etc.], polyvinyl alcohol [Liquitears, Refresh Classic, etc.], or wetting agents [Systane, Lacrilube])
  - Followed by at least 1 month of a different ocular lubricant that is non-preserved at optimal dosing and frequency (e.g., carboxymethylcellulose, polyvinyl alcohol)
  - **3-month trial of cyclosporine 0.05% unit-dose**
- Concomitant use of Restasis, Cequa, or Xiidra is NOT allowed
- **Cequa is approved if the patient has a diagnosis of VKC**

Other Non-FDA-approved uses are NOT approved
~~PA expires in one year.~~ **PA does not expire**

~~Renewal Criteria: Coverage will be approved indefinitely if all criteria are met:~~

- ~~The drug is prescribed by an ophthalmologist or optometrist.~~
- ~~The patient must have documented improvement in ocular discomfort.~~

~~The patient must have documented improvement in signs of dry eye disease~~

3. **cyclosporine 0.1% ophthalmic emulsion (Verkazia)**

   Updates from May 2023 are in BOLD and strikethrough

   Note that an age edit and automated look back apply.

   - Patients who are younger than 21 years of age who have a history of Restasis **or Cequa** do not require a PA; Verkazia is approved
   - Patients who are younger than 21 years of age who do not have a history of Restasis **or Cequa** require manual PA
   - Manual PA is required in all new patients 21 years of age and older

   Automated PA criteria: The patient is younger than age 21 years AND has filled a prescription for cyclosporine 0.05% ophthalmic solution (Restasis) **or cyclosporine 0.09% (Cequa)** at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 720 days.

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

   - Verkazia is prescribed by or in consultation with an optometrist or ophthalmologist
   - Patient has a diagnosis of moderate to severe VKC
   - Patient has tried and failed an adequate course of at least one mast cell stabilizer/antihistamine (i.e., olopatadine, azelastine, epinastine, lodoxamide, cromolyn)
   - Patient has tried and failed, or has a contraindication to an adequate course of cyclosporine 0.05% ophthalmic 3 (Restasis) **or the patient has tried and failed, or has a contraindication to an adequate course of cyclosporine 0.09% (Cequa)**

   Non-FDA-approved uses are NOT approved including dry eye disease, graft rejection/graft versus host disease (GvHD), corneal transplant, atopic keratoconjunctivitis (AKC), and LASIK associated dry eye
   PA does not expire

4. **varenicline nasal solution (Tyrvaya)**

   Note – there were no changes to the current PA criteria

   Manual PA criteria apply to all new users of Tyrvaya

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

   - The patient is 18 years of age or older
   - Tyrvaya is prescribed by an ophthalmologist or

- Patient has a diagnosis of dry eye disease as supported by both of the criteria below:
  - Positive symptomology screening for dry eye disease from an appropriate measure
  - At least one positive diagnostic test (e.g., Tear Film Breakup Time, Osmolarity, Ocular Surface Staining, Schirmer Tear Test)
- Patient must try and fail the following:
  - At least 1 month of one ocular lubricant used at optimal dosing and frequency (e.g., carboxymethylcellulose [Refresh, Celluvisc, Thera Tears, Genteal, etc.], polyvinyl alcohol [Liquitears, Refresh Classic, etc.], or wetting agents [Systane, Lacrilube])
  - Followed by at least 1 month of a different ocular lubricant that is non-preserved at optimal dosing and frequency (e.g., carboxymethylcellulose, polyvinyl alcohol)
- If the patient has moderate to severe dry eye disease:
  - Patient has tried and failed an adequate course (at least 6 weeks) of treatment of lifitegrast or cyclosporine treatment

Non-FDA-approved uses are not approved

Prior Authorization expires after 1 year

Renewal Criteria: (Initial TRICARE PA approval is required for renewal) Coverage will be approved indefinitely if all criteria are met:

- The drug is prescribed by an ophthalmologist or optometrist
- The patient must have documented improvement in ocular discomfort
- The patient must have documented improvement in signs of dry eye disease

E. Ophthalmic—Dry Eye Agents—UF, PA, and Implementation Period

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) an effective date of the first Wednesday 60 days after signing of the minutes in all points of service for Restasis, Cequa, Xiidra, Verkazia, and Tyrvaya, and an effective date of the first Wednesday 120 days after signing of the minutes in all points of service for Eysuvis. DHA will send letters to patients affected by the complete exclusion status of Eysuvis.

V. UF DRUG CLASS REVIEWS— Ophthalmic—Dry Eye Agents

BAP Comments

A. Ophthalmic—Dry Eye Agents—UF Recommendation

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

- UF
  - Restasis unit-dose, generics
  - Restasis Multidose
  - Cequa – *moves from NF to UF*
  - Xiidra
- NF
  - Verkazia
  - Tyrvaya
- Complete exclusion
  - Eysuvis – *moves from NF to complete exclusion*

BAP Comments

Concur: Non-Concur: Abstain: Absent:

B. Ophthalmic—Dry Eye Agents—Manual Prior Authorization Criteria

The P&T Committee recommended Manual PA criteria for dry eye agents as outlined above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

C. Ophthalmic—Dry Eye Agents—UF, PA, and Implementation Period

The P&T Committee recommended the implementation plan of 60 days for all the drugs, except for Eysuvis (120 days) as described above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

VI. NEWLY APPROVED DRUGS PER 32 CFR 199.21(g)(5)

P&T Comments

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

The products were divided into two groups when presented at the P&T Committee meeting. The generic names are provided below. Group 1 included Krazati, Atorvaliq, Orserdu, Rezvoglar, Konvomep, Stimufend, and Jaypirca; Group 2 was comprised of Amjevita, Altuviiio, Filspari, Pradaxa, Daybue, and Tezspire.

Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions—The P&T Committee agreed (for both group 1 and group 2: 17 for, 0 opposed, 0 abstained, 1 absent) with the relative clinical and cost-effectiveness analyses presented for the newly approved drugs reviewed according to 32 CFR 199.21(g)(5).

B. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF Recommendation

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

- UF
  - adagrasib (Krazati) – Oncological agent for advanced or metastatic non-small cell lung cancer
  - antihemophilic factor (recombinant), Fc-VWF-XTEN fusion protein-ehtl vial (Altuviiio) – Antihemophilic
  - elacestrant (Orserdu) – Oncological agent for breast cancer
  - omeprazole and sodium bicarbonate 2 mg/mL oral suspension (Konvomep) – Proton Pump Inhibitors
  - pegfilgrastim-fpgk injection (Stimufend) – White Blood Cell Stimulants: pegfilgrastims
  - pirtobrutinib (Jaypirca) – Oncological agent for relapsed or refractory mantle cell lymphoma
  - sparsentan (Filspari) – Nephrology Miscellaneous Agent for immunoglobulin A nephropathy
  - tezepelumab-ekko autoinjector (Tezspire) – Atopy Agent for add on maintenance severe asthma treatment
  - trofinetide 200 mg/mL oral solution (Daybue) – Neurological Miscellaneous Agent for treatment of Rett syndrome

- NF
  - adalimumab-atto injection (Amjevita) – Targeted Immunomodulatory Biologics (TIBS); Humira biosimilar
  - atorvastatin 20 mg/5 mL oral suspension (Atorvaliq) – Antilipidemics-1 agents
  - dabigatran oral pellet packets (Pradaxa pellets) – Direct Acting Oral Anticoagulant for treatment of venous thromboembolism (VTE) in pediatric patients aged 3 months to less than 12 years
  - insulin glargine KwikPen (Rezvoglar) – Basal Insulins; Lantus biosimilar
- Complete exclusion – None

C. Newly Approved Drugs per 32 CFR 199.21(g)(5)—PA Criteria

The P&T Committee recommended (for both group 1 and group 2: 17 for, 0 opposed, 0 abstained, 1 absent) the following PA criteria:

- Applying manual PA criteria to new users of the Amjevita (the biosimilar to Humira), similar to what is required for all non-step-preferred TIBs. A trial of brand Humira is required first before the biosimilar in new users.
- Oncologic drugs: Applying manual PA criteria to new users of Krazati, Jaypirca, and Orserdu.
- Applying manual PA criteria to new users of Atorvaliq oral suspension, Pradaxa oral pellets, Filspari, Rezvoglar, Konvomep oral suspension, Daybue oral solution, and Tezspire injection.
- Applying manual PA criteria to Stimufend, similar to what is in place for the other non-step-preferred pegfilgrastims. New patients receiving Stimufend or one of the other non-step-preferred pegfilgrastims (Neulasta, Neulasta Onpro, and Ziextenzo) will be required to have a trial of Nyvepria, Udenyca or Fulphila first.

The Manual PA criteria is as follows:

1. adagrasib (Krazati)

Manual PA criteria apply to all new users of adagrasib (Krazati)

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

- Patient is 18 years of age and older
- The medication is prescribed by or in consultation with a hematologist or oncologist

- The patient has a diagnosis of KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) as determined by an FDA-approved test
- The patient will be monitored for QTC prolongation, gastrointestinal adverse reactions, hepatotoxicity, and interstitial lung disease
- If patient is a female, the patient will avoid breastfeeding during treatment and for at least 1 week after cessation of treatment
- 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

Other non-FDA approved uses are NOT approved, except as noted above
PA does not expire

2. adalimumab-atto injection (Amjevita)

Manual PA criteria apply to all new and current users of adalimumab-atto (Amjevita)

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

- Provider acknowledges that the originator adalimumab (Humira) is the preferred product over biosimilar adalimumab formulations
- Provider must provide patient specific justification as to why the originator Humira product cannot be used in this patient
    - Acceptable responses include that the patient has an allergy to an inactive ingredient found in the originator Humira that is not in the Amjevita biosimilar
- If patient is younger than 18 years of age, coverage is provided for moderate to severe polyarticular juvenile idiopathic arthritis or moderate to severe Crohn's disease
    - If indication is moderate to severe polyarticular juvenile idiopathic arthritis, patient must 2 years of age or older
    - If indication is moderate to severe Crohn's disease, the patient must be 6 years of age or older AND must have had an inadequate response to non-biologic systemic therapy (For example: methotrexate, aminosalicylates [such as, sulfasalazine, mesalamine], corticosteroids, immunosuppressants [such as, azathioprine], etc. unless they have fistulizing Crohn's disease
- If patient is 18 years of age or older, coverage is provided for moderately to severely active rheumatoid arthritis, moderate to severe Crohn's disease, moderate to severe chronic plaque psoriasis where patient is candidate for

systemic or phototherapy or when other systemic therapies are medically less appropriate, psoriatic arthritis, ankylosing spondylitis, moderate to severe ulcerative colitis, and hidradenitis suppurativa

- If indication is moderate to severe chronic plaque psoriasis OR moderate to severe Crohn's disease OR moderate to severe ulcerative colitis then patient must have had an inadequate response, intolerance, or contraindication to non-biologic systemic therapy. (For example: methotrexate, aminosalicylates [e.g., sulfasalazine, mesalamine], corticosteroids, immunosuppressants [e.g., azathioprine, cyclosporine], acitretin, or phototherapy), etc. unless they have fistulizing Crohn's disease
- If indication is ankylosing spondylitis has patient must have had inadequate response to at least two NSAIDs over a period of at least 2 months

- Patient has not had case of worsening congestive heart failure (CHF) and new onset CHF has not been reported with TNF blockers, including Humira
- Patient had evidence of negative TB test in the past 12 months (or TB is adequately managed)
- Patient is not receiving other targeted immunomodulatory biologics with Humira, including but not limited to the following: certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), apremilast (Otezla), ustekinumab (Stelara), abatacept (Orencia), anakinra (Kineret), tocilizumab (Actemra), tofacitinib (Xeljanz/Xeljanz XR), rituximab (Rituxan), secukinumab (Cosentyx), ixekizumab (Taltz), brodalumab (Siliq), sarilumab (Kevzara), guselkumab (Tremfya), baricitinib (Olumiant), tildrakizumab (Ilumya), risankizumab (Skyrizi), or upadacitinib (Rinvoq ER)

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

3. atorvastatin 20 mg/5 mL oral suspension (Atorvaliq)

Manual PA criteria apply to all new users of atorvastatin oral suspension (Atorvaliq)

Age edit: PA does not apply to patients younger than 12 years of age

PA criteria apply to all new users of Atorvaliq 12 years of age and older

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

- Provider must explain why patient requires atorvastatin oral suspension and cannot take simvastatin, atorvastatin or rosuvastatin tablets or sprinkles

- Acceptable responses include that the patient requires a high intensity statin and cannot swallow the statin tablets due to some documented medical condition (e.g., dysphagia, oral candidiasis, systemic sclerosis), and not due to convenience, and cannot take rosuvastatin (Ezallor) sprinkles

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

4. dabigatran oral pellet (Pradaxa pellets)

Manual PA criteria apply to all new users of dabigatran oral pellets (Pradaxa)

PA does not apply to patients less than 8 years of age (age edit) AND who have tried Xarelto Suspension OR Lovenox Injection within the past 180 days

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

- Patient is between the ages of 3 months to 12 years
- Pradaxa pellets are prescribed by or in consultation with a pediatric hematologist/oncologist or pediatric cardiologist
- Patient is being treated for venous thromboembolic events AND has been treated with parenteral anticoagulant for at least 5 days
- Patient has tried and failed or has a contraindication to Xarelto Suspension AND Lovenox Injection
- Patient is between the ages of 8 and 12 years and cannot take the Pradaxa capsule

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

5. elacestrant (Orserdu)

Manual PA criteria apply to all new users of elacestrant (Orserdu)

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

- Patient is 18 years of age or older
- Patient is a male or a postmenopausal female
- The medication is prescribed by or in consultation with a hematologist or oncologist
- The patient has a diagnosis of ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer

- Patient had disease progression following at least one line of endocrine therapy, which must include a CDK4/6 inhibitor
- Patient does not have severe hepatic impairment (Child-Pugh C)
- 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

Other non-FDA approved uses are NOT approved except as noted above
PA does not expire

6. insulin glargine KwikPen (Rezvoglar)

Manual PA criteria apply to all new and current users of Rezvoglar Kwikpen

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

- Patient must have tried and failed insulin glargine (Lantus) first.

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

7. Omeprazole and sodium bicarbonate 2 mg/mL oral suspension (Konvomep)

Manual PA criteria apply to all new users of Konvomep

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

- Patients younger than 12 years of age do not require PA – Age edit
- Patients 12 years of age or older – manual PA required
- The provide must provide a patient-specific clinical rationale as to why the patient cannot take omeprazole capsules, pantoprazole tablets, or esomeprazole capsules.

  Acceptable reasons include: Patient has a G-tube or patient cannot swallow other PPI capsules or tablets due to some documents medical condition – dysphagia, oral candidiasis, systemic sclerosis, etc and not due to convenience.

Non-FDA approved uses are not approved

PA does not expire

8. pegfilgrastim-fpgk injection (Stimufend)

Manual PA criteria apply to all new users of pegfilgrastim (Neulasta), pegfilgrastim (Neulasta OnPro), pegfilgrastim-bmez (Ziextenzo) **and pegfilgrastim-fpgk (Stimufend)**

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

- Provider acknowledges that pegfilgrastim-cbqv (Udenyca), pegfilgrastim-jmdb (Fulphila) and pegfilgrastim-apgf (Nyvepria) are the preferred pegfilgrastims and are available without a PA
- Drug is prescribed by or in consultation with a hematologist/oncologist
- Patient has experienced an inadequate treatment response or intolerance to pegfilgrastim-cbqv (Udenyca), pegfilgrastim-jmdb (Fulphila) or pegfilgrastim-apgf (Nyvepria) and is expected to respond to pegfilgrastim (Neulasta), pegfilgrastim-bmez (Ziextenzo), or **pegfilgrastim-fpgk (Stimufend)**

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

9. pirtobrutinib (Jaypirca)

Manual PA criteria apply to all new users of pirtobrutinib (Jaypirca)

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

- Patient is 18 years of age or older
- The medication is prescribed by or in consultation with a hematologist or oncologist
- Patient has pathologically confirmed relapsed or refractory mantle cell lymphoma (MCL)
- Monitor for bleeding, infection (including opportunistic infection), cardiac arrhythmias, secondary primary malignancies, and cytopenias
- Patient will use sun protection in sun-exposed areas
- Female patients of childbearing age and are not pregnant confirmed by (-) HCG
- Female patients will not breastfeed during treatment and for at least 1 week after the cessation of treatment
- Female patients of childbearing potential agree to use effective contraception during treatment and for at least 1 week after the cessation of treatment
- 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, except as noted above
PA does not expire

10. sparsentan (Filspari)

Manual PA criteria apply to all new users of sparsentan (Filspari)

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

- Provider acknowledges that Filspari is only available through a Risk Evaluation and Mitigation Strategy (REMS) program due to the risk of hepatotoxicity and embryo-fetal toxicity, and will follow the monitoring requirements
- Patient is 18 years of age or older
- Filspari is prescribed by a nephrologist
- The patient has a diagnosis of biopsy-verified primary immunoglobulin A nephropathy (IgAN) without cellular crescents in more than 25% of sampled glomeruli
- Patient has a urine protein-to-creatinine ratio (UPCR) greater than or equal to 1.5 g/gram
- Patient has an estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73 m^2
- Patient is not currently receiving dialysis or has not undergone kidney transplant
- Patient has not received immunosuppressants, including corticosteroids, in the past 2 weeks and is not expected to need immunosuppressants in the next 6 months
- Patient has continued to have proteinuria despite maximal ACE-inhibitor or ARB therapy and is at high risk for disease progression
- The patient is not receiving concomitant renin-angiotensin-aldosterone system inhibitors (for example ACE-inhibitors or ARBs such as irbesartan, telmisartan, losartan; or spironolactone), endothelin receptors antagonists (for example ambrisentan or bosentan) or aliskiren
- The patient's baseline liver aminotransferase (AST and ALT) levels are not elevated to greater than 3 times the upper limit of normal
- If patient is a female of child-bearing age, the patient must be tested for pregnancy before, during and 1 month after treatment discontinuation
- If patient can become pregnant, they will use effective contraception before starting treatment, during and for 1 month after treatment discontinuation

Non-FDA approved uses are NOT approved, including IgAN due to systemic lupus erythematosus, liver cirrhosis, Henoch-Schonlein purpura, or pulmonary arterial hypertension, or focal segmental glomerulosclerosis (FSGS)

PA expires in 9 months

Renewal criteria: coverage will be approved indefinitely if all the following apply

- Patient has had a response to Filspari defined by:
  - reduction in urine protein-to-creatinine ratio (UPCR) from baseline OR
  - reduction in proteinuria from baseline
- Patient's eGFR rate ≥ 30 mL/min/1.73 m2
- Filspari is not being used in combination with any RAAS blocker (e.g., ACE-Is, ARB), endothelin receptor antagonists, or aliskiren

11. tezepelumab-ekko autoinjector (Tezspire)

Manual PA is required for all new users of tezepelumab (Tezspire)

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

- The patient is 12 years of age and older
- The patient has a diagnosis of severe persistent asthma
- The drug is prescribed by an allergist, immunologist, or pulmonologist
- Provider acknowledges the FDA warnings and precautions associated with Tezspire
- The patient's asthma must be uncontrolled, despite adherence to optimized medication therapy regimen, defined as requiring ONE of the following:
  - Hospitalization for asthma in past year OR
  - Two courses of corticosteroids for asthma exacerbation in past year OR
  - Daily high-dose inhaled corticosteroids with inability to taper off the inhaled corticosteroids
- The patient has tried and failed an adequate course (3 months) of TWO of the following while using a high-dose inhaled corticosteroid:
  - Long-acting beta agonist (LABA e.g., Serevent, Striverdi), OR
  - Long-acting muscarinic antagonist (LAMA e.g., Spiriva, Incruse), OR
  - Leukotriene receptor antagonist (e.g., Singulair, Accolate, Zyflo)

Non-FDA-approved uses are not approved
Prior authorization expires after 12 months

Renewal Criteria: Note initial Tricare PA approval is required for renewal.

Renewal PA criteria will be approved indefinitely if all the following apply

- The patient has had a positive response to therapy, as defined by one of the following:
  - a decrease in asthma exacerbations
  - improvements in forced expiratory volume in one second (FEV1)
  - decrease in oral corticosteroid use

12. trofinetide oral solution (Daybue)

Manual PA criteria apply to all new users of trofinetide (Daybue)

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

- Patient is 2 years of age and older
- The medication is prescribed by a geneticist, neurologist, or a developmental pediatrician
- The patient has a diagnosis of Rett Syndrome with documented MECP2 gene mutation.

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

D. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF and PA Implementation Period

The P&T Committee recommended (for group 1 and group 2: 17 for, 0 opposed, 0 abstain, 1 absent) an effective date of the following:

- **New Drugs Recommended for UF or NF Status:** an effective date of the first Wednesday two weeks after signing of the minutes in all points of service.

VII. NEWLY APPROVED DRUGS PER 32 CFR 199.21(g)(5)

BAP Comments

A. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF Recommendation

The P&T Committee recommended the formulary status for the newly approved drugs as discussed above.

- UF
  - Krazati

        - Altuviiio
        - Orserdu
        - Konvomep
        - Stimufend
        - Jaypirca
        - Filspari
        - Tezspire
        - Daybue
    - NF
        - Amjevita
        - Atorvaliq
        - Pradaxa
        - Rezvoglar
    - Complete exclusion
        - None

BAP Comments

Concur: Non-Concur: Abstain: Absent:

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

The P&T Committee recommended the PA criteria for new drugs as stated previously.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

C. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF, PA, and Implementation Period

The P&T Committee recommended the implementation plan of two weeks as described above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

VIII. UTILIZATION MANAGEMENT—NEW MANUAL PA CRITERIA

P&T Comments

A. New PA Manual Criteria

a) Thyroid Agents—levothyroxine sodium capsule (Tirosint)—Tirosint is a formulation that does not contain some common excipients (e.g., dyes, gluten, etc.) found in other levothyroxine formulations. However, Tirosint is not cost-effective relative to generic levothyroxine tablets or Synthroid. MTF providers support the addition of a prior authorization, to encourage use of more cost-effective levothyroxine formulations.

Manual PA criteria apply to all new users of levothyroxine capsules (Tirosint)

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

- Tirosint is prescribed by or in consultation with an endocrinologist
- Patient is 6 years of age or older
- Patient must have tried and failed or have a contraindication to levothyroxine tablets that is not expected to occur with levothyroxine capsules

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

b) Gastrointestinal-2 Agents—sacrosidase oral solution (Sucraid)—Sucraid is approved to treat patients with Congenital Sucrase-Isomaltase Deficiency (CSID). Sucraid was identified as a high-cost, specialty medication with increasing utilization. Many commercial health plans require PA for Sucraid, and MTF providers support the addition of a prior authorization restricting it to its FDA-approved indication.

Manual PA criteria apply to all new and current users of sacrosidase (Sucraid)

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

- Sucraid is prescribed by or in consultation with a gastroenterologist or geneticist
- Patient has a diagnosis of congenital sucrase-isomaltase deficiency (CSID)
- Prior to starting therapy with Sucraid, patient had symptomatic CSID (e.g., diarrhea, bloating, abdominal cramping)

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

c) **Targeted Immunomodulatory Biologics (TIBs): Tumor Necrosis Factor (TNF) Inhibitors Agents—adalimumab (Humira)—**The PA criteria for Humira were updated to allow for approval if the prescriber specialty is Rheumatology. Humira is a high value medication, and the inclusion of this new PA criteria enables rheumatologists, who possess advanced training and certification, to prescribe Humira without having to complete a PA. This change will also encourage appropriate use of this preferred product.

B. New Manual PA Criteria and Implementation Plan

a) **Thyroid Agents**—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) manual PA criteria in new users of Tirosint capsules requiring a trial or contraindication to generic levothyroxine tablets or Synthroid first. The new PA will become effective the first Wednesday 60 days after the signing of the minutes.

b) **Gastrointestinal-2 Agents—sacrosidase oral solution (Sucraid)**—The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) manual PA criteria in new and current users of Sucraid, limiting use to patients who have a CSID diagnosis and symptoms. The new PA will become effective the first Wednesday 60 days after the signing of the minutes, and DHA will send letters to affected patients.

c) **Targeted Immunomodulatory Biologics (TIBs): Tumor Necrosis Factor (TNF) Inhibitors Agents—adalimumab (Humira)**—The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 2 absent) updated manual PA criteria in new users of Humira allowing for PA approval if the prescriber is a rheumatologist. The new PA will become effective the first Wednesday 30 days after the signing of the minutes.

IX. UTILIZATION MANAGEMENT— NEW MANUAL PA CRITERIA

BAP Comments

A. New Manual Criteria

The P&T Committee recommended new manual PA criteria for Tirosint, Sucraid, and Humira as stated above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

B. New Manual PA Criteria and Implementation Plan

The P&T Committee recommended effective dates after signing of the minutes for the drugs discussed above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

X. UTILIZATION MANAGEMENT—UPDATED PA CRITERIA FOR NEW FDA-APPROVED INDICATIONS

P&T Comments

A. Updated PA Criteria for New FDA-Approved Indications

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) updates to the PA criteria for several drugs, due to new FDA-approved indications and expanded age ranges. The updated PA criteria outlined below will apply to new users.

a) **Atopy Agents: Oral Janus Kinase Inhibitor (JAK-1)—abrocitinib (Cibinqo)—** The manual PA criteria were updated to include the new expanded age indication for adolescents with refractory, moderate-to-severe atopic dermatitis. Cibinqo is now approved for patients 12 years of age and older. In addition, the new PA criteria were edited to allow for pediatric patients to try and fail, have a contraindication to, or intolerability to any topical corticosteroid (as opposed to a high potency topical corticosteroid).

b) **Breast Cancer Agents: CDK Inhibitors—abemaciclib (Verzenio)**—The manual PA criteria were updated to remove the requirement for patients to have a high Ki-67 score.

c) **Corticosteroid-Immune Modulators for Hereditary Angioedema Prophylaxis (HAE)—lanadelumab (Takhzyro)—**Expands the HAE prophylaxis indication to include patients 2 years of age and older.

d) **Leukemia and Lymphoma Agents: Bruton Tyrosine Kinase (BTK) Inhibitors—zanubrutinib (Brukinsa)—**A new indication was added for the treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) in adults.

e) **Immunological Agents Miscellaneous: Oral Agents—house dust mite allergen extract (Odactra)**—Manual PA criteria were updated to reflect the expanded pediatric age indication. Odactra is now approved for patients ranging from 12 to 65 years of age.

f) **Oncological Agents—tucatinib (Tukysa)—**The manual PA criteria were updated for Tukysa to allow for use in combination with trastuzumab for the treatment of RAS wild-type, HER2-positive, unresectable, or metastatic colorectal cancer in adults that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.

g) **Therapeutic Continuous Glucose Monitoring Systems—Freestyle Libre 2 and 3**—The Freestyle Libre 2 and 3 systems are now approved for use in pregnant patients. The manual PA criteria were updated to change the requirement that patient had a diagnosis of "type 1 or type 2 diabetes" to a requirement that patients just have a diagnosis of "diabetes". Patients will still need to meet all additional PA requirements as last specified at the November 2022 meeting.

B. Updated PA Criteria for New FDA-Approved Indications—Manual PA Criteria and Implementation Period

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) updates to the manual PA criteria for Brukinsa, Odactra, Takhzyro, Tukysa, Cibinqo, Verzenio and Freestyle Libre 2 and 3 in new users. Implementation will be effective the first Wednesday 60 days after the signing of the minutes.

XI. UTILIZATION MANAGEMENT—UPDATED PA CRITERIA FOR NEW FDA-APPROVED INDICATIONS

BAP Comments

A. Updated PA Criteria for New FDA-Approved Indications

The P&T Committee evaluated updates to the PA Criteria for several drugs, due to FDA as outlined above.

BAP Comments

Concur: ***Non-Concur:*** ***Abstain:*** ***Absent:***

B. Updated Manual PA Criteria for New FDA-Approved Indication Implementation Plan

The P&T Committee recommended an effective date of 60 days after signing of the minutes for the drugs discussed above.

BAP Comments

Concur: ***Non-Concur:*** ***Abstain:*** ***Absent:***

XII. UTILIZATION MANAGEMENT—UPDATED PA CRITERIA FOR REASONS OTHER THAN NEW INDICATIONS

P&T Comments

A. Updated PA Criteria for Reasons other than New Indications

a) Antipsychotic Agents: Atypical—olanzapine/samidorphan (Lybalvi)—Lybalvi was reviewed as an innovator at the November 2021 meeting and designated non-formulary with a PA. Although Lybalvi was associated with approximately 5 pounds less weight gain than olanzapine alone, several other options are available to mitigate antipsychotic-induced weight gain, including choosing a different antipsychotic (e.g., aripiprazole and ziprasidone) or adding on metformin. The P&T Committee recommended clarifying the PA criteria to include these other options.

b) Non-Insulin Diabetes Drugs: Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)—liraglutide (Victoza) and exenatide once weekly (Bydureon BCise)—Dulaglutide (Trulicity) is the DoD's preferred GLP1RA, and it was previously only indicated for adults. Victoza and Bydureon BCise are indicated for patients as young as 10 years of age. The Victoza and Bydureon BCise PAs currently bypass the requirement to try Trulicity first in pediatric patients. The Trulicity package label was recently updated to allow for use in children 10 years of age and older, based on the results of a clinical trial. The P&T Committee recommended removing both the PA that allow the bypass of a trial of Trulicity first for pediatric patients with prescriptions for Victoza and Bydureon BCise.

c) Oncological Agents: Lung Cancer—sotorasib (Lumakras)—Previously, Lumakras had only been available as a 120 mg tablet. In order to get the recommended dose of 960 mg, a patient needed to take eight tablets. A new 320 mg tablet is now available which only requires a patient to take three tablets, but it is significantly less cost-effective than the 120 mg formulation. Both the 120 mg and 320 mg tablets can be dispersed in 4 ounces of water for patients who have swallowing difficulties. MTF provider feedback supports the addition of prior authorization criteria preferring the Lumakras 120 mg tablets over the 320 mg tablets.

B. Updated PA Criteria for Reasons other than New Indications—Updated Manual PA criteria and Implementation Period

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) updates to the manual PA criteria olanzapine/samidorphan (Lybalvi), liraglutide (Victoza), and exenatide (Bydureon BCISE) in new users, and updates to the manual PA criteria for new

users of sotorasib (Lumakras) 320 mg tablets. Implementation will be effective the first Wednesday 60 days after signing of the minutes.

XIII. UTILIZATION MANAGEMENT—UPDATED PA CRITERIA FOR REASONS OTHER THAN NEW INDICATIONS

BAP Comments

A. Updated PA Criteria for Reasons other than New Indications

The P&T Committee recommended PA revisions as listed above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

B. Updated PA Criteria for Reasons other than New Indications Implementation Period

The P&T Committee recommended PA implementation period of 60 days as listed above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

XIV. UTILIZATION MANAGEMENT—REMOVAL OF PA CRITERIA AND IMPLEMENTATION PLAN

P&T Comments

Removal of PA Criteria and Implementation Plan

Diabetes Non-Insulin: Thiazolidinediones (TZDs) and Dipeptidyl Peptidase-4 inhibitors (DPP-4s)—Several diabetes drug classes are available on the formulary, and new products are now recommended first-line in addition to metformin, including the GLP1RAs (e.g. Trulicity) and SGLT-2 inhibitors (e.g., Jardiance). However, older classes still play a role in lowering glucose levels. The American Diabetes Association 2023 guidelines includes guidance for using the TZDs and DPP-4 inhibitors before metformin.

The UF preferred TZD pioglitazone (Actos) and UF preferred DPP-4 inhibitor sitagliptin (Januvia) and their combination products are cost-effective, with high PA approval rates. Additionally, the TZDs and DPP-4 inhibitors have a low likelihood for off-label use (in contrast to the GLP1RAs.) The P&T Committee recommended removing the PA requirements for the UF TZD and DDP-4 inhibitors. PA will still remain for the NF, non-step-preferred TZD (e.g., rosiglitazone) and DPP-4 inhibitors (e.g., linagliptin, saxagliptin).

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) removing the PA criteria for pioglitazone (Actos), pioglitazone/metformin (Actoplus Met), pioglitazone/glimepiride (Duetact), sitagliptin (Januvia), and sitagliptin/metformin (Janumet, Janumet XR). Implementation will be effective the first Wednesday 2 weeks after signing of the minutes.

XV. UTILIZATION MANAGEMENT—REMOVAL OF PA CRITERIA AND IMPLEMENTATION PERIOD

BAP Comments

Removal of PA Criteria and Implementation Period

The P&T Committee recommended removing the PA criteria for the TZDs and DPP4- inhibitors as listed above, with an implementation effective the first Wednesday 2 weeks after signing of the minutes as listed above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

XVI. BRAND OVER GENERIC AUTHORIZATION AND TIER 1 COPAY FOR FLUTICASONE/SALMETEROL INHALER (ADVAIR HFA), LENALIDOMIDE (REVLIMID) AND TOPIRAMATE ER (TROKENDI XR) AND IMPLEMENTATION PERIOD

P&T Comments

The Committee evaluated drugs from 3 classes that are currently UF:

- Pulmonary Is: Inhaled Corticosteroid/Long-Acting Beta Agonist Inhalers—fluticasone/salmeterol HFA inhaler (Advair HFA)
- Oncological Agents: Multiple Myeloma—lenalidomide (Revlimid)
- Anticonvulsant-Anti Mania Agents—topiramate ER (Trokendi XR)

AB-rated generic versions of all three drugs have entered the market; however, the generic products are less cost-effective compared to the branded agents. Therefore, the branded Advair HFA, Revlimid, and Trokendi XR will continue to be dispensed at all three points of service, and the generic will only be available with prior authorization (i.e., the reverse of the current brand to generic policy). The Tier 1 copay for brand Advair HFA, Revlimid, and Trokendi XR dose is recommended.

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent), requiring brand Advair HFA, Revlimid and Trokendi XR over their respective generic formulations in all new and current users at all points of service, based on cost effectiveness. The prescriber will provide patient-specific justifications as to why the branded product cannot be used. The Tier 1 (generic) copay will apply to the brand Advair HFA, Revlimid and Trokendi XR. The effective date will be the first Wednesday 60-days after signing of the minutes. The "brand over generic" requirement will be removed administratively when it is no longer cost-effective compared to AB-rated generics.

XVII. BRAND OVER GENERIC AUTHORIZATION AND TIER 1 COPAY FOR FLUTICASONE/SALMETEROL (ADVAIR HFA), LENALIDOMIDE (REVLIMID) AND TOPIRAMATE ER (TROKENDI XR) AND IMPLEMENTATION PERIOD

BAP Comments

The P&T Committee recommended brand over generic authorization for Brand Advair HFA, Revlimid, and Trokendi XR and the Tier 1 copay, with an implementation period of 60 days as stated above.

BAP Comments

Concur: Non-Concur: Abstain: Absent:

XVIII. OVER-THE-COUNTER (OTC) DRUG BENEFIT—NALOXONE NASAL SPRAY—UF RECOMMENDATION, COPAY, PRESCRIPTION REQUIREMENT, AND IMPLEMENTATION PERIOD

P&T Comments

Background: Pursuant to 32 CFR 199.21(h)(5)(i), an OTC drug may be included on the UF upon the recommendation of the P&T Committee and approval of the Director, DHA, based on a finding that it is cost-effective and clinically effective, as compared with other drugs in the same therapeutic class of pharmaceutical agents. OTC drugs placed on the UF, in general, will be treated the same as generic drugs on the UF for purposes of availability in the MTF pharmacies, retail pharmacies, and the mail order pharmacy program and other requirements. However, upon the recommendation of the P&T Committee and approval of the Director, DHA, the requirement for the prescription may be waived for a particular OTC drug for certain emergency care treatment

situations. In addition, a special copayment may be established under 32 CFR 199.21 (i)(2)(xii) for OTC drugs specifically used in certain emergency care treatment situations.

OTC Naloxone Nasal Spray: The P&T Committee evaluated the clinical and cost-effectiveness for the addition of OTC naloxone 4 mg/0.1mL nasal spray (OTC Narcan Nasal Spray) to the UF. Other prescription naloxone formulations are available on the UF (Kloxxado, Zimhi). The OTC naloxone nasal spray is the same as the prescription product.

Multiple references, including guidance from the Substance Abuse and Mental Health Services Administration, the National Institute on Drug Abuse, and the 2022 DoD/VA Guideline for the Use of Opioids in Management of Chronic Pain, as well as input from DoD pain management specialists, support the use of intranasal naloxone for the emergency treatment of known or suspected opioid overdose. Based on clinical effectiveness and ease of access, OTC naloxone nasal (4 mg/0.1mL) was recommended for addition to the UF, when the product is launched commercially (expected in summer 2023).

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

- adding OTC naloxone 4 mg/0.1 mL nasal spray to the UF
- waiving the copay requirement
- waiving the prescription requirement
- implementation plan of two weeks after signing of the minutes and market launch of OTC Narcan Nasal Spray in all points of service

The P&T Committee voted to waive the prescription and copay requirements. While the P&T Committee voted to waive the requirement for a prescription at all points of service, there may be state or operational limitations that require some provider input for processing. As an example, some states allow pharmacists who have National Provider Identifier (NPI) numbers to prescribe but the pharmacy claims adjudication systems may require a valid prescription. According to National Council for Prescription Drug Programs (NCPDP) rules, a provider NPI is required for claims to process.

Regarding copay, 32 CFR 199.21(i)(2)(xii) states as a general rule, OTC drugs placed on the UF will have copayments equal to those for generic drugs on the UF. However, upon the recommendation of the P&T Committee and approval of the Director, DHA, the copayment may be established at $0.00 for any particular OTC drug in the retail pharmacy network. The P&T Committee recommended the copay for OTC naloxone be zero at retail and the Tier 1 generic copay at mail.

XIX. OVER-THE-COUNTER (OTC) DRUG BENEFIT—NALOXONE NASAL—UF RECOMMENDATION, COPAY, PRESCRIPTION REQUIREMENT, AND IMPLEMENTATION PERIOD

BAP Comments

The P&T Committee recommended adding OTC naloxone 4 mg/0.1 mL nasal spray to the UF, with an implementation effective 2 weeks after signing of the minutes as listed above.

BAP Comments

Concur: ***Non-Concur:*** ***Abstain:*** ***Absent:***

From: Axsome MedInfo US
To: DHA NCR J-6 Mailbox BAPREQUESTS
Subject: [Non-DoD Source] AUVELITY Written Statement to UF BAP
Date: Tuesday, March 28, 2023 4:16:31 PM
Attachments: AUVELITY DoD UF BAP PA Comments 3.28.23.pdf

Dear Designated Federal Officer,

Please see attached written statement to the UF BAP on the proposed prior authorization criteria for AUVELITY.

Thank you in advance for your review and consideration.

Regards,
Lally Samuel, PharmD
Axsome Medical Information
[redacted]

March 28, 2023

UF BAP's Designated Federal Officer
7700 Arlington Boulevard
Suite 5101
Falls Church, VA 22042–5101
dha.ncr.j-6.mbx.baprequests@health.mil

Dear Uniform Formulary Benefit Advisory Panel:

Thank you for the opportunity to comment on the P&T committee's proposed prior authorization criteria for AUVELITY® (dextromethorphan HBr and bupropion HCl) extended-release tablets for the treatment of adults with major depressive disorder (MDD).

The proposed prior authorization criteria include that patient must have "tried and failed generic bupropion extended release at maximally tolerated dose **AND** the patient has a contraindication to, intolerability to, or has failed a trial of **TWO** other formulary antidepressant medications (note: failure of medication is defined as a minimum treatment duration of 4-6 weeks at maximally tolerated dose)."

We respectfully request that you remove the additional step of failure of generic bupropion extended release prior to use of AUVELITY and allow access to AUVELITY after two antidepressant trials. As discussed below, there is a pressing need for new MDD treatment options with novel mechanisms of action, rapid onset, early time to remission, and tolerable safety profiles.

Remission Rates Following Monoaminergic Antidepressant Failure
As you know, it is well documented that individuals with military service have a higher risk of depression than the civilian population.[1] The proposed criteria require failure of at least 3 antidepressants that all work primarily via the monoaminergic pathway[2] prior to being eligible to receive AUVELITY, the only oral NMDA receptor antagonist approved for MDD.[3]

While it is *possible* that individuals that fail to respond to one monoaminergic antidepressant, may respond to another, it should be noted that the likelihood of this occurring is low. The STAR*D study clearly demonstrated that after failure of the SSRI citalopram at a maximally tolerated dose, the likelihood of remission was low (~20%) with subsequent monoaminergic-based treatment with either bupropion, sertraline, or venlafaxine.[4] Remission rates decline further with third and fourth line monoaminergic-based treatment.[5] The declining remission rates seen in STAR*D may be partially explained by the lack of pharmacological diversity amongst the different treatments, i.e., all antidepressants employed are thought to work in generally the same way: monoamine modulation.[6]

Early and Sustained Remission is a Critical Treatment Goal in MDD
Time to initiation of effective treatment in MDD may be delayed by at least 3-5 months if symptomatic remission is not achieved by the initial 3 required antidepressant trials. Early symptom remission is key to obtaining improved clinical, functional, and psychosocial outcomes and is one of the strongest predictors of long-term favorable outcome in MDD.[7-10] The impact of the delay of potentially effective treatment is further compounded by the well-documented stigma around MDD that further results in many people, including those in the military, suffering with depression for months or years prior to receiving adequate evidence-based treatment.[11] This is particularly noteworthy since the duration of untreated depression has been shown to correlate with structural changes in the brains of people with MDD.[12]

Tricare beneficiaries suffering with MDD need improvement in depressive symptoms as soon as possible and should not be required to wait this long before their mental health provider can prescribe a differentiated treatment option for MDD. The mental health provider should be able to prescribe the medication they believe is most appropriate for the patient

without having to proceed through three steps with antidepressants with similar mechanisms of action (i.e., monoaminergic).

Differentiated Mechanism of Action
AUVELITY is the first oral antidepressant in approximately 60 years that is thought to work via a non-monoaminergic mechanism. AUVELITY targets the glutamatergic pathway via NMDA receptor antagonism and sigma-1 receptor agonism,[3] an approach that is different from other approved oral agents.[2] Dextromethorphan is an uncompetitive antagonist of the NMDA receptor (an ionotropic glutamate receptor) and a sigma-1 receptor agonist.[3] The primary role of bupropion in AUVELITY is to increase and prolong plasma levels of dextromethorphan by inhibiting its CYP2D6-mediated metabolism.[3] Requiring that patients also must fail bupropion before receiving a prescription for AUVELITY is ignoring the significant contribution of dextromethorphan to the efficacy of AUVELITY and its differentiated mechanism of action (further discussed below).

AUVELITY is a Rapid-Acting Antidepressant
Breakthrough therapy designation was granted to AUVELITY in 2019 by the FDA and it was approved in August 2022 based on a clinical development program of over 1100 patients. AUVELITY is the only rapid-acting oral antidepressant with labeling of statistically significant antidepressant efficacy compared to placebo starting at one week.[3]

In the pivotal, placebo-controlled, **GEMINI study[13]:**
- AUVELITY achieved the primary outcome: Change from baseline to week 6 in MADRS total score was -15.9 points in the AUVELITY group and -12.1 in the placebo group (P=0.002).[3,13]
- Statistically significant improvement in the MADRS was demonstrated starting at Week 1,[3,13] a time frame consistent with the draft FDA guidance for rapid-acting antidepressants.[14]
  - No other oral antidepressant has FDA-approved labeling stating improvement in depressive symptoms starting at Week 1.
- The improvements seen with AUVELITY on the MADRS total score at all timepoints measured were greater than the clinically meaningful threshold, which ranges from 1.6-1.9 points.[13,15]
- The key secondary endpoint of remission (MADRS Total Score ≤10) at Week 2 was also achieved, with AUVELITY demonstrating a statistically significant greater remission rate compared to placebo (AUVELITY 17%, Placebo 8%; P = 0.013).[13]
  - Symptom remission is considered the desired goal in depression treatment, because it is associated with better daily functioning and better long-term prognosis.[5]

In the confirmatory, active-controlled, **ASCEND study[16]:**
- AUVELITY achieved the primary outcome by demonstrating statistically significant improvement in change from baseline in MADRS total score over weeks 1-6 compared to bupropion 105 mg dosed twice daily (AUVELITY -13.7 points, Bupropion -8.8 points; $P < 0.001$).
- Rates of remission were also increased compared to bupropion starting at Week 2.

Boxed Warning and Other Safety Information
AUVELITY has a boxed warning for increased risk of suicidal thoughts and behaviors in pediatric and young adult patients. The most common adverse reactions with AUVELITY were dizziness, headache, diarrhea, somnolence, dry mouth, sexual dysfunction, and hyperhidrosis.[3] Please consult the AUVELITY full Prescribing Information for complete product details including contraindications, warnings and precautions, drug interactions, and adverse reactions available at: https://www.axsome.com/auvelity-prescribing-information.pdf

In summary, AUVELITY is a differentiated and appropriate option after failure or intolerance of initial monoaminergic antidepressant treatment. Clinicians need the option to prescribe a rapid-acting and differentiated antidepressant earlier in treatment without having to wait the crucial time it would take to evaluate treatment response with 3 monoaminergic antidepressants.

We respectfully request that you remove the additional step of failure of generic bupropion extended release prior to use of AUVELITY. By removing this step, healthcare providers will have the option to prescribe AUVELITY for Tricare beneficiaries after two monoaminergic antidepressant drug failures.

Thank you again for your consideration of this important treatment option for adults with MDD.

Sincerely,

Zach Thomas, PharmD, MPH
Executive Director, Medical Affairs

References:

1. Department of Veterans Affairs and the Department of Defense. VA/DoD clinical practice guideline for the management of major depressive disorder, version 4.0. Published April 2022. https://www.healthquality.va.gov/guidelines/MH/mdd/VADoDMDDCPGFinal508.pdf. Accessed March 27, 2023.
2. Machado-Vieira R, Henter ID, Zarate CA Jr. New targets for rapid antidepressant action. *Prog Neurobiol.* 2017;152: 21-37.
3. AUVELITY [Prescribing Information]. New York, NY: Axsome Therapeutics Inc.
4. Rush AJ, South C, Jha MK, Jain SB, Trivedi MH. What to expect when switching to a second antidepressant medication following an ineffective initial SSRI: A report from the randomized clinical STAR*D study. *J Clin Psychiatry.* 2020;81(5):19m12949. doi: 10.4088/JCP.19m12949.
5. Rush AJ, Trivedi MH, Wisniewski SR, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. *Am J Psychiatry.* 2006;163:1905–1917.
6. Giakoumatos CI, Osser D. The Psychopharmacology Algorithm Project at the Harvard South Shore Program: An update on unipolar nonpsychotic depression. *Harv Rev Psychiatry.* 2019;27(1):33-52.
7. Habert J, Katzman MA, Oluboka OJ, et al. Functional recovery in major depressive disorder: Focus on early optimized treatment. *Prim Care Companion CNS Disord.* 2016;18(5). doi: 10.4088/PCC.15r01926.
8. Nierenberg AA, Husain MM, Trivedi MH, et al. Residual symptoms after remission of major depressive disorder with citalopram and risk of relapse: a STAR*D report. *Psychol Med.* 2010;40:41-50.
9. Trivedi MH, Morris DW, Wisniewski SR, et al. Increase in work productivity of depressed individuals with improvement in depressive symptom severity. *Am J Psychiatry.* 2013;170(6):633-641. doi: 10.1176/appi.ajp.2012.12020250.
10. Ciudad A, Álvarez E, Roca M, et al. Early response and remission as predictors of a good outcome of a major depressive episode at 12-month follow-up: a prospective, longitudinal, observational study. *J Clin Psychiatry.* 2012; 73(2):185-191.
11. Goldberg SB, Simpson TL, Lehavot K, et al. A comparison among civilians and veterans of different service eras. *Psychiatr Serv.* 2019;70(5):358-366. doi: 10.1176/appi.ps.201800444.
12. Sheline YI, Gado MH, Kraemer HC. Untreated depression and hippocampal volume loss. *Am J Psychiatry.* 2003; 160(8):1516-1518.
13. Iosifescu DV, Jones A, O'Gorman C, et al. Efficacy and safety of AXS-05 (dextromethorphan-bupropion) in patients with major depressive disorder: A phase 3 randomized clinical trial (GEMINI). *J Clin Psychiatry.* 2022;83(4): 21m14345. DOI: 10.4088/JCP.21m14345
14. FDA. Major Depressive Disorder: Developing Drugs for Treatment Guidance for Industry: DRAFT GUIDANCE. June 2018. Revision 1.
15. Duru G, Fantino B. The clinical relevance of changes in the Montgomery-Asberg Depression Rating Scale using the minimum clinically important difference approach. *Curr Med Res Opin.* 2008;24(5): 1329-1335.
16. Tabuteau H, Jones A, Anderson A, Jacobson M, Iosifescu DV. Effect of AXS-05 (dextromethorphan-bupropion) in major depressive disorder: a randomized double-blind controlled trial. *Am J Psychiatry.* 2022;179(7):490-499. DOI: 10.1176/appi.ajp.21080800

From:	Christopher Ngai
To:	DHA NCR J-6 Mailbox BAPREQUESTS
Cc:	Jonathan Schur
Subject:	[Non-DoD Source] NEPHROLOGY AGENTS MISCELLANEOUS - Tarpeyo
Date:	Monday, April 3, 2023 1:50:42 PM
Attachments:	image001.jpg NeflgArd-top-line-presentation.pdf CEOR-389456-cost-effectiveness-analysis-of-nefecon-versus-best-supportiv.pdf NeflgArd Positive Data Eng.pdf
Importance:	High

To Designated Federal Officer:

I am writing to follow up on TARPEYO. We noticed that the P&T Committee recommended Tier 4 designation for TARPEYO, based on the surprising rationale that "[TARPEYO] provides little to no clinical advantages relative to other drugs used off-label for IgAN."

We would like to update the BAP Committees on the topline results from the confirmatory portion of the NeflgArd clinical trial, studying TAREPYO (referred to under its development name of Nefecon) in patients with primary IgAN. Calliditas announced on March 12, 2023 that NeflgArd successfully met the primary endpoint, intended to describe and verify TARPEYO's clinical benefit:

- Over a two-year period of 9-months of treatment with Nefecon or placebo and 15-months of follow-up off drug, mean change in baseline in estimated glomerular filtration rate (eGFR) were -2.47 ml/min/1.73 m^2 in the TARPEYO group and -7.52 ml/min/1.73 m^2 in the placebo group, a treatment benefit over placebo of 5.05 ml/min/1.73 m^2 (p value < 0.0001).
- Supportive 2-year total slope analyses similarly indicated a sustained treatment benefit.
- We observed the eGFR benefit was observed across the entire study population, irrespective of urine protein-to-creatinine ratio (UPCR) baseline.
- UPCR reductions observed were durable during the 15-month follow-up period off treatment.

Our initial review, subject to continuing analysis and regulatory review, is that these results show a clinically significant long-lasting treatment effect and support a regulatory filing which we will make in the near future for full approval in the study population. The press release announcing the NeflgArd results is attached as well as a summary presentation of the trial results.

We are concerned that TRICARE beneficiaries risk being denied access to this important new drug, in favor of unapproved, off-label treatments for which clinical studies, when available, in no way demonstrate a similar treatment effect and safety profile in a population comparable to that of TRICARE beneficiaries. Moreover, the cost effectiveness analysis manuscript now published in the journal of ClinicoEconomics and Outcomes Research, which you will find attached, supports the cost-effectiveness of TARPEYO treatment, even before taking into account the confirmatory trial results.

We ask that you provide these materials to the BAP Committees. New and significant confirmatory clinical trial results need to be taken into account before TRICARE beneficiaries are denied access to TARPEYO or being subject to unreasonable prior authorization criteria.

Best regards,

Christopher Ngai
Vice President Market Access
[redacted]
[redacted]

From: McCarthy, Jim
To: DHA NCR J-6 Mailbox BAPREQUESTS
Subject: [URL Verdict: Neutral][Non-DoD Source] Tarpeyo phase 3 data
Date: Monday, April 3, 2023 12:00:19 PM
Attachments: image001.png
NefIgArd Positive Data Eng.pdf

Colonel Carby, hello.

The March 31 Federal Register identifies you as the Designated Federal Official relative to BAP.

I'm part of the Payor-facing team working on behalf of Calliditas Therapeutics in its commercialization of Tarpeyo® (budesonide) delayed release capsules.
None of us are formally aligned to DHA as a focus-customer, but I monitor both DHA Pharmacy and Federal Register and have been asked in the past to share certain information. I've confirmed Calliditas' interest in having the attached provided to your team and I have made Calliditas aware of the 31 March Federal Register notice of tomorrow's UF BAP committee meeting and its impact on any opportunity for public comment.

The attached is recently published data relative to the concluded phase 3 trial for Tarpeyo's use in the management of IgA nephropathy (IgAN). This press release was provided to us for sharing with Payors just last Tuesday. Besides the possibility that the clinical data might be viewed very favorably by BAP relative to that of another recently approved IgAN therapy, there are clear implications relative to cost of drug treatment.

Understanding the role and function of BAP, this is not being shared with any expectation of P&T-like review, but in lieu of the now waived Public Comment window, only of informing the BAP Committee in advance of their vote on April 4. And, for the Committee's consideration, the simple ask that BAP vote for now against relegating Tarpeyo® to tier 4 and ask P&T to reinstate newly-approved drug criteria pending P&T review of the product's phase 3 trial results and possible full marketing approval and, possible full class review.

Thank you.

Respectfully,

Jim McCarthy
Director, National Accounts/Government Affairs
Reimbursement, Access & Distribution Solutions
Emerging Biopharma

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Stockholm, Sweden **March 12, 2023**

Calliditas Announces Primary Endpoint Successfully Met in Phase 3 NefIgArd Trial Evaluating Nefecon® in IgA Nephropathy

Calliditas Therapeutics AB (Nasdaq: CALT, Nasdaq Stockholm: CALTX) ("Calliditas") today announced positive topline results from the global, randomized, double-blind, placebo-controlled Phase 3 clinical trial NefIgArd, which investigated the effect of Nefecon (TARPEYO®/Kinpeygo® (budesonide) delayed release capsules) versus placebo in patients with primary IgA nephropathy (IgAN).

- The trial met its primary endpoint with Nefecon demonstrating a highly statistically significant benefit over placebo (p value < 0.0001) in estimated glomerular filtration rate (eGFR) over the two-year period of 9-months of treatment with Nefecon or placebo and 15-months of follow-up off drug.
- Supportive 2-year total slope analyses were statistically significant and clinically meaningful reflecting a sustained treatment benefit.
- The eGFR benefit was observed across the entire study population, irrespective of urine protein-to-creatinine ratio (UPCR) baseline, which the company believes supports a regulatory filing for full approval in the study population.
- UPCR reductions observed were durable, reflecting a long lasting treatment effect during the 15-month follow-up period off treatment.

"This is truly a great outcome for IgAN patients. This reflects sustained impact on kidney function across the entire study population with a treatment which was specifically designed to treat IgAN by downregulating pathogenic IgA1 antibodies at their presumed source and we believe this dataset supports regulatory filing for full approval based on the Phase 3 study population," said CEO Renée Aguiar-Lucander.

"These data show the kidney function protection delivered by Nefecon and demonstrate that the approach offers patients a truly disease modifying treatment with sustained reductions in proteinuria over two years and continued eGFR benefit. Importantly Nefecon was well tolerated and together with the proteinuria and eGFR data mean that Nefecon has cemented its place as a key treatment option for patients with IgA nephropathy at risk of progressive kidney function loss," said Dr Jonathan Barratt, Mayer Professor of Renal Medicine at Leicester University.

"These data establish that there is an option for patients with IgA nephropathy to specifically target their illness and to safely slow and delay progression of their kidney disease. The sustained effects on proteinuria and on eGFR are impressive and clinically meaningful," said Richard Lafayette, Professor of Medicine (Nephrology) at Stanford University.

This data readout from Part B provides longer term data from the Phase 3 NefIgArd trial, which read out topline data on Part A in November 2020. An additional 29 Chinese patients, required for local Chinese regulatory purposes only, are expected to complete Part B in Q3, 2023. Based on the Part A data, Calliditas received accelerated approval from the U.S Food and Drug Administration (FDA) in December 2021 and conditional marketing authorization from the European Commission (EC) in July 2022, marking the first time a drug was approved for the treatment of IgAN in the US and the European Economic Area (EEA). Nefecon is being marketed by Calliditas in the US under the brand name TARPEYO®, and by STADA Arzneimittel AG in the EEA, Switzerland and the UK under the brand name Kinpeygo®.

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"I am delighted with the positive outcome of the NefIgArd trial. This important milestone is the culmination of many years of hard work and dedication from so many people involved in the study. I would like to extend my thanks in particular to the investigators and site staff involved in the study, as well as of course the participating patients," said Calliditas' CMO, Dr. Richard Philipson.

On the basis of this data, Calliditas plans to file for full approval from the FDA, and support filing for full approval with EC and UK MHRA during 2023 for patients with primary IgAN based on the Phase 3 study population.

NefIgArd Topline Results

The analysis included 364 patients diagnosed with primary IgAN and who were on a background of optimized and stable renin-angiotensin system (RAS) inhibitor therapy. The patients were randomized in a 1:1 ratio into one of two treatment groups – Nefecon 16 mg/day orally or placebo – and treated for 9 months daily, and then monitored for 15 months off-drug.

<u>eGFR Data</u>

The key primary endpoint, eGFR over 2 years, was on average 5.05 mL/min/1.73 m^2 higher with Nefecon compared to placebo ($p<0.0001$). Mean change in eGFR over the 2-year period was -2.47 mL/min/1.73 m^2 for Nefecon 16 mg versus -7.52 mL/min/1.73 m^2 for placebo.

<u>Safety Profile</u>

The results indicate that Nefecon was generally well-tolerated and the safety profile was consistent with that observed in Part A of the trial.

Trial Design

The global clinical trial NefIgArd is an ongoing Phase 3, randomized, double-blind, placebo- controlled, multicenter study to evaluate the efficacy and safety of TARPEYO 16 mg once daily vs placebo in adult patients with primary IgAN as an addition to optimized RAS inhibitor therapy.

Part A of the study included a 9-month blinded treatment period and a 3-month follow-up period. The primary endpoint was UPCR, and eGFR was a secondary endpoint. Part B included a 12-month observational period off drug and assessed eGFR over the entire 2-year period for patients who were treated with the TARPEYO or placebo regimen in Part A in a total population of 360 patients.

The trial met its primary objective in Part A of demonstrating a statistically significant reduction in urine protein creatinine ratio (UPCR) or proteinuria after 9 months of treatment with 16 mg once daily of TARPEYO compared to placebo. Patients taking TARPEYO plus RAS inhibition (n=97) showed a statistically significant 34% reduction from baseline vs 5% with RASi alone (n=102) at 9 months, resulting in UPCR reduction of 31% (16% to 42%) p=0.0001.[3]

At 9 months, there was a 3.87 mL/min/1.73 m2 difference in eGFR absolute change with TARPEYO plus RASi vs RASi alone (-0.17 vs. -4.04).[4]

Topline data of the NefIgArd study were reported on March 12, 2023 in which the primary endpoint of eGFR was met as per above. The trial is expected to conclude in Q3 of 2023 when the final 29 patients in China (not required for global submission purposes) have completed 9 months of treatment and 15 months of observation.

Conference Call

The Company will host a live webcast for investors on Monday 13th March 2023 at 8 A.M. ET (13:00 CET). Interested participants may register for the webcast here: https://lifescievents.com/event/calliditas-webcast/

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Indication and important safety information

Indication: TARPEYO® (budesonide), named Kinpeygo in the EEA, a 4mg delayed release capsule, is a corticosteroid indicated in the US to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g and in the EEA for the treatment of IgAN in adults at risk of rapid disease progression with a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/gram.

This indication is approved by the FDA in the US under an accelerated approval and as a conditional marketing authorisation by the European Commission for the EEA based on a reduction in proteinuria. It has not been established whether TARPEYO/Kinpeygo slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

Important Safety Information

Contraindications: TARPEYO/Kinpeygo is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO/Kinpeygo. Serious hypersensitivity reactions, including anaphylaxis, have occurred with other budesonide formulations.

Warnings and Precautions

Hypercorticism and adrenal axis suppression: When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy [see Dosing and Administration] or switching between corticosteroids, monitor for signs of adrenal axis suppression.

Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

Risks of Immunosuppression: Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressive doses of corticosteroids. Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection; untreated fungal, bacterial, systemic viral, or parasitic infections; or ocular herpes simplex. Avoid exposure to active, easily transmitted infections (eg, chicken pox, measles). Corticosteroid therapy may decrease the immune response to some vaccines.

Other corticosteroid effects: TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma, cataracts, a family history of diabetes or glaucoma, or with any other condition in which corticosteroids may have unwanted effects.

Adverse reactions: In clinical studies, the most common adverse reactions with TARPEYO (occurring in ≥5% of TARPEYO/Kinpeygo patients and ≥2% higher than placebo) were hypertension (16%), peripheral edema (14%), muscle spasms (13%), acne (11%), dermatitis (7%), weight increase (7%), dyspnea (6%), face edema (6%), dyspepsia (5%), fatigue (5%), and hirsutism (5%).

Drug interactions: Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, and cyclosporine. Avoid ingestion of grapefruit juice with TARPEYO/Kinpeygo. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide.

Use in specific populations

Pregnancy: The available data from published case series, epidemiological studies, and reviews with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgAN. Infants exposed to in utero corticosteroids, including budesonide, are at risk for hypoadrenalism.

Please see Full Prescribing Information for TARPEYO here.

About Primary Immunoglobulin A Nephropathy

Primary immunoglobulin A nephropathy (IgA nephropathy or IgAN or Berger's Disease) is a rare, progressive, chronic autoimmune disease that attacks the kidneys and occurs when galactose-deficient IgA1 are recognized by autoantibodies, creating IgA1 immune complexes that become deposited in the glomerular mesangium of the kidney.[5,6] This deposition in the kidney can lead to progressive kidney damage and potentially a clinical course resulting in end-stage renal disease. IgAN most often develops between late teens and late 30s.[6,7]

For further information, please contact:
Marie Galay, IR Manager, Calliditas
Tel.: +44 79 55 12 98 45, email: marie.galay@calliditas.com

The information in the press release is information that Calliditas is obliged to make public pursuant to the EU Market Abuse Regulation. The information was sent for publication, through the agency of the contact person set out above, on March 12, 2023 at 6:30 p.m. CET.

About Calliditas

Calliditas Therapeutics is a commercial stage biopharma company based in Stockholm, Sweden focused on identifying, developing and commercializing novel treatments in orphan indications, with an initial focus on renal and hepatic diseases with significant unmet medical needs. Calliditas' lead product, developed under the name Nefecon, has been granted accelerated approval by the FDA under the trade name TARPEYO® and conditional marketing authorization by the European Commission under the trade name Kinpeygo®. Kinpeygo is being commercialized in the EEA, Switzerland, and the UK by Calliditas' partner, STADA Arzneimittel AG. Additionally, Calliditas is conducting a Phase 2b/3 clinical trial in primary biliary cholangitis and a Phase 2 proof-of-concept trial in head and neck cancer with its NOX inhibitor product candidate, setanaxib. Calliditas' common shares are listed on Nasdaq Stockholm (ticker: CALTX) and its American Depositary Shares are listed on the Nasdaq Global Select Market (ticker: CALT).

About TARPEYO/Kinpeygo

Calliditas has introduced TARPEYO/Kinpeygo, the first treatment to be approved for patients with IgAN. TARPEYO/Kinpeygo is an oral, delayed release formulation of budesonide, a corticosteroid with potent glucocorticoid activity and weak mineralocorticoid activity that undergoes substantial first pass metabolism. TARPEYO/Kinpeygo was designed as a 4 mg delayed release capsule and is enteric coated so that it would remain intact until it reaches the ileum. Each capsule contains coated beads of budesonide that target mucosal B-cells present in the ileum, including the Peyer's patches, which are responsible for the production of galactose-deficient IgA1 antibodies (Gd-Ag1) causing IgAN. It is unclear to what extent TARPEYO's/Kinpeygo's efficacy is mediated via local effects in the ileum vs systemic effects.[1]

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding Calliditas' strategy, planned regulatory submissions, anticipated regulatory approvals and clinical development plans, timing and data readouts. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties, and important factors that may

cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, any related to Calliditas' business, operations, continued and additional regulatory approvals for TARPEYO and Kinpeygo, market acceptance of TARPEYO and Kinpeygo, competitive products, clinical trials, supply chain, strategy, goals and anticipated timelines and other risks identified in the section entitled "Risk Factors" in Calliditas' reports filed with the Securities and Exchange Commission. Calliditas cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. Calliditas disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions, or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent Calliditas' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

References:

1. TARPEYO. Prescribing Information. Calliditas Therapeutics AB; 2021.
2. Hastings, M. C., Bursac, Z., Julian, B. A., Villa Baca, E., Featherston, J., Woodford, S. Y., Bailey, L., & Wyatt, R. J. (2018). Life Expectancy for Patients From the Southeastern United States With IgA Nephropathy. Kidney Int Rep, 3(1), 99-104. https://doi.org/10.1016/j. ekir.2017.08.008
3. Barratt, J., Lafayette, R., Kristensen, J., Stone, A., Cattran, D., Floege, J., Tesar, V., Trimarchi, H., Zhang, H., Eren, N., Paliege, A, Rovin, B. H., for theNeflgArd Trial Investigators, Results from part A of the multi-center, double-blind, randomized, placebo-controlled NeflgArd trial, which evaluated targeted-release formulation of budesonide for the treatment of primary immunoglobulin A nephropathy, Kidney International (2023) 103, 391–402; https://doi.org/10.1016/j.kint.2022.09.017.
4. Barratt, J., & Feehally, J. (2005). IgA nephropathy. J Am Soc Nephrol, 16(7), 2088-2097. https://doi.org/10.1681/ASN.2005020134
5. Barratt, J., Rovin, B. H., Cattran, D., et al. (2020). Why Target the Gut to Treat IgA Nephropathy? Kidney Int Rep, 5(10), 1620-1624. https://doi.org/10.1016/j.ekir.2020.08.009
6. Jarrick, S., Lundberg, S., Welander, A., et al. (2019). Mortality in IgA Nephropathy: A Nationwide Population-Based Cohort Study. J Am Soc Nephrol, 30(5), 866-876. https://doi.org/10.1681/ASN.2018101017

From:	Christopher Ngai
To:	DHA NCR J-6 Mailbox BAPREQUESTS
Cc:	Andrew Udell; Jonathan Schur
Subject:	[Non-DoD Source] Comments on Background Document for June 2023 BAP Meeting
Date:	Thursday, June 22, 2023 5:53:48 PM
Attachments:	image001.jpg CALHB TRICARE Letter (2023.06.22).pdf

Dear Colonel Carby:

Please see attached our comment on the Background Document for June 2023 BAP Meeting. I thank you for this opportunity to provide our comments to the BAP.

Best regards,

Christopher Ngai

[redacted]

calliditas
THERAPEUTICS

BY OVERNIGHT COURIER
Designated Federal Official [DFO]
Colonel Paul B Carby, PharmD
7700 Arlington Boulevard Suite 5101
Falls Church, VA 22042-5101

June 22, 2023

Re: Background Document for June 2023 Beneficiary Advisory Panel Meeting

Dear Colonel Carby:

On behalf of Calliditas Therapeutics US Inc. (Calliditas), I thank you for the opportunity to provide comments on the Beneficiary Advisory Panel (BAP) Background Document for the Uniform Formulary BAP Meeting taking place on June 28, 2023.

I would like to call your attention to the substantial differences between the assessment and recommendation of the Department of Defense Pharmacy and Therapeutics (P&T) Committee concerning FILSPARI, the second FDA approved treatment for IgA nephropathy (IgAN), as compared to TARPEYO, the first FDA approved treatment for IgAN:

1. To support the P&T Committee's recommendation in May 2022 to categorize TARPEYO as a Tier 4/Not Covered drug, it was stated that "the needs of TRICARE beneficiaries are met by available alternative agents," e.g., prednisone, methylprednisolone, and budesonide DR capsules (Entocort EC, generics). However, in the recent assessment of FILSPARI by the P&T Committee this May, it appears that there was a recognition of unmet needs among TRICARE beneficiaries diagnosed with IgAN, and that FILSPARI had demonstrated relative clinical effectiveness and cost effectiveness against the available alternative agents. The available clinical data for FILSPARI are at best comparable to that of TARPEYO and the chronic treatment cost with FILSPARI is likely more than the cost of TARPEYO treatment over a 2-year period. The unmet needs addressed by FILSPARI is also addressed by TARPEYO.
2. The P&T Committee in May 2022 compared TARPEYO to similar agents in its drug class. FILSPARI is an endothelin receptor antagonist (ERA) and angiotensin II receptor blocker

(ARB). Notably, in the assessment of FILSPARI's relative clinical effectiveness and cost effectiveness, the Committee did not compare FILSPARI to various combination of similar ERA and ARB agents, including generics.

3. Both TARPEYO and FILSPARI were approved by the FDA under the Accelerated Approval pathway. The intent to treat (ITT) population was similar for the Phase 3 clinical trials that supported their respective accelerated approvals. The primary endpoints of the trials were the same – a reduction in urine protein creatinine ratio (UPCR) compared to baseline. In published, peer-reviewed study results, FILSPARI reported a maximal 41% relative reduction in UPCR from baseline, and TARPEYO reported a maximal 48% relative reduction in UPCR from baseline. However, only TARPEYO reported a beneficial treatment effect on kidney function (eGFR) at the end of treatment compared to baseline.[1,2] Patients treated with TARPEYO had a statistically significant and clinically relevant eGFR stabilization at the end of the 9-month treatment period.

   Moreover, in March this year, positive results were announced from TARPEYO's confirmatory trial, required for drugs approved under the Accelerated Approval pathway. The confirmatory results were first presented at an international scientific congress this month. Not only did TARPEYO treatment resulted in eGFR stabilization at the end of the 9-month treatment period, but a statistically significant and clinically relevant eGFR treatment benefit was maintained during the 15 months observational follow-up. The primary endpoint of time-weighted average change from baseline in eGFR over the 2-year period was 5.05 mL/min/1.73^2. This treatment benefit supports a disease-modifying effect not yet demonstrated by FILSPARI.[3] On June 21, Calliditas announced that it has submitted the confirmatory study results to the FDA in a supplemental New Drug Application seeking full approval of TARPEYO.

4. In the P&T Committee's recommendation for FILSPARI's Manual PA criteria, it is recognized that there is a Black Box warning and that patients must be enrolled in a REMS program. Patients who can become pregnant must have pregnancy tests prior to treatment with FILSPARI, monthly during treatment, and one month after treatment discontinuation. In comparison, "the 9-month treatment regimen of Nefecon was well tolerated, with low rates of AEs that were generally of mild or moderate severity and reversible. Glucocorticoid-related AEs were as expected for an oral budesonide treatment and without the serious side effects associated with systemic glucocorticoids, which can be long-lasting and life-altering."[2]

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[1] Heerspink HJL, et al.; PROTECT Investigators. Sparsentan in patients with IgA nephropathy: a prespecified interim analysis from a randomised, double-blind, active-controlled clinical trial. Lancet. 2023 May 13;401(10388):1584-1594..

[2] Barratt J, et al.; NefIgArd Trial Investigators. Results from part A of the multi-center, double-blind, randomized, placebo-controlled NefIgArd trial, which evaluated targeted-release formulation of budesonide for the treatment of primary immunoglobulin A nephropathy. Kidney Int. 2023 Feb;103(2):391-402.

[3] Richard L, et al.; Long-term renal benefit over 2 years with Nefecon verified: The NefIgArd Phase 3 full trial results. 60th ERA Congress, Milan & Virtual, June 15-18, 2023.

In summary, as the BAP members assess the recommendation of the P&T Committee to include FILSPARI on the Uniform Formulary with the proposed Manual PA criteria, I respectfully request your support, on both clinical and relative cost grounds, in having the BAP revisit the decision that excludes TARPEYO from the Uniform Formulary. TARPEYO is the only approved treatment option specifically for IgAN that has provided evidence obtained through a confirmatory clinical trial of a statistically significant and clinically relevant benefit on kidney function.

Respectfully submitted,

Christopher Agai
Vice President Market Access

Cc: Andrew B. Udell, President, Calliditas Therapeutics US Inc.
Jonathan A. Schur, Esq., Calliditas NA Enterprises Inc.