Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
January 5, 2017
Washington, D.C.

Present Panel Members

- Dr. Michael Anderson, United Healthcare, Chairperson
- Dr. Sandra S. Delgado, Humana
- Ms. Theresa Buchanan, National Family Military Association
- Mr. Jon Ostrowski, Non-Commissioned Officers Association
- Dr. Sarika Joshi, HeathNet Federal Services
- Dr. Richard Bertin, Commissioned Officers Association of the United States Public Health Service
- Dr. Kevin Sommer, U.S. Family Health Plan
- Mr. John Du Teil, United States Army Warrant Officers Association
- Ms. Lisa Le Gette, Express Scripts Inc.
- Ms. Suzanne Walker, Military Officers Association of America

The meeting was held at Naval Heritage Center Theater, 701 Pennsylvania Ave., N.W., Washington, D.C., and Alternate DFO William Blanche called the meeting to order at 9:00 A.M.

Agenda

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

- Welcome and Opening Remarks
- Public Citizen Comments
- Therapeutic Class Reviews
    - Designated Newly-Approved Drugs
        - Pulmonary IIs−Long-Acting Muscarinic Antagonists (LAMAs): tiotropium soft mist inhaler (Spiriva Respimat)
    - Drug Class Reviews
        - Oral Anticoagulants
        - Antilipidemics-1 (LIP-1s)−Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors

- Innovator Drugs

  - Antiemtics: aprepitant oral suspension (Emend)
  - Antigout Agents: lesinurad (Zurampic)
  - Antihemophilc Agents: von Willebrand factor (Voncvendi)
  - Antiplatelet Agents: aspirin/omeprazole (Yosprala)
  - Beta Blocker Combination Antihypertensive Agents: nebivolol/valsartan (Byvalson)
  - LAMA/Long-Acting Beta Agonists (LABA) combinations: glycopyrrolate/formoterol oral inhaler (Bevespi Aeroshere)
  - Miscellaneous Cardiovascular Agents: nitroglycerin sublingual powder (GoNitro)
  - Multiple Sclerosis Drugs: daclizumab (Zinbryta)
  - Opthalmic Anti-Inflammatory Immunomodulatory Agents: lifitegrast ophthalmic solution (Xiidra)
  - Opioid-Induced Constipation Drugs: methylnaltrexone tablets (Relistor)
  - Oral Contraceptives: norethindrone/ethinyl estradiol/iron (Taytulla)
  - Renin-Angiotensin Antihypertensive Agens (RAAs): Lisinopril oral solution (Qbrelis)
  - Topicl Otic Antibiotic/Steroid Combinations: ciprofloxacin/fluocinolone acetonide otic solution (Otovel)

- Utilization Management Issues

  - Prior Authorization Criteria

    - Basal Insulins: insulin degludec (Tresiba)
    - Analgesics and Combinations: butalbital/acetaminophen/caffeine tablets (Allzital)
    - Targeted Immunomodulatory Biologics (TIBs): adalimumab (Humira) and ustekinumab (Stelara)
    - Ophthalmic Anti-Inflammatory/Immunomodulatory Agents─Ophthalmic Immunomodulatory Agents: cyclosporine 0.05% ophthalmic emulsion (Restasis)
    - Oral Oncology Agents: crizotinib (Xalkori)

- Formulary Update

  - Non-Insulin Diabetes Drugs─DPP-4 Inhibitors: linagliptin/metformin XR (Jentadueto XR)

- National Defense Authorization Act 2008, Section 703 Actions

- Panel Discussions

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

Opening Remarks

Mr. William Blanche introduced himself as the Alternate Designated Federal Officer (DFO) for the Uniform Formulary (UF) Beneficiary Advisory Panel (BAP). The Panel convened to comment on the recommendations of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee meeting, which occurred on November 16-17, 2016.

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

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

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

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

- To review and comment on the recommendations of the P&T Committee concerning the establishment of the UF and subsequently recommending changes. Comments to the Director of the DHA regarding recommended formulary status, pre-authorizations and the effective dates for changing drugs from "formulary" to "non-formulary" status must be reviewed by the Director before making a final decision.

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

- To prepare minutes of the proceedings and prepare comments of the Secretary or his designee regarding the Uniform Formulary or changes to the Formulary. The minutes will be available on the website, and comments will be prepared for the Director of DHA. As guidance to the Panel regarding this meeting, Mr. William Blanche said the role of the BAP is to comment on the UF recommendations made by the P&T Committee at their last meeting. While the department appreciates that the BAP maybe interested in the drug classes selected for review, drugs recommended for the basic core formulary (BCF) or specific pricing data, these items do not fall under the purview of the BAP.

The P&T Committee met for approximately 14 ½ hours conducting this review of the drug class recommendation presented today. Since this meeting is considerably shorter, the Panel will not receive the same extensive information as presented to the P&T Committee members. However, the BAP will receive an abbreviated version of each presentation and its discussion. The materials provided to the Panel are available on the TRICARE website. Detailed minutes of this meeting are being prepared. The BAP minutes, the DoD P&T Committee minutes, and the Director's decisions will be available on the TRICARE website in approximately four to six weeks.

The DFO provided ground rules for conducting the meeting:

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

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

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

Mr. Blanche introduced the individual Panel members (see list above) and noted housekeeping considerations.

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

Chairman's Opening Remarks

Dr. Anderson welcomes the audience and the new members of the Panel. This is the largest BAP since he’s participated.

DRUG CLASS REVIEW PRESENTATION

(PEC Script – CAP VON BERG)

GOOD MORNING. I am CAPT Edward Von Berg, Chief of the Formulary Management Branch. Joining me is doctor and retired Army Colonel John Kugler, the Chairman of the Pharmacy & Therapeutics Committee, who will provide the physician perspective and comments on the recommendations made by the P&T Committee. Also joining us from the Formulary Management Branch today is Dr. Angela Allerman, a clinical pharmacist and Deputy Chief, P&T Section. I would also like to recognize Mr. Bryan Wheeler, Acting General Counsel, DHA, and CAPT Nita Sood from the P&T Pharmacy Operations Division.

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

We are here to present an overview of the analyses presented to the P&T Committee. 32 Code of Federal Regulations (CFR) establishes procedures for inclusion of pharmaceutical agents on the Uniform Formulary based upon both relative clinical effectiveness and relative cost effectiveness.

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

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

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

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

4. The Committee reviewed the following:

    a. One newly approved drug: the long-acting muscarinic antagonist tiotropium soft mist inhaler (Spiriva Respimat**)** for chronic obstructive pulmonary disease.

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

- the Oral Anticoagulants; and
- the Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors

  A summary table of the UF drug class recommendations is found on a page 27 of the background document. It also contains the numbers of the unique utilizers affected by the recommendations.

c. The P&T Committee also evaluated 13 Innovator Drugs, which are currently in pending status and available under terms comparable to non-formulary drugs.

d. We will also discuss Prior Authorizations (PAs) for drugs in **5** drug classes.
   - Basal Insulins
   - Analgesics and Combinations
   - Targeted Immunomodulatory Biologics
   - Ophthalmic Anti-Inflammatory/Immunomodulatory Agents and
   - Oral Oncology Agents

e. There was also one formulary update for an oral non-insulin diabetes drug.

4. Lastly, there were two drugs under Section 703, National Defense Authorization Act (NDAA) for Fiscal Year 2008 reviewed at this meeting: aspirin extended release 162.5 mg capsules (Durlaza), and amphetamine 2.5 mg/mL oral suspension (Dyanavel XR).

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

I. REVIEW OF RECENTLY APPROVED U.S. FOOD AND DRUG (FDA) AGENTS

A. PULMONARY IIs:

(CAPT VON BERG)

1. Long-Acting Muscarinic Antagonist (LAMA) Agents: Tiotropium Soft Mist Inhaler (Spiriva Respimat)─Relative Clinical Effectiveness and Conclusion

Spiriva Respimat contains tiotropium, the same active ingredient, as found in the Spiriva HandiHaler, but in a new soft mist inhaler device. Spiriva HandiHaler was launched in 2004 and added to the BCF in May 2013, while Spiriva Respimat entered the market in 2014. Both formulations are FDA-approved for maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD, which includes emphysema and chronic bronchitis), and for reducing COPD exacerbations. Spiriva Respimat is also approved for treating asthma in patients older than 12 years of age. Improvements in forced expiratory volume in one second (FEV1) (a measure of how forcefully a person can exhale) were similar between Spiriva Respimat and Spiriva HandiHaler. The safety profile is similar to the other LAMAs.

Spiriva HandiHaler was not associated with an increased risk of mortality in the placebo-controlled UPLIFT trial. However, initial concerns of increased mortality with Spiriva Respimat were raised in meta-analyses of placebo-controlled trials. These concerns were allayed in the prospective TIOSPIR clinical trial, where Spiriva Respimat was non-inferior to Spiriva HandiHaler with regard to overall mortality and cardiovascular mortality.

Relative Clinical Effectiveness Conclusion—The P&T Committee **concluded (15 for, 0 opposed, 0 abstained, 0 absent)** that Spiriva Respimat, as with Spiriva HandiHaler, has advantages over the other LAMAs in terms of the reductions in COPD exacerbations and once daily dosing. Patients with dexterity issues may find initial assembly of the Respimat device difficult.

2. LAMA Agents: Tiotropium Soft Mist Inhaler (Spiriva Respimat)─Relative Cost-Effectiveness Analysis and Conclusion

Cost minimization analysis (CMA) was performed. The P&T Committee concluded **(14 for, 0 opposed, 0 abstained, 1 absent)** the following rankings from most-to-least cost effective: tiotropium soft mist inhaler (Spiriva Respimat), tiotropium bromide inhalation powder (Spiriva HandiHaler), aclidinium (Tudorza Pressair), umeclidinium (Incruse Ellipta), and glycopyrrolate (Seebri Neohaler).

3. **LAMA Agents: Tiotropium Soft Mist Inhaler (Spiriva Respimat)—UF Recommendation**

   The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** tiotropium soft mist inhaler (Spiriva Respimat) be designated as formulary on the UF, based on clinical and cost effectiveness.

4. **LAMA Agents: Tiotropium Soft Mist Inhaler (Spiriva Respimat)—Implementation Plan**

   The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** the implementation become effective upon signing of the minutes.

5. **Physician's Perspective**

   - Since the May 2013 class review of the COPD drugs, there have been several new products that have entered the market. The various inhaler devices all have some advantages and disadvantages between them. For Spiriva Respimat, the new device is easier to use than the Spiriva Handihaler device, since there is no need to insert a capsule into the inhaler. However, the initial priming of the device may be difficult for some patients.

   - In the DoD, the Handihaler product has 89% of the market share with over 54,000 unique users, compared to 9,500 users of the Respimat product. For the new Respimat formulation, over 88% of the usage is for patients with COPD, compared to 12% usage for patients with asthma.

   - The Committee was reassured when the UPLIFT trial was reviewed that the original safety concerns with the Respimat device were not found in this prospective trial. Having Spiriva Respimat on the formulary provides another treatment option for patients with COPD.

6. **Panel Questions and Comments:**

   There were no questions from the Panel. The Chair called for the vote on the UF Recommendation and Implementation Plan for the LAMA Agents : Triotropium Soft Mist Inhaler (Spiriva Respimate)

   - **LAMA Agents: Triotropium Soft Mist Inhaler (Spiriva Respimate) ─UF Recommendation**

     Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **LAMA Agents: Triotropium Soft Mist Inhaler (Spiriva Respimate) ─Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

II. UNIFORM FORMULARY CLASS REVIEWS

A. ORAL ANTICOAGULANTS

(DR. ALLERMAN)

1. Oral Anticoagulants—Relative Clinical Effectiveness and Conclusion

Background—The P&T Committee previously reviewed the oral anticoagulants at the May 2015 DoD P&T Committee meeting. The class is comprised of the vitamin K antagonist warfarin (Coumadin, generic) and the newer direct-acting oral anticoagulants (DOACs). "DOACs" is now the preferred terminology for apixaban (Eliquis), dabigatran (Pradaxa), edoxaban (Savaysa) and rivaroxaban (Xarelto). The majority of DOAC usage in the Military Health System (MHS) is for stroke prevention in patients with non-valvular atrial fibrillation (NVAF), which is an irregular heart rhythm—the clinical review focused on this indication.\

Since the May 2015 review, dabigatran gained approval for the prophylaxis (or prevention) of venous thromboembolism (VTE) (which include blood clots in the legs or the lungs) following hip replacement surgery in November 2015. Additionally idarucizumab (Praxbind) is now available as a reversal agent for the direct thrombin inhibitor dabigatran. The reversal agent will prevent further action of the blood thinner, and decrease or stop bleeding episodes. However, Praxbind is not part of the TRICARE pharmacy benefit as it an IV infusion. A reversal agent for the factor Xa inhibitors (apixaban, edoxaban, rivaroxaban) is in the FDA drug approval pipeline.

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

- There are no head-to-head trials to determine if one DOAC is more efficacious or safe than another.

- With respect to NVAF, the following conclusions were made:

  - Dabigatran and apixaban were superior to not optimally controlled warfarin, while edoxaban and rivaroxaban were non-inferior at preventing stroke and systemic embolism.

  - Intracranial bleeding was lower with all four DOACs compared with warfarin in the major trials used to obtain FDA approval.

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

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

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

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

- In terms of clinical coverage, warfarin is required on the BCF due to its wide number of FDA indications and long history of use. For the DOACs, apixaban and rivaroxaban are the most appropriate candidates for preferred formulary status due to the number of FDA-approved indications, pharmacokinetic profile, dosing regimen, and Military Treatment Facility (MTF) provider opinions, compared with dabigatran and edoxaban.

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

CMA, cost-effectiveness analysis (CEA), and budget impact analysis (BIA) were performed. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 0 absent**) the following:

- CMA and CEA results found that generic warfarin was the most cost-effective oral anticoagulant, followed by the apixaban, dabigatran, rivaroxaban, and edoxaban, in order from most cost effective to least cost effective.

- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results found that designating warfarin, apixaban, rivaroxaban, and dabigatran as formulary on the UF, with edoxaban designated as NF, demonstrated the largest estimated cost avoidance for the MHS.

3. **Oral Anticoagulants—UF Recommendation**

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

- **UF:**
  - Warfarin (Coumadin; generic)
  - Apixaban (Eliquis)
  - Dabigatran (Pradaxa)
  - Rivaroxaban (Xarelto)
- **NF:** Edoxaban (Savaysa)

4. **Oral Anticoagulants—Implementation Plan**

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

5. **Physician's Perspective**

- We have been reviewing the oral anticoagulants yearly since 2013. There were several reasons for reviewing the class again – there is an overall trend for declining warfarin use in DoD; the newer direct acting agents have now had enough time on the market to see if there are prescriber preferences for one newer product over another; the newer products have gained additional FDA indications; and to determine if the availability of a reversal agent would influence what newer products should be on the Formulary.

- We did talk with the Cardiology consultants – they recommended apixaban most often as being the preferred direct acting agent, however rivaroxaban was also mentioned due to the once daily dosing. Dabigatran is usually reserved for younger patients, due to bleeding risk. But dabigatran is the only product that has a reversal agent, and it was the first direct acting agent to gain FDA approval. Edoxaban was not endorsed by the cardiologists.

- Overall, the recommendation was unanimous for warfarin, apixaban, dabigatran and rivaroxaban to be on the Uniform Formulary. For edoxaban, non-formulary status was recommended; currently there are only 750 patients on it, compared to the over 200,000 patients on one of the other oral anticoagulants.

6. **Panel Questions and Comments**

Dr. Anderson asked if there is a step-therapy program to require trial/failure of warfarin before using a newer anticoagulant.

Dr. Allerman replied that they did not recommend step therapy and the prescriber is free to use whatever is appropriate for the patient.

There were no more question or comments from the Panel. The Chair called for a vote on the UF Recommendation and Implementaion for the Oral Anticoagulants.

- **Oral Anticoagulants─UF Recommendation**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Oral Anticoagulants─Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

B. ANTILIPIDEMICS-1s (LIP-1s)

(DR. ALLERMAN)

1. **LIP-1s: Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitor Subclass—Relative Clinical Effectiveness and Conclusion**

Background—The P&T Committee evaluated the PCSK9 inhibitors. Alirocumab (Praluent) and evolocumab (Repatha) are a new class of biologic drugs that reduce low-density lipoprotein (LDL) (or "bad") cholesterol. They are injectable monoclonal antibodies requiring biweekly or monthly administration. Prior authorization criteria and quantity limits were recommended for the PCSK9 inhibitors in November 2015, due to the lack of data on cardiovascular (CV) morbidity and mortality, unknown long-term safety profile, and high cost. Evolocumab was reviewed as an innovator drug and is currently NF.

Both products are indicated as an adjunct to diet and maximally-tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) (which is a genetic condition where patients have extremely high cholesterol levers) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of LDL cholesterol. Evolocumab has an additional indication for treatment of homozygous familial hypercholesterolemia (HoFH) in patients 13 years and older. All of these conditions increase the risk of heart attacks and strokes.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 0 absent)** the following for the PCSK9 Inhibitor Subclass:

- Dyslipidemia (or high cholesterol) treatment guidelines have been in flux, with an overall shift from LDL lowering targets to a focus on addressing risk reduction. However, clinical practice guidelines from several professional organizations consistently support the use of statins to reduce cardiovascular risk.

- The PCSK9 inhibitors significantly reduce LDL by 50% to 60% when added on to maximum tolerated statin therapy (drugs such as Zocor, Lipitor, or Crestor) in patients with HeFH or ASCVD.

- At this time, there are no direct head-to-head trials between alirocumab and evolocumab. Meta-analyses suggest that both drugs effectively lower LDL whether used as monotherapy, when compared to ezetimibe (Zetia – which is a drug that has a different mechanism of action than the statins), or when used as add-on therapy to standard care.

- CV outcomes trials are still pending to determine whether the LDL-lowering benefit of the PCSK9 inhibitor agents will produce significant improvements in mortality beyond that established with statins. The results of outcome trials are anticipated in 2017 to 2018.

- Both agents appear safe and well-tolerated during the short-term periods when they have been studied. The most commonly reported adverse events include injection site and hypersensitivity reactions. Long-term safety concerns have yet to be resolved, including neurocognitive effects and immunogenicity risk.

- The PCSK9 inhibitors are highly therapeutically interchangeable. There is extremely limited data to support switching between evolocumab and alirocumab once an initial product has been selected.

- The most appropriate place in therapy for the PCSK9 inhibitors is in high-risk patients with ASCVD, HeFH, or HoFH who require additional CV risk reduction through LDL- lowering despite maximally-tolerated statin and lipid-lowering therapy, including ezetimibe.

- Provider input solicited from cardiologists and endocrinologists slightly favored evolocumab. Of note, there was limited clinical experience of these products with most providers.

- For clinical coverage, at least one PCSK9 inhibitor is required on the UF to serve the needs of the majority of MHS patients who would most likely benefit from these products.

2. LIP-1s: PCSK9 Inhibitor Subclass—Relative Cost-Effectiveness Analysis and Conclusion

CMA and BIA were performed. The P&T Committee concluded **(15 for, 0 opposed, 0 abstained, 0 absent)** the following:

- CMA results showed alirocumab (Praluent) and evolocumab (Repatha) had comparable cost effectiveness.

- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. All modeled scenarios show cost avoidance against current MHS expenditures. BIA results showed that designating evolocumab as formulary and step-preferred, with alirocumab as formulary and non-step-preferred, demonstrated a cost-effective option for the MHS.

3. LIP-1s: PCSK9 Inhibitor Subclass—UF Recommendation

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

- UF and step-preferred: evolocumab (Repatha)

- UF and non-step-preferred: alirocumab (Praluent)

Note that as part of this recommendation, all new users of alirocumab are required to try evolocumab first.

4. LIP-1s: PCSK9 Inhibitor Subclass—Manual Prior Authorization (PA) Criteria

Manual PA criteria for both PCSK9 inhibitors were recommended at the August 2015 P&T Committee meeting and implemented on October 30, 2015. The P&T Committee recommended **(15 for 0 opposed, 0 abstained, 0 absent)** maintaining the current manual PA criteria for alirocumab and evolocumab. The renewal PA criteria were updated to include prescriptions written by a primary care provider in consultation with a specialist who initially prescribed the agent. The step therapy requirement for a trial of evolocumab prior to use of alirocumab in new users is included in the manual PA criteria.

<u>Full PA Criteria</u>

a. PCSK9 Inhibitor: Alirocumab (Praluent)

Changes from November 2016 meeting are in BOLD.

All new users of alirocumab (Praluent) are required to try evolocumab (Repatha) first.

Manual PA Criteria—Alirocumab is approved if:

- A cardiologist, lipidologist, or endocrinologist initially prescribes the drug.

- The patient is at least 18 years of age.

- The patient has heterozygous familial hypercholesterolemia (HeFH) and is on concurrent statin therapy at maximally-tolerated doses.

- 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 must have tried both atorvastatin (Lipitor) 40-80 mg and rosuvastatin (Crestor) 20-40 mg, OR

  - The patient must have tried any maximally-tolerated statin in combination with ezetimibe (Zetia), 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 (Tricor), niacin, or bile acid sequestrants [Questran]), 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. (These are signs of severe muscle breakdown leading to kidney damage, which a rare side effect of the statins.)

  - Contraindication to statin

    - The contraindication must be defined.

- Praluent is not approved for any indication other than HeFH or clinical ASCVD.

- 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 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, or lipidologist. Continued use of Praluent 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.

b. PCSK9 Inhibitor: Evolocumab (Repatha)

Changes from November 2016 meeting are in BOLD.

Manual PA criteria apply to all new users of evolocumab (Repatha).

Manual PA Criteria—Evolocumab is approved if:

- A cardiologist, lipidologist, or endocrinologist initially prescribes the drug.
- The patient is at least 18 years of age for HeFH and clinical ASCVD. For HoFH, patients as young as 13 years of age can receive the drug.
- 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.
- 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 must have tried both atorvastatin 40-80 mg 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.
- 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 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, OR 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.

5. **LIP-1s: PCSK9 Inhibitor Subclass—UF and PA Implementation Plan**

The P&T Committee recommended **(15 for, 0 opposed, 0 abstained, 0 absent)** an effective date of the first Wednesday after a 60-day implementation period.

6. **Physician's Perspective**

- This is the first drug class review for these products, although PA criteria have been in place for over a year. Existing utilization is approximately 50-50 for Praluent vs. Repatha; and clinically the two products are very similar. Even though Repatha was previously made non formulary as an innovator drug, the equal market share does show that some providers are preferring Repatha over Praluent.

- When the cardiologists were surveyed, they expressed a slight preference for Repatha, which supports a switch from non-formulary to uniform formulary status. These provider preferences and market share support having Repatha back on the formulary, and making it step-preferred. The patients currently on Praluent will be able to remain on therapy, and it will still be on the formulary.

- We are just now coming up to the one year expiration date for the patients originally placed on these drugs. We will be reviewing how many patients submit the paperwork for the renewal PA. We also recognize that a cardiologist will start therapy, but will now allow a non-cardiologist to continue therapy, after consulting with the specialist.

- Once the outcomes studies are published, we will also look at the studies and decide if another class review is warranted.

7. **Panel Questions and Comments**

Ms. Le Gette stated these drugs currently have manual prior authorization criteria. Will that stay in place, or will it be an automated step therapy?

Dr. Allerman replied that it will be a manual prior authorization for Praluent. The requirement is to try Repatha first. The patients currently on Praluent will be grandfathered. It will not be an automated prior authorization.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, and UF and PA Implementation Plan for LIP-1s : PCSK9 Inhibitoy Subclass.

- **LIP-1s: PCSK9 Inhibitor Subclass─UF Recommendation**

Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **LIP-1s: PCSK9 Inhibitor Subclass─Manual PA Criteria**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **LIP-1s : PCSK9 Inhibitor Subclass─UF and PA Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

III. UF CLASS REVIEWS

A. INNOVATOR DRUGS

(CAPT VON BERG)

1. Innovator Drugs—Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions

The P&T Committee agreed **(14 for, 0 opposed, 0 abstained, 1 absent)** with the relative clinical and cost-effectiveness analyses presented for the innovator drugs.

2. Innovator Drugs—UF Recommendation

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

- UF:
  - Antiemetics: aprepitant oral suspension (Emend)
  - Antihemophilic Factors: von Willebrand factor (Vonvendi)
  - Ophthalmic Anti-Inflammatory Immunomodulatory Agents: lifitegrast ophthalmic solution (Xiidra)
  - Topical Otic Antibiotic/Steroid Combinations: ciprofloxacin/fluocinolone acetonide otic solution (Otovel)
- NF:
  - Antigout Agents: lesinurad (Zurampic)
  - Antiplatelet Agents: aspirin/omeprazole (Yosprala)
  - Beta Blocker Combination Antihypertensive Agents: nebivolol/valsartan (Byvalson)

- LAMA/Long-Acting Beta Agonists (LABA) combinations: glycopyrrolate/formoterol oral inhaler (Bevespi Aerosphere)
- Miscellaneous Cardiovascular Agents: nitroglycerin sublingual (SL) powder (GoNitro)
- Multiple Sclerosis Drugs: daclizumab (Zinbryta)
- Opioid-Induced Constipation Drugs: methylnaltrexone tablets (Relistor)
- Oral Contraceptives: norethindrone/ethinyl estradiol/iron (Taytulla)
- Renin-Angiotensin Antihypertensive Agents (RAAs): lisinopril oral solution (Qbrelis)

3. Innovator Drugs—Manual PA Criteria

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** manual PA criteria for new users of Xiidra and Zinbryta, and for new and current users of Zurampic.

Full PA Criteria:

a. Innovator Drugs—Ophthalmic Anti-Inflammatory Immunomodulatory Agents: Lifitegrast Ophthalmic Solution (Xiidra)

Manual PA criteria apply to all new users of lifitegrast ophthalmic solution.
Manual PA Criteria

Coverage will be approved if:

1. Age ≥ 18 AND
2. Has documented diagnosis of moderate to severe inflammatory Dry Eye Disease AND
3. Drug is prescribed by an ophthalmologist or optometrist AND
4. Patient has failed to respond to an adequate trial of artificial tears.

Combination use of Xiidra and Restasis not allowed.

Off-label uses are NOT approved.

Prior Authorization does not expire.

b. Innovator Drugs—Multiple Sclerosis Drugs: Daclizumab (Zinbryta)

Manual PA criteria apply to all new users of daclizumab.

Manual PA Criteria

Coverage will be approved if:

1. Age ≥ 18 AND
2. Has documented diagnosis of relapsing multiple sclerosis AND
3. Has tried and had an inadequate response to two or more multiple sclerosis drugs.

Off-label uses are NOT approved.

Prior Authorization does not expire.

c. Innovator Drugs—Antigout Agents: Lesinurad (Zurampic)

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

Manual PA Criteria

Coverage will be approved if:

1. Age ≥ 18
2. The patient has chronic or tophaceous gout (where uric acid crystals form deposits around the joints)
3. The patient has a creatine clearance (CrCl) >45 mL/min (normal kidney function)
4. The gout patient has not achieved target serum uric acid level despite maximally-tolerated therapy with a xanthine oxidase inhibitor (drugs such as allopurinol).

Off-label uses are not approved.

Prior Authorization does not expire.

4. **Innovator Drugs—UF and PA Implementation Plan**

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** an effective date upon signing of the minutes in all points of service.

5. **Physician's Perspective**

- For the innovator drugs recommended as non-formulary, clinically and cost effective alternative therapies are available on the formulary.

- Some of the new innovator drugs we have reviewed have prompted a full drug class review – as you saw with the PCSK9 inhibitors from this meeting. We will also re-review the Hepatitis C drugs at the February 2017 P&T Committee meeting, since there have been several new products approved in the past year.

- PA criteria were recommended for the dry eye drug (Xiidra), since there is already a PA for another drug in the class, Restasis. PAs criteria were recommended for the gout drug Zurampic, since we have existing step therapy for the xanthine oxidase inhibitor drugs allopurinol and Uloric. (Zurampic will not be part of the step). A PA was also recommended for the MS drug Zinbryta due to the specific indication and risk of adverse events.

- We will be looking at some metrics for the innovator program at the upcoming February 2017 meeting to see how many different drug classes have been reviewed, and how many products have been designated as non-formulary vs. formulary.

6. **Panel Questions and Comments**

There were no questions from the Panel. The Chair called for the vote on the UF Recommendation, Manual PA Criteria, and UF and PA Implementation Plan for the Innovator Drugs.

- **Innovator Drugs—UF Recommendations**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Innovator Drugs—Manual PA Criteria**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Innovator Drugs—UF and PA Implementation**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

IV. UTILIZATION MANAGEMENT

A. BASAL INSULINS

(CAPT VONBERG)

1. Basal Insulins: Insulin Degludec (Tresiba)—Manual PA Criteria

Tresiba is a new basal insulin indicated for glycemic, or blood sugar, control in adults with diabetes mellitus. Tresiba was reviewed in February 2016 as an innovator product and designated NF.

The P&T Committee recommended (**14 for, 0 opposed, 0 abstained, 1 absent**) manual PA criteria for Tresiba in new and current users. Despite its ultra-long duration of action and steady-state profile, Tresiba offers no clinically compelling advantages over existing basal insulins used to treat Type I or Type II diabetes (such as Lantus or Levimir). Patients will be required to try insulin glargine before using Tresiba.

Full PA Criteria:

Basal Insulins: Insulin Degludec (Tresiba)

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

Manual PA Criteria

Tresiba is approved if:

a. Patient is age ≥ 18 AND

b. Patient has tried and failed or is intolerant to insulin glargine (Lantus).

Non-FDA approved uses are not approved.

Prior Authorization does not expire.

Basal Insulins: Insulin Degludec (Tresiba)—PA Implementation Period

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent**) an effective date of the first Wednesday after a 90-day implementation period in all points of service.

2. **Physician's Perspective**

- The Committee did recommend "no grandfathering" here, so all patients will have to go through the PA process, which will affect about 3,000 patients. Lantus and Levemir are clinical alternatives that are both on the formulary. The Committee will be reviewing the basal insulins later in 2017.

3. **Panel Questions and Comments**

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

- **Basal Insulins : Insulin Degludec (Tresiba)─Manual PA Criteria**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Basal Insulins : Insulin Degludec (Tresiba)─PA Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

B. ANGALGESICS AND COMBINATIONS

(CAPT VON BERG)

1. **Analgesics and Combinations: Butalbital/Acetaminophen (APAP) Tablets (Allzital)—Manual PA Criteria**

Allzital is an oral tablet formulation containing butalbital and acetaminophen that is approved for tension or muscle headaches.

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent**) manual PA criteria for Allzital in new and current users, due to cost disadvantages compared to generic butalbital/APAP combinations.

Full PA Criteria:

Analgesics and Combinations: Butalbital/APAP Tablets (Allzital)

All new and current users of butalbital/APAP are required to undergo manual prior authorization.

Manual PA Criteria

Coverage will be approved if:

- Patient cannot tolerate generic oral tablet or capsule formulations of butalbital/APAP or butalbital/APAP/caffeine.
- Off-label uses are not approved.
- PA does not expire.

2. Analgesics and Combinations: Butalbital/APAP Tablets (Allzital)—PA Implementation Plan

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** an effective date of the first Wednesday after a 90-day implementation period in all points of service.

3. Physician's Perspective

- This is the second bultalbital-containing product we have recommended a PA for. This product is another expensive formulation. Several cost effective generic formulations are available, and must be tried first, prior to Allzital.

4. Panel Questions and Comment

There were no questions or comments from the Panel. The Chair called for the vote on the Manual PA Criteria and PA Implementation Plan for the Analgesics and Combination: Butalbital/APAP Tablets (ALZITAL).

- **Analgesics and Combinations: Butalbital/APAP Tablets (Allzital)─Manual PA Criteria**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Analgesics and Combinations: Butalbital/APAP Tablets (Allzital)─PA Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

C. TARGETED IMMUNOMODULATORY BIOLOGIC (TIBs) (DR. ALLERMAN)

1. TIBs: Adalimumab (Humira) and Ustekinumab (Stelara)—Manual PA Criteria

The TIBs were reviewed by the P&T Committee in August 2014 and automated PA (step therapy) and manual PA criteria were recommended for the class. Adalimumab (Humira) was selected as the UF step-preferred agent. In June 2016, adalimumab (Humira) received FDA approval for treatment of non-infectious intermediate, posterior and panuveitis in adult patients. (This is an inflammation of the pigmented areas of the eye which can lead to blindness). The PA criteria were updated for Humira to reflect its new FDA indication. Clinical data supporting several off-label uses for Humira were reviewed; these will be considered for coverage.

Ustekinumab (Stelara) is UF and non-step-preferred; it is currently approved for rheumatoid arthritis and plaque psoriasis. In September 2016, Stelara received FDA approval for the treatment of adult patients with moderate to severely active Crohn's disease who have failed or were intolerant to treatment with immunomodulators, corticosteroids, or tumor necrosis factor (TNF) blockers. (Crohn's disease is a type of inflammatory bowel disease). The existing manual PA criteria were updated to include these new indications.

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** updating the manual PA criteria for Humira and Stelara to include their respective new indications.

<u>Full PA Criteria</u>

Targeted Immunomodulatory Biologics: Adalimumab (Humira)

Prior Authorization criteria was originally approved in August 2014 and implemented on February 18, 2015. **November 2016 changes to PA criteria are in BOLD.**

Manual PA criteria for non-infectious intermediate, posterior and panuveitis in adults apply to new patients.

- **Non-infectious intermediate, posterior and panuveitis in adults patients (November 2016)**

Coverage approved for patients ≥ 18 years with:

- Moderate to severe active rheumatoid arthritis, active psoriatic arthritis, or active ankylosing spondylitis

- Moderate to severe chronic plaque psoriasis who are candidates for systemic or phototherapy, and when other systemic therapies are medically less appropriate

- Moderate to severely active Crohn's disease following an inadequate response to conventional therapy, loss of response to Remicade, or an inability to tolerate Remicade

- Moderate to severely active ulcerative colitis following inadequate response to immunosuppressants

- Moderate to severe hidradenitis suppurativa (November 2015)

- **Non-infectious intermediate, posterior and panuveitis in adults patients (November 2016)**

Coverage approved for pediatric patients (age 4-17 years) with:

- Moderate to severe active polyarticular juvenile idiopathic arthritis

- Moderate to severely active Crohn's disease (≥ 6 years) who have had an inadequate response to corticosteroids, azathioprine, 6-mercaptopurine, or methotrexate.

Coverage for off-label uses not listed above. Please provide diagnosis and rationale for treatment. Supportive evidence will be considered.

PA does not expire.

Coverage is NOT provided for concomitant use with other TIBs including, but not limited to, adalimumab (Humira), anakinra (Kineret), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), abatacept (Orencia), tocilizumab (Actemra), tofacitinib (Xeljanz), ustekinumab (Stelara), apremilast (Otezla), or rituximab (Rituxan).

2. Targeted Immunomodulatory Biologics: Ustekinumab (Stelara)

November 2016 changes to PA criteria in bold.

Manual PA criteria for moderate to severe active Crohn's disease in adults applies to new patients.

<u>Automated PA Criteria</u>

The patient has filled a prescription for adalimumab (Humira) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA Criteria

If automated criteria are not met, coverage is approved for Stelara if:

- Contraindications exist to Humira
- Inadequate response to Humira (need for different anti-TNF or non-TNF)
- There is no formulary alternative: patient requires a non-TNF TIB for symptomatic CHF
- Adverse reactions to Humira not expected with requested non step-preferred TIB

AND

Coverage approved for patients ≥ 18 years with:

- Active psoriatic arthritis
- Moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy
- **Moderate to severe active Crohn's disease who have failed or intolerant to immunomodulators, corticosteroids, or TNF blockers. (November 2016)**

PA does not expire.

Non-FDA approved uses are not approved.

Coverage is NOT provided for concomitant use with other TIBs including, but not limited to, adalimumab (Humira), anakinra (Kineret), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), abatacept (Orencia), tocilizumab (Actemra), tofacitinib (Xeljanz), ustekinumab (Stelara), apremilast (Otezla), or rituximab (Rituxan).

3. TIBs: Adalimumab (Humira) and Ustekinumab (Stelara)—PA Implementation Plan

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** the implementation become effective upon signing of the minutes.

4. Physician's Perspective

- Once again, we are updating the PAs for this drug class to be consistent with either new FDA approved indications or for off-label use where there is supporting literature. For Humira, there is supporting literature for ocular inflammatory disorders, including scleritis and Behcet'sdisease; pyoderma

gangrenosum, and sarcoidosis. If a provider sends in supporting literature for the TIBs, this can be considered for the PA.

5. **Panel Questions and Comments**

There were no questions or comments from the Panel. The Chair called for the vote on the Manual PA Criteria and PA Implementation Plan for the TIBs: Adalimumab (Humira) and Ustekinumab (Stelara).

- **TIBs: Adalimumab (Humira) and Ustekinumab (Stelara)─Manual PA Criteria**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **TIBs: Adalimumab (Humira) and Ustekinumab (Stelara)─PA Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

D. OPHTHALMIC ANTI-INFLAMMATORY/IMMUNOMODULATORY AGENTS: OPHTHALMIC IMMUNOMODULATORY AGENTS SUBCLASS

(DR. ALLERMAN)

1. **Ophthalmic Anti-Inflammatory/Immunomodulatory Agents: Ophthalmic Immunomodulatory Agents Subclass: Cyclosporine 0.05% Ophthalmic Emulsion (Restasis)—Updated Manual PA Criteria**

Restasis was reviewed in February 2016, with manual PA criteria recommended. Based on feedback from MTF providers and supporting literature, updates were made to the criteria to include treatment of atopic keratoconjunctivitis and vernal keratoconjunctivitis in pediatric patients (these are severe forms of allergies affecting the eyes, involving the corneas and eyelids) and in adults following LASIK surgery.

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** updating the Restasis manual PA criteria.

Full PA Criteria:

November 2016 updates are in BOLD.

Manual PA criteria apply to all new and current users of cyclosporine 0.05% ophthalmic emulsion.

PA criteria apply to all new users of Restasis.

- Current User is defined as a patient who has had Restasis dispensed during the previous 365 days at a Military Treatment Facility (MTF), a retail network pharmacy, or the Mail Order Pharmacy.
    - If there is a Restasis prescription in the past 365 days (automated lookback with Restasis as the qualifying drug), the claim goes through and no manual PA is required.
- New User is defined as a patient who has no had Restasis dispensed in the past 365 days.
    - If there is no Restasis prescription in the past 365 days, a manual PA is required.

<u>Manual PA Criteria:</u>

- Coverage is approved if one of the following is fulfilled:
    - Patient has diagnosis of keratoconjunctivitis sicca (KCS), **dry eye disease or dry eye syndrome** with lack of therapeutic response to at least 2 OTC artificial tears agents
    - Patient has ocular graft versus host disease
    - Patient has corneal transplant rejection
    - Patient has experienced documented corneal surface damage while using frequent artificial tears
    - **Restasis is prescribed by an ophthalmology/corneal specialist for a pediatric patient with a diagnosis of atopic keratoconjunctivitis (AKC) or vernal keratoconjunctivitis (VKC)**
    - **Patient has had LASIK surgery not more than 3 months previously. Note that therapy is limited to a maximum of 3 months of therapy after the procedure.**
- **The combination of Xiidra and Restasis is not allowed.**
- **For all indications, the patient must have had a trial of artificial tears.**
- Coverage is not approved for off-label uses such as, but not limited to:
    - Pterygia, which is growth of pink, fleshy tissue on the white part of the eye, and is common in people who spend a lot of time outdoors or have long periods of exposure to sunlight.
    - Blepharitis, which is chronic inflammation of the eyelids.

- Ocular rosacea, where patients with rosacea develop eye symptoms, including a watery or bloodshot appearance, as well as irritation and burning or stinging of the eyes.

- Contact lens intolerance

Prior Authorization expires in one year.

- If there is a break in therapy, the patient will be subject to the PA again.

2. Ophthalmic Anti-Inflammatory/Immunomodulatory Agents: Ophthalmic Immunomodulatory Agents Subclass: Cyclosporine 0.05% Ophthalmic Emulsion (Restasis)—PA Implementation Plan

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** the implementation become effective upon signing of the minutes.

3. Physician's Perspective

The Restasis PA was updated based on some feedback from providers to expand the allowable off-label uses. Once again, there is supporting evidence for these conditions, or else there are no therapeutic alternatives, in the case of the pediatric population

4. Panel Questions and Comments

Mr. Du Teil asked if there is a specific reason why it is limited to 3 months for use with LASIK surgery patients.

Dr. Allerman replied that was based on supporting literature. The LASIK is an off-label use; however, there are some data that suggests that it is appropriate for use at least 3 months afterwards. We didn't want to have that continued forever because the benefits decrease.

There were no more questions from the Panel. The Chair called for the vote on the Updated Manual PA Criteria and PA Implementation Plan for the Ophthalmic Anti-Inflammatory/Immunomodulatory Agents: Ophthalmic Immunomodulatory Agents Subclass: Cyclosporine 0.05% Ophthalmic Emulsion (Restasis)

- **OphthalmicAnti-Inflammatory/Immunomodulatory Agents: Ophthalmic Immunomodulatory Agents Subclass: Cyclosporine 0.05% Ophthalmic Emulsion (Restasis)—Updated Manual PA Criteria**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **OphthalmicAnti-Inflammatory/Immunomodulatory Agents: Ophthalmic Immunomodulatory Agents Subclass: Cyclosporine 0.05% Ophthalmic Emulsion (Restasis)—PA Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

E. ORAL ONCOLOGY AGENTS

(DR. ALLERMAN)

1. Oral Oncology Agents: Crizotinib (Xalkori)—Updated Manual PA Criteria

Xalkori is an oral oncologic agent used for the treatment of non-small cell lung cancer (NSCLC). Xalkori inhibits tyrosine kinases including anaplastic lymphoma kinase (ALK) and c-ros oncogene 1 (ROS). (This is a very specific target for the drug, which required a genetic test). Manual PA criteria have been in place since February 2012. The criteria were updated to add additional indications.

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** updating the manual PA criteria.

<u>Full PA Criteria</u>

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

Manual PA Criteria—Xalkori is approved if:

a. Patient has a documented diagnosis of ALK-positive NSCLC

OR

b. Patient has a documented diagnosis of ROS-1 positive NSCLC (November 2016)

PA does not expire.

Non-FDA approved uses are not approved.

2. Oral Oncology Agents: Crizotinib (Xalkori)—PA Implementation Plan

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent)** the implementation become effective upon signing of the minutes.

3. Physician's Perspective

- This is another example of keeping up with expanded FDA approved indications for the oral oncology drugs.

4. Panel Questions and Comments

There were no questions from the Panel. The Chair called for the vote on the Oral Oncology Agents: Crizotinib (Xalkori).

- **Oral Oncology Agents: Crizotinib (Xalkori)—Updated Manual PA Criteria**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Oral Oncology Agents: Crizotinib (Xalkori)—PA Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

IV. FORMULARY STATUS UPDATE—NON-INSULIN DIABETES DRUGS (CAPT VONBERG)

A. Dipeptidyl Peptidase-4 (DPP-4) Inhibitors: Linagliptin/Metformin ER (Jentadueto XR)—Formulary Status Update

Linagliptin/metformin ER (Jentadueto XR) was reviewed as an innovator drug in August 2016 and designated NF and non-step preferred. Linagliptin/metformin IR (Jentadueto) is UF and non-step-preferred. Price parity now exists between Jentadueto and Jentadueto XR.

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 1 absent) designating Jentadueto XR as UF and non-step-preferred, with implementation upon signing of the minutes.

1. Physician's Perspective

- Jentadueto XR has the same ingredients as Jentadueto, with the exception that the metformin component has extended release properties. This is an innovator drug where we have already reviewed the class, and since the cost effectiveness of Jentadueto XR was similar to the formulary product Jentadueto, the XR product was placed back on the formulary.

2. Panel Questions and Comments

There were no questions from the Panel. The Chair called for the vote Formulary Status Update and the Implementation Plan for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors: Linagliptin/Metformin ER (Jentadueto XR)

- **Dipeptidyl Peptidase-4 (DPP-4) Inhibitors: Linagliptin/Metformin ER (Jentadueto XR)—Formulary Status Update**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Dipeptidyl Peptidase-4 (DPP-4) Inhibitors: Linagliptin/Metformin ER (Jentadueto XR)—Implementation**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

V. SECTION 703, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR 2008 (FY08) (CAPT VONBERG)

A. Section 703, NDAA FY08—Drugs Designated NF

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

The P&T Committee recommended (**14 for, 0 opposed, 0 abstained, 1 absent**) the following products be designated NF on the UF:

- New Haven Pharma: aspirin ER (Durlaza) 162.5 mg oral capsules
- Tris Pharma: amphetamine (Dyanavel XR) 2.5mg/mL oral suspension

Note that both Durlaza and Dyanavel XR were previously recommended for NF placement as innovator drugs at the February 2016 P&T Committee meeting. The Director, DHA, approved the recommendation and implementation became effective in all points of service on May 5, 2016.

1. Section 703, NDAA FY08—Pre-Authorization Criteria

The P&T Committee recommended **(14 for, 0 opposed, 0 abstained, 1 absent**) the following pre-authorization criteria for Durlaza and Dyanavel XR:

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

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

c. These pre-authorization criteria do not apply to any other point of service other than retail network pharmacies.

Dyanavel XR is a Schedule II controlled substance, but is not typically used as first line therapy for attention deficit hyperactivity disorder, or used for acute therapy. If the home delivery requirement for Dyanavel XR impacts availability through the Mail Order Pharmacy, the P&T Committee will allow an exception to the Section 703 rule, and allow dispensing at the Retail Pharmacy Network.

2. Section 703, NDAA FY08—Implementation Plan

The P&T Committee recommended (**14 for, 0 opposed, 0 abstained, 1 absent)** 1) an effective date of the first Wednesday after a 90-day implementation period for Durlaza and Dyanavel XR; and, 2) DHA send letters to beneficiaries affected by this decision.

3. Physician's Perspective

For both products we recommended for NF status because there are cost-effective generic formulations or therapeutic alternatives available on the UF. The Pharmacy Operations Division does follow up with the affected manufacturers, to try to ensure compliance with the Section 703 requirements.

4. Panel Questions and Comments

There were no questions from the Panel. The Chair called for the vote the Section 703, NDAA FY 08 Drugs Designated NF, Pre-Authorization Criteria, and Implementation Plan.

- **Section 703, NDAA FY08—Drugs Designated NF**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Section 703, NDAA FY08—Pre-Authorization Criteria**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

- **Section 703, NDAA FY08—Implementation Plan**

  Concur : 10 Non-Concur : 0 Abstain : 0 Absent : 0

Dr. Anderson thanked the DHA staff and P&T committee and thanks the new BAP members.

DFO Blanche thanks the BAP and audience. Meeting concludes at 10:20 a.m.

Dr. Michael Anderson, Chair UF BAP

Brief Listing of Acronyms Used in this Summary

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

- AB-Rated – Generic Drugs
- AKC – Atopic Kertoconjunctivitis
- ALK – Anaplastic Lymphoma Kinase
- APAP – Butalbital/Acetaminophen
- ASCVD – Atherosclerotic Cardiovascular Disease
- BAP – Beneficiary Advisory Panel
- BCF – Basic Core Formula
- BIA – Budget Impact Analysis
- CEA – Cost-Effectiveness Analysis
- CFR – Code of Federal Regulations
- CHF – Congestive Heart Failure
- CK – Creatine Kinase
- CMA – Cost Minimization Analysis
- COPD – Chronic Obstructive Pulmonary Disease
- CrCL – Creatine Clearance
- CV – Cardiovascular
- DFO – Designated Federal Office
- DHA – Defense Health Agency
- dL – Deciliter
- DOAC – Direct Oral Anticoagulant
- DoD – Department of Defense
- DPP-4 – Non-Insulin Diabetes Drugs
- FACA – Federal Advisory Committee Act
- FDA – Food & Drug Administration
- FEV1 – Forced Expiratory Volume in One Second
- GI – Gastrointestinal
- HeFH - Heterozygous Familial Hypercholesterolemia
- HoFH - Homozygous Familial Hypercholesterolemia
- KCS - Keratoconjunctivitis Sicca
- LABA - Long Acting Beta Agonists
- LAMA – Long-Acting Muscarinic Antagonist
- LASIK - Laser-Assisted in Situ Keratomileusis
- LDL – Low-Density Lipoprotein

- LIP-1S - Antilipidemics-1
- MHS – Military Health Service
- mL – Milliliter
- MTF – Military Treatment Facility
- NDAA – National Defense Authorization Act
- NF – Non-Formulary
- NSCLC – Non-Small Cell Lung Cancer
- NVAF – Non-Valvular Atrial Fibrillation
- P&T – Pharmacy & Therapeutics
- PA – Prior Authorization
- PCSK9 - Proprotein Convertase Subtilisin/Kexin Type 9
- ROS - Receptor Tyrosine Kinase
- TIBs – Targeted Immunomodulatory Biologic
- TIOSPIR – trial demonstrates comparable long-term safety of tiotropium delivered via Respimat and HandiHaler in COPD patients
- TNF – Tumor Necrosis Factor
- UF – Uniform Formulary
- ULN – Upper Limit of Normal
- UPLIFT – Use Portable Lifts in Facilitating Transfers
- VKC – Vernal Keratoconjunctivitis
- VTE – Venous Thromboembolism
- XR – Extended Release