DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

INFORMATION FOR THE UNIFORM FORMULARY
BENEFICIARY ADVISORY PANEL

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), on formulary status, prior authorization (PA), pre-authorizations, and the effective date for a drug's change from formulary to nonformulary (NF) status are received from the Beneficiary Advisory Panel (BAP), which must be reviewed by the Director before making a final decision.

II. REVIEW OF RECENTLY APPROVED U.S. FOOD AND DRUG (FDA) AGENTS: PULMONARY IIs

P&T Comments

A. 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), 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 (FEV_1) 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.

B. 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).

C. 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.

D. 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.

III. REVIEW OF RECENTLY APPROVED FDA AGENTS—PULMONARY IIs

BAP Comments

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

The P&T Committee recommended Spiriva Respimat be designated as formulary on the UF, based on clinical and cost effectiveness.

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

The P&T Committee recommended that implementation be effective upon signing of the minutes.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

IV. UF CLASS REVIEWS—ORAL ANTICOAGULANTS

P&T Comments

A. 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)—the clinical review focused on this indication.

Since the May 2015 review, dabigatran gained approval for venous thromboembolism (VTE) prophylaxis following hip replacement surgery in November 2015. Additionally idarucizumab (Praxbind) is now available as a reversal agent for the direct thrombin inhibitor dabigatran. 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 (GI) bleeding, and a higher risk of stroke in patients with normal renal function (creatinine clearance greater than 95 mL/min).
    - Dabigatran was the only 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.

B. 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.

C. 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)

D. 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.

V. UF CLASS REVIEWS—ORAL ANTICOAGULANTS

BAP Comments

A. Oral Anticoagulants—UF Recommendation

The P&T Committee recommended the following:

- **UF:**
  - Coumadin; generic
  - Eliquis
  - Pradaxa
  - Xarelto

- **NF:** Savaysa

B. Oral Anticoagulants—Implementation Plan

The P&T Committee recommended an effective date of the first Wednesday after a 90-day implementation and DHA send letters to beneficiaries who are affected by the UF decision.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissension

VI. UF CLASS REVIEWS—ANTILIPIDEMICS-1s (LIP-1s)

P&T Comments

A. 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) 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) 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.

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 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 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, 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.

B. 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.

C. 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.

D. 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 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.

Full PA Criteria

1. 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 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 creatinine 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.
- 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:
  - 5 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, and 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.

2. 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 creatinine 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, 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. 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.

VII. UF CLASS REVIEWS—LIP-1s

BAP Comments

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

The P&T Committee recommended the following, based on clinical and cost effectiveness:

- UF and step-preferred: Repatha
- UF and non step-preferred: Praluent

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

B. LIP-1s: PCSK9 Inhibitor Subclass—Manual PA Criteria

The P&T Committee recommended 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.

The full prior authorization criteria were stated previously.

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

The P&T Committee recommended an effective date of the first Wednesday after a 60-day implementation period.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

VIII. UF CLASS REVIEWS—INNOVATOR DRUGS

P&T Comments

A. 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.

B. 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)

C. 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:

1. 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.

2. 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.

3. 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
3. The patient has a creatinine clearance (CrCl) >45 mL/min
4. The gout patient has not achieved target serum uric acid level despite maximally-tolerated therapy with a xanthine oxidase inhibitor

Off-label uses are not approved.

Prior Authorization does not expire.

D. 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.

IX. UF CLASS REVIEWS—INNOVATOR DRUGS

BAP Comments

A. Innovator Drugs—UF Recommendation

The P&T Committee recommended the following:

- UF:
  - Emend
  - Vonvendi
  - Xiidra
  - Otovel

- **NF:**
    - Zurampic
    - Yosprala
    - Byvalson
    - Bevespi Aerosphere
    - GoNitro
    - Zinbryta
    - Relistor
    - Taytulla
    - Qbrelis

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissension

B. Innovator Drugs—Manual PA Criteria

The P&T Committee recommended manual PA criteria for new users of Xiidra and Zinbryta, and for new and current users of Zurampic.

The full prior authorization criteria were stated previously.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissension

C. Innovator Drugs—UF and PA Implementation Plan

The P&T Committee recommended an effective date upon signing of the minutes in all points of service.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissension

X. UTILIZATION MANAGEMENT—BASIL INSULINS

P&T Comments

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

Tresiba is a new basal insulin indicated for glycemic 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. 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:

1. Patient is age ≥ 18 AND
2. Patient has tried and failed or is intolerant to insulin glargine.

Non-FDA approved uses are not approved.
Prior Authorization does not expire.

B. 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.

XI. UTILIZATION MANAGEMENT—BASIL INSULINS

BAP Comments

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

The P&T Committee recommended manual PA criteria for Tresiba in new and current users.

The full prior authorization criteria were stated previously.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

B. Basal Insulins: Insulin Degludec (Tresiba)—PA Implementation Plan

The P&T Committee recommended an effective date of the first Wednesday after a 90-day implementation period in all points of service.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

XII. UTILIZATION MANAGEMENT—ANALGESICS AND COMBINATIONS

P&T Comments

A. 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.

B. 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.

XIII. UTILIZATION MANAGEMENT—ANALGESICS AND COMBINATIONS

BAP Comments

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

The P&T Committee recommended manual PA criteria for Allzital in new and current users.

The full prior authorization criteria were stated previously.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

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

The P&T Committee recommended an effective date of the first Wednesday after a 90-day implementation period in all points of service.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

XIV. UTILIZATION MANAGEMENT—TARGETED IMMUNOMODULATORY BIOLOGIC (TIBs)

P&T Comments

A. 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. 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. 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.

Full PA Criteria

1. 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 applies 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.

Automated PA Criteria

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).

B. 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.

XV. UTILIZATION MANAGEMENT—TIBs

BAP Comments

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

The P&T Committee recommended updating the manual PA criteria for Humira and Stelara to include their respective new indications.

The full prior authorization criteria were stated previously.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

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

The P&T Committee recommended the implementation become effective upon signing of the minutes.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

XVI. UTILIZATION MANAGEMENT—OPHTHALMIC ANTI-INFLAMMATORY/ IMMUNOMODULATORY AGENTS: OPHTHALMIC IMMUNOMODULATORY AGENTS SUBCLASS

P&T Comments

A. 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; 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.

Manual PA Criteria:

- 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
  - Blepharitis
  - Ocular rosacea
  - 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.

B. 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.

XVII. UTILIZATION MANAGEMENT—OPHTHALMIC ANTI-INFLAMMATORY/ IMMUNOMODULATORY AGENTS: OPHTHALMIC IMMUNOMODULATORY AGENTS SUBCLASS

BAP Comments

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

The P&T Committee recommended updating the Restasis manual PA criteria.

The full prior authorization criteria were stated previously.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

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

The P&T Committee recommended the implementation become effective upon signing of the minutes.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissension

XVIII. UTILIZATION MANAGEMENT—ORAL ONCOLOGY AGENTS

P&T Comments

A. 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). 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.

Full PA Criteria

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.

B. 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.

XIX. UTILIZATION MANAGEMENT—ORAL ONCOLOGY AGENTS

BAP Comments

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

The P&T Committee recommended updating the manual PA criteria for Xalkori.

The full prior authorization criteria were stated previously.

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

The P&T Committee recommended the implementation become effective upon signing of the minutes.

XX. FORMULARY STATUS UPDATE—NON-INSULIN DIABETES DRUGS

P&T Comments

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.

XXI. FORMULARY STATUS UPDATE—NON-INSULIN DIABETES DRUGS

BAP Comments

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

The P&T Committee recommended designating Jentadueto XR as UF and non step-preferred, with implementation upon signing of the minutes.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

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

P&T Comments

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.

B. 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:

1. Obtaining the product by home delivery would be detrimental to the patient; and,
2. For branded products with products with AB-rated generic availability, use of the generic product would be detrimental to the patient.

These pre-authorization criteria do not apply to any other 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.

C. 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.

XXIII. SECTION 703, NDAA FY08

BAP Comments

A. Section 703, NDAA FY08—Drugs Designated NF

The P&T Committee recommended 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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

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

The P&T Committee recommended the pre-authorization criteria for Durlaza and Dyanavel XR as previously stated.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

C. Section 703, NDAA FY08—Implementation Plan

The P&T Committee recommended an effective date of the first Wednesday after a 90-day implementation period for Durlaza and Dyanavel XR and DHA send letters to beneficiaries affected by this decision.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissension

Table of Implementation Status of UF Recommendations/Decisions Summary

Date	DoD PEC Drug Class	Type of Action	UF Medications	Nonformulary Medications	Implementation	Notes & Unique Utilizers Affected
Nov 2016	**Antilipidemics–1 (LIP-1s) Agents PCSK9 Inhibitors Subclass**	UF subclass review; not previously reviewed	**UF PCSK9 – Step-Preferred:** ▪evolocumab (Repatha) **UF PCSK9 – Non Step-Preferred:** ▪alirocumab (Praluent)	None	Pending signing of the minutes / 60 days	▪Manual PA applies to evolocumab and alirocumab. ▪Step therapy applies to all new users of the PCSK9 inhibitor products. ▪Evolocumab is the preferred PCSK9 inhibitor. ▪PA must be renewed after one year.
Nov 2016	**Oral Anticoagulants**	UF class reviewed May 2015	▪apixaban (Eliquis) ▪dabigatran (Pradaxa) ▪rivaroxaban (Xarelto) ▪warfarin generic	▪edoxaban (Savaysa)	Pending signing of the minutes / 90 days	Note: Savaysa made NF <u>Savaysa UUs Affected</u> ▪ Retail: 130 ▪ Mail: 560 ▪ MTF: 60 **Total: 750**
Nov 2016	**Pulmonary II Agents: Long-Acting Muscarinic Antagonists (LAMAs)**	UF class review; subclass not previously reviewed; Pulmonary II drugs reviewed May 2013	▪ aclidinium (Tudorza Pressair) ▪ tiotropium bromide inhalation powder (Spiriva HandiHaler) ▪tiotropium soft mist inhaler (Spiriva Respimat) ▪ umeclidinium (Incruse Ellipta)	▪ glycopyrrolate (Seebri Neohaler)	Pending signing of the minutes	None

TRICARE Formulary Search tool: http://www.express-scripts.com/tricareformulary
UUs: unique utilizers

November 2016 Drugs with Prior Authorization Criteria
Unique Utilizers Affected Per Drug

Drug	MTF	Mail Order	Retail	Total
Allzital	0	0	0	0
Tresiba	145	1,960	977	3,082