EXECUTIVE SUMMARY

Uniform Formulary Beneficiary Advisory Panel (BAP)
June 22, 2017

A. UNIFORM FORMULARY CLASS REVIEWS

A. PULMONARY-1 DRUG CLASS: PULMONARY MISCELLANEOUS SUBCLASS

1. Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—UF Recommendation

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

- **UF and Step-Preferred:** pirfenidone (Esbriet)
- **UF and Non Step-Preferred:** nintedanib (Ofev)
- **NF:** no products

Note that as part of this recommendation, all new users of an IPF agent are required to try Esbriet first.

2. Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—Manual Prior Authorization (PA) Criteria

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) updating the current manual PA criteria to require a trial of pirfenidone (Esbriet) in new users, prior to use of nintedanib (Ofev). The step therapy requirement for a trial of Esbriet in new users is included in the manual PA criteria.

Updated PA Criteria

1. nintedanib (Ofev)

   Changes from the May 2017 meeting are in BOLD

   All new users of nintedanib (Ofev) are required to try pirfenidone (Esbriet) first.
   Pirfenidone (Esbriet) is the preferred IPF agent; coverage is approved for nintedanib (Ofev) if:

- **The patient has had a trial of pirfenidone (Esbriet) and either:**

  a) **Failed therapy with Esbriet due to progression of IPF, e.g. improvement or effectiveness of therapy is defined by a less than 10% decline in percent predicted forced vital capacity (FVC) OR**

  b) **Experienced intolerable adverse effects (e.g., rash, photosensitivity; GI AEs) OR**

- **The patient has clinical factors where Esbriet is not appropriate**

  a) **The patient is taking a drug which will interact with Esbriet that does not interact with Ofev [moderate to strong CYP inhibitors – CYP 450-1A2 (e.g., fluvoxamine)] OR**

  b) **The patient has end stage renal disease (ESRD) on dialysis**

3. **Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—UF and PA Implementation Plan**

   The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) an effective date of the first Wednesday after a 30-day implementation.

   Summary of Physician's Perspective:

   This was the first time reviewing the drug class. IPF is a very debilitating disease with a high mortality rate, and these two drugs don't improve survival. The goal of therapy is NOT to improve lung function, but to slow the rate of decline.

   In terms of efficacy, the results from the individual clinical trials show that Esbriet and Ofev are very similar in efficacy. Current Military Health System utilization is about 50-50 for Esbriet vs. Ofev. The average age for the patients in DoD is 75 years, and 91% of patients are over age 65.

   The recommendation was unanimous to have both drugs remain on the formulary, with Esbriet as step-preferred. The intent of the step therapy is that in new patients, Esbriet should be tried first, if it is clinically appropriate. This requirement will be on the manual PA form. There are some differences in the adverse event and drug interaction profile, which was taken into account for the Prior Authorization criteria. Currently we have about 900 patients per quarter on Esbriet and Ofev, however, the step therapy requirement will only affect new patients with an Ofev prescription, which is about 150 patients per quarter.

We did survey three pulmonologists who treat patients with IPF. Their opinions were that prescribing should be limited to pulmonologists, and that combination therapy is not appropriate. These factors were already in the PA criteria. One provider felt that Esbriet was preferred over Ofev, but admitted that this was his opinion and was not definitive. The majority of providers prescribes only one drug, and don't switch from one product to another.

When we analyzed DoD data, we found that after 18 months, only 40% of Esbriet patients and 24% of Ofev patients were still taking the drugs. We don't know the reason why patients stopped therapy, whether it was due to death, adverse events or lack of efficacy– we don't have that data. However, based on these results, we are recommending that the PA criteria be renewed yearly, to ensure the patient is still benefitting from therapy.

Summary of Panel Questions and Comments:

Dr. Bertin asked a question about the anticipated duration of the trial period.

CAPT VonBerg replied the renewal is one year.

Dr. Bertin clarified that he is referring to the step therapy trial. How long do patients need to try the medication?

CAPT VonBerg replied that is up to the physician.

Dr. Anderson asked whether the choice to use Esbriet or Ofev is simply based on prescriber preference.

Dr. Kugler and CAPT VonBerg both replied with yes.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria and UF and PA implementation plan for the Pulmonary-1 Drug Class.

- **Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—UF Recommendation**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

- **Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

- **Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—UF and PA Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:
  CJS These comments were taken under consideration prior to my final decision

B. OPHTHALMIC-1s

1. Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—UF Recommendation

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following, based on clinical and cost effectiveness:

- **UF:**
  a) olopatadine 0.1% (generic Patanol)
  b) olopatadine 0.7% (Pazeo)
  c) azelastine 0.05% (generic Optivar)
  d) epinastine 0.05% (generic Elestat)
- **NF:**
  a) olopatadine 0.2% (Pataday)
  b) alcaftadine 0.25% (Lastacaft)

c) bepotastine 1.5% (Bepreve)

d) emedastine 0.05% (Emadine)

2. **Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—Manual PA Criteria**

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for the dual acting AH/MCS. All new and current users of a NF product, olopatadine 0.2% (Pataday), Lastacaft, Bepreve, and Emadine, require a trial of two formulary products within the past 90 days, unless the patient has experienced intolerable adverse events from the formulary products, or is pregnant.

Full PA Criteria

Manual PA criteria apply to all new and current users of Lastacaft, Bepreve, Emadine, and olopatadine 0.2% (Pataday).

- The patient has ocular symptoms of allergic conjunctivitis AND

  a) The patient has tried and failed two formulary alternatives (olopatadine 0.1%, olopatadine 0.7% (Pazeo), azelastine, or epinastine) in the last 90 days, OR

  b) Use of two formulary alternatives (olopatadine, azelastine, or epinastine) has resulted in intolerable adverse effects, OR

  c) The patient is pregnant (for Lastacaft and Emadine only)

PA does not expire.

3. **Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—UF and PA Implementation Plan**

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

Summary of Physician's Perspective:

These drugs treat the ocular itching caused by allergic conjunctivitis, which is generally a seasonal condition, and not a chronic problem. Patients will commonly use the eye drops during the spring allergy season, and then stop

therapy until the next spring. MHS utilization shows this seasonal variation in use.

The drugs in the class are highly therapeutically interchangeable. The main recommendation here is that Pataday which was previously formulary, will now move to non-formulary status, and Pazeo will move to formulary status. We are basically just changing olopatadine formulations, since Patanol, Pataday, and Pazeo all contain the same active ingredient. Overall, almost 90% of the market share is from olopatadine (all formulations counted together).

Additionally, we are going to have the non-formulary drugs also have manual Prior Authorization criteria. Because of the seasonal variation in allergy symptoms, the recommendation is that both current and new patients will undergo the PA process – in other words, patients will not be grandfathered here. Approximately 33,000 patients will be affected by the PA, including about 29,000 patients currently receiving Pataday.

Summary of Panel Questions and Comments:

Mr. Du Teil asked about the person who opposed the relative clinical effectiveness conclusion.

Dr. Kugler replied that we utilize electronic voting and we think that the oppose vote was a mistake. We asked for comments. No one had comments regarding the relative clinical effectiveness criteria.

Ms. Le Gette asked why the committee did not place a true automated step therapy drug rather than just asking about the prior former usage of the manual PA. I do realize it's seasonal and only looking back 90 days for new and current users.

CAPT VonBerg replied that this approach will allow us to capture all of those patients.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, and UF and PA implementation plan for the Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers.

- **Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—UF Recommendation**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

- **Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

- **Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—UF and PA Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

II. NEWLY APPROVED DRUGS PER CFR 199.21 (g)(5) (INNOVATOR DRUGS)

A. Newly Approved Drugs UF Recommendation

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

- **UF:**

  a) deflazacort (Emflaza) – Corticosteroids – Immune Modulators – for Duchenne Muscular Dystrophy (DMD)

b) deutetrabenazine (Austedo) – Neurological Agents Miscellaneous for Huntington's Disease

c) dupilumab (Dupixent) – Corticosteroids – Immune Modulators – Immune Modulators Subclass for Atopic Dermatitis

d) ribociclib (Kisqali) – Oral Oncologic Agents for Breast Cancer

e) telotristat (Xermelo) – GI-2 Miscellaneous Agents

- **NF:**

a) crisaborole (Eucrisa) – Corticosteroids – Immune Modulators – Immune Modulators Subclass for Atopic Dermatitis

b) insulin degludec/liraglutide (Xultophy) – Glucagon-Like Peptide-1 Receptor Agonist (GLP1RA)

c) morphine sulfate extended release (Arymo ER) – Narcotic Analgesics and Combinations

d) oxymetazoline (Rhofade) – Acne Agents – Topical Acne and Rosacea Agents Subclass

e) plecanatide (Trulance) – GI-2 Miscellaneous Agents

B. Newly Approved Drugs—PA Criteria

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

- Applying the same manual PA criteria for insulin degludec/liraglutide (Xultophy) in new and current users, as is currently in place for insulin glargine/lixisenatide (Soliqua) and the other non-step-preferred GLP1RAs. Patients must first try metformin or a sulfonylurea, and exenatide weekly injection (Bydureon) and albiglutide weekly injection (Tanzeum) prior to Xultophy. Additionally, for Xultophy, patients are required to be on basal insulin at a dosage of less than 50 units daily.

- Applying the same step therapy and manual PA criteria for topical oxymetazoline (Rhofade) in new and current users as is currently in place for the non-step-preferred topical rosacea products. Patients must first try one generic metronidazole step-preferred formulation and topical azelaic acid prior to Rhofade.

- Applying PA criteria to the following: new and current users of crisaborole (Eucrisa), dupilumab (Dupixent), deflazacort (Emflaza), plecanatide (Trulance), and telotristat (Xermelo);and in new users of deutetrabenazine (Austedo) and ribociclib (Kisqali).

  Full PA Criteria for the Newly Approved Drugs

  a. **Crisaborole (Eucrisa) – Corticosteroids – Immune Modulators – Immune Modulators Subclass**

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

     Manual PA Criteria: coverage will be approved if:

     - Patient has mild to moderate atopic dermatitis AND
     - Prescribed by a dermatologist AND
     - Patient has a contraindication to, intolerability to, or failed treatment with at least one high potency / class 1 topical corticosteroid.

     Off-label uses are NOT approved.

     PA does not expire.

  b. **Dupilumab (Dupixent) – Corticosteroids – Immune Modulators – Immune Modulators Subclass**

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

     Manual PA Criteria: Coverage will be approved for initial therapy for 6 months if:

     - Patient has moderate to severe or uncontrolled atopic dermatitis AND
     - Patient must be 18 years of age or older AND
     - Prescribed by a dermatologist AND
     - Patient has a contraindication to, intolerability to, or failed treatment with at least **ONE** high potency / class 1 topical corticosteroid AND
     - Patient has a contraindication, intolerability to, or failed treatment with at least **ONE** systemic immunosuppressant.

     PA expires after 6 months.

Renewal PA Criteria: Coverage will be approved indefinitely for continuation of therapy if:

- The patient has had a positive response to therapy, e.g., an Investigator's Static Global Assessment (ISGA) score of clear (0) or almost clear (1)

Off-label uses are NOT approved.

c. **Deflazacort (Emflaza) – Corticosteroids – Immune Modulators**
Manual PA criteria apply to all new and current users of Emflaza.

Manual PA Criteria: Coverage will be approved for one year indefinitely if all criteria are met:

- Patient has a diagnosis of Duchenne Muscular Dystrophy AND
- Prescribed by a neurologist AND
- Patient is age 5 or greater AND
- Patient has tried prednisone for at least 6 months and has experienced at least one of the following adverse events:

  a) Unmanageable weight gain OR

  b) Patient has experienced severe behavioral adverse events that requires a reduction in prednisone dose

Off-label uses are NOT approved

PA does not expire.

d. **Plecanatide (Trulance) – GI-2 Miscellaneous Drugs**

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

Manual PA Criteria: Coverage approved if:

- Patient is ≥ 18 years of age AND
- Patient has clinically diagnosed chronic idiopathic constipation AND
- Patient does not have gastrointestinal obstruction AND

- Patient has failed or is intolerant to linaclotide (Linzess) AND

- Dual therapy with another guanylate cyclase-C agonist is not allowed.

Off-label uses are not approved.

PA expires in one year.

- PA criteria for renewal for new and current users: After one year, PA must be resubmitted. Continued use of Trulance will be approved if there has been improvement in constipation symptoms and NO dual therapy with another guanylate cyclase-C agonist.

Renewal PA criteria is limited to one year.

e. **Telotristat (Xermelo) – GI-2 Miscellaneous Drugs**

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

Manual PA Criteria: Coverage approved for one year if all criteria are met:

- Patient has diagnosis of carcinoid syndrome diarrhea.

- Patient has had an inadequate treatment response to at least a 3-month trial of somatostatin analog therapy.

- Telotristat must be used in combination with a somatostatin analog (i.e., octreotide or lanreotide).

- Patient has $\geq$ 4 bowel movements daily.

Off-label uses are NOT approved.

PA expires in one year.

- PA criteria for renewal for new and current users: After one year, PA must be resubmitted. Continued use of Xermelo will be approved when

  a) used in combination with a somatostatin analog,

  b) decrease from baseline in amount of average daily bowel movements,

c) prescriber agrees to continue to assess the patient for severe constipation and abdominal pain and discontinue the medication if either develops,

d) no severe constipation or abdominal pain develops.

- Renewal PA criteria is limited to one year.

f. **Deutetrabenazine (Austedo) – Neurological Agents Miscellaneous**
Manual PA criteria apply to all new users of Austedo.

Manual PA Criteria: Coverage approved for initial therapy for indefinitely if all criteria are met:

- Prescribed by or in consultation with a neurologist
- Patient has a diagnosis of chorea associated with Huntington's Disease
- Patient is not actively suicidal
- Patient does not have depression, or is being adequately treated for depression
- Patient does not have severe hepatic impairment
- Patient is not taking any of the following:

  a) MAOI inhibitor within the past 14 days

  b) Reserpine

  c) tetrabenazine (Xenazine) or another VMAT-2 inhibitor

- Patient has had an adequate trial of tetrabenazine for 12 weeks and had one of the following:

  a) Experienced treatment failure

  b) Experienced an adverse event that is not expected to occur with Austedo

PA expires in one year.

Manual PA Criteria (Renewal Criteria): Coverage approved indefinitely for continuation of therapy if all criteria are met:

- Patient has demonstrated improvement in chorea based on clinician assessment and is being monitored for depression and suicidal ideation

Off-label uses are NOT approved (Tourette's, tardive dyskinesia, dystonia).

g. **Oxymetazoline (Rhofade) – Topical Acne and Rosacea Agents: Miscellaneous Topical Agents**

Manual PA Criteria apply to all new and current users of Rhofade.
Automated PA Criteria:

The patient has filled a prescription for one generic topical step-preferred metronidazole product (1% gel, or 0.75% lotion, or 0.75% cream) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or TRICARE Mail Order Pharmacy) during the previous 180 days

Manual PA Criteria: If automated PA criteria are not met, Rhofade will be approved if:

The patient is at least 18 years of age and has the following diagnosis:

- For Rhofade, the patient has persistent facial erythema of rosacea

  AND

- The patient has tried and failed one generic step-preferred formulary topical metronidazole product (1% gel, 0.75% lotion or 0.75% cream)

  AND

- The patient has tried and failed topical azelaic acid 15%

PA expires in one year

Off-label uses are not approved

h. **Ribociclib (Kisqali) – Oral Oncologic Agents**

Manual PA criteria apply to all new users of Kisqali.

Manual PA Criteria: Kisqali is approved if:

- Patient has advanced (metastatic) estrogen receptor-positive (ER+) disease; AND

- Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND

- The patient is postmenopausal woman and will be used as first-line endocrine therapy in combination with an aromatase inhibitor.

Off-label uses are not approved.

PA does not expire.

C. Newly Approved Drugs—UF and PA Implementation

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) an effective date upon signing of the minutes in all points of service, including the new PAs for dupilumab (Dupixent), crisaborole (Eucrisa), deflazacort (Emflaza), plecanatide (Trulance), telotristat (Xermelo), liraglutide/insulin degludec (Xultophy), deutetrabenazine (Austedo), oxymetazoline (Rhofade), and ribociclib (Kisqali).

Summary of Physician's Perspective:

For the newly approved drugs recommended for non-formulary status, clinically and cost effective alternative therapies are available on the formulary. Additionally, we do consult with the appropriate specialists for some of the products that are in classes that have not been previously reviewed, or for some of the orphan drugs.

Manual PA criteria were recommended for 9 of the 10 newly approved drugs.

- For the drugs used to treat atopic dermatitis, PAs were recommended for both Eucrisa and Dupixent. We did reach out to the dermatologists who said that for atopic dermatitis, a trial of a high potency topical steroid is considered first line therapy. For Dupixent, we did recommend having the PA expire after six months with renewal requiring the patient to have a response to therapy. This was because in the clinical trials, there was only a 38% response rate for the primary endpoint.

- The PAs for Xultophy and Rhofade reflect the current step-therapy requirements in their respective classes (GLP1-RAs for Xultophy for diabetes, and topical acne and rosacea for Rhofade), since the P&T Committee has already reviewed these classes.

- The PAs recommended for the orphan drugs Emflaza, Austedo, and Kisqali are consistent with their FDA approved indications. Also, Kisqali has a similar mechanism of action as Ibrance, which has had a PA in place since November 2016.

- PAs were also recommended for Trulance and Xermelo, since other cost effective drugs are available to treat chronic idiopathic constipation and carcinoid syndrome diarrhea. For Xermelo, there is also renewal PA criteria recommended after one year, due to the 40% response rate for efficacy.

  Summary of Panel Questions and Comments:

  Dr. Anderson – noted regarding Rhofade that persistent facial erythema is a potential approval pathway in the prior authorization criteria. This should partially address concerns raised in the public comment.

  Ms. Buchanan asked for clarification regarding Emflaza. You said for children under age 8 or greater, but the packet says age 5.

  Allerman replied that the insert in the packaging stated that the requirement is that the child has to be at least 5. The studies for Emflaza were conducted in the 1990s, but that was one of the inclusion criteria for the study. This has not been studied in children younger than 5. Prednisone is the favorite. The child will be placed on prednisone when they are prescribed the medication.

  Buchanan reiterated that it is age 5 not age 8.

  Allerman confirmed it is age 5 not age 8.

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

  - **Newly-Approved Drugs—UF Recommendation**

    Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

    Director, DHA:

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

  - **Newly-Approved Drugs—PA Criteria**

    Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

    Director, DHA:

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

- **Newly-Approved Drugs—UF and Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

III. UTILIZATION MANAGEMENT—NON-INSULIN DIABETES DRUG: BIGUANIDES

A. Non-Insulin Diabetes Drug: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza—New Manual PA Criteria

Fortamet and Glumetza are branded formulations of metformin ER (Glucophage XR), which were designated as NF at the November 2010 meeting, and maintained as NF in August 2016. Glumetza and Fortamet are available in 500 mg and 1000 mg tablets while generic metformin ER products are available in 500 mg and 750 mg tablets.

Due to the significant cost differences between Fortamet and Glumetza and generic metformin ER, and the lack of clinically compelling benefits over generic metformin ER, the Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) manual PA in all new and current users of Glumetza and Fortamet. The patient will be required to try generic metformin ER first. Prior authorization will not expire.

Full PA Criteria:

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

The provider must explain why the patient cannot take two generic 500mg ER tablets separately (for patients taking requiring 1000 mg metformin ER).

PA will be approved if patient is on a dose-alternating schedule (e.g., 500 mg alternating with 1000 mg every other day).

PA does not expire.

Off-label uses are not approved.

B. Non-Insulin Diabetes Drug: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza—Manual PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the new manual PA for extended-release metformin (Fortamet, Glumetza, generics) become effective on the first Wednesday after a 90-day implementation period in

all points of service.

Summary of Physician's Perspective:

Fortamet and Glumetza are considerably more expensive than generic metformin ER, and do not offer any clinical advantages over the generic. The PA criteria do take into account patients who have dose alternating schedules, since generic metformin ER is not available in a 1,000 mg tablet.

Approximately 6,500 patients will be affected by the PA requirements, since the PA will apply to both new and current users ("no grandfathering"). The committee was unanimous in recommending the PA criteria.

Summary of Panel Questions and Comments:

Dr. Anderson asked if this is the strongest action we can take regarding these drugs.

Dr. Allerman replied correct. We have the non-formulary recommendation; we looked at prices again last summer; and we can't come up with a clinical reason. There is a significant cost different. That is our next step, to make everyone fill out a piece of paper.

Dr. Anderson agreed, in his opinion, it is wasteful spending on these drugs. There is no therapeutic advantage.

There were no more questions or comments from the Panel. The Chair called for a vote on the New Manual PA Criteria and Manual PA Implementation Plan for the Non-Insulin Diabetes Drugs: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza.

- **Non-Insulin Diabetes Drug: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza—New Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

- **Non-Insulin Diabetes Drug: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza—Manual PA Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

IV. UTILIZATION MANAGEMENT—DIURETICS CARBONIC ANHYDRASE INHIBITOR

A. Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis)—New Manual PA Criteria

Keveyis is an orphan drug approved for treating primary hyperkalemic or hypokalemic periodic paralysis, or related variants. The active ingredient dichlorphenamide was first marketed in 1958 under the brand name Daranide, but discontinued from the market. Keveyis was FDA-approved in August 2015, but just recently launched.

Acetazolamide is commonly used off-label for this condition, but only one published retrospective trial is available. FDA approval for Keveyis was based on two clinical trials enrolling a total of 65 patients. The mechanism of action of Keveyis for treating periodic paralysis is unknown.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) new manual PA criteria for Keveyis, requiring a diagnosis of hypo- or hyperkalemic periodic paralysis as outlined in the product labeling, and a trial of acetazolamide. Prior authorization will expire after two months. If the patient has responded to therapy, then Keveyis will be approved indefinitely.

Full PA Criteria:

Manual PA criteria apply to all new and current users of Keveyis for treatment of Hypo/Hyperkalemic Periodic Paralysis (HypoPP/HyperPP) and Related Variants.

Manual PA Criteria: Initial Therapy. Keveyis is approved for 2 months if the patient meets the following criteria (i, ii, iii, iv, and v):

i. Patient has a confirmed diagnosis of primary hypokalemic or hyperkalemic periodic paralysis by meeting at least ONE of the following (a, b, or c):

   a) Patient with HypoPP has had a serum potassium concentration of less than 3.5 mEq/L during a paralytic attack; OR for patient with HyperPP, patient

has had an increase from baseline in serum potassium concentration of greater than or equal to 1.5 mEq/L during a paralytic attack; OR for patient with HyperPP, patient has had a serum potassium concentration during a paralytic attack of greater than 5.0 mEq/L;

OR

b) Patient has a family history of the condition; OR

c) Patient has a genetically confirmed skeletal muscle calcium or sodium channel mutation; AND

ii. Patient has had improvements in paralysis attack symptoms with potassium intake; AND

iii. Patient has tried and failed oral acetazolamide therapy (e.g., Diamox tablets, Diamox Sequels extended-release capsules, generics); AND

iv. According to the prescribing physician, acetazolamide therapy did not worsen the paralytic attack frequency or severity in the patient; AND

v. Keveyis is prescribed by or in consultation with a neurologist or a physician who specializes in the care of patients with primary periodic paralysis (e.g., muscle disease specialist, or Physical Medicine and Rehabilitation [PMNR]).

PA expires after two months.

Renewal Manual PA Criteria:

- Patients Continuing Therapy. Keveyis is approved indefinitely if the patient has responded to Keveyis (e.g., decrease in the frequency or severity of paralytic attacks) as determined by the prescribing physician.

Off-label uses are not approved.

B. Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis)—PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the new manual PA for dichlorphenamide (Keveyis) become effective on the first Wednesday after a 90-day implementation period in all points of service.

Summary of Physician's Perspective:

This is a new version of an old drug from the 1950s that was originally used as a diuretic. It now has a very specific indication for patients with periodic paralysis

caused by fluctuations in potassium levels, and was brought back to the market as an orphan drug. Acetazolamide (Diamox) has been used off label for this condition for several years, and has the same mechanism of action. Diamox does have some retrospective data supporting its use for periodic paralysis.

Manual PA criteria were recommended to ensure Keveyis is used in accordance to the package insert. We also did look at PA criteria from some commercial health care plans. The PA criteria will also recommend a trial of Diamox first.

So far we have one patient in DoD who has received a prescription for Keveyis. We will require that patient to go through the PA process, along with any new patients.

Summary of Panel Questions and Comments:

There were no questions or comments from the Panel. The Chair called for the vote on the Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis) New Manual PA Criteria and PA Implementation Plan,

- **Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis)—New Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

- **Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis)—PA Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

V. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA

The P&T Committee recommended updated manual PA criteria for nine drugs from seven classes. Updates to the manual PA criteria were recommended for a variety of reasons, including expanded FDA-approved indications, FDA safety alerts, or availability of low cost generics for NF drugs in classes where there is existing step therapy.

A. Updated Manual PA Criteria

1. **Gastrointestinal-2 Miscellaneous Agents: Eluxadoline (Viberzi)**
   Viberzi was reviewed in February 2016 with manual PA criteria recommended. An update to the manual PA criteria was recommended, based on a recent FDA safety alert. Patients who have had a cholecystectomy will be excluded from using Viberzi.

   Updated PA Criteria

   - **Patient does not have a history of cholecystectomy.**

2. **Anticonvulsants and Anti-Mania Drugs: Topiramate ER (Qudexy XR)**
   Qudexy XR was reviewed in May 2016 with manual PA criteria recommended. Criteria were updated to add the additional indication for migraine prophylaxis.

   Updated PA Criteria

   Changes from the May 2017 meeting are in BOLD and strikethrough

   - Coverage approved **for Migraine prophylaxis in adults (Trokendi XR and Qudexy XR)**

   - Coverage not approved for non-FDA approved indications, including weight loss

3. **Non-Opioid Pain Syndromes: Pregabalin (Lyrica)**

   Lyrica was reviewed in November 2011 with step therapy and manual PA criteria recommended. A trial of gabapentin is required prior to use of Lyrica, except in patients with seizure disorders. The manual PA criteria were updated to require a trial of duloxetine in addition to gabapentin for disorders not related to seizures or post-herpetic neuralgia.

   Updated PA Criteria

   Changes from the May 2017 meeting are in BOLD and will apply to new users of Lyrica.

   - Indication: Seizure disorder **and post-herpetic neuralgia** – (no changes to the criteria for these indications)

   OR

- **Indication: Non-seizure related disorder (diabetic peripheral neuropathy and fibromyalgia)**

  a) The patient has tried and failed gabapentin therapy (trial of Gralise or Horizant does not qualify) **AND**

  b) **Patient has tried and failed duloxetine**

  c) The patient has a contraindication to gabapentin or **duloxetine** that is not expected to occur with pregabalin

  d) The patient experienced adverse events with gabapentin or **duloxetine** that are not expected to occur with pregabalin

  e) The patient previously responded to pregabalin and changing to gabapentin or **duloxetine** would incur unacceptable risk

4. **Hepatitis C Virus Direct-Acting Antivirals: Ledipasvir/Sofosbuvir (Harvoni) and Sofosbuvir (Sovaldi)**

   The direct-acting antivirals were most recently reviewed for formulary status in February 2017. The manual PA criteria were updated to reflect FDA approval in children 12 years of age and older.

   Updated PA Criteria for both ledipasvir/sofosbuvir (Harvoni) and sofosbuvir (Sovaldi)

   Coverage approved for patients **≥ 12 years**

5. **Nasal Allergy Drugs: Fluticasone/Azelastine (Dymista)**

   Dymista was reviewed in May 2014, with step therapy and manual PA criteria recommended. Currently, a trial of one step-preferred formulary nasal allergy drug (nasal formulations of generic fluticasone, flunisolide, azelastine, or ipratropium) is required prior to use of Dymista. Since the May 2014 class review, several nasal allergy drugs are now available in generic formulations, or OTC. Criteria were updated to include a trial of at least two formulary step-preferred drugs prior to use of Dymista.

   Updated PA Criteria

   Changes from May 2017 meeting are in BOLD

   Manual PA Criteria: Dymista is approved (e.g., trial of azelastine 137 mcg, flunisolide, fluticasone propionate, azelastine, or ipratropium is NOT required) if:

- Patient has experienced any of the following issues with **at least two** of the following step-preferred nasal allergy drugs (fluticasone propionate, flunisolide, azelastine, or ipratropium), which is not expected to occur with the non-preferred nasal allergy drugs

  a) inadequate response to the step-preferred drugs

  b) intolerable adverse effects (persistent epistaxis, significant nasal irritation, pharyngitis)

  c) contraindication

6. Sedative Hypnotic-1s: Newer Sedative Hypnotics—Eszopiclone (Lunesta) and Zolpidem ER (Ambien CR)

Lunesta and Ambien CR were reviewed in May 2012 with the newer sedative hypnotics drug class, and both drugs are designated as UF and non-step-preferred. Step therapy for the class requires a trial of a step-preferred drug (zolpidem IR or zaleplon) prior to use of non-step-preferred agents. Cost-effective generic formulations of Lunesta and Ambien CR are now available.

The step therapy criteria and manual criteria for the newer sedative hypnotics were updated to remove step therapy for eszopiclone and zolpidem ER. Eszopiclone and zolpidem ER will be step-preferred agents in addition to zolpidem IR and zaleplon. Step therapy remains for non-step-preferred agents including Rozerem, Intermezzo, Edluar, Silenor, and Zolpimist. Belsomra and Hetlioz have additional manual PA criteria.

Updated PA Criteria

Changes from May 2017 meeting are in BOLD

Manual PA Criteria: Coverage is approved if: The patient has an inadequate response to, been unable to tolerate due to adverse effects, or has a contraindication to zolpidem IR, zaleplon, **zolpidem ER, or eszopiclone**.

7. OAB Drugs: Mirabegron (Myrbetriq)

The OAB drugs were most recently reviewed for formulary status in November 2012, with step therapy requiring a 12-week trial of one cost-effective generic formulation of tolterodine ER, oxybutynin ER, or trospium IR prior to use of the non-step-preferred drugs. Mirabegron was reviewed as a new drug at the May 2014 meeting, and was designated as UF and non-step-preferred. Since the previous P&T Committee review, several cost-effective generic formulations of other OAB drugs have entered the market.

Overactive bladder is characterized by a high placebo response rate, and benefits are seen with behavioral therapies. There do not appear to be clinically relevant differences in efficacy between mirabegron and the antimuscarinic OAB drugs, based on meta-analyses and clinical practice guidelines.

The manual PA criteria for mirabegron were updated to recommend a trial of two formulary step-preferred products first. The criteria will continue to allow patients who are at significant risk for central nervous system effects from antimuscarinic drugs to receive mirabegron. The criteria were also updated to reflect package insert cautions regarding use in patients with compromised renal function. Additionally, a trial of behavioral interventions (including pelvic floor muscle training in women and bladder training) is recommended, based on the clinical practice guidelines.

Updated PA Criteria

Changes from May 2017 meeting are in BOLD

Manual PA Criteria—If automated criteria are not met, Myrbetriq is approved if:

1. Patient has confirmed diagnosis of OAB with symptoms of urge incontinence, urgency, and urinary frequency **AND**

2. **Patient has tried and failed behavioral interventions to include pelvic floor muscle training in women, and bladder training, AND**

3. Patient has had a 12-week trial with **2** formulary step-preferred products and had therapeutic failure **OR**

4. Patient has experienced central nervous system AEs with oral OAB medications **OR** is at increased risk for such central nervous system effects due to comorbid conditions or other medications, **AND**

5. **Patient does not have a creatinine clearance (CrCl) < 15 mL/min OR**

6. If CrCl 15-29 mL/min, dosage does not exceed 25 mg daily

B. Updated Manual PA Criteria PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) updates to the current PAs for eluxadoline (Viberzi), topiramate ER (Qudexy XR), pregabalin (Lyrica), ledipasvir/sofosbuvir (Harvoni), sofosbuvir (Sovaldi), fluticasone/azelastine (Dymista) and the step therapy changes for eszopiclone (Lunesta) and zolpidem ER (Ambien CR) and recommended (12 for, 0 opposed, 0 abstained, 4 absent) the manual PA update for mirabegron (Myrbetriq) become effective upon signing of the minutes in

all points of service.

Summary of Physician's Perspective:

These updates to existing PA criteria are done routinely at every P&T meeting to take into account either new indications (Qudexy XR for migraine prophylaxis, or the Hepatitis C drugs with a new pediatric indication), or safety warnings from the FDA (Viberzi). We also monitor prices of generic drugs in classes where we have existing step therapy requirements. For the sedative hypnotics, the change was made to put more cost effective generic formulations in front of the step.

Summary of Panel Questions and Comments:

Dr. Anderson had a question regarding the Lyrica criteria. If the beneficiary were already taking an antidepressant or SSRI, would the beneficiary be required to take duloxetine per the manual PA.?

Dr. Allerman replied that since Lyrica is not approved for depression, we were specifically looking for gabapentin or duloxetine. Duloxetine does have indications as previously discussed.

Dr. Anderson asked if someone were already on Prozac, would it be a problem to take both.

Dr. Allerman replied that they would probably have the PA approved for Lyrica if they met the requirement. I don't recall us going back to look at or combinations in anti-depressant therapies with Lyrica. I do not have a good answer right now.

Dr. Anderson asked her to follow up on that. His concern would be forcing someone in a situation where they were taking two (2) SSRIs.

Dr. Allerman replied that if they've had a contraindication, that would apply in this case and the beneficiary would not be required to use two (2) SSRIs in combination.

There were no more questions or comments. The Chair called for a vote on the updated Manual PA Criteria and PA Criteria Implementation Plan.

- **Updated Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

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

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

  ___These comments were taken under consideration prior to my final decision

VI. RE-EVALUATION OF NF GENERICS

A. Re-evaluation of Generics—UF Recommendations and Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following actions, to become effective upon signing of the minutes:

- Selective Serotonin Reuptake Inhibitors: All fluoxetine capsules currently designated as NF will be returned to UF status.

- Testosterone Replacement Therapies: Generic Androgel 1% gel will be returned to UF status and designated as step-preferred, with appropriate changes made to PA criteria to require an unsuccessful trial, contraindication, or intolerance to either Fortesta or generic Androgel 1% before receiving a non-preferred product.

Summary of Physician's Perspective:

We are continuing to go through all the classes evaluated several years ago to assess new clinical and cost information for the products that are non-formulary that now have generics available. The last time this topic was presented to the panel was from the August 2016 P&T meeting.

For the classes reviewed (the antidepressants and the testosterone replacement therapies), the recommendations for which generics remain NF and which should go back to UF status was based on cost effectiveness. The generic fluoxetine capsules and the generic Androgel 1% formulation are now recommended to change to UF status.

Summary of Panel Questions and Comments:

There were no questions or comments from the Panel. The Chair called for a vote on the UF Recommendation and Implementation plan for the Re-evaluation of Generics.

- **Re-evaluation of Generics—UF Recommendations and Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

VII. SECTION 703, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR (FY) 2008

A. Section 703, NDAA FY08—Drugs Designated NF

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

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) the following product be designated NF on the UF:

- CSL Behring LLC: antihemophilic factor, recombinant single chain (Afstyla) 500 units, 1000 units, 2000 units, and 3000 units injection

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

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) the following pre-authorization criteria for Afstyla:

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

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

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

Should the mail order requirement impact availability of a drug, the P&T Committee will allow an exception to the Section 703 rule. The following drug will not be available in the Mail Order:

- Afstyla (antihemophilic factor, recombinant single chain), 500 units, 1000 units, 2000 units, and 3000 units subcutaneous injection is only available in the Retail Network.

C. Section 703, NDAA FY08—Implementation Plan

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) an effective date of the first Wednesday after a 90-day implementation period for Afstyla and DHA send letters to beneficiaries affected by this decision.

Summary of Physician's Perspective:

(Normally no comments for Dr. Kugler on the Section 703 drugs)

Summary of Panel Questions and Comments:

Ms. Le Gette asked for clarification. The drug is only limited to retail. Is it just moving to non-formulary or is there a requirement for a prior authorization?

CAPT VonBerg replied the non-formulary normally would be restricted to one point of service, but now allowing it to be dispensed at retail.

Ms. Le Gette replied that she's trying to understand is there a prior authorization but isn't available in mail order.

CAPT VonBerg replied the legalese and interpretation is that it will be allowed in retail.

There were no more questions or comments from the Panel. The Chair called for a vote on the Section 703, NDAA FY08 Drugs Designated NF.

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

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

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

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

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

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

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

  Director, DHA:

  CG These comments were taken under consideration prior to my final Decision

RADM Colin Chinn, MC, USN
Acting Deputy Director, DHA
for R.C. Bono, VADM, MC, USN
Director

Date: 12/7/17

Appendix A: Public Citizen Comments
Appendix B: Brief Listing of Acronyms Used in the Summary

Appendix 1 **06/22/2017 BAP Meeting**

Private Citizen Comments

- Pfizer, Inc. submitted a written comment regarding the prior authorization criteria Eucrisa. The letter was presented to the Panel for review.

- Mr. Eric V. Busby, Scientific Director under the Global Medical Excellence Team at Allergen gave a presentation on the prior authorization for Rhofade. A summary of the presentation are as follows:

    1. Mr. Busby spoke about the newly proposed prior authorization of Rhofade and respectfully request further examination of the clinical data for the preferred treatment options within the Rosacea category.

    2. The first line products within the PA metronidazole and azelaic acid are used for rosacea. The focus and only FDA approved indication is treating the bumps and lesions or the papulars or pustulars that are associated with rosacea. They are not indicated for the persistent erythema that is associated with rosacea. As you may know, rosacea is a dermatological disease involving four major sub-types or manifestations. Evidence in the literature supports that disease progression may occur from the most common sub-types to the persistent erythema to papulars or pustulars, ocular or even privitas rosacea.

    3. The two key pathological factors associated with rosacea symptoms include the augmented immune responses and also neurovascular dysregulation. They are not mutually exclusive; however, one predominates over the other. If the augmented immune response is predominating then this is where the patients will develop the papulars and pustulars that are associated with rosacea. Metronidazole and azelaic acid targets this pathogenic process. If the neurovascular dysregulation is predominant then the patient develops the persistent or background erythema, and Rhofade targets this process.

    4. Consensus recommendations from the American Acne and Rosacea Society recommend clinicians consider the two pathogenic factors and symptoms. They also note that alpha-agonists such as Rhofade to be an important independent category of topical agent in the treatment persistent diffused facial erythema.

    5. According to the Cochran Collaboration Review 2015, metronidazole and azelaic acid were shown to be effective and safe in reducing rosacea symptoms, but their improvements tended after 3-6 weeks. The primary end point was focused more on the bumps and lesions. Erythema, generally speaking, was a secondary end point, but results were inadequately recorded. They were unable to demonstrate improvement beyond paralesional redness.

6. Therefore, these products are only FDA approved to treat the bumps and lesions. The clinical evidence does not support the use of persistent erythema. Rhofade is an alpha-1 adrenalceptor agonist that addresses the persistent erythema by causing basal constriction of the abnormally dilated vasculature under the skin. A pea-sized amount of Rhofade is applied to the entire face, once a day, has been shown to reduce facial erythema, the most common symptoms of rosacea. The effect of Rhofade is seen as early as day 1. Rhofade is safe and tolerable with no evidence of clinically relevant rebound following discontinuation of treatment. The most common adverse reaction was application site dermatitis, pruritis, and also worsening inflammatory lesions. All which were recorded in 1-2% of patients.

7. We ask that you consider the pathophysiological aspects of rosacea symptoms, further evaluate the clinical data for your preferred treatment options in your proposed PA criteria, and also consider adjusting or limiting the step-through requirements for Rhofade.

Mr. Busby thanks the Panel for their time and attention.

Appendix 2 **06/22/2017 BAP Meeting**

Brief Listing of Acronyms Used in the 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.

- AE – Adverse Events
- AH/MCS – Adverse Events
- BCF – Antihistamine/Mast Cell Stabilizer
- BIA – Budget Impact Analyisis
- CFR – Code of Federal Regulations
- CMA – Cost-Minimization Analysis
- CR – Extended Release
- CYP - Cytochrome
- DHA – Defense Health Agency
- DMD = Duchenne Muscular Dystrophy
- DoD – Department of Defense
- ER – Extended Release
- ER+ - Estrogen Receptor - Positive
- ESERD – End Stage Renal Disease
- FDA – Food & Drug Administration
- FVC – Forced Vital Capacity
- FY – Fiscal Year
- g - gram
- GI - Gastrointestinal
- GI AE – Gastrointestinal Adverse Events
- GI-2 – Gastrointestinal 2
- GLP1RA – Glucagon-Like Peptide-1 Receptor Agonist
- HER2 – Human Epidermal Growth Receptor 2
- IPF – Idiopathic Pulmonary Fibrosis
- IR – Insulin Resistance
- ISGA – Investigator’s Static Global Assessment
- LLC – Limited Liability Company
- MAOI – Monoamine Oxidase Inhibitors
- mEq/L – mil equivalent per liter
- mg - milligram
- MHS – Military Health System
- Ml - Milliliter
- MTF – Military Treatment Facility

- NDAA – National Defense Authorization Act
- NF – Non Formulary
- OAB – Overactive Bladder
- OTC – Over the Counter
- PA – Prior Authorization
- PMDD – Premenstrual Dysphoric Disorder
- PMN – Physical Medicine and Rehabilitation
- POS – Point of Service
- PP – Periodic Paralysis
- SSRI – Selective Serotonin Reuptake Inhibitors
- SU - Sulfonylurea
- TRICARE – Healthcare Network
- TRT – Testosterone Replacement Therapy
- UF – Uniform Formulary
- VMAT-2 – Vesicular Monoamine Transporter 2
- XR – Extended Release

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
June 22, 2017
Washington, D.C.

Present Panel Members

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

Absent Panel Members

- Mr. Charles Hostettler, AMSUS, The Society of Federal Health Professionals

The meeting was held at Naval Heritage Center Theater, 701 Ave., N.W., Washington, D.C., and Alternate DFO CAPT Edward Norton called the meeting to order at 9:15 A.M.

Agenda

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

- Welcome and Opening Remarks

- Public Citizen Comments

- Therapeutic Class Reviews

    1. Drug Class Reviews

        a) Pulmonary I Drug Class—Pulmonary Miscellaneous Subclass Idiopathic Pulmonary Fibrosis Drugs

        b) Ophthalmic-1s—Dual Acting Antihistamine/Mast Cell Stabilizers Subclass

    2. Newly-Approved Drugs Per CFR 199.21 (g)(5) (Innovator Drugs)

        a) Crisaborole (Eucrisa)—Corticosteroids – Immune Modulators – Immune Modulators Subclass for Atopic Dermatitis

b) Deflazacort (Emflaza)—Corticosteroids – Immune Modulators – for Duchenne Muscular Dystrophy

c) Deutetrabenazine (Austedo)—Neurological Agents Miscellaneous for Huntington's Disease

d) Dupilumab (Dupixent)—Corticosteroids – Immune Modulators – Immune Modulators Subclass for Atopic Dermatitis

e) Insulin degludec/liraglutide (Xultophy)—Glucagon-Like Peptide-1 Receptor Agonist (GLP1RA)

f) Morphine sulfate ER (Arymo ER —Narcotic Analgesics and Combinations

g) Oxymetazoline (Rhofade)—Acne Agents – Topical Acne and Rosacea Agents Subclass

h) Plecanatide (Trulance)—GI-2 Miscellaneous Agents for chronic idiopathic constipation

i) Ribociclib (Kisqali)—Oral Oncologic Agents for Breast Cancer

j) Telotristat (Xermelo)—GI-2 Miscellaneous Agents for carcinoid syndrome diarrhea

3. Utilization Management Issues

a) Prior Authorization Criteria—New Criteria

- Non-Insulin Diabetes Drugs—Biguanides: metformin extended release (Fortamet, Glumetza)
- Diuretics Carbonic Anhydrase Inhibitor: dichlorphenamide
- (Keveyis)

b) Prior Authorization Criteria—Updated Criteria

- GI-2 Miscellaneous Agents: eluxadoline (Viberzi)
- Anticonvulsant and Anti-Mania Drugs: topiramate extended release (Qudexy XR)
- Non-Opioid Pain Syndrome Drugs: pregabalin (Lyrica)
- Hepatitis C Direct-Acting Antivirals: ledipasvir/sofosbuvir

- (Harvoni) and sofosbuvir (Sovaldi)
- Nasal Allergy Drugs: fluticasone/azelastine (Dymista)
- Sedative Hypnotic-1s—Newer Sedative Hypnotics: eszopiclone
- (Lunesta), and zolpidem ER (Ambien CR)
- Overactive Bladder (OAB) Drugs—mirabegron (Myrbetriq)

4. Re-Evaluation of Generic Non Formulary Agents
    a) Selective Serotonin Receptor Inhibitors
    b) Testosterone Replacement Therapies (TRT)
5. National Defense Authorization Act 2008, Section 703 Actions
6. 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

CAPT Edward Norton introduced himself as the Designated Federal Officer (DFO) for the Uniform Formulary (UF) Beneficiary Advisory Panel (BAP). The Panel has convened to comment on the recommendations of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee meeting, which occurred on May 11-12, 2017.

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

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

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

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

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

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

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

- The P&T Committee met for approximately 12 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 meetings, 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 meetings:

- 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.

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

Private Citizen Comments**:**

- Pfizer, Inc. submitted a written comment regarding the prior authorization criteria Eucrisa. The letter was presented to the Panel for review.

- Mr. Eric V. Busby, Scientific Director under the Global Medical Excellence Team at Allergen gave a presentation on the prior authorization for Rhofade. A summary of the presentation are as follows:

    1. Mr. Busby spoke about the newly proposed prior authorization of Rhofade and respectfully request further examination of the clinical data for the preferred treatment options within the Rosacea category.

    2. The first line products within the PA metronidazole and azelaic acid are used for rosacea. The focus and only FDA approved indication is treating the bumps and lesions or the papulars or pustulars that are associated with rosacea. They are not indicated for the persistent erythema that is associated with rosacea. As you may know, rosacea is a dermatological disease involving four major sub-types or manifestations. Evidence in the literature supports that disease progression may

occur from the most common sub-types to the persistent erythema to papulars or pustulars, ocular or even privitas rosacea.

3. The two key pathological factors associated with rosacea symptoms include the augmented immune responses and also neurovascular dysregulation. They are not mutually exclusive; however, one predominates over the other. If the augmented immune response is predominating then this is where the patients will develop the papulars and pustulars that are associated with rosacea. Metronidazole and azelaic acid targets this pathogenic process. If the neurovascular dysregulation is predominant then the patient develops the persistent or background erythema, and Rhofade targets this process.

4. Consensus recommendations from the American Acne and Rosacea Society recommend clinicians consider the two pathogenic factors and symptoms. They also note that alpha-agonists such as Rhofade to be an important independent category of topical agent in the treatment persistent diffused facial erythema.

5. According to the Cochran Collaboration Review 2015, metronidazole and azelaic acid were shown to be effective and safe in reducing rosacea symptoms, but their improvements tended after 3-6 weeks. The primary end point was focused more on the bumps and lesions. Erythema, generally speaking, was a secondary end point, but results were inadequately recorded. They were unable to demonstrate improvement beyond paralesional redness.

6. Therefore, these products are only FDA approved to treat the bumps and lesions. The clinical evidence does not support the use of persistent erythema. Rhofade is an alpha-1 adrenalceptor agonist that addresses the persistent erythema by causing basal constriction of the abnormally dilated vasculature under the skin. A pea-sized amount of Rhofade is applied to the entire face, once a day, has been shown to reduce facial erythema, the most common symptoms of rosacea. The effect of Rhofade is seen as early as day 1. Rhofade is safe and tolerable with no evidence of clinically relevant rebound following discontinuation of treatment. The most common adverse reaction was application site dermatitis, pruritis, and also worsening inflammatory lesions. All which were recorded in 1-2% of patients.

7. We ask that you consider the pathophysiological aspects of rosacea symptoms, further evaluate the clinical data for your preferred treatment options in your proposed PA criteria, and also consider adjusting or limiting the step-through requirements for Rhofade.

8. Mr. Busby thanks the Panel for their time and attention.

Chairman's Opening Remarks

Dr. Anderson welcomes everyone, states he has no further comments, and starts the meeting.

DRUG CLASS REVIEW PRESENTATION

(PEC Script – CAPT VONBERG)

GOOD MORNING. I am CAPT Edward VonBerg, 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, Deputy General Counsel.

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

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

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

- A brief overview of the relative clinical effectiveness analyses considered by the DoD P & T Committee. All reviews include but are not limited to the sources of information listed in 32 CFR 199.21 (e)(1) and (g)(5). Also note that 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.

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

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

- The Committee reviewed the following:

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

a) the Pulmonary 1-s Drug Class, Pulmonary Miscellaneous subclass – the drugs for idiopathic pulmonary fibrosis; and

b) the Ophthalmic Is, Dual-Acting Antihistamine/Mast Cell Stabilizers

A summary table of the UF drug class recommendations is found on pages 27-28 of the background document. It also contains the numbers of the unique utilizers affected by the recommendations.

2. The P&T Committee also evaluated 10 Newly Approved Drug per CFR 199.21 (g)(5) (recently approved drugs formerly known as Innovator Drugs), which are currently in pending status and available under terms comparable to non-formulary drugs.

3. We will also discuss Prior Authorizations (PAs) for 11 drugs in 9 drug classes.

   a) Non-Insulin Diabetes Drugs – metformin ER products

   b) Diuretic Carbonic Anhydrase Inhibitors

   c) Gastrointestinal-2 Miscellaneous Agents

   d) Anticonvulsant and Anti-Mania Drugs

   e) Non-Opioid Pain Syndrome

   f) Hepatitis C Direct Acting Antivirals

   g) Nasal Allergy Drugs

   h) Sedative Hypnotics

   i) Overactive Bladder Drugs

4. There was a re-evaluation of non-formulary generic drugs in the Selective Serotonin Reuptake Inhibitors and the Testosterone Replacement Therapies drug classes.

5. There was one drug under Section 703, National Defense Authorization Act (NDAA) for Fiscal Year 2008 reviewed at this meeting

- 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.

UNIFORM FORMULARY DRUG CLASS REVIEWS

I. UNIFORM FORMULARY CLASS REVIEWS

A. PULMONARY-1 DRUG CLASS: PULMONARY MISCELLANEOUS SUBCLASS

(CAPT VONBERG)

1. Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—Relative Clinical Effectiveness and Conclusion

Background—The IPF drugs have not been previously reviewed for UF status. Currently, there are manual prior authorization (PA) requirements in place since February 2016 for both nintedanib (Ofev) and pirfenidone (Esbriet).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

- IPF is difficult to diagnose and has limited therapeutic options. Nintedanib (Ofev) and pirfenidone (Esbriet) are the first therapeutic advances for the disease, and have different mechanisms of action. How Ofev and Esbriet slow the decline of lung function in IPF is not fully understood.

- There are no studies directly comparing Ofev and Esbriet. These two drugs may delay disease progression; however, the most appropriate subset of IPF patients who will respond to therapy and who will tolerate the adverse effects is difficult to predict.

- While neither agent is curative, FDA approval was based on studies showing Ofev and Esbriet may reduce the rate of inexorable decline in lung function that is the hallmark of IPF.

- Available meta-analyses suggest that Ofev and Esbriet favorably affect endpoints of lung function including forced vital capacity over 52 weeks. Overall, the available evidence suggests these two drugs have similar efficacy when compared to placebo.

- The most commonly reported adverse events for Ofev and Esbriet include gastrointestinal (GI) effects. Esbriet uniquely can cause rash/photosensitivity, while Ofev is rated as pregnancy Category D. Esbriet should not be used in patients with renal dysfunction, and is associated with more drug interactions.

- Both products are associated with significant discontinuation rates, and may require dosage reductions or temporary stoppage due to adverse effects.

2. Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—Relative Cost-Effectiveness Analysis and Conclusion

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

- CMA results showed that pirfenidone (Esbriet) was the most cost-effective IPF agent, followed by nintedanib (Ofev).

- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating pirfenidone (Esbriet) as formulary and step-preferred, with nintedanib (Ofev) as formulary and non-step-preferred, demonstrated the largest estimated cost avoidance for the Military Health System (MHS).

3. Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—UF Recommendation

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

- **UF and Step-Preferred:** pirfenidone (Esbriet)

- **UF and Non Step-Preferred:** nintedanib (Ofev)

- **NF:** no products

Note that as part of this recommendation, all new users of an IPF agent are required to try Esbriet first.

4. Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—Manual Prior Authorization (PA) Criteria

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) updating the current manual PA criteria to require a trial of pirfenidone (Esbriet) in new users, prior to use of nintedanib (Ofev). The step therapy requirement for a trial of Esbriet in new users is included in the manual PA criteria.

Updated PA Criteria

1. nintedanib (Ofev)

   Changes from the May 2017 meeting are in BOLD

   All new users of nintedanib (Ofev) are required to try pirfenidone (Esbriet) first.

   Pirfenidone (Esbriet) is the preferred IPF agent; coverage is approved for nintedanib (Ofev) if:

   - **The patient has had a trial of pirfenidone (Esbriet) and either:**

     a) **Failed therapy with Esbriet due to progression of IPF, e.g. improvement or effectiveness of therapy is defined by a less than 10% decline in percent predicted forced vital capacity (FVC) OR**

     b) **Experienced intolerable adverse effects (e.g., rash, photosensitivity; GI AEs) OR**

   - **The patient has clinical factors where Esbriet is not appropriate**

     a) **The patient is taking a drug which will interact with Esbriet that does not interact with Ofev [moderate to strong CYP inhibitors – CYP 450-1A2 (e.g., fluvoxamine)] OR**

     b) **The patient has end stage renal disease (ESRD) on dialysis**

5. Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—UF and PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) an effective date of the first Wednesday after a 30-day implementation.

6. Physician's Perspective

This was the first time reviewing the drug class. IPF is a very debilitating disease with a high mortality rate, and these two drugs don't improve survival. The goal of therapy is NOT to improve lung function, but to slow the rate of decline.

In terms of efficacy, the results from the individual clinical trials show that Esbriet and Ofev are very similar in efficacy. Current Military Health System

utilization is about 50-50 for Esbriet vs. Ofev. The average age for the patients in DoD is 75 years, and 91% of patients are over age 65.

The recommendation was unanimous to have both drugs remain on the formulary, with Esbriet as step-preferred. The intent of the step therapy is that in new patients, Esbriet should be tried first, if it is clinically appropriate. This requirement will be on the manual PA form. There are some differences in the adverse event and drug interaction profile, which was taken into account for the Prior Authorization criteria. Currently we have about 900 patients per quarter on Esbriet and Ofev, however, the step therapy requirement will only affect new patients with an Ofev prescription, which is about 150 patients per quarter.

We did survey three pulmonologists who treat patients with IPF. Their opinions were that prescribing should be limited to pulmonologists, and that combination therapy is not appropriate. These factors were already in the PA criteria. One provider felt that Esbriet was preferred over Ofev, but admitted that this was his opinion and was not definitive. The majority of providers prescribes only one drug, and don't switch from one product to another.

When we analyzed DoD data, we found that after 18 months, only 40% of Esbriet patients and 24% of Ofev patients were still taking the drugs. We don't know the reason why patients stopped therapy, whether it was due to death, adverse events or lack of efficacy– we don't have that data. However, based on these results, we are recommending that the PA criteria be renewed yearly, to ensure the patient is still benefitting from therapy.

7. Panel Questions and Comments

Dr. Bertin asked a question about the anticipated duration of the trial period.

CAPT VonBerg replied the renewal is one year.

Dr. Bertin clarified that he is referring to the step therapy trial. How long do patients need to try the medication?

CAPT VonBerg replied that is up to the physician.

Dr. Anderson asked whether the choice to use Esbriet or Ofev is simply based on prescriber preference.

Dr. Kugler and CAPT VonBerg both replied with yes.
There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria and UF and PA implementation plan for the Pulmonary-1 Drug Class.

- **Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—UF Recommendation**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

- **Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

- **Pulmonary-1 Drug Class: Pulmonary Miscellaneous Subclass: Idiopathic Pulmonary Fibrosis (IPF) Drugs—UF and PA Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

II. OPHTHALMIC-1s

(CAPT VONBERG)

1. Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—Relative Clinical Effectiveness and Conclusion

Background—The Ophthalmic-1 Dual Acting Antihistamine and Mast Cell Stabilizer (AH/MCS) Drug Class was previously reviewed for UF status in August 2010. Ketotifen (Zaditor, generic) is available over-the-counter (OTC) and was not included in the review.

Three products containing the active ingredient olopatadine are available. Olopatadine 0.1% (Patanol) is administered twice daily, is available as a generic formulation, and is the current BCF selection for the class. Olopatadine 0.2% (Pataday) has been marketed since 2004 and is administered once daily; generic formulations are expected later this year. Olopatadine 0.7% (Pazeo) entered the market in 2015 and is administered once daily; it was designated NF at the February 2016 meeting.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 1 opposed, 0 abstained, 0 absent) the following for the ophthalmic AH/MCS:

- The ophthalmic AH/MCS are the standard of care for treating the signs and symptoms of allergic conjunctivitis. Allergic conjunctivitis is a highly seasonal condition, and MHS utilization for the class reflects this variability.

- Clinical practice guidelines from the American Academy of Ophthalmology and the American Optometric Association recommend the AH/MCS as first-line therapy for acute and chronic allergic conjunctivitis. The guidelines do not prefer one product over another.

- A 2015 Cochrane review and 2016 meta-analysis concluded there is insufficient evidence to discern whether one AH/MCS is the more effective than another. Olopatadine may be more effective than OTC ketotifen, but less effective than alcaftadine; however, these differences among products may not be clinically relevant.

- In terms of efficacy and safety, head-to-head studies show olopatadine 0.1% (Patanol) is comparable to olopatadine 0.2% (Pataday). Olopatadine 0.7% (Pazeo) reduced ocular itching to a greater extent than olopatadine 0.2%; however, although these results were statistically significant 24 hours following administration (when the next daily dose is due), the result did not meet the threshold for clinical significance.

- With regard to safety and tolerability, the overall adverse event rate is low. All the products can cause burning, stinging, headaches, dry eye, blurred vision, and hyperemia. Bepotastine (Bepreve) may cause taste perversion in up to 25% of patients.

- There is no new data to change the conclusion from the previous review that the AH/MCS are highly therapeutically interchangeable.

2. Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—Relative Cost-Effectiveness Analysis and Conclusion

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

- CMA results showed that generic azelastine (Optivar) was the most cost-effective AH/MCS, followed by generic epinastine (Elestat), brand olopatadine 0.7% (Pazeo), generic olopatadine 0.1% (Patanol), brand olopatadine 0.1% (Patanol), brand emedastine (Emadine), brand bepotastine (Bepreve), brand alcaftadine (Lastacaft), and brand olopatadine 0.2% (Pataday).

- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating generic olopatadine 0.1% (Patanol), generic azelastine (Optivar), generic epinastine (Elestat), and brand olopatadine 0.7% (Pazeo) as UF, and brand emedastine (Emadine), brand bepotastine (Bepreve), brand alcaftadine (Lastacaft), and brand olopatadine 0.2% (Pataday) as NF, demonstrated the largest estimated cost avoidance for the MHS.

3. Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—UF Recommendation

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following, based on clinical and cost effectiveness:

- **UF:**

  a) olopatadine 0.1% (generic Patanol)

  b) olopatadine 0.7% (Pazeo)

  c) azelastine 0.05% (generic Optivar)

  d) epinastine 0.05% (generic Elestat)

- **NF:**

  a) olopatadine 0.2% (Pataday)

  b) alcaftadine 0.25% (Lastacaft)

  c) bepotastine 1.5% (Bepreve)

  d) emedastine 0.05% (Emadine)

4. Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—Manual PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for the dual acting AH/MCS. All new and current users of a NF product, olopatadine 0.2% (Pataday), Lastacaft, Bepreve, and Emadine, require a trial of two formulary products within the past 90 days, unless the patient has experienced intolerable adverse events from the formulary products, or is pregnant.

Full PA Criteria

Manual PA criteria apply to all new and current users of Lastacaft, Bepreve, Emadine, and olopatadine 0.2% (Pataday).

- The patient has ocular symptoms of allergic conjunctivitis AND

  a) The patient has tried and failed two formulary alternatives (olopatadine 0.1%, olopatadine 0.7% (Pazeo), azelastine, or epinastine) in the last 90 days, OR

  b) Use of two formulary alternatives (olopatadine, azelastine, or epinastine) has resulted in intolerable adverse effects, OR

  c) The patient is pregnant (for Lastacaft and Emadine only)

PA does not expire.

5. Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—UF and PA Implementation Plan

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

6. Physician's Perspective

These drugs treat the ocular itching caused by allergic conjunctivitis, which is generally a seasonal condition, and not a chronic problem. Patients will commonly use the eye drops during the spring allergy season, and then stop therapy until the next spring. MHS utilization shows this seasonal variation in use.

The drugs in the class are highly therapeutically interchangeable. The main recommendation here is that Pataday which was previously formulary, will now move to non-formulary status, and Pazeo will move to formulary status. We are basically just changing olopatadine formulations, since Patanol, Pataday, and Pazeo all contain the same active ingredient. Overall, almost 90% of the market share is from olopatadine (all formulations counted together).

Additionally, we are going to have the non-formulary drugs also have manual Prior Authorization criteria. Because of the seasonal variation in allergy symptoms, the recommendation is that both current and new patients will undergo the PA process – in other words, patients will not be grandfathered here. Approximately 33,000 patients will be affected by the PA, including about 29,000 patients currently receiving Pataday.

7. Panel's Questions and Comments

Mr. Du Teil asked about the person who opposed the relative clinical effectiveness conclusion.

Dr. Kugler replied that we utilize electronic voting and we think that the oppose vote was a mistake. We asked for comments. No one had comments regarding the relative clinical effectiveness criteria.

Ms. Le Gette asked why the committee did not place a true automated step therapy drug rather than just asking about the prior former usage of the manual PA. I do realize it's seasonal and only looking back 90 days for new and current users.

CAPT VonBerg replied that this approach will allow us to capture all of those patients.

There were no more questions or comments from the Panel. The Chair called for a vote on the UF Recommendation, Manual PA Criteria, and UF and PA implementation plan for the Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers.

- **Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—UF Recommendation**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

- **Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

- **Ophthalmic-1s: Dual Acting Antihistamines/Mast Cell Stabilizers—UF and PA Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

II. NEWLY APPROVED DRUGS PER CFR 199.21 (g)(5) (INNOVATOR DRUGS) (DR. ALLERMAN)

A. Newly Approved Drugs —Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions

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

1. Newly Approved Drugs UF Recommendation

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

- **UF:**

  a) deflazacort (Emflaza) – Corticosteroids – Immune Modulators – for Duchenne Muscular Dystrophy (DMD)

  b) deutetrabenazine (Austedo) – Neurological Agents Miscellaneous for Huntington's Disease

  c) dupilumab (Dupixent) – Corticosteroids – Immune Modulators – Immune Modulators Subclass for Atopic Dermatitis

  d) ribociclib (Kisqali) – Oral Oncologic Agents for Breast Cancer

  e) telotristat (Xermelo) – GI-2 Miscellaneous Agents

- **NF:**

  a) crisaborole (Eucrisa) – Corticosteroids – Immune Modulators – Immune Modulators Subclass for Atopic Dermatitis

  b) insulin degludec/liraglutide (Xultophy) – Glucagon-Like Peptide-1 Receptor Agonist (GLP1RA)

  c) morphine sulfate extended release (Arymo ER) – Narcotic Analgesics and Combinations

  d) oxymetazoline (Rhofade) – Acne Agents – Topical Acne and Rosacea Agents Subclass

  e) plecanatide (Trulance) – GI-2 Miscellaneous Agents

2. Newly Approved Drugs—PA Criteria

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

- Applying the same manual PA criteria for insulin degludec/liraglutide (Xultophy) in new and current users, as is currently in place for insulin glargine/lixisenatide (Soliqua) and the other non-step-preferred GLP1RAs. Patients must first try metformin or a sulfonylurea, and exenatide weekly

injection (Bydureon) and albiglutide weekly injection (Tanzeum) prior to Xultophy. Additionally, for Xultophy, patients are required to be on basal insulin at a dosage of less than 50 units daily.

- Applying the same step therapy and manual PA criteria for topical oxymetazoline (Rhofade) in new and current users as is currently in place for the non-step-preferred topical rosacea products. Patients must first try one generic metronidazole step-preferred formulation and topical azelaic acid prior to Rhofade.

- Applying PA criteria to the following: new and current users of crisaborole (Eucrisa), dupilumab (Dupixent), deflazacort (Emflaza), plecanatide (Trulance), and telotristat (Xermelo);and in new users of deutetrabenazine (Austedo) and ribociclib (Kisqali).

Full PA Criteria for the Newly Approved Drugs

a. Crisaborole (Eucrisa) – Corticosteroids – Immune Modulators – Immune Modulators Subclass

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

Manual PA Criteria: coverage will be approved if:

- Patient has mild to moderate atopic dermatitis AND

- Prescribed by a dermatologist AND

- Patient has a contraindication to, intolerability to, or failed treatment with at least one high potency / class 1 topical corticosteroid.

Off-label uses are NOT approved.

PA does not expire.

b. Dupilumab (Dupixent) – Corticosteroids – Immune Modulators – Immune Modulators Subclass

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

Manual PA Criteria: Coverage will be approved for initial therapy for 6 months if:

- Patient has moderate to severe or uncontrolled atopic dermatitis AND

- Patient must be 18 years of age or older AND

- Prescribed by a dermatologist AND

- Patient has a contraindication to, intolerability to, or failed treatment with at least **ONE** high potency / class 1 topical corticosteroid AND

- Patient has a contraindication, intolerability to, or failed treatment with at least **ONE** systemic immunosuppressant.

PA expires after 6 months.

Renewal PA Criteria: Coverage will be approved indefinitely for continuation of therapy if:

- The patient has had a positive response to therapy, e.g., an Investigator's Static Global Assessment (ISGA) score of clear (0) or almost clear (1)

Off-label uses are NOT approved.

c. Deflazacort (Emflaza) – Corticosteroids – Immune Modulators
Manual PA criteria apply to all new and current users of Emflaza.

Manual PA Criteria: Coverage will be approved for one year indefinitely if all criteria are met:

- Patient has a diagnosis of Duchenne Muscular Dystrophy AND

- Prescribed by a neurologist AND

- Patient is age 5 or greater AND

- Patient has tried prednisone for at least 6 months and has experienced at least one of the following adverse events:

  a) Unmanageable weight gain OR

  b) Patient has experienced severe behavioral adverse events that requires a reduction in prednisone dose

Off-label uses are NOT approved

.

PA does not expire.

d. Plecanatide (Trulance) – GI-2 Miscellaneous Drugs

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

Manual PA Criteria: Coverage approved if:

- Patient is ≥ 18 years of age AND
- Patient has clinically diagnosed chronic idiopathic constipation AND
- Patient does not have gastrointestinal obstruction AND
- Patient has failed or is intolerant to linaclotide (Linzess) AND
- Dual therapy with another guanylate cyclase-C agonist is not allowed.

Off-label uses are not approved.

PA expires in one year.

- PA criteria for renewal for new and current users: After one year, PA must be resubmitted. Continued use of Trulance will be approved if there has been improvement in constipation symptoms and NO dual therapy with another guanylate cyclase-C agonist.

Renewal PA criteria is limited to one year.

e. **Telotristat (Xermelo) – GI-2 Miscellaneous Drugs**

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

Manual PA Criteria: Coverage approved for one year if all criteria are met:

- Patient has diagnosis of carcinoid syndrome diarrhea.
- Patient has had an inadequate treatment response to at least a 3-month trial of somatostatin analog therapy.
- Telotristat must be used in combination with a somatostatin analog (i.e., octreotide or lanreotide).
- Patient has ≥ 4 bowel movements daily.

Off-label uses are NOT approved.

PA expires in one year.

- PA criteria for renewal for new and current users: After one year, PA must be resubmitted. Continued use of Xermelo will be approved when

  a) used in combination with a somatostatin analog,

  b) decrease from baseline in amount of average daily bowel movements,

  c) prescriber agrees to continue to assess the patient for severe constipation and abdominal pain and discontinue the medication if either develops,

  d) no severe constipation or abdominal pain develops.

- Renewal PA criteria is limited to one year.

f. **Deutetrabenazine (Austedo) – Neurological Agents Miscellaneous**
Manual PA criteria apply to all new users of Austedo.

Manual PA Criteria: Coverage approved for initial therapy for indefinitely if all criteria are met:

- Prescribed by or in consultation with a neurologist

- Patient has a diagnosis of chorea associated with Huntington's Disease

- Patient is not actively suicidal

- Patient does not have depression, or is being adequately treated for depression

- Patient does not have severe hepatic impairment

- Patient is not taking any of the following:

  a) MAOI inhibitor within the past 14 days

  b) Reserpine

  c) tetrabenazine (Xenazine) or another VMAT-2 inhibitor

- Patient has had an adequate trial of tetrabenazine for 12 weeks and had one of the following:

a) Experienced treatment failure

b) Experienced an adverse event that is not expected to occur with Austedo

PA expires in one year.

Manual PA Criteria (Renewal Criteria): Coverage approved indefinitely for continuation of therapy if all criteria are met:

- Patient has demonstrated improvement in chorea based on clinician assessment and is being monitored for depression and suicidal ideation

Off-label uses are NOT approved (Tourette's, tardive dyskinesia, dystonia).

g. **Oxymetazoline (Rhofade) – Topical Acne and Rosacea Agents: Miscellaneous Topical Agents**

Manual PA Criteria apply to all new and current users of Rhofade.
Automated PA Criteria:

The patient has filled a prescription for one generic topical step-preferred metronidazole product (1% gel, or 0.75% lotion, or 0.75% cream) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or TRICARE Mail Order Pharmacy) during the previous 180 days

Manual PA Criteria: If automated PA criteria are not met, Rhofade will be approved if:

The patient is at least 18 years of age and has the following diagnosis:

- For Rhofade, the patient has persistent facial erythema of rosacea

  AND

- The patient has tried and failed one generic step-preferred formulary topical metronidazole product (1% gel, 0.75% lotion or 0.75% cream)

  AND

- The patient has tried and failed topical azelaic acid 15%

PA expires in one year

Off-label uses are not approved

h. **Ribociclib (Kisqali) – Oral Oncologic Agents**

Manual PA criteria apply to all new users of Kisqali.

Manual PA Criteria: Kisqali is approved if:

- Patient has advanced (metastatic) estrogen receptor-positive (ER+) disease; AND
- Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
- The patient is postmenopausal woman and will be used as first-line endocrine therapy in combination with an aromatase inhibitor.

Off-label uses are not approved.

PA does not expire.

3. Newly Approved Drugs—UF and PA Implementation

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) an effective date upon signing of the minutes in all points of service, including the new PAs for dupilumab (Dupixent), crisaborole (Eucrisa), deflazacort (Emflaza), plecanatide (Trulance), telotristat (Xermelo), liraglutide/insulin degludec (Xultophy), deutetrabenazine (Austedo), oxymetazoline (Rhofade), and ribociclib (Kisqali).

4. Physician's Perspective

For the newly approved drugs recommended for non-formulary status, clinically and cost effective alternative therapies are available on the formulary. Additionally, we do consult with the appropriate specialists for some of the products that are in classes that have not been previously reviewed, or for some of the orphan drugs.

Manual PA criteria were recommended for 9 of the 10 newly approved drugs.

- For the drugs used to treat atopic dermatitis, PAs were recommended for both Eucrisa and Dupixent. We did reach out to the dermatologists who said that for atopic dermatitis, a trial of a high potency topical steroid is considered first line therapy. For Dupixent, we did recommend having the PA expire after six months with renewal requiring the patient to have a response to therapy. This was because in the clinical trials, there was only a 38% response rate for the primary endpoint.

- The PAs for Xultophy and Rhofade reflect the current step-therapy requirements in their respective classes (GLP1-RAs for Xultophy for diabetes, and topical acne and rosacea for Rhofade), since the P&T Committee has already reviewed these classes.

- The PAs recommended for the orphan drugs Emflaza, Austedo, and Kisqali are consistent with their FDA approved indications. Also, Kisqali has a similar mechanism of action as Ibrance, which has had a PA in place since November 2016.

- PAs were also recommended for Trulance and Xermelo, since other cost effective drugs are available to treat chronic idiopathic constipation and carcinoid syndrome diarrhea. For Xermelo, there is also renewal PA criteria recommended after one year, due to the 40% response rate for efficacy.

5. **Panel's Questions and Comments**

Dr. Anderson – noted regarding Rhofade that persistent facial erythema is a potential approval pathway in the prior authorization criteria. This should partially address concerns raised in the public comment.

Ms. Buchanan asked for clarification regarding Emflaza. You said for children under age 8 or greater, but the packet says age 5.

Allerman replied that the insert in the packaging stated that the requirement is that the child has to be at least 5. The studies for Emflaza were conducted in the 1990s, but that was one of the inclusion criteria for the study. This has not been studied in children younger than 5. Prednisone is the favorite. The child will be placed on prednisone when they are prescribed the medication.

Buchanan reiterated that it is age 5 not age 8.

Allerman confirmed it is age 5 not age 8.

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

- **Newly-Approved Drugs—UF Recommendation**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

- **Newly-Approved Drugs—PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

- **Newly-Approved Drugs—UF and Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

III. UTILIZATION MANAGEMENT—NON-INSULIN DIABETES DRUG: BIGUANIDES

(DR. ALLERMAN)

For the updates to the drugs that have existing manual PAs, we are going to simplify how these are presented. We will only read what the actual update was. Refer to your handout for the full PA criteria for all the drugs discussed.

A. Non-Insulin Diabetes Drug: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza—New Manual PA Criteria

Fortamet and Glumetza are branded formulations of metformin ER (Glucophage XR), which were designated as NF at the November 2010 meeting, and maintained as NF in August 2016. Glumetza and Fortamet are available in 500 mg and 1000 mg tablets while generic metformin ER products are available in 500 mg and 750 mg tablets.

Due to the significant cost differences between Fortamet and Glumetza and generic metformin ER, and the lack of clinically compelling benefits over generic metformin ER, the Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) manual PA in all new and current users of Glumetza and Fortamet. The patient will be required to try generic metformin ER first. Prior authorization will not expire.

Full PA Criteria:

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

The provider must explain why the patient cannot take two generic 500mg ER tablets separately (for patients taking requiring 1000 mg metformin ER).

PA will be approved if patient is on a dose-alternating schedule (e.g., 500 mg alternating with 1000 mg every other day).

PA does not expire.

Off-label uses are not approved.

B. Non-Insulin Diabetes Drug: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza—Manual PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the new manual PA for extended-release metformin (Fortamet, Glumetza, generics)

become effective on the first Wednesday after a 90-day implementation period in all points of service.

C. Physician's Perspective

Fortamet and Glumetza are considerably more expensive than generic metformin ER, and do not offer any clinical advantages over the generic. The PA criteria do take into account patients who have dose alternating schedules, since generic metformin ER is not available in a 1,000 mg tablet.

Approximately 6,500 patients will be affected by the PA requirements, since the PA will apply to both new and current users ("no grandfathering"). The committee was unanimous in recommending the PA criteria.

D. Panel Questions and Comments

Dr. Anderson asked if this is the strongest action we can take regarding these drugs.

Dr. Allerman replied correct. We have the non-formulary recommendation; we looked at prices again last summer; and we can't come up with a clinical reason. There is a significant cost different. That is our next step, to make everyone fill out a piece of paper.

Dr. Anderson agreed, in his opinion, it is wasteful spending on these drugs. There is no therapeutic advantage.

There were no more questions or comments from the Panel. The Chair called for a vote on the New Manual PA Criteria and Manual PA Implementation Plan for the Non-Insulin Diabetes Drugs: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza.

- **Non-Insulin Diabetes Drug: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza—New Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

- **Non-Insulin Diabetes Drug: Biguanides—Metformin Extended Release (ER), Fortamet, and Glumetza—Manual PA Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

IV. UTILIZATION MANAGEMENT—DIURETICS CARBONIC ANHYDRASE INHIBITOR

(DR. ALLERMAN)

A. Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis)—New Manual PA Criteria

Keveyis is an orphan drug approved for treating primary hyperkalemic or hypokalemic periodic paralysis, or related variants. The active ingredient dichlorphenamide was first marketed in 1958 under the brand name Daranide, but discontinued from the market. Keveyis was FDA-approved in August 2015, but just recently launched.

Acetazolamide is commonly used off-label for this condition, but only one published retrospective trial is available. FDA approval for Keveyis was based on two clinical trials enrolling a total of 65 patients. The mechanism of action of Keveyis for treating periodic paralysis is unknown.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) new manual PA criteria for Keveyis, requiring a diagnosis of hypo- or hyperkalemic periodic paralysis as outlined in the product labeling, and a trial of acetazolamide. Prior authorization will expire after two months. If the patient has responded to therapy, then Keveyis will be approved indefinitely.

Full PA Criteria:

Manual PA criteria apply to all new and current users of Keveyis for treatment of Hypo/Hyperkalemic Periodic Paralysis (HypoPP/HyperPP) and Related Variants.

Manual PA Criteria: Initial Therapy. Keveyis is approved for 2 months if the patient meets the following criteria (i, ii, iii, iv, and v):

i. Patient has a confirmed diagnosis of primary hypokalemic or hyperkalemic periodic paralysis by meeting at least ONE of the following (a, b, or c):

   a) Patient with HypoPP has had a serum potassium concentration of less than 3.5 mEq/L during a paralytic attack; OR for patient with HyperPP, patient has had an increase from baseline in serum potassium concentration of greater than or equal to 1.5 mEq/L during a paralytic attack; OR for patient with HyperPP, patient has had a serum potassium concentration during a paralytic attack of greater than 5.0 mEq/L;

      OR

   b) Patient has a family history of the condition; OR

c) Patient has a genetically confirmed skeletal muscle calcium or sodium channel mutation; AND

ii. Patient has had improvements in paralysis attack symptoms with potassium intake; AND

iii. Patient has tried and failed oral acetazolamide therapy (e.g., Diamox tablets, Diamox Sequels extended-release capsules, generics); AND

iv. According to the prescribing physician, acetazolamide therapy did not worsen the paralytic attack frequency or severity in the patient; AND

v. Keveyis is prescribed by or in consultation with a neurologist or a physician who specializes in the care of patients with primary periodic paralysis (e.g., muscle disease specialist, or Physical Medicine and Rehabilitation [PMNR]).

PA expires after two months.

Renewal Manual PA Criteria:

- Patients Continuing Therapy. Keveyis is approved indefinitely if the patient has responded to Keveyis (e.g., decrease in the frequency or severity of paralytic attacks) as determined by the prescribing physician.

Off-label uses are not approved.

B. Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis)—PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the new manual PA for dichlorphenamide (Keveyis) become effective on the first Wednesday after a 90-day implementation period in all points of service.

C. Physician's Perspective

This is a new version of an old drug from the 1950s that was originally used as a diuretic. It now has a very specific indication for patients with periodic paralysis caused by fluctuations in potassium levels, and was brought back to the market as an orphan drug. Acetazolamide (Diamox) has been used off label for this condition for several years, and has the same mechanism of action. Diamox does have some retrospective data supporting its use for periodic paralysis.

Manual PA criteria were recommended to ensure Keveyis is used in accordance to the package insert. We also did look at PA criteria from some commercial health care plans. The PA criteria will also recommend a trial of Diamox first.

So far we have one patient in DoD who has received a prescription for Keveyis. We will require that patient to go through the PA process, along with any new patients.

D. Panel Questions and Comments

There were no questions or comments from the Panel. The Chair called for the vote on the Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis) New Manual PA Criteria and PA Implementation Plan,

- **Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis)—New Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

- **Diuretics Carbonic Anhydrase Inhibitor: Dichlorphenamide (Keveyis)—PA Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

V. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA

(DR. ALLERMAN)

The P&T Committee recommended updated manual PA criteria for nine drugs from seven classes. Updates to the manual PA criteria were recommended for a variety of reasons, including expanded FDA-approved indications, FDA safety alerts, or availability of low cost generics for NF drugs in classes where there is existing step therapy.

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) updates to the current PAs for eluxadoline (Viberzi), topiramate ER (Qudexy XR), pregabalin (Lyrica), ledipasvir/sofosbuvir (Harvoni), sofosbuvir (Sovaldi), fluticasone/azelastine (Dymista), eszopiclone (Lunesta), and zolpidem ER (Ambien CR); and the P&T Committee recommended (12 for, 0 opposed, 0 abstained, and 4 absent) the updated manual PA criteria for mirabegron (Myrbetriq). The updated manual PA for all the drugs discussed will apply to new users.

A. Updated Manual PA Criteria

1. **Gastrointestinal-2 Miscellaneous Agents: Eluxadoline (Viberzi)**
   Viberzi was reviewed in February 2016 with manual PA criteria recommended. An update to the manual PA criteria was recommended, based on a recent FDA safety alert. Patients who have had a cholecystectomy will be excluded from using Viberzi.

Updated PA Criteria

- **Patient does not have a history of cholecystectomy.**

2. **Anticonvulsants and Anti-Mania Drugs: Topiramate ER (Qudexy XR)**
Qudexy XR was reviewed in May 2016 with manual PA criteria recommended. Criteria were updated to add the additional indication for migraine prophylaxis.

Updated PA Criteria

Changes from the May 2017 meeting are in BOLD and strikethrough

- Coverage approved **for Migraine prophylaxis in adults (Trokendi XR and Qudexy XR)**

- Coverage not approved for non-FDA approved indications, including weight loss

3. **Non-Opioid Pain Syndromes: Pregabalin (Lyrica)**

Lyrica was reviewed in November 2011 with step therapy and manual PA criteria recommended. A trial of gabapentin is required prior to use of Lyrica, except in patients with seizure disorders. The manual PA criteria were updated to require a trial of duloxetine in addition to gabapentin for disorders not related to seizures or post-herpetic neuralgia.

Updated PA Criteria

Changes from the May 2017 meeting are in BOLD and will apply to new users of Lyrica.

- Indication: Seizure disorder **and post-herpetic neuralgia** – (no changes to the criteria for these indications)

OR

- **Indication: Non-seizure related disorder (diabetic peripheral neuropathy and fibromyalgia)**

  a) The patient has tried and failed gabapentin therapy (trial of Gralise or Horizant does not qualify) **AND**

  b) Patient has tried and failed duloxetine

c) The patient has a contraindication to gabapentin or **duloxetine** that is not expected to occur with pregabalin

d) The patient experienced adverse events with gabapentin or **duloxetin**e that are not expected to occur with pregabalin

e) The patient previously responded to pregabalin and changing to gabapentin or **duloxetine** would incur unacceptable risk

4. Hepatitis C Virus Direct-Acting Antivirals: Ledipasvir/Sofosbuvir (Harvoni) and Sofosbuvir (Sovaldi)

The direct-acting antivirals were most recently reviewed for formulary status in February 2017. The manual PA criteria were updated to reflect FDA approval in children 12 years of age and older.

Updated PA Criteria for both ledipasvir/sofosbuvir (Harvoni) and sofosbuvir (Sovaldi)

Coverage approved for patients **≥ 12 years**

5. Nasal Allergy Drugs: Fluticasone/Azelastine (Dymista)

Dymista was reviewed in May 2014, with step therapy and manual PA criteria recommended. Currently, a trial of one step-preferred formulary nasal allergy drug (nasal formulations of generic fluticasone, flunisolide, azelastine, or ipratropium) is required prior to use of Dymista. Since the May 2014 class review, several nasal allergy drugs are now available in generic formulations, or OTC. Criteria were updated to include a trial of at least two formulary step-preferred drugs prior to use of Dymista.

Updated PA Criteria

Changes from May 2017 meeting are in BOLD

Manual PA Criteria: Dymista is approved (e.g., trial of azelastine 137 mcg, flunisolide, fluticasone propionate, azelastine, or ipratropium is NOT required) if:

- Patient has experienced any of the following issues with **at least two** of the following step-preferred nasal allergy drugs (fluticasone propionate, flunisolide, azelastine, or ipratropium), which is not expected to occur with the non-preferred nasal allergy drugs

  a) inadequate response to the step-preferred drugs

b) intolerable adverse effects (persistent epistaxis, significant nasal irritation, pharyngitis)

c) contraindication

6. Sedative Hypnotic-1s: Newer Sedative Hypnotics—Eszopiclone (Lunesta) and Zolpidem ER (Ambien CR)

Lunesta and Ambien CR were reviewed in May 2012 with the newer sedative hypnotics drug class, and both drugs are designated as UF and non-step-preferred. Step therapy for the class requires a trial of a step-preferred drug (zolpidem IR or zaleplon) prior to use of non-step-preferred agents. Cost-effective generic formulations of Lunesta and Ambien CR are now available.

The step therapy criteria and manual criteria for the newer sedative hypnotics were updated to remove step therapy for eszopiclone and zolpidem ER. Eszopiclone and zolpidem ER will be step-preferred agents in addition to zolpidem IR and zaleplon. Step therapy remains for non-step-preferred agents including Rozerem, Intermezzo, Edluar, Silenor, and Zolpimist. Belsomra and Hetlioz have additional manual PA criteria.

Updated PA Criteria

Changes from May 2017 meeting are in BOLD

Manual PA Criteria: Coverage is approved if: The patient has an inadequate response to, been unable to tolerate due to adverse effects, or has a contraindication to zolpidem IR, zaleplon, **zolpidem ER, or eszopiclone**.

7. OAB Drugs: Mirabegron (Myrbetriq)

The OAB drugs were most recently reviewed for formulary status in November 2012, with step therapy requiring a 12-week trial of one cost-effective generic formulation of tolterodine ER, oxybutynin ER, or trospium IR prior to use of the non-step-preferred drugs. Mirabegron was reviewed as a new drug at the May 2014 meeting, and was designated as UF and non-step-preferred. Since the previous P&T Committee review, several cost-effective generic formulations of other OAB drugs have entered the market.

Overactive bladder is characterized by a high placebo response rate, and benefits are seen with behavioral therapies. There do not appear to be clinically relevant differences in efficacy between mirabegron and the antimuscarinic OAB drugs, based on meta-analyses and clinical practice guidelines.

The manual PA criteria for mirabegron were updated to recommend a trial of two formulary step-preferred products first. The criteria will continue to

allow patients who are at significant risk for central nervous system effects from antimuscarinic drugs to receive mirabegron. The criteria were also updated to reflect package insert cautions regarding use in patients with compromised renal function. Additionally, a trial of behavioral interventions (including pelvic floor muscle training in women and bladder training) is recommended, based on the clinical practice guidelines.

Updated PA Criteria

C**hanges from May 2017 meeting are in BOLD**

Manual PA Criteria—If automated criteria are not met, Myrbetriq is approved if:

1. Patient has confirmed diagnosis of OAB with symptoms of urge incontinence, urgency, and urinary frequency **AND**

2. **Patient has tried and failed behavioral interventions to include pelvic floor muscle training in women, and bladder training, AND**

3. Patient has had a 12-week trial with **2** formulary step-preferred products and had therapeutic failure **OR**

4. Patient has experienced central nervous system AEs with oral OAB medications **OR** is at increased risk for such central nervous system effects due to comorbid conditions or other medications, **AND**

5. **Patient does not have a creatinine clearance (CrCl) < 15 mL/min OR**

6. If CrCl 15-29 mL/min, dosage does not exceed 25 mg daily

B. Updated Manual PA Criteria PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) updates to the current PAs for eluxadoline (Viberzi), topiramate ER (Qudexy XR), pregabalin (Lyrica), ledipasvir/sofosbuvir (Harvoni), sofosbuvir (Sovaldi), fluticasone/azelastine (Dymista) and the step therapy changes for eszopiclone (Lunesta) and zolpidem ER (Ambien CR) and recommended (12 for, 0 opposed, 0 abstained, 4 absent) the manual PA update for mirabegron (Myrbetriq) become effective upon signing of the minutes in all points of service.

C. Physician's Perspective

These updates to existing PA criteria are done routinely at every P&T meeting to take into account either new indications (Qudexy XR for migraine prophylaxis, or the Hepatitis C drugs with a new pediatric indication), or safety warnings from the FDA (Viberzi). We also monitor prices of generic drugs in classes where we have existing

step therapy requirements. For the sedative hypnotics, the change was made to put more cost effective generic formulations in front of the step.

D. Panel Questions and Comments

Dr. Anderson had a question regarding the Lyrica criteria. If the beneficiary were already taking an antidepressant or SSRI, would the beneficiary be required to take duloxetine per the manual PA.?

Dr. Allerman replied that since Lyrica is not approved for depression, we were specifically looking for gabapentin or duloxetine. Duloxetine does have indications as previously discussed.

Dr. Anderson asked if someone were already on Prozac, would it be a problem to take both.

Dr. Allerman replied that they would probably have the PA approved for Lyrica if they met the requirement. I don't recall us going back to look at or combinations in anti-depressant therapies with Lyrica. I do not have a good answer right now.

Dr. Anderson asked her to follow up on that. His concern would be forcing someone in a situation where they were taking two (2) SSRIs.

Dr. Allerman replied that if they've had a contraindication, that would apply in this case and the beneficiary would not be required to use two (2) SSRIs in combination.

There were no more questions or comments. The Chair called for a vote on the updated Manual PA Criteria and PA Criteria Implementation Plan.

- **Updated Manual PA Criteria**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

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

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

VI. RE-EVALUATION OF NF GENERICS

(CAPT VONBERG)

A. Re-evaluation of Generics—Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions

The P&T Committee reviewed the current utilization, formulary status, generic availability, comparative clinical effectiveness, and relative cost effectiveness,

including the weighted average cost per unit, for all generically available NF agents in two previously reviewed UF drug classes: the antidepressants, and the testosterone replacement therapies.

The P&T Committee concluded that for the drug classes, there was no new pertinent efficacy or safety information to change the clinical effectiveness conclusions from when the classes were originally reviewed for UF placement. Specific comments, including the results of comparative cost reviews, are below:

- *Selective Serotonin Reuptake Inhibitors (SSRIs): Fluoxetine tablets and capsules* Fluoxetine is available in several formulations, including tablets and capsules, products with special packaging for Premenstrual Dysphoric Disorder (PMDD) (Sarafem) and a higher dosing strength for weekly administration (Prozac Weekly). Fluoxetine capsules are substantially more cost effective than these other formulations of fluoxetine. The vast majority of utilization across all POS is for the lowest cost generic fluoxetine capsules.

- *Testosterone Replacement Therapy (TRT):* This class was last reviewed in August of 2012, and the P&T Committee agreed there are no clinically relevant differences in efficacy or safety among available products, since they all contain testosterone. Fortesta (testosterone gel) was designated as UF and the sole step-preferred product. Androgel 1% and 1.62% gel were designated as NF and non-step-preferred. As of May 2017, a number of the TRT products have become generically available, including Fortesta, Testim, Androgel 1% gel, and Androgel 1.62% gel. However, only generic Androgel 1% is now comparable to Fortesta in terms of weighted average cost across points of service and less costly than Fortesta at MTFs.

B. Re-evaluation of Generics—UF Recommendations and Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 0 absent) the following actions, to become effective upon signing of the minutes:

- Selective Serotonin Reuptake Inhibitors: All fluoxetine capsules currently designated as NF will be returned to UF status.

- Testosterone Replacement Therapies: Generic Androgel 1% gel will be returned to UF status and designated as step-preferred, with appropriate changes made to PA criteria to require an unsuccessful trial, contraindication, or intolerance to either Fortesta or generic Androgel 1% before receiving a non-preferred product.

C. Physician's Perspective

- We are continuing to go through all the classes evaluated several years ago to assess new clinical and cost information for the products that are non-formulary that now

have generics available. The last time this topic was presented to the panel was from the August 2016 P&T meeting.

- For the classes reviewed (the antidepressants and the testosterone replacement therapies), the recommendations for which generics remain NF and which should go back to UF status was based on cost effectiveness. The generic fluoxetine capsules and the generic Androgel 1% formulation are now recommended to change to UF status.

D. Panel Questions and Comments

There were no questions or comments from the Panel. The Chair called for a vote on the UF Recommendation and Implementation plan for the Re-evaluation of Generics.

- **Re-evaluation of Generics—UF Recommendations and Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

VII. SECTION 703, NATIONAL DEFENSE AUTHORIZATION ACT (NDAA) FOR FISCAL YEAR (FY) 2008

(CAPT VONBERG)

A. Section 703, NDAA FY08—Drugs Designated NF

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

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) the following product be designated NF on the UF:

- CSL Behring LLC: antihemophilic factor, recombinant single chain (Afstyla) 500 units, 1000 units, 2000 units, and 3000 units injection

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

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) the following pre-authorization criteria for Afstyla:

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

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

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

Should the mail order requirement impact availability of a drug, the P&T Committee will allow an exception to the Section 703 rule. The following drug will not be available in the Mail Order:

- Afstyla (antihemophilic factor, recombinant single chain), 500 units, 1000 units, 2000 units, and 3000 units subcutaneous injection is only available in the Retail Network.

C. Section 703, NDAA FY08—Implementation Plan

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) an effective date of the first Wednesday after a 90-day implementation period for Afstyla and DHA send letters to beneficiaries affected by this decision.

D. Physician's Perspective

(Normally no comments for Dr. Kugler on the Section 703 drugs)

E. Panel Questions and Comments

Ms. Le Gette asked for clarification. The drug is only limited to retail. Is it just moving to non-formulary or is there a requirement for a prior authorization?

CAPT VonBerg replied the non-formulary normally would be restricted to one point of service, but now allowing it to be dispensed at retail.

Ms. Le Gette replied that she's trying to understand is there a prior authorization but isn't available in mail order.

CAPT VonBerg replied the legalese and interpretation is that it will be allowed in retail.

There were no more questions or comments from the Panel. The Chair called for a vote on the Section 703, NDAA FY08 Drugs Designated NF.

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

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

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

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

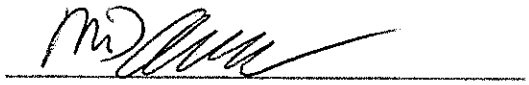
- **Section 703, NDAA FY08—Implementation Plan**

  Concur: 9 Non-Concur: 0 Abstain: 0 Absent: 1

Anderson thanks the Panel and the P&T Committee for all of the great work, and on behalf of TRICARE beneficiaries, thanks you.

The DFO adjourns the meeting.

(Meeting concludes)



Dr. Michael Anderson, Chair UF BAP

Brief Listing of Acronyms Used in the 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.

- AE – Adverse Events
- AH/MCS – Adverse Events
- BCF – Antihistamine/Mast Cell Stabilizer
- BIA – Budget Impact Analyisis
- CFR – Code of Federal Regulations
- CMA – Cost-Minimization Analysis
- CR – Extended Release
- CYP - Cytochrome
- DHA – Defense Health Agency
- DMD = Duchenne Muscular Dystrophy
- DoD – Department of Defense
- ER – Extended Release
- ER+ - Estrogen Receptor - Positive
- ESERD – End Stage Renal Disease
- FDA – Food & Drug Administration
- FVC – Forced Vital Capacity
- FY – Fiscal Year
- g - gram
- GI - Gastrointestinal
- GI AE – Gastrointestinal Adverse Events
- GI-2 – Gastrointestinal 2
- GLP1RA – Glucagon-Like Peptide-1 Receptor Agonist
- HER2 – Human Epidermal Growth Receptor 2
- IPF – Idiopathic Pulmonary Fibrosis
- IR – Insulin Resistance
- ISGA – Investigator’s Static Global Assessment
- LLC – Limited Liability Company
- MAOI – Monoamine Oxidase Inhibitors
- mEq/L – mil equivalent per liter
- mg - milligram
- MHS – Military Health System
- Ml - Milliliter
- MTF – Military Treatment Facility
- NDAA – National Defense Authorization Act
- NF – Non Formulary
- OAB – Overactive Bladder

- OTC – Over the Counter
- PA – Prior Authorization
- PMDD – Premenstrual Dysphoric Disorder
- PMN – Physical Medicine and Rehabilitation
- POS – Point of Service
- PP – Periodic Paralysis
- SSRI – Selective Serotonin Reuptake Inhibitors
- SU - Sulfonylurea
- TRICARE – Healthcare Network
- TRT – Testosterone Replacement Therapy
- UF – Uniform Formulary
- VMAT-2 – Vesicular Monoamine Transporter 2
- XR – Extended Release