EXECUTIVE SUMMARY

Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) Comments
31 July 2014

I. UF DRUG CLASS REVIEWS – NASAL ALLERGY DRUGS

A. Nasal Allergy Drugs – UF Recommendation

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following for the Nasal Allergy Drugs, based on the high degree of therapeutic interchangeability and on cost effectiveness:

- UF and step-preferred ("in front of the step"): generic Astelin 137 mcg, Nasarel, Nasonex, and Atrovent.
- NF and non-preferred ("behind the step"): Astepro, QNASL, Beconase AQ, Omnaris, Zetonna, Rhinocort Aqua, Veramyst, Dymista, Nasonex, and Patanase.
- This recommendation includes step therapy, which requires a trial of a generic product (Astelin 137 mcg, Nasarel, Nasonex, Atrovent) in all new and current users of the Nasal Allergy Drugs who are older than 4 years. In other words, there is no grandfathering for patients older than 4.
- Generic formulations of Nasonex are expected later in 2014. When the generics to Nasonex become cost-effective relative to the step-preferred agents, the generic will become step-preferred without further action by the P&T Committee, Beneficiary Advisory Panel, or Director, DHA. A generic agent is cost-effective relative to step-preferred agents when its total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the step-preferred agent.

B. Nasal Allergy Drugs – PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) automated (step therapy) and manual PA criteria in all new and current users of Astepro, QNASL, Beconase AQ, Omnaris, Zetonna, Rhinocort Aqua, Veramyst, Dymista, Nasonex, and Patanase who are older than 4 years of age. A trial of a generic product (Astelin 137 mcg, Nasarel, Flonase, or Atrovent) is required before the non step-preferred drugs.

Automated PA criteria: The patient has filled a prescription for generic product (Astelin 137 mcg, Nasarel, Flonase, or Atrovent) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria: The non-formulary drugs, Astepro, Beconase AQ, QNASL, Rhinocort Aqua, Zetonna, Omnaris, Veramyst, Dymista, Nasonex, or Patanase is approved (e.g., trial of a generic product is NOT required) if:

- Patient has experienced any of the following issues with **at least one** of the following step-preferred Nasal Allergy Drugs (generic Astelin 137 mcg, Nasarel, Flonase, or Atrovent) which is not expected to occur with the non-preferred Nasal Allergy drug:
  - Inadequate response to the step-preferred drugs
  - Intolerable adverse effects (persistent epistaxis ("*nose bleed*"), significant nasal irritation, pharyngitis ("*sore throat*")
  - Contraindication ("*a contraindication is the opposite of 'indication' so it means a reason to not give a drug, usually an allergy or certain medical condition.")*
  - No formulary alternative for the following
    - For Rhinocort Aqua: patient is pregnant ("*Rhinocort is the only Nasal Allergy drug that is pregnancy category B, which carries a lower risk of harm to the fetus than the other products.*")
    - For Beconase AQ and Nasonex: patient has nasal polyps and cannot be treated with one of the step-preferred products ("*nasal polyps are non-cancerous growths in the nose (like grape clusters) which can cause stuffiness and loss of the sense of smell*").

C. Nasal Allergy Drugs – UF and PA Implementation Period

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

Summary of Physician Perspective:

The P&T Committee has reviewed this drug class 3 times, and now there are some new generics, plus an over-the-counter product.

There was no evidence to suggest that any one product within a class is better at controlling allergy symptoms than another. Generally, the nasal steroids are used 1st line, and the nasal antihistamines are used 2nd line. The nasal steroids take about 2 weeks to show effect, and the nasal antihistamines have a much quicker onset of action. However, commonly you'll have the patient start the nasal steroid a couple of weeks before allergy season starts, so that it is effective when the patient starts to have symptoms.
There was no controversy with the decision. There is "no grandfathering" here – all patients have to try one of the preferred generics. However, for most patients, these drugs are taken on a seasonal basis during allergy season, and not taken year round. DoD

utilization reflects this, since there are just as many patients starting a nasal allergy drug (92,000 new starts) as there discontinuations (90,000) per quarter.

The Committee did take into account some of the differences in the FDA-approved labeling – that is why the step therapy and "no grandfathering" does not apply to children younger than 4 years of age; Flonase is approved for 4 years olds, and Nasonex is approved for children as young as 2. A pediatrician is on the Committee and he agreed with the recommendation.

Also, for the step therapy criteria, the Committee recognized the "safer" pregnancy category rating for Rhinocort Aqua, and also that Nasonex is FDA-approved for patients with polyps. If a patient has adverse effects from Flonase, including nosebleeds, that is also in the PA criteria as a reason to receive a branded product.

Generic Flonase and the other generics to Astelin, Nasalide and Atrovent are the preferred products for the step therapy. Flonase has the highest utilization in DoD. The Committee did realize that currently Nasonex is 2nd in utilization for the class and that the majority of these patients are at the MTFs, and that the recommendation will affect about 19,000 patients. As soon as cost-effective generics to Nasonex come out, the Committee will act quickly and move the generic in front of the step.

Summary of Panel Vote/Comments:

The Panel asked if the P&T Committee gave any consideration to a trial of multiple agents rather than one agent. More specifically, it looks as if a patient can start with the antihistamine, Astelin, and get to a nasal steroid without a trial of Fluticosone.

In response, the presenter stated that the Committee did discuss the requirement of a trial of multiple agents but decided to a trial of one agent. Meade replies the discussion took place, and the committee decided to go with the one.

Without further discussion, the Chair called for a vote on the Nasal Allergy Drugs.

D. Nasal Allergy Drugs – UF Recommendation

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

Director, DHA:

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

E. Nasal Allergy Drugs – PA Criteria

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

Director, DHA:

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

F. Nasal Allergy Drugs – UF and PA Implementation Plan

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

Director, DHA:

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

II. UF DRUG CLASS REVIEWS – INHALED CORTICOSTEROIDS

P&T Committee Comments

A. Inhaled Corticosteroids (ICS) – UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following for the inhaled steroids, based on the high degree of therapeutic interchangeability and cost effectiveness:

- UF and step-preferred ("in front of the step"): Flovent Diskus and Flovent HFA
- NF and non-preferred ("behind the step"): QVAR, Pulmicort Flexhaler, Alvesco, Aerospan, and Asmanex Twisthaler
- This recommendation includes step therapy, which requires a trial of Flovent Diskus or Flovent HFA in all new users of QVAR, Pulmicort Flexhaler, Alvesco, Aerospan, or Asmanex Twisthaler who are older than 12 years.
- Budesonide nebulized solution (Pulmicort) was reviewed in 2009 and was not part of the class review for this meeting; it remains on the UF and is not subject to step therapy.

B. Inhaled Corticosteroids (ICS) – PA Criteria

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) automated (step therapy) and manual PA criteria in all new users of QVAR, Pulmicort Flexhaler, Alvesco, Aerospan, or Asmanex Twisthaler who are older than 12 years of age. A trial of Flovent Diskus or Flovent HFA is required before the non-step preferred drugs.

Automated PA criteria: The patient has filled a prescription for Flovent Diskus or Flovent HFA at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria: QVAR, Pulmicort Flexhaler, Alvesco, Aerospan, and Asmanex Twisthaler is approved (e.g., trial of Flovent Diskus or Flovent HFA is NOT required) if:

- Patient has experienced any of the following issues with Flovent Diskus or Flovent HFA, which is not expected to occur with the non-preferred ICS:
  - Inadequate response to the step preferred drugs
  - Intolerable adverse effects (patient has a history of adrenal suppression and the request is for Alvesco)
  - Contraindication
  - Patient previously responded to non-formulary agent and changing to a formulary agent would incur unacceptable risk
  - No formulary alternative for the following: Pulmicort Flexhaler: patient is pregnant

C. Inhaled Corticosteroids (ICS) – UF and PA Implementation Plan

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

Summary of Physician Perspective:

This class has been reviewed once before, back in 2009. There were no new products approved by the FDA since the last review.

The combination inhalers (inhaled steroid plus a long-acting beta agonist) were reviewed by the Committee in February of this year. Advair, which has Flovent as the steroid component was chosen as the preferred product. The recommendation for the inhaled steroids to have Flovent as the preferred product is consistent with the previous decision for the combination inhalers. Flovent by far has the highest utilization in the class. Some of the products recommended for non-formulary use have very low utilization (for example Aerospan).

Patients are "grandfathered" here – the step therapy only applies to new patients. When the Committee looked at the cost avoidance, if there had been "no grandfathering", it would have affected a lot more patients without generating a lot of cost savings.
The step therapy does not apply to children 12 years and younger. This is conservative, because when we looked at the utilization in kids, children younger 8 years comprised the

majority of use. Out of 54,000 total users in the ICS class, about 17,000 are younger than 12 years of age. However, there are only 3,000 children younger than 12 who are a non-Flovent user. The pediatrician on the Committee agreed with the recommendation.

Summary of Panel Vote/Comments:

There were no questions or comments from the Panel. Without further discussion, the Chair called for a vote on the Inhaled Corticosteroids drugs.

D. Inhaled Corticosteroids (ICS) – UF Recommendation

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

Director, DHA:

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

E. Inhaled Corticosteroids (ICS) – PA Criteria

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

Director, DHA:

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

F. Inhaled Corticosteroids (ICS) – UF Implementation Plan

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

Director, DHA:

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

III. UF DRUG CLASS REVIEWS – OSTEOPOROSIS DRUGS: ORAL BISPHOSPHONATES SUBCLASS

P&T Committee Comments

A. Osteoporosis Drugs: Oral Bisphosphonates Subclass – UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following, based on the high degree of therapeutic interchangeability and cost-effectiveness:

- UF and step-preferred (e.g., "in front of the step"): generic Fosamax

- UF and non-step-preferred (e.g., "behind the step"): generic Boniva
- NF and non-step-preferred: Actonel, Atelvia, Binosto, and Fosamax Plus D
- This recommendation includes step therapy, which requires the following:
  - A trial of generic Fosamax is required prior to use of generic Boniva only in new users, as the patient impact is less than if all current and new users were affected by the step *(existing patients using Boniva will be 'grandfathered'* ")
  - A trial of generic Fosamax is required prior to use of Actonel, Atelvia, Binosto, and Fosamax Plus D in all new and current users. (*"Patients are not grandfathered here"*)

B. Osteoporosis Drugs: Oral Bisphosphonates Subclass – PA Criteria

P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) automated (step therapy) and manual PA criteria in all new users of generic Boniva, and all new and current users of Actonel, Atelvia, Binosto, and Fosamax Plus D. A trial of alendronate is required before the non-step-preferred drugs.

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

AND

Manual PA criteria—ibandronate, Actonel, Atelvia, Binosto, and Fosamax Plus D is approved (e.g., trial of alendronate is NOT required) if:

- Patient has experienced any of the following issues with alendronate, which is not expected to occur with the non-preferred oral bisphosphonates:
  - Intolerable adverse effects
    - » Patient requires once monthly ibandronate or Actonel 150 mg due to gastrointestinal adverse events from alendronate weekly dosing
    - » Patient has experienced significant adverse effects from formulary agents
    - » For Binosto: No alternative formulary agent and patient has swallowing difficulties and cannot consume 8 oz of water and has no sodium restrictions
    - » For Fosamax Plus D: No alternative formulary agent and patient cannot take alendronate and vitamin D separately
  - Contraindication

C. Osteoporosis Drugs: Oral Bisphosphonates Subclass –UF and PA Implementation Plan:

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

Summary of Physician Perspective:

This drug class was last reviewed back in 2008. There has been a steady decline in MHS utilization of the bisphosphonates, most likely due to safety concerns.

Generic Fosamax was recommended as the preferred product, and it currently has the highest utilization in the subclass.

Boniva is recommended to remain Uniform Formulary, but be subject to step therapy. However, existing Bonvia users will be "grandfathered", due to the convenience of once monthly dosing, compared to the once weekly dosing with Fosamax and Actonel.

Overall, adherence to the bisphosphonates is poor, and the Committee did take into consideration a study done in 2008 showing improved adherence in DoD patients taking Boniva (about a 20% improvement). Another reason to grandfather the Boniva patients is that the majority of use is at the MTFs, and "grandfathering" impacted significantly fewer patients than having "no grandfathering" (about 25,000 fewer patients affected). Additionally, we are expecting the price of the generic Boniva to drop.

For the other drugs, Actonel, Atelvia, Binosto, and Fosamax Plus Vitamin D, there is no grandfathering, and they are recommended for non-formulary placement.

Fosamax Plus Vitamin D is now recommended for non-formulary placement. There are no generics available. At one time, before the regular Fosamax was available in a generic, we were getting the Vitamin D essentially for free, but this is no longer the case. Inexpensive OTC Vitamin D products that are taken daily are available. One of the members of the Committee is an endocrinologist, and he agreed with the recommendations.

Summary of Panel Vote/Comments:

There were no questions or comments from the Panel members. Without further discussion, the Chair called for a vote on the Osteoporosis Drugs.

D. Osteoporosis Drugs: Oral Bisphosphonates Subclass – UF Recommendations

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

Director, DHA:

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

E. Osteoporosis Drugs: Oral Bisphosphonates Subclass – PA Criteria

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

Director, DHA:

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

F. Osteoporosis Drugs: Oral Bisphosphonates Subclass – UF Implementation Plan

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

Director, DHA:

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

IV. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

A. Hepatitis C Virus Drugs: Sofosbuvir tablets (Sovaldi) UF Recommendation

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

- Sovaldi be designated with formulary status on the UF. Patients are encouraged to fill Sovaldi prescriptions at Military Treatment Facilities (MTFs) or Mail Order Pharmacy points of service (POS), and
- Sovaldi, and the other Direct Acting Agents Incivek and Victrelis, be added to the TRICARE Specialty Drug list to facilitate recapture from the Retail Network to the Mail Order Pharmacy.

CAPT Downs interjects with a correction regarding relative clinical effectiveness. The P&T Committee voted (16 for, 0 Against, 0 Abstained, 1 Absent)

B. Hepatitis C Virus Drugs: Sofosbuvir tablets (Sovaldi) Prior Authorization Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for Sovaldi for new users, consistent with guidelines and FDA-approved labeling. Prior authorization will expire after 12 or 24 weeks for Sovaldi, based on the treatment regimen selected.

Manual PA Criteria:

- Age ≥ 18
- Has laboratory evidence of chronic HCV infection
- Has laboratory evidence of HCV with the appropriate genotype
  - State the HCV genotype on the PA form.
- Sovaldi is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.
- The patient is not co-infected with Hepatitis B virus (HBV).
- Sovaldi is not prescribed as monotherapy; ribavirin with or without PEG-interferon is also prescribed

Treatment Regimens and Duration of Therapy

- Treatment and duration of therapy are approved for the following regimens outlined below, based on HCV genotype or unique population.

Genotype 1

- Approved in patients who meet ONE of the following criteria: (1 or 2)
  1. Interferon eligible: Sovaldi + interferon + ribavirin for 12 weeks
  2. Interferon ineligible: Sovaldi + Olysio for 12 weeks
- Interferon ineligible is defined as ONE of the following:
  1. Intolerance to interferon (patient has previously taken interferon)
  2. Autoimmune hepatitis or other autoimmune disorders
  3. Hypersensitivity to peginterferon or any of its components
  4. Decompensated hepatic disease
  5. History of depression or clinical features consistent with depression
  6. Baseline CBC: neutrophil count < 1,500/μ or PLTs < 90,000/μ or Hgb<10 g/dl *("these are standard laboratory blood tests drawn to see if the patient has anemia, a higher risk of bleeding, or is at risk of infection")*
  7. History of preexisting cardiac disease

Genotype 2

- Sovaldi + ribavirin approved for 12 weeks

Genotype 3

- Approved in patients who meet ONE of the following criteria: (1 or 2):
  1. Sovaldi + ribavirin approved for 24 weeks
  2. Sovaldi + ribavirin + interferon approved for 12 weeks as an alternative in cirrhotic individuals or treatment experienced

Genotype 4

- Sovaldi + ribavirin+ interferon approved for 12 weeks

Regimen other than those listed above:

- Explain the rationale for treatment and duration of therapy. Consult the guidelines for new updates and guidelines.

While we are on the topic of Hepatitis C, we will also discuss PA criteria for three other DAAs – Incivek, Victrelis and Olysio.

C. Hepatitis C Virus Drugs: Incivek and Victrelis Prior Authorization Criteria

PA criteria for Incivek and Victrelis were recommended at the November 2012 P&T Committee meeting. Because of the new the AASLD/IDSA guidelines, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revised PA criteria for Victrelis and Incivek for new users. Current users of boceprevir or telaprevir are allowed to complete their course of therapy without interruption.

Manual PA Criteria:

Incivek and Victrelis are NO LONGER RECOMMENDED for ANY HCV treatment by the guidelines.

- Although regimens of PEG-interferon and ribavirin plus Incivek or Victrelis for 24 to 48 weeks using response-guided therapy are also FDA-approved; they are **markedly inferior** to the currently available regimens.
- Incivek and Victrelis regimens are associated with higher rates of serious adverse events than recommended current regimens with Sovaldi.
- Consider treatment with Sovaldi-containing regimens OR future highly effective pan-genotypic (*"covering all types of HCV"*) DAA combination regimens that are interferon-free.
- The justification and dosing/duration for Incivek and Victrelis must be documented (e.g., allergic to all other known regimens; inability to wait for treatment).

Prior authorization will expire after 12 weeks for Incivek and 44 weeks for Victrelis.

D. Hepatitis C Virus Drugs: Olysio Prior Authorization Criteria

Olysio is a Direct Acting Agent approved by the FDA in December 2013. It will be reviewed as a new drug at an upcoming meeting.

Olysio is indicated for use with ribavirin and PEG interferon, but the guidelines recommend a non-FDA-approved regimen with Sovaldi and ribavirin as an alternative treatment for genotype 1 patients who are ineligible to take interferon.

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for new users of simeprevir (Olysio) consistent with guidelines.

Manual PA Criteria:

- Age ≥18
- Has laboratory evidence of chronic HCV (quantified viral load above undetectable)
- Has laboratory evidence of genotype 1 HCV infection
- The patient HCV genotype 1a without any indication of resistance.
- Is not co-infected with HIV or Hepatitis B Virus
- The patient has not previously used a HCV protease inhibitor (Victrelis, Incivek, or Olysio)
- Simeprevir is not approved for monotherapy
    - The guidelines recommend a regimen of Olysio plus Sovaldi either with or without ribavirin for 12 weeks.
- The patient is interferon ineligible. Interferon ineligible as defined previously

Prior authorization will expire after 12 weeks.

E. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio Prior Authorization Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of no later than the first Wednesday after a 30-day implementation period in all POS.

Summary of Physician Perspective:

There was a lot of discussion on the topic of Hepatitis C, however, there was no question that Sovaldi has advantages over the first drugs in the class, Incivek and Victrelis. There are several drugs in the pipeline, so that even though Sovaldi is the drug of choice today, in 6 months we are likely to see new combination drugs out that will be preferred over Sovaldi.

The recommendations will change again if and when a regimen gets approved by the FDA that does not require interferon for patients with genotype 1 (the most common genotype in the U.S.).

We did speak to two DOD hepatologists for their input, and there is a GI physician on the Committee. The Prior Authorization for Sovaldi is one of the most complicated that we've ever done. Because this area is changing so rapidly, the PA criteria recommended by the Committee reflect what is in the guidelines, based on the clinical evidence available, and not necessarily the FDA package insert. These guidelines will be updated quickly when new data or new products come out, and the Committee will review new information, in order to keep the PA criteria as up to date as possible. This is why the Incivek and Victrelis PAs were updated too, and why PA criteria were placed on Olysio, even though it (Olysio) hasn't been reviewed yet.

Summary of Panel Vote/Comments:

The Panel members asked if the P&T committee considered promoting a 12-week combination therapy of Sovaldi and Olysio as well as give consideration to risk stratification of patients based on disease severity and treating patients based on a metavir score or some kind of indicator of disease severity.

In response, the presenters stated that the P&T committee based their decisions on current FDA-approved guidelines and regimens. The issues/concerns mentioned are decisions that should be discussed between the patient and their physician.

Without further discussion, the Chair asked for a vote on the Hepatitis C Virus Drugs.

F. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio - UF Recommendation

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

Director, DHA:

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

G. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio - PA Criteria

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

Director, DHA:

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

H. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio - UF and PA Implementation Plan

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

Director, DHA:

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

V. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

A. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq) – UF Recommendation

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

- Myrbetriq be designated UF and non-step-preferred ("behind the step"). Step therapy will require that all new users of Myrbetriq try Detrol LA or a preferred generic (Ditropan, Ditropan XL, Sanctura) prior to the use of the other OAB drugs.
- Automated PA criteria (step therapy) and manual PA criteria for all new users of Myrbetriq were recommended at the February 2014 P&T Committee meeting and implemented on June 11, 2014.

Summary of Physician Perspective:

This drug does not show better efficacy than the other OAB drugs (Detrol LA, Vesicare, etc), but it does have better tolerability.

Step therapy for all new Myrbetriq patients was recommended at the February 2014 P&T meeting, and implemented on June 11, 2014. The step therapy requires a trial of a Detrol LA or a generic OAB drug, unless the patient has had side effects to one of these drugs in the past, or if the patient is at risk for CNS side effects due other existing illnesses (like Parkinson's disease) or other concurrent drugs.

Myrbetriq was recommended to remain on the Uniform Formulary, even though it is more costly than the OAB step preferred drugs, since it has a different adverse event profile that does not include anticholinergic effects (dry mouth and constipation).

Summary of Panel Vote/Comments:

There were no questions or comments from the Panel members. Without further discussion, the Chair asked for a vote on the Overactive Bladder Drugs.

B. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq) – UF Recommendation

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

Director, DHA:

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

VI. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

A. Oral Anticoagulants: Apixaban (Eliquis) UF Recommendation

The P&T Committee recommended (12 for, 0 against, 0 abstained, 5 absent) Eliquis remain designated formulary on the UF.

Summary of Physician Perspective:

There was no debate with the recommendation for Eliquis to remain on the formulary – it is cost-effective compared to the other newer anticoagulants

The three new drugs, Eliquis, Xarelto, and Pradaxa, are all staring to pick up additional indications from the FDA. Eliquis is likely to get approval by the FDA this summer for treatment of DVT and PE.

The newer agents and Coumadin were reviewed by the Committee for formulary status back in February 2013, but Eliquis didn't get approved by the FDA until late December 2013, so it was not part of the original class review. We are anticipating a fourth product, edoxaban, to be approved in early 2015, and will do a full class review when it is on the market.

Summary of Panel Vote/Comments:

There were no questions or comments from the Panel members. Without further discussion, the Chair asked for a vote on the Oral Anticoagulant Drugs.

B. Oral Anticoagulants: Apixaban (Eliquis) UF Recommendations

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

Director, DHA:

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

VII. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

A. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) Farxiga be designated NF, due to the lack of compelling clinical advantages, safety concerns, lack of long-term outcome, and cost disadvantage compared to UF products.

B. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – PA Criteria

Existing automated PA (step therapy) for the SGLT2 inhibitors requires a trial of metformin, or a sulfonylurea, and a DPP-4 inhibitor first, based on positive long-term outcomes data with metformin and the sulfonylureas.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) a trial of metformin or a sulfonylurea and a DPP-4 inhibitor in all new and current users of Farxiga, due to the modest hemoglobin Alc lowering and safety concerns.

Automated PA criteria: The patient has filled a prescription for metformin, a SU, AND a DPP-4 inhibitor at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria: If automated criteria are not met, Farxiga is approved (e.g., trial of metformin or SU AND a DPP-4 inhibitor is NOT required) if:

- The patient has experienced any of the following issues on metformin:
  - Impaired renal function (*"decreased kidney function"*) precluding treatment with metformin
  - History of lactic acidosis (*"the build-up of lactic acid in the blood, which can be a sign of reduced blood flow"*)
- The patient has experienced any of the following issues on a sulfonylurea:
  - Hypoglycemia (*"low blood sugar"*) requiring medical treatment
- The patient has had inadequate response (*"blood sugars have not been adequately controlled"*) to metformin or a SU or a DPP-4 inhibitor
- The patient has a contraindication to metformin or a SU or DPP-4 inhibitor

C. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – UF and PA Implementation Plan

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

Summary of Physician Perspective:

As I mentioned previously an endocrinologist is on the committee. Lack of long term safety effect is a concern, and the Committee recognized the higher risk of fungal infections with this subclass. Other subclasses for treating diabetes have a longer history of use, and are more effective at lowering blood glucose levels (as measured by the HgA1c).

The Committee recommended non-formulary status for Farxiga, and also recommended that Farxiga have the same step therapy criteria that is currently in place for Invokana, the other drug in this subclass. All of the oral diabetes drugs have the step therapy requirement that a patient try metformin or a sulfonylurea first.

There are several drugs with this same mechanism of action in the pipeline, and the Committee will likely review the subclass sometime in 2015. The Committee also mentioned that consideration will be given to enhancing the step therapy recommendations with injectable drugs (insulin, or Exenatide and Victoza) in the future, when the subclass is reviewed.

Summary of Panel Vote/Comments:

The Panel members asked for clarification regarding the non-formulary status of Invocana. The Panel also expressed concerns about patients being able to obtain the newer drugs without a trial of metformin even if they do have a contraindication of metformin.

In response, the presenters stated that Invocana is currently non-formulary and patients are technical required to try sulfonylurea first but with the guidelines the way they are metformin is prevalent. Also, the decisions of the P&T Committee considered the advice of the endocrinologist on the committee.

Without further discussion, the Chair asked for a vote on the Sodium-Glucose Contransporter 2 Inhibitor Drugs.

D. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) UF Recommendation

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

Director, DHA:

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

E. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) PA Criteria

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

Director, DHA:

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

F. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) UF and PA Implementation Plan

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

Director, DHA:

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

VIII. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

A. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) Relative Clinical Effectiveness and Conclusion

Indacaterol (Arcapta) is a LABA that is dosed once daily. It is not available in a fixed-dose combination with an inhaled steroid.

Figure 8 on page 9 of the handout shows overall a decrease in utilization of the LABAs. Serevent has the highest utilization, and there has been very low usage of Arcapta.

The U.S. approved dose of 75 mcg administered once daily ("*higher doses are approved in Europe*") was based on two trials showing indacaterol produced statistically and clinically significant improvement in forced expiratory volume in one second (FEV1), "(*which measures how forcefully air is exhaled from the lungs*") compared to placebo; there are no comparative

trials available with this dose (*"in other words, no trials of Arcapta with another LABA"*). The safety profile appears similar to the other LABAs, including a black box warning against use in patients with asthma.

The P&T Committee concluded (17 for, 0 against, 0 abstained, 0 absent) that although indacaterol is the only LABA dosed once daily, other drug classes, including the ICS/LABA combinations (Advair) and long-acting muscarinic agents (for example Spiriva and Tudorza), are more effective than LABAs at improving pulmonary function, and decreasing hospitalizations or exacerbations (*"flare ups"*) in patients with COPD (*"emphysema"*).

B. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) Relative Cost Effectiveness and Conclusion

CMA was performed to evaluate Arcapta with other LABAs available on the UF that are used in the treatment of COPD. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA results showed that Arcapta was not cost-effective compared to Serevent and Foradil.

C. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) UF Recommendation

Despite the convenience of once daily dosing, the P&T Committee recommended (16 for, 0 against, 1 abstained, 0 absent) Arcapta be designated NF due to the lack of compelling advantages over the other LABAs and cost effectiveness. Additionally, the P&T Committee recommended reclassifying the LABAs to the Pulmonary II drug class, which includes other drug classes used for treating COPD.

D. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) UF Implementation Plan

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

Summary of Physician Perspective:

There was also no controversy here. This is the first new LABA to reach the market in several years. The Committee did recognize the convenience to the patient of once daily dosing, but patients with COPD are usually on several other drugs, so Arcapta would not necessarily simplify their medication regimen.

The COPD pipeline is very robust – three products were approved earlier this year, and we are expecting more combination products on the market. We want to move the LABAs over into the Pulmonary II drug class, which contains other drugs for COPD, which makes sense clinically (since the LABAs alone are no longer recommended for treating asthma), and to help increase competition within the class.

Summary of Panel Vote/Comments:

There were no questions or concerns from the Panel members. Without further discussion, the Chair asked for a vote on the Long-Acting Beta Adrenertic Inhalers.

F. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) UF Recommendation

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

Director, DHA:

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

G. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) Implemenation Plan

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

Director, DHA:

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

IX. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

A. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – UF Recommendation

The P&T Committee recommended (16 for, 0 against, 1 abstained, 0 absent) Uceris be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

B. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – UF Implementation Plan

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

Summary of Physician Perspective:

Once again, there was no controversy here, and the GI physician on the Committee agreed with the recommendation. Other drugs, including the aminosalicylates – Lialda, and the other mesalamine products, and biologics (Humira) are used to induce remission in patients with ulcerative colitis. There are also rectal steroid preparations on the Uniform Formulary which are used for this indication, and oral prednisone.

There are no step therapy requirements here, so if a patient needs Uceris, a medical necessity form can be filled out.

Summary of Panel Vote/Comments:

There were no questions or concerns from the Panel members. Without further discussion, the Chair asked for a vote on the Gastrointestinal (GI-1s) Steroid subclass.

C. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – UF Recommendation

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

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

D. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – Implementation Plan

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

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

X. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

A. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) UF Recommendation

The P&T Committee recommended (13 for, 0 against, 0 abstained, 4 absent) diclofenac low dose 18 mg and 35 mg capsules (Zorvolex) be designated NF, based on clinical and cost effectiveness.

B. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) UF Implementation Plan

The P&T Committee recommended (13 for, 0 against, 0 abstained, 4 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS; and, 2) DHA send a letter to beneficiaries affected by the UF decision.

Summary of Physician Perspective:

The Committee recommended non-formulary placement based on the FDA review of the drug and cost-effectiveness. The vote was unanimous here.

A generic formulation of Celebrex was approved by the FDA in late May 2014, and is expected to launch soon. In addition to Celebrex, there are several generic NSAIDs on the Uniform Formulary, including the diclofenac products Voltaren and Cataflam.

Summary of Panel Vote/Comments:

There were no questions or comments from the Panel. Without further discussion, the Chair asked for a vote on the Non-Steroidal Anti-Inflammatory Drugs.

C. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) - UF Recommendation

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

Director, DHA:

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

D. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) - Implementation Plan

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

Director, DHA:

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

XI. UTILIZATION MANAGEMENT-PRIOR AUTHORIZATIONS

P&T Comments

A. Cystic Fibrosis Drugs: Ivacaftor (Kalydeco)

Ivacaftor (Kalydeco) is a potentiator of the cystic fibrosis transmembrane conductance regulator (CFTR). *("Basically, this drug is what is called 'personalized medicine' or 'genomic medicine'")* The drug initially targeted a specific subgroup of patients with cystic fibrosis (CF) who had a G551D gene mutation. The FDA has expanded Kalydeco's approved indication to include additional mutations in the CFTR gene. PA criteria were recommended by the P&T Committee for Kalydeco in February 2012 and were implemented in July 2012. There are several FDA-approved in-vitro molecular diagnostic tests designed to simultaneously detect and identify mutations in the CFTR gene.

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) updating the existing PA criteria to include the expanded FDA-approved indication.

(1) Coverage will be approved for the treatment of CF patients aged 6 years and older who have a G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R mutation in the CFTR gene, detected by an FDA-approved test.

(2) Coverage is not approved for patients who are homozygous for the F508del mutation in the CFTR gene.

(3) The approved PA limits coverage of the drug to its labeled use. DHA will expedite review of the required test to determine its coverage under 32 CFR 199.4(g)(15). Providers and beneficiaries will be advised to retain receipts for the test to submit for reimbursement following the coverage determination.

B. Cystic Fibrosis Drugs: Invacaftor (Kalydeco) —PA Authorization

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

Director, DHA:

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

XII. UTILIZATION MANAGEMENT – PRIOR AUTHORIZATIONS

P&T Comments

A. Targeted Immunomodulatory Biologics (TIBSs): Tofacitinib (Xeljanz) and Apremilast (Otezla)—PA criteria currently apply to the TIBs, *which are injectable drugs used to treat a*

variety of conditions, including arthritis, psoriasis and inflammatory bowel disease. Tofacitinib (Xeljanz) is a janus kinase inhibitor approved for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had inadequate response or intolerance to methotrexate. Xeljanz is the first oral TIB to reach the market. Apremilast (Otezla) is an oral phosphodiesterase-4 inhibitor approved for the treatment of psoriatic arthritis.

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) PA criteria for tofacitinib (Xeljanz) and apremilast (Otezla), consistent with the product's labeling.

Tofacitinib (Xeljanz) PA Criteria: Coverage approved for patients ≥ 18 years with:

- Moderate to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.
- Not approved for use in combination with other biologics or potent immunosuppressants (aziathioprine and cyclosporine).

Apremilast (Otezla) PA Criteria: Coverage approved for patients ≥ 18 years with:

- Active psoriatic arthritis
- Coverage not approved for use in combination with other biologics

Summary of Physician Perspective:

The Committee does routinely review new FDA approved indications for drugs where we already have Prior Authorizations, so that the PA criteria are up to date. The updated PA criteria for these 3 drugs reflect this, and there was no discussion by the Committee.

Summary of Panel Vote/Comments:

There were no questions or comments from the Panel. Without further discussion, the Chair asked for a vote on the Targeted Immunomodulatory Biologics (TIBS).

B. Targeted Immunomodulatory Biologics (TIBSs): Tofacitinib (Xeljanz) and Apremilast (Otezla) —Expanded the FDA food product labeling

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

Director, DHA: 

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

XIII. UTILIZATION MANAGEMENT – PRIOR AUTHORIZATIONS

P&T Comments

Meade explains looking at prior authorization for generic to brand changes. Reason being, the manufacturers of branded products are giving such good price breaks. There are significant differences between the price available to the generics, which are more expensive than the branded price available. We are looking to put prior authorizations on these drugs so that the patient can get the branded product and not go to the generic substitution. One point is both do carry a generic co-pay. The beneficiary will not see a difference in the co-pay charge between brand and generic on these particular drugs.

A. Generic to Brand Changes: PA Criteria for the Retail Network for Niacin ER (Niaspan)

AB-rated generic formulations (*"this is a rating by the FDA which essentially means the generic drug has the same blood levels as the branded product"*) for niacin ER (Niaspan) were launched in August 2013; however, pricing for the branded product is lower than the generic formulations. The manufacturer of Niaspan offered a Voluntary Agreement for Retail Refunds, and the Tier 1 (generic) copayment was assigned to the branded product at the November 2013 P&T Committee meeting.

The mandatory generic drug policy is in place at the Retail Network; however, brand Niaspan is the preferred product for the MHS. PA criteria allowing for a patient to receive generic niacin ER instead of branded Niaspan is needed as a result of the generic to brand change (i.e., the reverse of the current brand to generic policy).

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) manual PA criteria for generic niacin ER in the Retail Network. The prescriber will provide patient-specific justification as to why the brand Niaspan product cannot be used. Acceptable reasons include the following, which have occurred or are likely to occur with the branded Niaspan product: allergy to the branded Niaspan; contraindication; sub-therapeutic response; physical restriction (e.g., swallowing issues); and brand availability issues.

There were no questions or comments from the Panel. Without further discussion, the Chair asked for a vote on the PA Criteria for the retail network for Niacin ER (Niaspan)

B. Generic to Brand Changes: PA Criteria for the Retail Network for Niacin ER (Niaspan) - PA Criteria

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

Director, DHA:

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

XIV. UTILIZATION MANAGEMENT – PRIOR AUTHORIZATIONS

P&T Comments

A. Generic to Brand Changes: PA Criteria for the Retail Network for Esomeprazole (Nexium)

Nexium) and omeprazole (generic Prilosec) are BCF and step-preferred in the Proton Pump Inhibitor (PPI) drug class. The patent for Nexium expired in May 2014; however, the launch date for generic formulations is unknown, due to manufacturing issues with the company granted exclusivity by the FDA. Market research indicates generic Nexium entrants will be less cost-effective than the branded formulation, leaving branded Nexium as the preferred product in the MHS. Therefore, PA criteria are needed to allow a patient to receive the generic esomeprazole instead of branded Nexium (i.e., the reverse of the current brand to generic policy).

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) manual PA criteria for generic esomeprazole in the Retail Network. The prescriber will provide patient-specific justification as to why the branded Nexium product cannot be used. Acceptable reasons include the following, which have occurred or are likely to occur with the branded Nexium product: allergy to branded Nexium; contraindication; sub-therapeutic response; physical restriction (e.g., swallowing issues); and brand availability issues. Implementation will occur when generic esomeprazole products reach the market.

Summary of Panel Vote/Comments:

The Panel members asked if there is a process to communicate the "reverse of the current generic policy" to the network pharmacies. It is standard practice to substitute the generic for a brand name drug.

The presenter replied he "thinks" the information could be messaged.

Without further discussion, the Chair asked for a vote on the PA Criteria for the retail network for Esomeprazole (Nexium).

B. Generic to Brand Changes: PA Criteria for the Retail Network for Esomeprazole (Nexium) PA Criteria

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

Director, DHA: 

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

XV. FISCAL YEAR 2008 NDAA, Section 703

The P&T Committee reviewed drugs from manufacturers that were not included on a DoD Retail Refund Pricing Agreement; these drugs are not in compliance with the Fiscal Year 2008 National Defense Authorization Act, Section 703. The law stipulates that if a drug is not compliant with Section 703, these drugs will be designated NF on the UF and will require pre-authorization prior to use in the Retail POS and medical necessity in the MTFs. These NF drugs will remain available in the Mail Order POS without preauthorization.

A. Section 703: Drugs Designated NF and Pre-Authorization Criteria

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) that the following products be designated NF on the UF:

- CorePharma: dextroamphetamine sulfate capsules
- Lupin: fenofibrate capsules; Wymzya Fe tablets
- Royal: Derma-Smoothe/FS Body Oil topical oil; DermOtic Oil otic drops
- Savient: Oxandrin tablets

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) the following pre-authorization criteria for the drugs recommended NF above: 1) obtaining the product by home delivery would be detrimental to the patient; and, 2) for branded products with AB generic availability, use of the generic product would be detrimental to the patient. These pre-authorization criteria do not apply to any POS other than retail network pharmacies.

B. Section 703: Implementation Plan for Pre-Authorization Criteria

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS; and, 2) DHA send a letter to beneficiaries affected by these decisions.

Without further discussion, the Chair asked for a vote on the Implementation plan for Pre-Authorization Criteria for the Section 703 Drugs designated non-formulary.

C. Section 703: Implementation Period for PA Criteria

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

Director, DHA: 

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

Uniform Formulary Beneficiary Advisory Panel (BAP)

Meeting Summary
July 31, 2014
Washington, D.C.

Present Panel Members

- Robert Lewis, the Chief Warrant and Warrant Officer's Association
- Bryan Hammons, Express Scripts, Inc.
- John Wagoner, HealthNet Federal Services
- Robert Duane Tackitt, Association of Military Surgeons of the United States
- Michael Anderson, United Healthcare
- Theresa Buchanan, National Association of the Uniformed Services
- Katherine O. Tracy, Military Officers Association of America
- Steven Hein, National Association of Uniformed Services

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave, N.W., Washington D.C. Colonel Spilker called the proceedings to order at 9:00 A.M. The Panel convened to review and comment on the therapeutic drug class recommendations resulting from the November 13 & 14 Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee meeting held in San Antonio, TX.

Agenda

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

- Welcome and Opening Remarks
- Public Citizen Comments
- Review and Panel discussion of P&T Committee recommendations for the following therapeutic drug class:
    - Drug Class and Subclass Reviews
        - Nasal Allergy Drugs
        - Inhaled Corticosteroid Drugs
        - Osteoporosis Drugs – Oral Biphosphonates Subclass
    - Designated Newly Approved Drugs
        - Hepatitis C Virus Drugs – Sofosbuvir tablets (Sovaldi)
        - Overactive Bladder (OAB) Drugs – Mirabegron (Myrbtriq)
        - Oral Anticoagulants – Apixaban (Eliquis)
        - Sodium-Glucose cotransporter 2 (SGLT2) Inhibitors – Dapagliflozin (Farxiga)

- Long-Acting Beta Adrenegic (LABA) Inhalers – Indacaterol (Arcapta Neohaler)
- Gastrointestinal (GI-1s): GI steroid subclass – budesonide extended release tablets (Uceris)
- Non-Steroid Anti-inflammatory Drugs (NSAIDs) – Diclofenac low dose (Zorvolex)

➢ Utilization Management Issues

- Prior Authorization Criteria
  - Ivactor (Kalydeco)
  - Hepatitis C drugs: Sofosbuvir (Sovaldi), Simeprevir (Olysio), telaprevir (Incivek), boceprevir (Victrelis)
  - Tofacitinib (Xeljanz) and Apremilast (Otezia)
  - Niacin ER (Niaspan) and Esomeprazole (Nexium)

➢ Section 703 Review

➢ Panel Discussions

Opening Remarks

Col J. Michael Spilker, DFO, indicated that Title 10, United States Code (USC) section 1074g, subsection b requires the Secretary of Defense to establish a DoD Uniform Formulary (UF) of pharmaceutical agent and establish the P&T committee to review the formulary on a periodic basis and 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. Comments of the panel must be considered by the Director of the Defense Health Agency (DHA) before establishing the UF or implementing changes to the UF.

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

The duties of the 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 of 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 his 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 by DHA.

As guidance to the Panel regarding this meeting, Col Spilker 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 will review, drugs recommended for the basic core formulary (BCF) or specific pricing data, these titles 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 minutes, and the Director's decisions will be available on the TRICARE website in approximately four to six weeks.

The DFO provided ground rules for conducting the meeting:

- All discussions take place in an open public forum. There is to be no committee discussion outside the room, during breaks, or at lunch.
- Audience participation is limited to private citizens who signed up to address the Panel.
- Members of the Pharmacoeconomic 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.

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

There were no public citizen comments submitted nor any sign-ups prior to the meeting.

Chairman's Opening Remarks

Mr. Robert Duane Tackitt welcomes the BAP and audience and gives the floor to Dr. Meade.

DRUG CLASS REVIEW PRESENTATION:

(PEC Script – Dr. Meade)

I'm Dave Meade, Director of Clinical Operations at the Pharmacoeconomic Branch ("PEC Branch" for short). Joining me is Doctor and retired Army Colonel John Kugler, the Chairman of the P & T Committee, who will provide the physician perspective and comment on the recommendations made by the P & T Committee. Also joining us from the PEC Branch today are LTC Chris Conrad, the PEC Branch Director; CAPT Walter Downs, the Navy Physician and Angela Allerman, one of the clinical pharmacists.

The DoD PEC Branch supports the DoD P & T Committee by conducting the relative (relative meaning in comparison to the other agents defined in the same class) 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 (UF).

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

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

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

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

3) The DoD P & T Committee's Uniform Formulary recommendation is based upon its collective professional judgment when considering the analyses from both the relative clinical- and relative cost-effectiveness evaluations. The Committee reviewed three Uniform Formulary Drug Classes (or sub-classes): Inhaled Corticosteroids (ICS), Nasal Allergy Drugs, and the Bisphosphonate subclass of the Osteoporosis Agents.

   Additionally, 7 newly approved drugs were reviewed – sofosbuvir (Sovaldi) from the Hepatitis C drugs class; mirabegron (Myrbetriq), a drug for Overactive Bladder (OAB); apixaban (Eliquis) a new oral anticoagulant; dapagliflozin (Farxiga) from the sodium-glucose co-transporter 2 subclass of the non-insulin diabetes drugs; indacaterol (Arcapta), a new Long-Acting Beta Agonist; budesonide extended release (Uceris) a new gastrointestinal

steroid; and diclofenac low dose (Zorvolex), from the Non-steroidal Anti-inflammatory Drugs (NSAIDs) class.

We will also discuss Prior Authorizations for a drug for cystic fibrosis, ivacaftor (Kalydeco); the Hepatitis C drugs Sovaldi, simeprevir (Olysio), telaprevir (Incivek) and boceprevir (Victrelis); and two oral Targeted Immunomodulatory Biologics (or TIBs), tofacitinib (Xeljanz) and apremilast (Otezla). Additionally we'll discuss new Prior Authorizations for generic esomeprazole (Nexium) and generic niacin extended release (Niaspan).

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

We've given you a handout which includes the Uniform Formulary recommendations for all the drugs discussed today; these are found on pages 2 through 12. There are tables and utilization figures for each of the drug classes. We'll be using trade names as much as possible, so you can refer to your handout throughout the presentation.

I. UF DRUG CLASS REVIEWS – NASAL ALLERGY DRUGS

P&T Committee Comments

(Dr. Allerman)

A. Nasal Allergy Drugs – Relative Clinical Effectiveness and Conclusion

The P&T Committee evaluated the clinical effectiveness of the Nasal Allergy Drugs, which includes the nasal steroids, nasal antihistamines, and nasal anticholinergics. The class was last reviewed for Uniform Formulary (UF) status in May 2011. Since the last review, three new drugs have been marked. There are two new hydrofluoroalkane (HFA) or "aerosol" formulations of ciclesonide (Zetonna) and beclomethasone (QNASL); the parent drugs are liquids (Omnaris and Beconase AQ). There is also the 1st combination steroid with an antihistamine, fluticasone/azelastine (Dymista). Triamcinolone (Nasacort OTC) is available over-the-counter (OTC) and is not included in the review.

Military Health System (MHS) expenditures for the class were $65 million in the period from March 2012 to February 2013. The handout on page 2, Figure 1, shows that across all the three points of service (Retail Network, Mail Order Pharmacy, and the Military Treatment Facilities (MTFs), generic Flonase has the highest utilization (about 175,000 30-day equivalent prescriptions dispensed monthly), followed by Nasonex, at about 60,000 30-day equivalent prescriptions dispensed monthly). There is very little use of the remaining products.

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

1. There is no new evidence that substantively changes the conclusions of the class review completed in 2011. Nasal steroids are first-line agents in reducing allergic rhinitis ("*allergies*") symptoms of rhinorrhea ("*runny nose"*), congestion ("*stuffy nose*"), and itching.
2. Available data from placebo-controlled trials ("*where a 'dummy' pill is given"*) and head-to-head trials ("*where one nasal allergy drug is compared with another"*) is not sufficient to clearly show superiority of one nasal allergy drug over another with regard to relief of allergy symptoms, or lower risk of harm ("*side effects*").
3. The nasal steroid HFA aerosol formulations (Zetonna and QNASL) have advantages over aqueous ("*liquid")* formulations including not causing a post nasal drip, longer retention in the nasal cavity ("*staying in the nose longer*"), potentially better taste, once daily dosing, and inclusion of a dose counter. The disadvantages include a higher incidence of epistaxis ("*nose bleed*") and burning, and the fact that they are FDA approved only for children older than 12 years, ("*whereas the other products are approved in children down to the age of 6 years, and some of them are approved down to the age of 2").*
4. Dymista is the first combination nasal steroid/nasal antihistamine. It has not been compared with the individual components (generic Flonase and Astelin) given separately, or with concomitant *(or "current")* use of another nasal steroid/oral antihistamine.
5. The nasal antihistamines are generally less effective than nasal steroids for treating allergic rhinitis, but may be used as first-line therapy, and in non-allergic rhinitis. ("*Non-allergic rhinitis occurs when you have a runny nose from eating spicy foods or going out in very cold weather*"). Nasal antihistamines have a quicker onset of effect than the nasal steroids. They are associated with a clinically significant effect on reducing nasal congestion ("*stuffy nose*"). Somnolence ("*drowsiness")* is considered a class effect.

(Dr. Meade)

B. Nasal Allergy Drugs – Relative Cost Effectiveness and Conclusion

A pharmacoeconomic analysis and budget impact analysis (BIA) were performed to evaluate the Nasal Allergy Drugs. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- The pharmacoeconomic analysis showed generic formulations of fluticasone propionate (Flonase), ipratropium (Atrovent), flunisolide (Nasarel), and azelastine 137 mcg (Astelin) were the most cost-effective agents in this class, followed by the branded agents Nasonex, Veramyst, Astepro, Rhinocort Aqua, QNASL, Omnaris, Patanase, Zetonna, Beconase AQ, and Dymista.
- A BIA was performed to evaluate the potential impact of scenarios with selected agents designated with formulary or Nonformulary (NF) status on the UF. BIA

results showed that the scenario with generic Astelin, Nasarel, Flonase, and Atrovent all designated as formulary and step-preferred, and with all branded agents designated as NF and non-step-preferred, was the most cost-effective for the MHS.

(Dr. Allerman)

C. Nasal Allergy Drugs – UF Recommendation

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following for the Nasal Allergy Drugs, based on the high degree of therapeutic interchangeability and on cost effectiveness:

- UF and step-preferred ("in front of the step"): generic Astelin 137 mcg, Nasarel, Nasonex, and Atrovent.
- NF and non-preferred ("behind the step"): Astepro, QNASL, Beconase AQ, Omnaris, Zetonna, Rhinocort Aqua, Veramyst, Dymista, Nasonex, and Patanase.
- This recommendation includes step therapy, which requires a trial of a generic product (Astelin 137 mcg, Nasarel, Nasonex, Atrovent) in all new and current users of the Nasal Allergy Drugs who are older than 4 years. In other words, there is no grandfathering for patients older than 4.
- Generic formulations of Nasonex are expected later in 2014. When the generics to Nasonex become cost-effective relative to the step-preferred agents, the generic will become step-preferred without further action by the P&T Committee, Beneficiary Advisory Panel, or Director, DHA. A generic agent is cost-effective relative to step-preferred agents when its total weighted average cost per day of treatment is less than or equal to the total weighted average cost per day of treatment for the step-preferred agent.

(Dr. Allerman)

D. Nasal Allergy Drugs – PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) automated (step therapy) and manual PA criteria in all new and current users of Astepro, QNASL, Beconase AQ, Omnaris, Zetonna, Rhinocort Aqua, Veramyst, Dymista, Nasonex, and Patanase who are older than 4 years of age. A trial of a generic product (Astelin 137 mcg, Nasarel, Flonase, or Atrovent) is required before the non-step-preferred drugs.

Automated PA criteria: The patient has filled a prescription for generic product (Astelin 137 mcg, Nasarel, Flonase, or Atrovent) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria: The non-formulary drugs, Astepro, Beconase AQ, QNASL, Rhinocort Aqua, Zetonna, Omnaris, Veramyst, Dymista, Nasonex, or Patanase is approved (e.g., trial of a generic product is NOT required) if:

- Patient has experienced any of the following issues with **at least one** of the following step-preferred Nasal Allergy Drugs (generic Astelin 137 mcg, Nasarel, Flonase, or Atrovent) which is not expected to occur with the non-preferred Nasal Allergy drug:
  - Inadequate response to the step-preferred drugs
  - Intolerable adverse effects (persistent epistaxis ("*nose bleed*"), significant nasal irritation, pharyngitis ("*sore throat*")
  - Contraindication ("*a contraindication is the opposite of 'indication' so it means a reason to not give a drug, usually an allergy or certain medical condition.")*
  - No formulary alternative for the following
    - For Rhinocort Aqua: patient is pregnant ("*Rhinocort is the only Nasal Allergy drug that is pregnancy category B, which carries a lower risk of harm to the fetus than the other products*.")
    - For Beconase AQ and Nasonex: patient has nasal polyps and cannot be treated with one of the step-preferred products ("*nasal polyps are non-cancerous growths in the nose (like grape clusters) which can cause stuffiness and loss of the sense of smell*").

(Dr. Allerman)

E. Nasal Allergy Drugs – UF and PA Implementation Period

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

F. Nasal Allergy Drugs – Physician Perspective

The P&T Committee has reviewed this drug class 3 times, and now there are some new generics, plus an over-the-counter product.

There was no evidence to suggest that any one product within a class is better at controlling allergy symptoms than another. Generally, the nasal steroids are used 1st line, and the nasal antihistamines are used 2nd line. The nasal steroids take about 2 weeks to show effect, and the nasal antihistamines have a much quicker onset of action. However, commonly you'll have the patient start the nasal steroid a couple of weeks before allergy season starts, so that it is effective when the patient starts to have symptoms.
There was no controversy with the decision. There is "no grandfathering" here – all patients have to try one of the preferred generics. However, for most patients, these

drugs are taken on a seasonal basis during allergy season, and not taken year round. DoD utilization reflects this, since there are just as many patients starting a nasal allergy drug (92,000 new starts) as there discontinuations (90,000) per quarter.

The Committee did take into account some of the differences in the FDA-approved labeling – that is why the step therapy and "no grandfathering" does not apply to children younger than 4 years of age; Flonase is approved for 4 years old, and Nasonex is approved for children as young as 2. A pediatrician is on the Committee and he agreed with the recommendation.

Also, for the step therapy criteria, the Committee recognized the "safer" pregnancy category rating for Rhinocort Aqua, and also that Nasonex is FDA-approved for patients with polyps. If a patient has adverse effects from Flonase, including nosebleeds, that is also in the PA criteria as a reason to receive a branded product.

Generic Flonase and the other generics to Astelin, Nasalide and Atrovent are the preferred products for the step therapy. Flonase has the highest utilization in DoD. The Committee did realize that currently Nasonex is 2nd in utilization for the class and that the majority of these patients are at the MTFs, and that the recommendation will affect about 19,000 patients. As soon as cost-effective generics to Nasonex come out, the Committee will act quickly and move the generic in front of the step.

G. Nasal Allergy Drugs – Panel Questions and Comments:

The Panel asked if the P&T Committee gave any consideration to a trial of multiple agents rather than one agent. More specifically, it looks as if a patient can start with the antihistamine, Astelin, and get to a nasal steroid without a trial of Fluticosone.

In response, the presenter stated that the Committee did discuss the requirement of a trial of multiple agents but decided to a trial of one agent. Meade replies the discussion took place, and the committee decided to go with the one.

Without further discussion, the Chair called for a vote on the Nasal Allergy Drugs.

H. Nasal Allergy Drugs – UF Recommendation

The BAP voted:

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

I. Nasal Allergy Drugs – PA Criteria

The BAP voted:

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

J. Nasal Allergy Drugs – UF and PA Implementation Plan

The BAP voted:

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

II. UF DRUG CLASS REVIEWS – INHALED CORTICOSTEROIDS

P&T Committee Comments

(Dr. Allerman)

A. Inhaled Corticosteroids (ICS) - Relative Clinical Effectiveness and Conclusion

The P&T Committee evaluated the clinical effectiveness of the inhaled steroids, which were last reviewed for UF status in February 2009. One product, fluticasone, is available in a dry powder inhaler (Flovent Diskus) and an HFA aerosol (Flovent HFA). Mometasone (Asmanex HFA) metered dose inhaler was recently approved and has an August 2014 launch date; it will be reviewed at an upcoming meeting. MHS expenditures for the class the past year were $37.7 million.

The Handout on page 3, Figure 2, shows that Flovent has the highest utilization, at about 25,000 30-day equivalent prescriptions dispensed monthly, followed by Asmanex.

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

1. There is no new evidence that substantively changes the conclusions of the class review completed in 2009.
2. In patients with asthma, there is fair-to-moderate evidence that the inhaled steroids do not differ with regard to controlling symptoms *("wheezing, or shortness of breath"*), need for rescue medication ("*need to have another inhaler to immediately treat symptoms, such as albuterol"),* and exacerbations *("periods of an asthma flare up*")
3. There is insufficient evidence to conclude there are clinically relevant differences in efficacy among the inhaled products for treating symptoms COPD ("*emphysema*"). The inhaled steroids are not FDA-approved for treating COPD, ("*but are often used off-label here*").
4. In terms of safety, there is insufficient evidence to determine whether there are clinically relevant differences among the inhaled steroid products in terms of minor adverse events ("*mild side effects like coughing, sore throat, or hoarseness"*) or systemic adverse events ("*adverse events that affect the whole body like cataracts or thinning bones*.")

(Dr. Meade)

B. Inhaled Corticosteroids (ICS) - Relative Cost Effectiveness and Conclusion

A pharmacoeconomic analysis and BIA were performed to evaluate the inhaled steroids. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) the following:

- The pharmacoeconomic analysis showed Pulmicort Flexhaler and Flovent Diskus and Flovent HFA were the most cost-effective agents in this class; followed by QVAR and Asmanex Twisthaler; and by Alvesco and Aerospan.
- BIA results showed that the scenario with Flovent Diskus and Flovent HFA designated as step-preferred and formulary on the UF, with Aerospan, Alvesco, Asmanex Twisthaler, Pulmicort Flexhaler and QVAR designated as non-preferred and NF on the UF, was the most cost-effective option for the MHS.

(Dr. Allerman)

C. Inhaled Corticosteroids (ICS) – UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following for the inhaled steroids, based on the high degree of therapeutic interchangeability and cost effectiveness:

- UF and step-preferred ("in front of the step"): Flovent Diskus and Flovent HFA
- NF and non-preferred ("behind the step"): QVAR, Pulmicort Flexhaler, Alvesco, Aerospan, and Asmanex Twisthaler
- This recommendation includes step therapy, which requires a trial of Flovent Diskus or Flovent HFA in all new users of QVAR, Pulmicort Flexhaler, Alvesco, Aerospan, or Asmanex Twisthaler who are older than 12 years.
- Budesonide nebulized solution (Pulmicort) was reviewed in 2009 and was not part of the class review for this meeting; it remains on the UF and is not subject to step therapy.

(Dr. Allerman)

D. Inhaled Corticosteroids (ICS) – PA Criteria

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) automated (step therapy) and manual PA criteria in all new users of QVAR, Pulmicort Flexhaler, Alvesco, Aerospan, or Asmanex Twisthaler who are older than 12 years of age. A trial of Flovent Diskus or Flovent HFA is required before the non-step preferred drugs.

Automated PA criteria: The patient has filled a prescription for Flovent Diskus or Flovent HFA at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria: QVAR, Pulmicort Flexhaler, Alvesco, Aerospan, and Asmanex Twisthaler is approved (e.g., trial of Flovent Diskus or Flovent HFA is NOT required) if:

- Patient has experienced any of the following issues with Flovent Diskus or Flovent HFA, which is not expected to occur with the non-preferred ICS:
  - Inadequate response to the step preferred drugs
  - Intolerable adverse effects (patient has a history of adrenal suppression and the request is for Alvesco)
  - Contraindication
  - Patient previously responded to non-formulary agent and changing to a formulary agent would incur unacceptable risk
  - No formulary alternative for the following: Pulmicort Flexhaler: patient is pregnant

(Dr. Allerman)

E. Inhaled Corticosteroids (ICS) – UF and PA Implementation Plan

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

F. Inhaled Corticosteroids (ICS) – Physician Perspective

This class has been reviewed once before, back in 2009. There were no new products approved by the FDA since the last review.

The combination inhalers (inhaled steroid plus a long-acting beta agonist) were reviewed by the Committee in February of this year. Advair, which has Flovent as the steroid component was chosen as the preferred product. The recommendation for the inhaled steroids to have Flovent as the preferred product is consistent with the previous decision for the combination inhalers. Flovent by far has the highest utilization in the class. Some of the products recommended for non-formulary use have very low utilization (for example Aerospan).

Patients are "grandfathered" here – the step therapy only applies to new patients. When the Committee looked at the cost avoidance, if there had been "no grandfathering", it would have affected a lot more patients without generating a lot of cost savings.
The step therapy does not apply to children 12 years and younger. This is conservative, because when we looked at the utilization in kids, children younger 8 years comprised the majority of use. Out of 54,000 total users in the ICS class, about 17,000 are younger than 12 years of age. However, there are only 3,000 children younger than 12 who are a non-Flovent user. The pediatrician on the Committee agreed with the recommendation.

G. Inhaled Corticosteroids (ICS) – Panel Questions and Comments

There were no questions or comments from the Panel. Without further discussion, the Chair called for a vote on the Inhaled Corticosteroids drugs.

H. Inhaled Corticosteroids (ICS) – UF Recommendation

The BAP voted:

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

I. Inhaled Corticosteroids (ICS) – PA Criteria

The BAP voted:

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

J. Inhaled Corticosteroids (ICS) – UF Implementation Plan

The BAP voted:

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

III. UF DRUG CLASS REVIEWS – OSTEOPOROSIS DRUGS: ORAL BISPHOSPHONATES SUBCLASS

P&T Committee Comments

(Dr. Allerman)

A. Osteoporosis Drugs: Oral Bisphosphonates Subclass – Relative Clinical Effectiveness and Conclusion

The oral bisphosphonates are a subclass of the Osteoporosis drugs, which were last reviewed for UF placement in June 2008. *These drugs are used to treat osteoporosis, which is thinning of the bones and that can lead to bone fractures.* Generic formulations are available for alendronate (Fosamax), which is commonly administered once a week, and ibandronate (Boniva) which is administered once a month; the generic for Boniva reached the market about a year ago.

MHS expenditures for the bisphosphonates were $30.5 million in calendar year 2013. The Handout on page 4, Figure 3, shows the utilization for the entire Osteoporosis drug class. For the bisphosphonates, generic Fosamax (the top blue line) has the highest utilization, followed by branded Boniva (green line), and branded Actonel (purple line) The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) the following:

1. There was no new significant efficacy data since the last review; however, there is substantial new safety information for the bisphosphonates.
2. Relative superiority of one agent versus another cannot be determined by bone mineral density data alone. ("*Bone mineral density measures how thin the bones are, but it is a surrogate measure, since patients are interested in whether these drugs prevent a bone fracture").* For fracture prevention, available data from placebo-controlled trials and head-to-head trials is not sufficient to clearly establish superiority of one bisphosphonate versus another.
3. Clinical guidelines list ibandronate (Boniva, generics) as second-line therapy due to the lack of data for hip fracture prevention and lack of long-term data. *("The oral bisphosphonates help reduce the risk of fractures of the hip, neck and spinal column, along with other bones. The other bisphosphonates (Fosamax and Actonel) have data they prevent hip fractures, which is important because hip fractures are associated with a high risk of death*"). However, ibandronate has the convenience of once monthly dosing and an MHS study showed improved persistence with the once monthly ibandronate formulation over the other bisphosphonates ("*which are dosed once weekly. Poor persistence (adherence) is common with the oral bisphosphonates, as they have strict administration requirements.").*
4. ("*Atelvia and Binosto are branded formulations of risdedronate (Actonel)").* Atelvia (once weekly regimen) and Binosto (effervescent tablet) offer no clinically compelling advantages over the other bisphosphonate formulations.
5. Potential adverse events of osteonecrosis of the jaw ("*rotting of the jaw bone"*), atrial fibrillation ("*irregular heartbeat*"), esophageal cancer (*"cancer of the hollow tube that runs from the mouth to the stomach"),* and atypical femur fractures ("*fractures of the leg that aren't associated with trauma")* are considered a class effect by the FDA.

(Dr. Meade)

B. Osteoporosis Drugs: Oral Bisphosphonates Subclass – Relative Cost Effectiveness and Conclusion

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

- CMA results showed generic alendronate (Fosamax) was the most cost-effective agent, followed by generic ibandronate (Boniva), branded risedronate (Actonel), risedronate delayed release (Atelvia), alendronate/vitamin D (Fosamax Plus D), and alendronate effervescent tablet (Binosto).

- BIA was performed to evaluate the potential impact of scenarios, with selected agents designated step-preferred and UF or non-preferred and NF on the UF. BIA results showed the scenario with generic Fosamax designated as formulary and step-preferred, generic Boniva as UF and non-step-preferred for new users, and all branded agents (Actonel,

Atelvia, Binosto, and Fosamax Plus D) designated as NF and non-step-preferred for new and current users was the most cost-effective option for the MHS.

(Dr. Allerman)

C. Osteoporosis Drugs: Oral Bisphosphonates Subclass – UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following, based on the high degree of therapeutic interchangeability and cost-effectiveness:

- UF and step-preferred (e.g., "in front of the step"): generic Fosamax
- UF and non-step-preferred (e.g., "behind the step"): generic Boniva
- NF and non-step-preferred: Actonel, Atelvia, Binosto, and Fosamax Plus D
- This recommendation includes step therapy, which requires the following:
  - A trial of generic Fosamax is required prior to use of generic Boniva only in new users, as the patient impact is less than if all current and new users were affected by the step *(existing patients using Boniva will be 'grandfathered'* ")
  - A trial of generic Fosamax is required prior to use of Actonel, Atelvia, Binosto, and Fosamax Plus D in all new and current users. ("*Patients are not grandfathered here"*)

(Dr. Allerman)

D. Osteoporosis Drugs: Oral Bisphosphonates Subclass – PA Criteria

P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) automated (step therapy) and manual PA criteria in all new users of generic Boniva, and all new and current users of Actonel, Atelvia, Binosto, and Fosamax Plus D. A trial of alendronate is required before the non-step-preferred drugs.

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

AND

Manual PA criteria—ibandronate, Actonel, Atelvia, Binosto, and Fosamax Plus D is approved (e.g., trial of alendronate is NOT required) if:

- Patient has experienced any of the following issues with alendronate, which is not expected to occur with the non-preferred oral bisphosphonates:
  - Intolerable adverse effects

- » Patient requires once monthly ibandronate or Actonel 150 mg due to gastrointestinal adverse events from alendronate weekly dosing
- » Patient has experienced significant adverse effects from formulary agents
- » For Binosto: No alternative formulary agent and patient has swallowing difficulties and cannot consume 8 oz of water and has no sodium restrictions
- » For Fosamax Plus D: No alternative formulary agent and patient cannot take alendronate and vitamin D separately
  - o Contraindication

(Dr. Allerman)

E. Osteoporosis Drugs: Oral Bisphosphonates Subclass –UF and PA Implementation Plan:

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

F. Osteoporosis Drugs: Oral Bisphosphonates Subclass – Physician Perspective

This drug class was last reviewed back in 2008. There has been a steady decline in MHS utilization of the bisphosphonates, most likely due to safety concerns.

Generic Fosamax was recommended as the preferred product, and it currently has the highest utilization in the subclass.

Boniva is recommended to remain Uniform Formulary, but be subject to step therapy. However, existing Bonvia users will be "grandfathered", due to the convenience of once monthly dosing, compared to the once weekly dosing with Fosamax and Actonel.

Overall, adherence to the bisphosphonates is poor, and the Committee did take into consideration a study done in 2008 showing improved adherence in DoD patients taking Boniva (about a 20% improvement). Another reason to grandfather the Boniva patients is that the majority of use is at the MTFs, and "grandfathering" impacted significantly fewer patients than having "no grandfathering" (about 25,000 fewer patients affected). Additionally, we are expecting the price of the generic Boniva to drop.

For the other drugs, Actonel, Atelvia, Binosto, and Fosamax Plus Vitamin D, there is no grandfathering, and they are recommended for non-formulary placement.

Fosamax Plus Vitamin D is now recommended for non-formulary placement. There are no generics available. At one time, before the regular Fosamax was available in a generic, we were getting the Vitamin D essentially for free, but this is no longer the case. Inexpensive

OTC Vitamin D products that are taken daily are available. One of the members of the Committee is an endocrinologist, and he agreed with the recommendations.

G. Osteoporosis Drugs: Oral Bisphosphonates Subclass – Panel Questions and Comments

There were no questions or comments from the Panel members. Without further discussion, the Chair called for a vote on the Osteoporosis Drugs.

H. Osteoporosis Drugs: Oral Bisphosphonates Subclass – UF Recommendations

The BAP voted:

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

I. Osteoporosis Drugs: Oral Bisphosphonates Subclass – PA Criteria

The BAP voted:

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

J. Osteoporosis Drugs: Oral Bisphosphonates Subclass – UF Implementation Plan

The BAP voted:

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

IV. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

(CAPT Downs)

A. Hepatitis C Virus Drugs: Sofosbuvir tablets (Sovaldi) Relative Clinical Effectiveness and Conclusion

Sofosbuvir (Sovaldi) is a new oral direct acting antiviral (DAA) indicated for the treatment of chronic hepatitis C virus (HCV) infection. The American Association for the Study of Liver Diseases and the Infectious Disease Society of America released new HCV treatment guidelines in February 2014 (*"which are found on the web at"* www.hcvguidelines.org). "*The information presented here for the clinical effectiveness review and for the PA criteria comes from these guidelines*". Several drugs for Hepatitis C virus /are in the pipeline, including interferon-free regimens *("the interferons are injectable drugs used for Hepatitis C; they are associated with side effects that make them difficult to tolerate, and often require treatment for 24-48 weeks").*

MHS expenditures for Hepatitis C drugs in the past year were $43.4 million. Figure 4 on page 5 of the Handout shows the steep increase in Sovaldi utilization since its FDA approval in December 2013. Figure 4 also shows the steady decline in use of the two other Direct Acting Antivrials, telaprevir (Incivek) and boceprevir (Victrelis).

"The goal of treating Hepatitis C is to prevent the progression to liver cirrhosis and liver cancer. The endpoint for treating Hepatitis C infection is the 'sustained virologic response' or SVR, which shows that the virus is no longer circulating in the blood."

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

- The guidelines consider Sovaldi as the standard of care for HCV infection. Solvadi should be a component of a combination antiviral regimen (e.g., including ribavirin with or without peginterferon); it must not be used as monotherapy ("*alone*"). Sustained virologic response (SVR) rates of 90% are achieved in HCV genotypes *("types of HCV virus*") 1 through 6 when Sovaldi is combined with ribavirin (dual therapy) and interferon (triple therapy).

- Advantages of sofosbuvir over the Incivek and Victrelis include reduced frequency of administration, lower tablet burden ("*decreased number of tablets taken each day*"), higher SVR rates, shorter treatment courses, fewer drug interactions, and improved tolerability profile.

- Incivek and Victrelis are no longer recommended in the guidelines as they are inferior to Sovaldi and should not be used.

(Dr. Meade)

B. Hepatitis C Virus Drugs: Sofosbuvir tablets (Sovaldi) Relative Cost Effectiveness and Conclusion

Initial CMA and cost-effectiveness analysis (CEA) were performed. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA showed that Sovaldi is the most costly DAA currently available for treating HCV.
- CEA evaluated the potential benefit associated with improved efficacy data and improved tolerability associated with Sovaldi compared to other HCV treatment regimens. Preliminary findings suggested that the cost per SVR achieved with Sovaldi was comparable with previously prescribed DAAs for HCV infection.

(Dr. Meade)

C. Hepatitis C Virus Drugs: Sofosbuvir tablets (Sovaldi) UF Recommendation

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

- Sovaldi be designated with formulary status on the UF. Patients are encouraged to fill Sovaldi prescriptions at Military Treatment Facilities (MTFs) or Mail Order Pharmacy points of service (POS), and
- Sovaldi, and the other Direct Acting Agents Incivek and Victrelis, be added to the TRICARE Specialty Drug list to facilitate recapture from the Retail Network to the Mail Order Pharmacy.

(CAPT Downs)

CAPT Downs interjects with a correction regarding relative clinical effectiveness. The P&T Committee voted (16 for, 0 Against, 0 Abstained, 1 Absent)

D. Hepatitis C Virus Drugs: Sofosbuvir tablets (Sovaldi) Prior Authorization Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for Sovaldi for new users, consistent with guidelines and FDA-approved labeling. Prior authorization will expire after 12 or 24 weeks for Sovaldi, based on the treatment regimen selected.

Manual PA Criteria:

- Age ≥ 18
- Has laboratory evidence of chronic HCV infection
- Has laboratory evidence of HCV with the appropriate genotype
  - State the HCV genotype on the PA form.
- Sovaldi is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician.
- The patient is not co-infected with Hepatitis B virus (HBV).
- Sovaldi is not prescribed as monotherapy; ribavirin with or without PEG-interferon is also prescribed

Treatment Regimens and Duration of Therapy

- Treatment and duration of therapy are approved for the following regimens outlined below, based on HCV genotype or unique population.

Genotype 1

- Approved in patients who meet ONE of the following criteria:
  (1 or 2)
  1. Interferon eligible: Sovaldi + interferon + ribavirin for 12 weeks
  2. Interferon ineligible: Sovaldi + Olysio for 12 weeks
- Interferon ineligible is defined as ONE of the following:
  1. Intolerance to interferon (patient has previously taken interferon)

2. Autoimmune hepatitis or other autoimmune disorders
3. Hypersensitivity to peginterferon or any of its components
4. Decompensated hepatic disease
5. History of depression or clinical features consistent with depression
6. Baseline CBC: neutrophil count < 1,500/μ or PLTs < 90,000/μ or Hgb<10 g/dl *("these are standard laboratory blood tests drawn to see if the patient has anemia, a higher risk of bleeding, or is at risk of infection")*
7. History of preexisting cardiac disease

Genotype 2

- Sovaldi + ribavirin approved for 12 weeks

Genotype 3

- Approved in patients who meet ONE of the following criteria: (1 or 2):
  1. Sovaldi + ribavirin approved for 24 weeks
  2. Sovaldi + ribavirin + interferon approved for 12 weeks as an alternative in cirrhotic individuals or treatment experienced

Genotype 4

- Sovaldi + ribavirin+ interferon approved for 12 weeks

Regimen other than those listed above:

- Explain the rationale for treatment and duration of therapy. Consult the guidelines for new updates and guidelines.

While we are on the topic of Hepatitis C, we will also discuss PA criteria for three other DAAs – Incivek, Victrelis and Olysio.

(CAPT Downs)

E. Hepatitis C Virus Drugs: Incivek and Victrelis Prior Authorization Criteria

PA criteria for Incivek and Victrelis were recommended at the November 2012 P&T Committee meeting. Because of the new the AASLD/IDSA guidelines, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revised PA criteria for Victrelis and Incivek for new users. Current users of boceprevir or telaprevir are allowed to complete their course of therapy without interruption.

Manual PA Criteria:

Incivek and Victrelis are NO LONGER RECOMMENDED for ANY HCV treatment by the guidelines.

- Although regimens of PEG-interferon and ribavirin plus Incivek or Victrelis for 24 to 48 weeks using response-guided therapy are also FDA-approved; they are **markedly inferior** to the currently available regimens.
- Incivek and Victrelis regimens are associated with higher rates of serious adverse events than recommended current regimens with Sovaldi.
- Consider treatment with Sovaldi-containing regimens OR future highly effective pan-genotypic ("*covering all types of HCV*") DAA combination regimens that are interferon-free.
- The justification and dosing/duration for Incivek and Victrelis must be documented (e.g., allergic to all other known regimens; inability to wait for treatment).

Prior authorization will expire after 12 weeks for Incivek and 44 weeks for Victrelis.

(CAPT Downs)

F. Hepatitis C Virus Drugs: Olysio Prior Authorization Criteria

Olysio is a Direct Acting Agent approved by the FDA in December 2013. It will be reviewed as a new drug at an upcoming meeting.

Olysio is indicated for use with ribavirin and PEG interferon, but the guidelines recommend a non-FDA-approved regimen with Sovaldi and ribavirin as an alternative treatment for genotype 1 patients who are ineligible to take interferon.

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for new users of simeprevir (Olysio) consistent with guidelines.

Manual PA Criteria:

- Age ≥18
- Has laboratory evidence of chronic HCV (quantified viral load above undetectable)
- Has laboratory evidence of genotype 1 HCV infection
- The patient HCV genotype 1a without any indication of resistance.
- Is not co-infected with HIV or Hepatitis B Virus
- The patient has not previously used a HCV protease inhibitor (Victrelis, Incivek, or Olysio)
- Simeprevir is not approved for monotherapy

- The guidelines recommend a regimen of Olysio plus Sovaldi either with or without ribavirin for 12 weeks.

- The patient is interferon ineligible. Interferon ineligible as defined previously

Prior authorization will expire after 12 weeks.

(CAPT Downs)

G. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio Prior Authorization Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of no later than the first Wednesday after a 30-day implementation period in all POS.

H. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio – Physician Perspective

There was a lot of discussion on the topic of Hepatitis C, however, there was no question that Sovaldi has advantages over the first drugs in the class, Incivek and Victrelis. There are several drugs in the pipeline, so that even though Sovaldi is the drug of choice today, in 6 months we are likely to see new combination drugs out that will be preferred over Sovaldi.

The recommendations will change again if and when a regimen gets approved by the FDA that does not require interferon for patients with genotype 1 (the most common genotype in the U.S.).

We did speak to two DOD hepatologists for their input, and there is a GI physician on the Committee. The Prior Authorization for Sovaldi is one of the most complicated that we've ever done. Because this area is changing so rapidly, the PA criteria recommended by the Committee reflect what is in the guidelines, based on the clinical evidence available, and not necessarily the FDA package insert. These guidelines will be updated quickly when new data or new products come out, and the Committee will review new information, in order to keep the PA criteria as up to date as possible. This is why the Incivek and Victrelis PAs were updated too, and why PA criteria were placed on Olysio, even though it (Olysio) hasn't been reviewed yet.

I. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio – Panel Questions and Comments

The Panel members asked if the P&T committee considered promoting a 12-week combination therapy of Sovaldi and Olysio as well as give consideration to risk stratification of patients based on disease severity and treating patients based on a metavir score or some kind of indicator of disease severity.

In response, the presenters stated that the P&T committee based their decisions on current FDA-approved guidelines and regimens. The issues/concerns mentioned are decisions that should be discussed between the patient and their physician.

Without further discussion, the Chair asked for a vote on the Hepatitis C Virus Drugs.

J. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio - UF Recommendation

The BAP voted:

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

K. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio - PA Criteria

The BAP voted:

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

L. Hepatitis C Virus Drugs: Hepatitis C Drugs Sovaldi, Incivek, Victrelis and Olysio - UF and PA Implementation Plan

The BAP voted:

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

V. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

(CAPT Downs)

A. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq) – Relative Clinical Effectiveness and Conclusion

Myrbetriq is a beta-3 receptor agonist, which promotes urine storage by increasing bladder capacity. This mechanism of action is unique from the antimuscarinic OAB drugs *("which inhibit the contraction of the bladder.")* Examples of the antimuscarinic OAB drugs include Detrol LA, generic Ditropan, Vesicare, and Sanctura.

Figure 5 on page 6 of the Handout shows the utilization of the OAB drug class. Step therapy requiring use of Detrol LA or a generic was implemented in May 2013. The top blue line shows the effect of the step therapy, which is a Detrol LA prescription. Myrbetriq utilization is shown by the light blue line, which has passed 10,000 prescriptions in March 2014.

Compared to placebo, Myrbetriq produced statistically significant reductions in incontinence episodes, but the clinical effect is small and there is a high placebo response rate. An analysis of MHS prescription data showed that the medication possession ratio (adherence) was higher at six months with Myrbetriq than the OAB drugs (72% versus 61%).

The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 0 absent) that although there do not appear to be clinically relevant differences in efficacy between mirabegron and the antimuscarinic OAB drugs, it is well-tolerated and does not produce the anticholinergic effects of dry mouth and constipation seen with the other OAB drugs.

(Dr. Meade)

B. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq) – Relative Cost Effectiveness and Conclusion

A CMA was performed to evaluate mirabegron (Myrbetriq), a new entrant in the OAB Drug Class. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA results showed that generic Ditropan was the most cost-effective agent, followed by generic Ditropan XL, generic Sanctura, Gelnique, Detrol LA, generic Detrol IR Vesicare, Myrbetriq, Oxytrol patch, Enablex, Sanctura XR, Toviaz, and Gelnique Pump.

(Dr. Meade)

C. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq) – UF Recommendation

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

- Myrbetriq be designated UF and non-step-preferred ("behind the step"). Step therapy will require that all new users of Myrbetriq try Detrol LA or a preferred generic (Ditropan, Ditropan XL, Sanctura) prior to the use of the other OAB drugs.
- Automated PA criteria (step therapy) and manual PA criteria for all new users of Myrbetriq were recommended at the February 2014 P&T Committee meeting and implemented on June 11, 2014.

D. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq) – Physician Perspective

This drug does not show better efficacy than the other OAB drugs (Detrol LA, Vesicare, etc), but it does have better tolerability.

Step therapy for all new Myrbetriq patients was recommended at the February 2014 P&T meeting, and implemented on June 11, 2014. The step therapy requires a trial of a Detrol LA or a generic OAB drug, unless the patient has had side effects to one of these drugs in the past, or if the patient is at risk for CNS side effects due other existing illnesses (like Parkinson's disease) or other concurrent drugs.

Myrbetriq was recommended to remain on the Uniform Formulary, even though it is more costly than the OAB step preferred drugs, since it has a different adverse event profile that does not include anticholinergic effects (dry mouth and constipation).

E. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq) – Panel Comments and Questions

There were no questions or comments from the Panel members. Without further discussion, the Chair asked for a vote on the Overactive Bladder Drugs.

F. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq) –UF Recommendation

The BAP voted:

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

VI. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

(Dr. Allerman)

A. Oral Anticoagulants: Apixaban (Eliquis) Relative Clinical Effectiveness and Conclusion

Apixaban is a new oral anticoagulant (NOAC) (" or *blood thinner")*). The other NOACs on the market include rivaroxaban (Xarelto) and dabigatran (Pradaxa). The NOACs have a different mechanism of action than warfarin (generic Coumadin).

Figure 6 on page 7 of the handout shows the utilization of warfarin and the NOACs. Warfarin has the highest utilization, followed by Xarelto, Pradaxa and Eliquis.

Eliquis and the other NOACs have the advantages of predictable anticoagulant effect, fixed dosing, and fewer drug interactions compared to warfarin, and the convenience of no laboratory monitoring and no dietary restrictions. Eliquis was superior to poorly controlled warfarin at preventing stroke and systemic embolism *("blood clots")* in patients with atrial fibrillation ("*irregular heartbeat*") in one large trial. (ARISTOTLE trial). Apixaban was non-inferior to ("*no different than")* Lovenox when used for prevention of venous thromboembolism or VTE ("*blood clots in the lungs or legs")* following hip or knee replacement surgery.

The P&T Committee concluded (12 for, 0 against, 0 abstained, 5 absent) the main benefit of Eliquis and the other NOACs over warfarin is the reduced rate of intracranial hemorrhage ("*bleeding into the brain*") when used to prevent strokes in patients with non-valvular atrial fibrillation ("*irregular heartbeat not due to leaking heart valves*"). The NOACs and warfarin will be re-reviewed at an upcoming meeting for UF and BCF placement.

(Dr. Allerman)

B. Oral Anticoagulants: Apixaban (Eliquis) Relative Cost Effectiveness and Conclusion

Relative Cost-Effectiveness Analysis and Conclusion—CMA was performed to evaluate Eliquis with other NOACs in the prevention of stroke and systemic embolism in atrial fibrillation and prevention of VTE in patients undergoing orthopedic surgery. The P&T Committee concluded (12 for, 0 opposed, 0 abstained, 5 absent) the following:

- CMA showed that warfarin, including drug monitoring costs, remains the least costly agent in the class. Among the NOACs, Eliquis was less costly than Xarelto and more costly than Pradaxa.

(Dr. Allerman)

C. Oral Anticoagulants: Apixaban (Eliquis) UF Recommendation

The P&T Committee recommended (12 for, 0 against, 0 abstained, 5 absent) Eliquis remain designated formulary on the UF.

D. Oral Anticoagulants: Apixaban (Eliquis) - Physician's Perspective

There was no debate with the recommendation for Eliquis to remain on the formulary – it is cost-effective compared to the other newer anticoagulants

The three new drugs, Eliquis, Xarelto, and Pradaxa, are all staring to pick up additional indications from the FDA. Eliquis is likely to get approval by the FDA this summer for treatment of DVT and PE.

The newer agents and Coumadin were reviewed by the Committee for formulary status back in February 2013, but Eliquis didn't get approved by the FDA until late December 2013, so it was not part of the original class review. We are anticipating a fourth product, edoxaban, to be approved in early 2015, and will do a full class review when it is on the market.

E. Oral Anticoagulants: Apixaban (Eliquis) – Panel Questions and Comments

There were no questions or comments from the Panel members. Without further discussion, the Chair asked for a vote on the Oral Anticoagulant Drugs.

F. Oral Anticoagulants: Apixaban (Eliquis) UF Recommendations

The BAP voted:

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

VII. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

(Dr. Meade)

A. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – Relative Clinical Effectiveness and Conclusion

Farxiga is the second FDA-approved SGLT2 inhibitor. SGLT2 inhibitors are a relatively new subclass of the Non-Insulin Diabetes Drug Class and have a novel mechanism of action *("they cause blood sugar to be eliminated in the urine").*

Figure 7 on page 8 shows the utilization of the Farxiga and Invokana, the two SGLT2 inhibitors on the market.

Farxiga is effective in lowering hemoglobin A1c *("a lab test that measures control of blood sugar")* by about 0.4% to 1% when used as monotherapy ("*used alone"),* by about 0.5% to 2% as part of dual therapy ("*when added on to another drug, such as metformin*"), and about 0.3% to 1% as part of triple therapy ("*a three drug regimen").* It is similar to Invokana in terms of beneficial effects (decreasing triglycerides, increasing HDL ("*good*") cholesterol, and decreasing systolic blood pressure and body weight); and unwanted effects, increasing LDL ("*bad*") cholesterol.

The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) Farxiga offers no clinically compelling advantages over the existing UF non-insulin diabetes drugs, given the modest decrease in A1c; risk of adverse reactions, including female genital mycotic ("*fungal*") infections and urinary tract infections; and unknown long-term cardiovascular safety profile.

(Dr. Meade)

B. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – Relative Cost effectiveness and Conclusion

CMA was performed to evaluate Farxiga with other oral products on the Uniform Formulary used in the treatment of diabetes. The P&T Committee concluded (16 for, 0 opposed, 1abstained, 0 absent) the following:

- CMA results showed that Farxiga was not cost-effective compared with existing formulary agents in the non-insulin diabetes class including metformin, sulfonylureas, thiazolidinediones (TZDs), and dipeptidyl-dipeptidase-4 (DPP-4) inhibitors.

- Current costs for Farxiga show it was comparable to Invokana, the other product available in the SGLT2 subclass.

(Dr. Meade)

C. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) Farxiga be designated NF, due to the lack of compelling clinical advantages, safety concerns, lack of long-term outcome, and cost disadvantage compared to UF products.

(Dr. Meade)

D. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – PA Criteria

Existing automated PA (step therapy) for the SGLT2 inhibitors requires a trial of metformin, or a sulfonylurea, and a DPP-4 inhibitor first, based on positive long-term outcomes data with metformin and the sulfonylureas.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) a trial of metformin or a sulfonylurea and a DPP-4 inhibitor in all new and current users of Farxiga, due to the modest hemoglobin Alc lowering and safety concerns.

Automated PA criteria: The patient has filled a prescription for metformin, a SU, AND a DPP-4 inhibitor at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria: If automated criteria are not met, Farxiga is approved (e.g., trial of metformin or SU AND a DPP-4 inhibitor is NOT required) if:

- The patient has experienced any of the following issues on metformin:
  - Impaired renal function ("*decreased kidney function*") precluding treatment with metformin
  - History of lactic acidosis ("*the build-up of lactic acid in the blood, which can be a sign of reduced blood flow")*
- The patient has experienced any of the following issues on a sulfonylurea:
  - Hypoglycemia ("*low blood sugar*") requiring medical treatment
- The patient has had inadequate response (*"blood sugars have not been adequately controlled")* to metformin or a SU or a DPP-4 inhibitor

- The patient has a contraindication to metformin or a SU or DPP-4 inhibitor

(Dr. Meade)

E. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – UF and PA Implementation Plan

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

F. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) Physician Perspective

As I mentioned previously an endocrinologist is on the committee. Lack of long term safety effect is a concern, and the Committee recognized the higher risk of fungal infections with this subclass. Other subclasses for treating diabetes have a longer history of use, and are more effective at lowering blood glucose levels (as measured by the HgA1c).

The Committee recommended non-formulary status for Farxiga, and also recommended that Farxiga have the same step therapy criteria that is currently in place for Invokana, the other drug in this subclass. All of the oral diabetes drugs have the step therapy requirement that a patient try metformin or a sulfonylurea first.

There are several drugs with this same mechanism of action in the pipeline, and the Committee will likely review the subclass sometime in 2015. The Committee also mentioned that consideration will be given to enhancing the step therapy recommendations with injectable drugs (insulin, or Exenatide and Victoza) in the future, when the subclass is reviewed.

G. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) – Panel Questions and Comments

The Panel members asked for clarification regarding the non-formulary status of Invocana. The Panel also expressed concerns about patients being able to obtain the newer drugs without a trial of metformin even if they do have a contraindication of metformin.

In response, the presenters stated that Invocana is currently non-formulary and patients are technical required to try sulfonylurea first but with the guidelines the way they are metformin is prevalent. Also, the decisions of the P&T Committee considered the advice of the endocrinologist on the committee.

Without further discussion, the Chair asked for a vote on the Sodium-Glucose Contransporter 2 Inhibitor Drugs.

H. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) UF Recommendation

The BAP voted:

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

I. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) PA Criteria

The BAP voted:

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

J. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Dapagliflozin (Farxiga) UF and PA Implementation Plan

The BAP voted:

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

VIII. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

(LTC Conrad)

A. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) Relative Clinical Effectiveness and Conclusion

Indacaterol (Arcapta) is a LABA that is dosed once daily. It is not available in a fixed-dose combination with an inhaled steroid.

Figure 8 on page 9 of the handout shows overall a decrease in utilization of the LABAs. Serevent has the highest utilization, and there has been very low usage of Arcapta.

The U.S. approved dose of 75 mcg administered once daily ("*higher doses are approved in Europe*") was based on two trials showing indacaterol produced statistically and clinically significant improvement in forced expiratory volume in one second (FEV1), "(*which measures how forcefully air is exhaled from the lungs"*) compared to placebo; there are no comparative trials available with this dose *("in other words, no trials of Arcapta with another LABA*"). The safety profile appears similar to the other LABAs, including a black box warning against use in patients with asthma.

The P&T Committee concluded (17 for, 0 against, 0 abstained, 0 absent) that although indacaterol is the only LABA dosed once daily, other drug classes, including the ICS/LABA

combinations (Advair) and long-acting muscarinic agents (for example Spiriva and Tudorza), are more effective than LABAs at improving pulmonary function, and decreasing hospitalizations or exacerbations ("*flare ups")* in patients with COPD ("*emphysema").*

(LTC Conrad)

B. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) Relative Cost Effectiveness and Conclusion

CMA was performed to evaluate Arcapta with other LABAs available on the UF that are used in the treatment of COPD. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA results showed that Arcapta was not cost-effective compared to Serevent and Foradil.

(LTC Conrad)

C. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) UF Recommendation

Despite the convenience of once daily dosing, the P&T Committee recommended (16 for, 0 against, 1 abstained, 0 absent) Arcapta be designated NF due to the lack of compelling advantages over the other LABAs and cost effectiveness. Additionally, the P&T Committee recommended reclassifying the LABAs to the Pulmonary II drug class, which includes other drug classes used for treating COPD.

(LTC Conrad)

D. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) UF Implementation Plan

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

E. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) - Physician Perspective:

There was also no controversy here. This is the first new LABA to reach the market in several years. The Committee did recognize the convenience to the patient of once daily dosing, but

patients with COPD are usually on several other drugs, so Arcapta would not necessarily simplify their medication regimen.

The COPD pipeline is very robust – three products were approved earlier this year, and we are expecting more combination products on the market. We want to move the LABAs over into the Pulmonary II drug class, which contains other drugs for COPD, which makes sense clinically (since the LABAs alone are no longer recommended for treating asthma), and to help increase competition within the class.

F. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) – Panel Questions and Comments:

There were no questions or concerns from the Panel members. Without further discussion, the Chair asked for a vote on the Long-Acting Beta Adrenertic Inhalers.

G. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) UF Recommendation

The BAP voted:

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

H. Long-Acting Beta Adrenergic (LABA) Inhalers: Indacaterol (Arcapta Neohaler) Implemenation Plan

The BAP voted:

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

IX. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

(LTC Conrad)

A. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) - Relative Clinical Effectiveness and Conclusion

Budesonide is a GI steroid used to treat inflammatory bowel disease. Budesonide is available in generic capsules (Entocort), and a new extended release tablet, Uceris. Figure 9 on page 10 of the handout shows some of the drugs in the GI-1 class. The green line shows generic Entocort capsules, and the bottom two lines (light blue and orange) show branded Entocort capsules and Uceris tablets.

Uceris differs from the Entocort capsules currently on the market in its delivery mechanism ("*how it releases drug into the GI tract*") and FDA-approved indication. The Uceris tablet releases drug in the distal colon, making it effective for ulcerative colitis ("*a type of inflammatory bowel disease which affects the lower GI tract*"), while Entocort is released in the distal ileum and right colon and is only indicated for the treatment of Crohn's disease ("*another type of inflammatory bowel disease*"). There are no head-to-head studies comparing Uceris to the oral aminosalicylates ("*another subclass of the GI-1s*"), but an indirect comparison to the branded mesalamine product Lialda suggests reduced efficacy at inducing remission after eight weeks of treatment.

The P&T Committee concluded (17 for, 0 against, 0 abstained, 0 absent) that although Uceris offers a locally-acting steroid option for patients with mild to moderate ulcerative colitis, it failed to demonstrate clinically compelling advantages over existing UF agents for this indication.

(LTC Conrad)

B. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) - Relative Cost Effectiveness and Conclusion

CMA was performed to evaluate Uceris with other oral GI steroids and mesalamine products on the UF for induction of remission in patients with mild to moderate ulcerative colitis. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) Uceris was not cost-effective compared with other GI steroid alternatives and mesalamine products on the UF.

(LTC Conrad)

C. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – UF Recommendation

The P&T Committee recommended (16 for, 0 against, 1 abstained, 0 absent) Uceris be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

(LTC Conrad)

D. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – UF Implementation Plan

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

E. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – Physician's Perspective

Once again, there was no controversy here, and the GI physician on the Committee agreed with the recommendation. Other drugs, including the aminosalicylates – Lialda, and the other mesalamine products, and biologics (Humira) are used to induce remission in patients with ulcerative colitis. There are also rectal steroid preparations on the Uniform Formulary which are used for this indication, and oral prednisone.

There are no step therapy requirements here, so if a patient needs Uceris, a medical necessity form can be filled out.

F. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – Panel Questions and Comments

There were no questions or concerns from the Panel members. Without further discussion, the Chair asked for a vote on the Gastrointestinal (GI-1s) Steroid subclass.

G. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – UF Recommendation

The BAP voted:

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

H. Gastrointestinal (GI-1s): GI steroid subclass—Budesonide Extended Release (ER) Tablets (Uceris) – Implementation Plan

The BAP voted:

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

X. REVIEW OF NEWLY APPROVED DRUGS

P&T Committee Comments

(LTC Conrad)

A. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) Relative Clinical Effectiveness and Conclusion

Zorvolex is a low dose formulation of diclofenac available in 18 mg and 35 mg capsules. The formulation is intended for faster dissolution and absorption compared to other diclofenac products (diclofenac potassium 50 mg and 100 mg; e.g., Cataflam). Generic diclofenac sodium (Voltaren) is another product.

According to the FDA, the manufacturer failed to demonstrate these theoretical advantages, as there were no differences in the pharmacokinetic profile ("*profile of how drugs are absorbed and eliminated from the body")* when Zorvolex was compared to diclofenac potassium. In the clinical trial used to obtain FDA approval, over 80% of patients received rescue narcotics for pain control. The Zorvolex package insert contains usual black box warnings and precautions for NSAIDs.

The P&T Committee concluded (13 for, 0 against, 0 abstained, 4 absent) that there were no clinical compelling advantages between Zorvolex and the other UF NSAIDs.

(LTC Conrad)

B. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) Relative Cost Effectiveness and Conclusion

CMA was performed to evaluate Zorvolex with other oral NSAIDs available on the UF used in the treatment of mild to moderate pain. The P&T Committee concluded (13 for, 0 opposed, 0 abstained, 4 absent) the following:

- CMA results showed that Zorvolex 18 and 35 mg capsules were not cost-effective compared to generic formulations of meloxicam (Mobic), ibuprofen (Motrin), diclofenac sodium (Voltaren), and diclofenac potassium (Cataflam).
- Zorvolex was comparable in cost to Celebrex. However, generic formulations of Celebrex are expected later this year and should result in further cost reductions for celecoxib.

(LTC Conrad)

C. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) UF Recommendation

The P&T Committee recommended (13 for, 0 against, 0 abstained, 4 absent) diclofenac low dose 18 mg and 35 mg capsules (Zorvolex) be designated NF, based on clinical and cost effectiveness.

(LTC Conrad)

D. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) UF Implementation Plan

The P&T Committee recommended (13 for, 0 against, 0 abstained, 4 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS; and, 2) DHA send a letter to beneficiaries affected by the UF decision.

E. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) - Physician's Perspective

The Committee recommended non-formulary placement based on the FDA review of the drug and cost-effectiveness. The vote was unanimous here.

A generic formulation of Celebrex was approved by the FDA in late May 2014, and is expected to launch soon. In addition to Celebrex, there are several generic NSAIDs on the Uniform Formulary, including the diclofenac products Voltaren and Cataflam.

F. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) - Panel Questions and Comments

There were no questions or comments from the Panel. Without further discussion, the Chair asked for a vote on the Non-Steroidal Anti-Inflammatory Drugs.

G. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) - UF Recommendation

The BAP voted:

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

H. Non-Steroidal Anti-inflammatory Drugs (NSAIDs): Diclofenac Low Dose (Zorvolex) - Implementation Plan

The BAP voted:

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

XI. UTILIZATION MANAGEMENT-PRIOR AUTHORIZATIONS

P&T Comments

(Dr. Allerman)

A. Cystic Fibrosis Drugs: Ivacaftor (Kalydeco)

Ivacaftor (Kalydeco) is a potentiator of the cystic fibrosis transmembrane conductance regulator (CFTR). *("Basically, this drug is what is called 'personalized medicine' or 'genomic medicine'")* The drug initially targeted a specific subgroup of patients with cystic fibrosis (CF) who had a G551D gene mutation. The FDA has expanded Kalydeco's approved indication to include additional mutations in the CFTR gene. PA criteria were recommended by the P&T Committee for Kalydeco in February 2012 and were implemented in July 2012. There are several FDA-approved in-vitro molecular diagnostic tests designed to simultaneously detect

and identify mutations in the CFTR gene.

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) updating the existing PA criteria to include the expanded FDA-approved indication.

(1) Coverage will be approved for the treatment of CF patients aged 6 years and older who have a G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R mutation in the CFTR gene, detected by an FDA-approved test.

(2) Coverage is not approved for patients who are homozygous for the F508del mutation in the CFTR gene.

(3) The approved PA limits coverage of the drug to its labeled use. DHA will expedite review of the required test to determine its coverage under 32 CFR 199.4(g)(15). Providers and beneficiaries will be advised to retain receipts for the test to submit for reimbursement following the coverage determination.

B. Cystic Fibrosis Drugs: Invacaftor (Kalydeco) —PA Authorization

The BAP voted:

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

XII. UTILIZATION MANAGEMENT – PRIOR AUTHORIZATIONS

P&T Comments

(CAPT Downs)

A. Targeted Immunomodulatory Biologics (TIBSs): Tofacitinib (Xeljanz) and Apremilast (Otezla)—PA criteria currently apply to the TIBs, *which are injectable drugs used to treat a variety of conditions, including arthritis, psoriasis and inflammatory bowel disease.* Tofacitinib (Xeljanz) is a janus kinase inhibitor approved for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had inadequate response or intolerance to methotrexate. Xeljanz is the first oral TIB to reach the market. Apremilast (Otezla) is an oral phosphodiesterase-4 inhibitor approved for the treatment of psoriatic arthritis.

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) PA criteria for tofacitinib (Xeljanz) and apremilast (Otezla), consistent with the product's labeling.

Tofacitinib (Xeljanz) PA Criteria: Coverage approved for patients $\geq$ 18 years with:

- Moderate to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.
- Not approved for use in combination with other biologics or potent immunosuppressants (aziathioprine and cyclosporine).

Apremilast (Otezla) PA Criteria: Coverage approved for patients $\geq$ 18 years with:

- Active psoriatic arthritis
- Coverage not approved for use in combination with other biologics

B. Targeted Immunomodulatory Biologics (TIBSs): Tofacitinib (Xeljanz) and Apremilast (Otezla)— Physician's Perspective

The Committee does routinely review new FDA approved indications for drugs where we already have Prior Authorizations, so that the PA criteria are up to date. The updated PA criteria for these 3 drugs reflect this, and there was no discussion by the Committee.

C. Targeted Immunomodulatory Biologics (TIBSs): Tofacitinib (Xeljanz) and Apremilast (Otezla)— Panel Questions and Comments

There were no questions or comments from the Panel. Without further discussion, the Chair asked for a vote on the Targeted Immunomodulatory Biologics (TIBS).

D. Targeted Immunomodulatory Biologics (TIBSs): Tofacitinib (Xeljanz) and Apremilast (Otezla) —Expanded the FDA food product labeling

The BAP voted:

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

XIII. UTILIZATION MANAGEMENT – PRIOR AUTHORIZATIONS

P&T Comments

(Dr. Meade)

Meade explains looking at prior authorization for generic to brand changes. Reason being, the manufacturers of branded products are giving such good price breaks. There are significant differences between the price available to the generics, which are more expensive than the branded price available. We are looking to put prior authorizations on these drugs so that the patient can get the branded product and not go to the generic substitution. One point is both do carry a generic co-pay. The beneficiary will not see a difference in the co-pay charge between brand and generic on these particular drugs.

A. Generic to Brand Changes: PA Criteria for the Retail Network for Niacin ER (Niaspan)

AB-rated generic formulations *("this is a rating by the FDA which essentially means the generic drug has the same blood levels as the branded product"*) for niacin ER (Niaspan) were launched in August 2013; however, pricing for the branded product is lower than the generic formulations. The manufacturer of Niaspan offered a Voluntary Agreement for Retail

Refunds, and the Tier 1 (generic) copayment was assigned to the branded product at the November 2013 P&T Committee meeting.

The mandatory generic drug policy is in place at the Retail Network; however, brand Niaspan is the preferred product for the MHS. PA criteria allowing for a patient to receive generic niacin ER instead of branded Niaspan is needed as a result of the generic to brand change (i.e., the reverse of the current brand to generic policy).

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) manual PA criteria for generic niacin ER in the Retail Network. The prescriber will provide patient-specific justification as to why the brand Niaspan product cannot be used. Acceptable reasons include the following, which have occurred or are likely to occur with the branded Niaspan product: allergy to the branded Niaspan; contraindication; sub-therapeutic response; physical restriction (e.g., swallowing issues); and brand availability issues.

There were no questions or comments from the Panel. Without further discussion, the Chair asked for a vote on the PA Criteria for the retail network for Niacin ER (Niaspan)

B. Generic to Brand Changes: PA Criteria for the Retail Network for Niacin ER (Niaspan) - PA Criteria

The BAP voted:

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

XIV. UTILIZATION MANAGEMENT – PRIOR AUTHORIZATIONS

P&T Comments

(Dr. Meade)

A. Generic to Brand Changes: PA Criteria for the Retail Network for Esomeprazole (Nexium)

Nexium) and omeprazole (generic Prilosec) are BCF and step-preferred in the Proton Pump Inhibitor (PPI) drug class. The patent for Nexium expired in May 2014; however, the launch date for generic formulations is unknown, due to manufacturing issues with the company granted exclusivity by the FDA. Market research indicates generic Nexium entrants will be less cost-effective than the branded formulation, leaving branded Nexium as the preferred product in the MHS. Therefore, PA criteria are needed to allow a patient to receive the generic esomeprazole instead of branded Nexium (i.e., the reverse of the current brand to generic policy).

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) manual PA criteria for generic esomeprazole in the Retail Network. The prescriber will provide patient-specific justification as to why the branded Nexium product cannot be used. Acceptable reasons include the following, which have occurred or are likely to occur with the branded

Nexium product: allergy to branded Nexium; contraindication; sub-therapeutic response; physical restriction (e.g., swallowing issues); and brand availability issues. Implementation will occur when generic esomeprazole products reach the market.

B. Generic to Brand Changes: PA Criteria for the Retail Network for Esomeprazole (Nexium) – Panel Questions and Comments

The Panel members asked if there is a process to communicate the "reverse of the current generic policy" to the network pharmacies. It is standard practice to substitute the generic for a brand name drug.

The presenter replied he "thinks" the information could be messaged.

Without further discussion, the Chair asked for a vote on the PA Criteria for the retail network for Esomeprazole (Nexium).

C. Generic to Brand Changes: PA Criteria for the Retail Network for Esomeprazole (Nexium) PA Criteria

The BAP voted:

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

XV. FISCAL YEAR 2008 NDAA, Section 703

(Dr. Meade)

The P&T Committee reviewed drugs from manufacturers that were not included on a DoD Retail Refund Pricing Agreement; these drugs are not in compliance with the Fiscal Year 2008 National Defense Authorization Act, Section 703. The law stipulates that if a drug is not compliant with Section 703, these drugs will be designated NF on the UF and will require pre-authorization prior to use in the Retail POS and medical necessity in the MTFs. These NF drugs will remain available in the Mail Order POS without preauthorization.

A. Section 703: Drugs Designated NF and Pre-Authorization Criteria

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) that the following products be designated NF on the UF:

- CorePharma: dextroamphetamine sulfate capsules
- Lupin: fenofibrate capsules; Wymzya Fe tablets
- Royal: Derma-Smoothe/FS Body Oil topical oil; DermOtic Oil otic drops
- Savient: Oxandrin tablets

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) the following pre-authorization criteria for the drugs recommended NF above: 1) obtaining the product by home delivery would be detrimental to the patient; and, 2) for branded products with AB generic availability, use of the generic product would be detrimental to the patient. These pre-authorization criteria do not apply to any POS other than retail network pharmacies.

B. Section 703: Implementation Plan for Pre-Authorization Criteria

The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 4 absent) 1) an effective date of the first Wednesday after a 90-day implementation period in all POS; and, 2) DHA send a letter to beneficiaries affected by these decisions.

Without further discussion, the Chair asked for a vote on the Implementation plan for Pre-Authorization Criteria for the Section 703 Drugs designated non-formulary.

C. Section 703: Implementation Period for PA Criteria

The BAP voted:

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

Colonel Spilker adjourns meeting at approximately 11:00 A.M.

Robert Duane Tackitt

Mr. Robert Duane Tackitt

Brief Listing of Acronyms Used in This Summary

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

- BAP – Beneficiary Advisory Panel
- AB - Bioequivalence
- Baseline CBC – Baseline Complete Blood Count
- BCF – Basic Core Formula
- Beconase AQ – Beclomethasone Nasal
- BIA – Budget Impact Analysis
- CEA – Cost-Effectiveness Analysis
- CF – Cystric Fibrosis
- CFR – Code of Federal Regulations
- CFTR – Cystic Fibrosis Transmembrane Conductance Regulator
- CMA – Cost Minimization Analysis
- COPD – Chronic Obstructive Pulmonary Disease
- DAA – Direct Acting Antiviral
- DFO – Designated Federal Officer
- DHA – Defense Health Agency
- DoD – Department of Defense
- DPP-4 – Dipeptidyl-Dipeptidase-4
- ER – Extended Release
- FACA – Federal Advisory Committee Act
- FDA – Food and Drug Administration
- FEV1 – Forced Expiratory Volume in one second
- GI-1s – Gastrointestinal
- HCV – Hepatitis C Virus
- HDL – High Density Lipoprotein
- HFA – Hysrofluoralkane
- Hgb – Hemoglobin
- ICS – Inhaled Corticosteroids
- IR – Immediate Release
- LA – Long-Acting
- LABA – Long-Acting Beta Adrenegic
- LDL – Low Density Lipoprotein
- Mcg – Microgram
- MHS – Military Health System
- MTF – Military Treatment Facility
- NDAA – National Defense Authorization Act

- NF – Nonformulary
- NOAC – New Oral Anticoagulant
- NSAIDs – Non-Steroid Anti-Inflammatory Drugs
- OAB – Overactive Bladder
- OTC – Over-the-Counter
- P&T – DoD Pharmacy & Therapeutics Committee
- PA – Prior Authorization
- PEC – Pharmacoeconomic Branch
- PEG interfernon – Peginterferon alfa-2a
- POS – Points of Service
- QNASL – Beclomenthasone
- QVAR – Beclomethasone Dipropionate HFA
- SGLT2 – Sodium-Glucose cotransporter 2
- SU – Sulphonylurea
- SVR – Sustained Virologic Response
- TIBs – Targeted Immunomodulatory Biologics
- TRICARE – Military Health Care System
- TZDs – Thiazolidinediones
- UF – Uniform Formulary
- USC – United States Code
- VTE – Venous Thromboembolism
- XL – Extended Release
- XR – Extended Release