EXECUTIVE SUMMARY

Uniform Formulary (UF) Beneficiary Advisory Panel (BAP) Comments
20 March 2014

UF CLASS REVIEWS – INHALED CORTICOSTEROIDS/LONG-ACTING BETA AGONISTA (ICS/LABAs) COMBINATIONS

A. ICS/LABAs Combinations—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) the following for the ICA/LABAs, based on clinical and cost effectiveness:

- UF and step-preferred: Advair Diskus/Advair HFA)
- NF and non-preferred: Dulera, Symbicort, and Breo Ellipta.
- This recommendation includes step therapy, which requires a trial of Advair Diskus or Advair HFA in all new and current users of Symbicort, Dulera, and Breo Ellipta who are older than 12 years.

B. ICS/LABAs Combinations—Prior Authorization (PA) Criteria

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) automated (step therapy) and manual PA criteria in all new and current users of Symbicort, Dulera, and Breo Ellipta who are older than 12 years of age; a trial of Advair Diskus or Advair HFA is required before the non-step preferred drugs.

Automated PA criteria

- The patient has filled a prescription for Advair or Advair HFA at any MHS pharmacy point of service [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

AND

Manual PA criteria—If automated criteria are not met, Symbicort, Dulera, or Breo Ellipta is approved (e.g., trial of Advair Diskus or Advair HFA is NOT required) if:

- Patient has experienced any of the following issues with either Advair Diskus or Advair HFA, which is not expected to occur with the non-preferred ICS/LABA combination drug:
    - inadequate response to Advair Diskus or Advair HFA
    - intolerable adverse effects

- contraindication
- patient previously responded to the nonformulary agent and changing to a formulary agent would incur unacceptable risk

C. ICS/LABAs Combinations—UF and PA Implementation Plan

The P&T Committee recommended (13 for, 2 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service (POS); and, 2) DHA send a letter to beneficiaries affected by the UF decision; and, 3) that the ICS/LABA Drug Class be added to the safety net program (Rapid Response Program).

Summary of Physician Perspective:

This is the 2nd time that the Committee has reviewed the class. Previously, all of the ICS/LABAs were on the Uniform Formulary; however, the recommendations now are to have Advair Diskus and Advair HFA as the preferred products (Step therapy), and the other drugs (Symbicort, Dulera, and Breo-Ellipta) as non-formulary. The reasons for choosing Advair were because there wasn't compelling evidence that one product clinically was superior to the others, and due to cost effectiveness; Advair will now have the lowest cost per month of therapy.

The Committee was unanimous in the formulary recommendations and in recommending step therapy – patient will need to try Advair first, before one of the other products. There is no grandfathering in the class – patients currently receiving Symbicort, Dulera and Breo Ellipta will need to switch to Advair, unless they had an inadequate response, couldn't tolerate Advair, have a contraindication to Advair, or risk deterioration in symptoms if changed to Advair. Currently Advair is the highest utilized ICS/LABA in the MHS; it has over 72% of the market share.

The Committee did acknowledge that there are a large number of beneficiaries affected by the decision. Around 40,000 patients will be affected by the non-formulary recommendations and the step therapy. However, this drug class will be added to the "safety net" (Rapid Response) program. ESI will send out letters to those patients who are affected by the step therapy who don't subsequently get their prescription filled for one of the inhalers. Also, children younger than 12 will be exempted from the step therapy requirements– the Committee recognized the importance of this patient population and didn't want to run the risk of a disrupting therapy in children.

Two Committee members disagreed with the implementation date of 60 days; they both recommended an implementation plan of 90 days, due to the numbers of patients affected.

Summary of Panel Vote/Comments:

The Panel members requested clarification regarding the implementation date for the ICS/LABAs Combinations. The implementation date is 60 days.

Without further discussion, the Panel voted on the following:

1. **ICS/LABAs Combinations – UF Recommendations**

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

Director, DHA:

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

2. **ICS/LABAs Combinations – Panel Vote on PA Criteria**

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

Director, DHA:

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

3. **ICS/LABAs Combinations—Panel Vote UF and PA Implementation Plan**

Concur: 6 Non-concur: 1 Abstain: 0 Absent: 0

Additional Panel Comments:

The Panel member that non-concurred agrees with dissention of the 90 day implementation period.

Director, DHA:

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

UF CLASS REVIEWS—GASTROINTESTINAL (GI-1s) DRUG CLASS

A. GI-1s: Oral Aminosalicylates Subclass—UF Recommendation

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

- UF: sulfasalazine, balsalazide 750 mg (Colazal, generics), olsalazine (Dipentum), and the mesalamine products Delzicol, Lialda, and Apriso
- NF: Pentasa, Asacol HD and the balsalazide 1,100 mg product (Giazo)

B. GI-1s: Oral Aminosalicylates Subclass—UF Implementation Plan

The P&T Committee recommended (15 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 class review included the 5-aminosalicylate products; the entire class (GI steroids, and rectal products) had previously been reviewed in February 2011. Several of the products (Delzicol, Asacol HD, Pentasa, Lialda, and Apriso) all contain the same active ingredient – mesalamine. The drugs in the class are highly interchangeable, but there are some differences in the numbers of tablets administered daily, and the frequency of dosing.

Lialda, Apriso, Delzicol Colazol, and Dipentum were recommended for Uniform Formulary placement. Lialda and Apriso have the advantages of once daily dosing. Two mesalamine products, Asacol HD and Pentasa were recommended for non-formulary. Giazo was also recommended for non-formulary placement due to it's limited FDA approval for use only in men. Overall, there was no controversy in the Uniform Formulary recommendation, and the decision was unanimous.

Summary of Panel Vote/Comments:

The Panel members' questions and concerns focused on the methods used to determine whether the P&T Committee recommends and implementation date of 60, 90 or 180 days. More specifically, were there considerations about the doctor changing the prescription and the costs associated with the changes. Additionally, a Panel member commented that when compared to the previous class of drugs, the rational and logic regarding the implementation dates is unclear.

The costs associated with a doctor changing the prescription were taken in to considerations. Other factors are the impact on the member beneficiary; cost analysis; the ability for the contractor to get the information out; and the cost to delay something across the system for an extra 30 or 60 days.

Without further discussion, the Panel voted on the following:

1. GI-1s: Oral Aminosalicylates Subclass – UF Recommendation

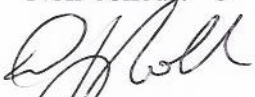
Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

Director, DHA:

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

2. 5-ARIs Subclass – Panel Vote on UF Implementation Plan

Concur: 7 Non-concur: 0 Abstained: 0 Absent: 0

Director, DHA: 

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

UF CLASS REVIEWS—PANCREATIC ENZYME PRODUCTS (PEPs)

A. PEPs—UF Recommendation

The P&T Committee recommended (13 for, 2 opposed, 1 abstained, 0 absent) Creon, Pancreaze, Zenpep, and Viokace remain on the UF, and that Pertzye and Ultresa be designated as NF.

B. PEPs—UF Implementation Plan

The P&T Committee recommended (15 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 Pancreatic Enzyme products were reviewed, primarily because there are 3 new products on the market since the last review in Feb 2011, and also because the class is now a Basic Core Formulary class, rather than an Extended Core Formulary Class.

There are only minor differences between the products; they all contain the same active ingredient, with varying percentages of lipase, amylase, and protease. Overall, the Committee felt that this class was highly interchangeable.

Creon, Zenpep, Pancreaze, and Viokace were recommended for Uniform Formulary placement. Ultresa and Pertzye were recommended for non-formulary placement; these two product had only 65 prescriptions in the MHS. The two opposing votes for the Uniform Formulary recommendation were because the Committee members felt that Viokace should be non-formulary; Viokace has 0.7% of the market share, while Creon, Zenpep and Pancreaze together account for 99% of the market share for the class.

Summary of Panel Vote/Comments:

The Panel members asked questions regarding the budget impact analysis (BIA) for Viokace and why committee members abstain.

As stated in the relative cost-effectiveness analysis and conclusions, a BIA was performed for Viokace and other agents. It did take into consideration that Viokace was an uncoated tablet.

The VA normally abstains because they do not provide comments on the formulary. They normally attend to provide information.

Without further discussion, the Panel voted on the following:

1. **PEPs – Panel Vote on UF Recommendation**

   Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

   Director, DHA:

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

2. **PEPs – Panel Vote on UF Implementaion Plan**

   Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

   Director, DHA:

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

RECENTLY APPROVED U.S. FDA AGENTS—ANTIDEPRESSANTS (AD-1s)

A. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—UF Recommendation

The P&T Committee recommended (15 for, 0 against, 0 absent, 1 abstain) bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), levomilnacipran (Fetzima), and vortioxetine (Brintellix) be designated NF, based on clinical and cost effectiveness. Additionally, the P&T Committee recommended Khedezla, Fetzima, and Brintellix be non-step preferred ("behind the step"), which requires a trial of a formulary AD-1 prior to use in all current and new patients. See Prior Authorization section, below.

B. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—PA Criteria

The P&T Committee recommended (15 for, 0 against, 0 absent, 1 abstain) PA criteria should apply to Khedezla, Fetzima, and Brintellix.

1. Desvenlafaxine ER (Khedezla): For all new users of Khedezla, patients are required to try venlafaxine IR or ER (Effexor, Effexor XR; generics) first.

2. Levomilnacipran (Fetzima) and vortioxetine (Brintellix): For new users of Fetzima or Brintellix, patients are required to try a generic SSRI, duloxetine, SNRI (except milnacipran), tricyclic antidepressant (TCA), mirtazapine, bupropion, serotonin antagonist reuptake inhibitor (trazodone or nefazodone), or mononamine oxidase inhibitor (MAOI) first.

   - **Desvenlafaxine ER (Khedezla)**—PA criteria apply to all new users of Khedezla.

     Automated PA criteria

     - The patient has filled a prescription for venlafaxine IR or venlafaxine ER 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, Khedezla is approved in new users (e.g., trial of venlafaxine IR or venlafaxine ER is NOT required) if:

     - Use of the formulary SNRI (venlafaxine) is contraindicated (e.g., hypersensitivity to a dye or other inert ingredient) and use of any other formulary antidepressant is not clinically appropriate.
     - The patient has previously responded to Khedezla, and changing to a formulary medication would incur unacceptable risk (e.g., the patient is currently stabilized on therapy with Khedezla and changing to a formulary medication would present a risk of destabilization).
     - The patient is being treated for depression, requires treatment with a SNRI (e.g., due to failure of SSRI therapy), and has failed an adequate trial of venlafaxine. Note: an adequate trial is generally considered to be at least 4–8 weeks in duration, due to the delay in achieving maximal benefit.
     - The patient requires treatment with a SNRI (e.g., due to failure of SSRI therapy), and has been unable to tolerate venlafaxine.

   - **Levomilnacipran (Fetzima) and vortioxetine (Brintellix)**—PA criteria apply to all new users of Fetzima and Brintellix.

     Automated PA criteria

     - The patient has filled a prescription for a formulary SSRI, duloxetine, SNRIs (except milnacipran), TCA, mirtazapine, buproprion, trazodone or nefazodone, or an MAOI at any MHS

pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria—For new users, Fetzima or Brintellix is approved (e.g., trial of a formulary AD-1 listed above is NOT required) if:

- Use of a formulary antidepressant (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI) is contraindicated (e.g., hypersensitivity to a dye or other inert ingredient) and use of any other formulary antidepressant is not clinically appropriate.
- The patient has previously responded to Fetzima or Brintellix, and changing to a formulary medication would incur unacceptable risk (e.g., the patient is currently stabilized on therapy with Fetzima or Brintellix and changing to a formulary medication would present a risk of destabilization).
- The patient is being treated for depression and has failed therapy with the formulary antidepressants (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI). Note: an adequate trial is generally considered to be at least 4–8 weeks in duration, due to the delay in achieving maximal benefit.
- The patient is being treated for depression and has been unable to tolerate the formulary antidepressants (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI).

C. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—UF and PA Implementation Plan

The P&T Committee recommended (15 for, 0 against, 0 absent, 1 abstain) 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 no controversy in the non-formulary recommendations for the four new antidepressants; there is only limited clinical information available, and they are not cost-effective. There hasn't been a lot of utilization so far for these new products; there were only 83 prescriptions dispensed. Three of the drugs, ForFivo, Khedezla and Fetzima are only minor variations of existing products.

The Uniform Formulary already has a wide selection of several drugs from the different sub-classes that are cost effective. The Committee did recommend step therapy for these four drugs, which is similar to what has been done previously in the class.

Summary of Panel Vote/Comments:

The Panel member asked questions regarding the number of formulary agents that patient has to try and fail prior to use for all current and new patients; specific PA requirement recommendations for Bupropion ER 450 mg (Forfivo XL); and if the system looks for 4-8 week trials in the automated PA criteria.

Current and new patients are only required to try one of the formulary agents, not all. There were no specific PA recommendations for Bupropion ER 450 (Forfivio XL) addressed by the committee but Dr. Meade will follow-up and confirm that there were none.

The systems will to confirm adequate 4-8 week trials in the automated PA criteria. It is assumed that the manual process with verify an adequate trial.

Without further discussion, the Panel voted on the following:

1. **AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Panel Vote on UF Recommenation**

   Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

   Director, DHA:

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

2. **AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Panel Vote on PA Criteria**

   Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

   Director, DHA:

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

3. **AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Panel Vote on Implementation Plan:**

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

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

UTILIZATION MANAGEMENT

A. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—PA Criteria

Mirabegron was FDA-approved for OAB in June 2012 and launched in October 2013. It will be reviewed as a new drug at an upcoming meeting. Mirabegron is a beta-3 agonist, which is a unique mechanism compared to the antimuscarinic OAB drugs. In placebo-controlled trials, the efficacy of mirabegron on OAB symptoms appears similar to that of the other OAB drugs; however, mirabegron causes less anticholinergic AEs (dry mouth, constipation). The OAB drugs were reviewed for UF placement in November 2012, and automated PA (step therapy) was implemented, requiring a trial of a generic OAB drug or Detrol LA in all new and current users of an OAB drug.

The P&T Committee recommended (13 for, 1 opposed, 1 abstained, 1 absent) PA criteria for all new users of mirabegron (Myrbetriq) for OAB.

- **Mirabegron (Myrbetriq)**—PA criteria apply to all new users of Myrbetriq.

  Automated PA criteria

  - The patient has filled a prescription for tolterodine ER (Detrol LA), oxybutynin ER, oxybutynin IR, or generic trospium IR (Sanctura) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

  - Coverage is only approved for the FDA-approved indication of OAB with symptoms of urge incontinence, urgency, and urinary frequency
  - Patient has failed a 12-week trial with at least one of the following step-preferred OAB drugs (Detrol LA, oxybutynin ER, oxybutynin IR, or trospium IR) due to a treatment failure or intolerable adverse effects.
  - Patient has experienced central nervous system (CNS) adverse effects with oral OAB medications or is at increased risk for such CNS effects due to comorbid conditions or other medications.

B. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—PA Implementation

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 30-day implementation period in all POS.

Summary of Physician Perspective:

Mirabegron (Myrbetriq) – Myrbetriq is a new drug for treating overactive bladder that has a different mechanism of action than the anticholinergic drugs (Detrol LA, Ditropan, Vesicare, etc). The Committee will review Myrbetriq as a new drug at an upcoming meeting. However PA criteria were recommended because the other OAB drugs have PA criteria that require the use of Detrol LA or a generic drug first. The PA criteria for Myrbetriq will apply to new users of the drug. New users will be required to try Detrol LA or a generic first. However, the manual PA criteria for Myrbetriq is different from what is in place for the other OAB drugs; the PA criteria reflect that the product is better tolerated than the anticholinergic drugs.

The one opposing vote for the PA criteria was because the Committee member felt that the PA criteria should mention that Myrbetriq is not on the Beer's list, which is a list of drugs that should not be used in elderly patients, due to the risk of adverse events.

Summary of Panel Vote/Comments:

The Panel members asked questions about the Automated PA criteria and the method used to confirm that there was an adequate 12 week trial by the patient as well as the utilization of the IR and ER products for this particular class of drugs. More specifically, is a trial and fail of the ER product required.

There is no way to monitor whether a patient had an adequate 12 week trial of the medication. The manual form is used in an effort to make the physician check to confirm the trial.

The Panel made a recommendation to provide education and provider outreach to ensure that an adequate 12 week has occurred to for the generic and formulary OAB.

In response to the question regarding the utilization and possible trials for the IR and ER products, patients used the ER product more than the IR product.

Without further discussion, the Panel voted on the following:

1. **Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—Panel Vote on the PA Criteria**

   Concur: 6 Non-concur: 1 Abstain: 0 Absent: 0

Additional Panel Comments: It appears that there should be a step behind ER products, that the IR products wouldn't get them to where they want to be in the formulary.

Director, DHA:

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

2. **Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—Panel Vote on PA Implementation**

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

Director, DHA:

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

UTILIZATION MANAGEMENT

1. **Phosphodiesterase-5 (PDE-5) Inhibitor: Avanafil (Stendra)—PA Criteria**

Avanafil is a new PDE-5 inhibitor approved by the FDA in April 2012, but not launched until January 2014. It is only approved for erectile dysfunction (ED). Currently, automated PA (step therapy) applies to the class for ED; Viagra is the step-preferred PDE-5 for ED.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) PA criteria for all users of Avanafil (Stendra) for ED. A trial of sildenafil (Viagra) for ED is required prior to using Stendra. Uses other than ED, including benign prostatic hypertrophy, following prostatectomy, pulmonary arterial hypertension, or Raynaud's phenomenon are not allowed.

- **Avanafil (Stendra)**—PA applies to all new and current users of avanafil (Stendra).

  Automated PA criteria

  - The patient has received a prescription for sildenafil (Viagra) at any MHS point of service (MTFs, Retail Network or Mail Order) during the previous 180 days.

  - The patient is a male, aged 40 years of older with ED.

  Manual PA criteria—if automated criteria are not met. Stendra is approved if:

- The patient has tried sildenafil (Viagra) and has had an inadequate response or was unable to tolerate treatment due to adverse effects.

- Treatment with Viagra is contraindicated.

Note: Coverage is approved only for erectile dysfunction (ED). Use for benign prostatic hyperplasia (BPH), following prostatectomy, pulmonary arterial hypertension, and Raynaud's phenomenon is not allowed. Additionally, use is not allowed for treatment of ED in males younger than age 18, for ED due to psychogenic origin, or in women for female sexual dysfunction.

Summary of Physician Perspective:

This is the 4th PDE-5 inhibitor on the market. The other PDE-5 inhibitors (Viagra, Cialis and Levitra) have PA criteria. For Stendra, the recommendation was to have the same PA criteria for treating erectile dysfunction as the other products.

Summary of Panel Vote/Comments

No questions or comments from the Panel.

Without further discussion, the Panel voted on the following:

1. **Phosphodiesterase-5 (PDE-5) Inhibitor: Avanafil (Stendra)—Panel Vote on PA Criteria:**

   Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

RE-EVALUATION OF NF AGENTS

1. **Duloxetine (Cymbalta)—UF Recommendation and Implementation**

   On an ongoing basis, the DHA Pharmacoeconomic Branch monitors changes in the clinical information, current costs, and utilization trends to determine whether the UF status of agents designated as NF needs to be readdressed. The P&T Committee's process for reevaluating NF agents was established at the May 2007 meeting and approved by the Director, TMA, on June 24, 2007.

   The P&T Committee reevaluated the UF status of duloxetine (Cymbalta) in light of recent price reductions in generic formulations across all three POS. Additionally, automated PA (step therapy) requires a trial of a generic formulary antidepressant or generic non-opioid pain syndrome drug before receiving Cymbalta. As of the meeting, the generic duloxetine products were not cost-effective relative to the price of branded Cymbalta.

   The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) maintaining

Cymbalta as NF and continuing the current step therapy. When generic formulations of Cymbalta become cost-effective relative to the step-preferred agents, generic duloxetine will move to UF status, become step-preferred (e.g., "in front of the step"), and existing PA criteria will be removed 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 the generic agent's 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.

Meade says once that happened we would come back to you and let you know.

Summary of Physician Perspective:

Generic formulations of Cymbalta were launched in the fall of 2013, however, the price of branded Cymbalta is still less expensive than the generics. We are closely watching the price of the generics, and wanted this section included in the minutes, so that when the generics become cost-effective, we can quickly act to designate Cymbalta as a Uniform Formulary product, and also remove the current Prior Authorization criteria.

Summary of Panel Vote/Comments;

No questions or comments from the Panel.

Without further discussion, the Panel voted on the following:

1. **Duloxetine (Cymbalta)—Panel Vote on UF Recommendation and Implementation**

Concur: 7 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
March 20, 2014
Washington, D.C.

Present Panel Members

- Lisa Le Gette
- Kathryn Buchta
- Amit Khurana
- Robert Duane Tackitt
- Elizabeth Sampsel
- Robert L. Lewis
- Steven Hein

The meeting was held at the Naval Heritage Center Theater, 701 Pennsylvania Ave. N.W., Washington D.C. Colonel J. Michael Spilker called the proceedings to order at 9:00 A.M. Col J. Michael Spilker indicated that the Panel has been convened to review and comment on the therapeutic drug class recommendations resulting from the February 13, 2014 Department of Defense (DoD) Pharmacy and Therapeutics 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 discussions of the P&T Committee recommendations for the following:
    - *Drug Class Reviews*
        - Long acting beta agonist/inhaled corticosteroids
        - Pancreatic enzyme products
        - GI-l amino salisylate subclass
    - *Designated Newly Approved Drugs*
        - Antidepressant 1 – Bupropion 450 mg (ForFivo)
        - Antidepressant 1 – Desvenlafaxine extended release (Khedezla)
        - Antidepressant 1 – Vortioxetine (Brintellix)
        - Antidepressant 1 – Levomilnacipran (Fetzima)

- *Utilization Management Issues*

  - Prior Authorization Criteria
    - A vanafil (Stendra)
    - Mirabegron (Myrbetriq)

Opening Remarks

Col Spilker 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 the pharmaceutical agent and establishes 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 panels 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 approved 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, Colonel 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 classes selected for review, drugs recommended for the basic core formulary (BCF) or specific pricing data, these topics do not fall under the purview of the BAP.

The P&T Committee met for approximately 9 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 TRICARE 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.

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

Chairman's Opening Remarks

The DFO turned the meeting over to Mr. Robert Duane Tackitt.

Mr. Tackitt greeted with, "Happy first day of spring." He is the interim Chairman for today's meeting. He turns the meeting over to Dr. David 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 is LTC Chris Conrad the PEC Branch Director.

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.

    a. 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/Long Acting Beta Agonist (ICS/LABAs), Aminosalicylates subclass from the GE-1 class and the Pancreatic Enzyme Product (PEP) class Additionally, 4 newly approved drugs from the AD-1 class were reviewed – Bupropion Extended Release (ER) 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix). We will also discuss prior authorizations for Mirabegron (Myrbetriq) and Avanafil (Stendra), as well as the formulary status of Duloxetine (Cymbalta).

3. 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 8. 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.

UF CLASS REVIEWS—INHALED CORTICOSTEROIDS/LONG-ACTING BETA AGONISTS (ICS/LABAs) COMBINATIONS

P&T Comments

A. ICS/LABAs Combinations—Relative Clinical Effectiveness and Conclusion

The P&T Committee evaluated the clinical effectiveness of the ICS/LABA combinations, which were last reviewed for UF status in February 2009. Since the last review, one new drug, fluticasone/vilanterol (Breo Ellipta) has been marketed. Military Health System (MHS) expenditures for the class were $168 million in calendar year 2013. The P&T Committee agreed (16 for, 0 opposed, 0 abstained, 0 absent) with the following conclusions:

1. Fluticasone/salmeterol (Advair) and budesonide/formoterol (Symbicort) are highly therapeutically interchangeable for asthma. For asthma, head-to-head trials and systematic reviews show no significant differences in efficacy.
2. For chronic obstructive pulmonary disease (COPD), there is insufficient evidence to conclude that there are clinically relevant differences in efficacy between Advair and Symbicort.
3. Advair Diskus, Symbicort, and Breo Ellipta are all FDA-approved for maintenance treatment of COPD; however, only Advair Diskus and Breo Ellipta are specifically approved for decreasing COPD exacerbations. Symbicort does have data from observational studies showing decreases in COPD exacerbations.
4. For mometasone/formoterol (Dulera), there are no head-to-head trials with another ICS/LABA in asthma; clinically relevant differences in efficacy are not expected. Dulera is not approved for COPD; two trials have shown benefit in improving lung volume breathing tests in COPD.
5. There is only limited data for Breo Ellipta in patients with asthma, and it is not FDA-approved for this indication.
6. Breo Ellipta offers the convenience of once-a-day dosing in COPD. However, the long-term safety of the LABA component vilanterol is not known. One large trial evaluating mortality is underway.
7. Advair Diskus in the only drug approved for treatment of asthma in children down to the age of four years; however, for this age range, a metered dose inhaler (MDI) with a spacer is more commonly used. It also has the advantage of availability in both a breath actuated inhaler and a propellant driven inhaler.
8. For safety, a systematic review did not show clinically relevant differences between Advair and Symbicort in asthma. Advair Diskus, Advair HFA, Symbicort, Dulera, and Breo Ellipta all contain the same black box warnings and precautions. All drugs containing a LABA carry a black box warning for the increased risk of death in asthma.
9. Breo Ellipta and Dulera have a lower degree of interchangeability with Advair and Symbicort, due to their limited FDA-approved indications.

10. The Pharmacy Outcomes Research Team (PORT) presented an analysis of the use of ICS/LABAs by indications and found that asthma represents the majority of MHS use (67% of beneficiaries had diagnosis codes indicative of asthma, while 37% had codes for COPD, and 17% had codes for neither diagnosis). There was considerable overlap between the COPD and asthma diagnosis codes.

B. ICS/LABAs Combinations—Relative Cost-Effectiveness Analysis and Conclusion

A pharmacoeconomic analysis and budget impact analysis (BIA) were performed to evaluate the ICS/LABAs. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

- The pharmacoeconomic analysis showed that Advair Diskus/Advair HFA was the most cost-effective agent in this class, followed by Dulera, Symbicort, and Breo Ellipta.
- A BIA was performed to evaluate the potential impact of scenarios, with selected agents designated step-preferred and formulary or non-preferred and NF on the UF. BIA results showed that the scenario where Advair Diskus and Advair HFA are designated as step-preferred and formulary, with Dulera, Symbicort, and Breo Ellipta designated as non-preferred and NF, was the most cost-effective option for the MHS.

C. ICS/LABAs Combinations—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) the following for the ICA/LABAs, based on clinical and cost effectiveness:

- UF and step-preferred: Advair Diskus/Advair HFA)
- NF and non-preferred: Dulera, Symbicort, and Breo Ellipta.
- This recommendation includes step therapy, which requires a trial of Advair Diskus or Advair HFA in all new and current users of Symbicort, Dulera, and Breo Ellipta who are older than 12 years.

D. ICS/LABAs Combinations—Prior Authorization (PA) Criteria

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) automated (step therapy) and manual PA criteria in all new and current users of Symbicort, Dulera, and Breo Ellipta who are older than 12 years of age; a trial of Advair Diskus or Advair HFA is required before the non-step preferred drugs.

<u>Automated PA criteria</u>

- The patient has filled a prescription for Advair or Advair HFA at any MHS pharmacy point of service [Military Treatment Facilities (MTFs), retail network

pharmacies, or mail order] during the previous 180 days.

AND

Manual PA criteria—If automated criteria are not met, Symbicort, Dulera, or Breo Ellipta is approved (e.g., trial of Advair Diskus or Advair HFA is NOT required) if:

- Patient has experienced any of the following issues with either Advair Diskus or Advair HFA, which is not expected to occur with the non-preferred ICS/LABA combination drug:
    - inadequate response to Advair Diskus or Advair HFA
    - intolerable adverse effects
    - contraindication
    - patient previously responded to the nonformulary agent and changing to a formulary agent would incur unacceptable risk

E. ICS/LABAs Combinations—UF and PA Implementation Plan

The P&T Committee recommended (13 for, 2 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service (POS); and, 2) DHA send a letter to beneficiaries affected by the UF decision; and, 3) that the ICS/LABA Drug Class be added to the safety net program (Rapid Response Program).

F. ICS/LABAs Combinations – Physician's Perspective:

This is the 2nd time that the Committee has reviewed the class. Previously, all of the ICS/LABAs were on the Uniform Formulary; however, the recommendations now are to have Advair Diskus and Advair HFA as the preferred products (Step therapy), and the other drugs (Symbicort, Dulera, and Breo-Ellipta) as non-formulary. The reasons for choosing Advair were because there wasn't compelling evidence that one product clinically was superior to the others, and due to cost effectiveness; Advair will now have the lowest cost per month of therapy.

The Committee was unanimous in the formulary recommendations and in recommending step therapy – patient will need to try Advair first, before one of the other products. There is no grandfathering in the class – patients currently receiving Symbicort, Dulera and Breo Ellipta will need to switch to Advair, unless they had an inadequate response, couldn't tolerate Advair, have a contraindication to Advair, or risk deterioration in symptoms if changed to Advair. Currently Advair is the highest utilized ICS/LABA in the MHS; it has over 72% of the market share.

The Committee did acknowledge that there are a large number of beneficiaries affected by the decision. Around 40,000 patients will be affected by the non-formulary recommendations and the step therapy. However, this drug class will be added to the "safety net" (Rapid Response) program. ESI will send out letters to those patients who are affected by the step therapy who don't subsequently get their prescription filled for one of the inhalers. Also, children younger than 12 will be exempted from the step therapy requirements– the Committee recognized the importance of this patient population and didn't want to run the risk of a disrupting therapy in children.

Two Committee members disagreed with the implementation date of 60 days; they both recommended an implementation plan of 90 days, due to the numbers of patients affected.

G. ICS/LABAs Combinations – Panel Questions and Comments:

The Panel members requested clarification regarding the implementation date for the ICS/LABAs Combinations. The implementation date is 60 days.

H. ICS/LABAs Combinations – Panel Vote on the UF Recommendations

The Chair called for the vote on the Uniform Formulary recommendations on the ICS/LABAs Combinations.

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

- UF and step-preferred: fluticasone/salmetrerol (Advair Diskus and Advair HFA)
- NF and non-preferred: budesonide/formoterol (Symbicort), mometasone/formoterol (Dulera), and fluticasone/vilanterol (Breo Ellipta)
- This recommendation includes step therapy, which requires a trial of Advair Diskus or Advair HFA in all new and current users of Symbicort, Dulera, and Breo Ellipta who are older than 12 years.

There was no further discussion by the panel.

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

I. ICS/LABAs Combinations – Panel Vote on PA Criteria

The Chair called for the vote on the PA Criteria.

The P&T Committee recommended automated (step therapy) and manual PA criteria in all new and current users of Symbicort, Dulera, and Breo Ellipta who are older than 12 years of age; a trial of Advair Diskus or Advair HFA is required before the non-step preferred drugs.

Automated PA criteria

- The patient has filled a prescription for Advair or Advair HFA 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, Symbicort, Dulera, or Breo Ellipta is approved (e.g., trial of Advair Diskus or Advair HFA is NOT required) if:

- Patient has experienced any of the following issues with either Advair Diskus or Advair HFA, which is not expected to occur with the non-preferred ICS/LABA combination drug:
    - Inadequate response to Advair Diskus or Advair HFA
    - Intolerable adverse effects
    - Contraindication
    - Patient previously responded to the nonformulary agent and changing to a formulary agent would incur unacceptable risk

The BAP voted:

Concur: 7	Non-concur: 0	Abstain: 0	Absent: 0

J. ICS/LABAs Combinations—Panel Vote UF and PA Implementation Plan

The P&T Committee recommended (13 for, 2 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service (POS); and, 2) DHA send a letter to beneficiaries affected by the UF decision; and, 3) that the ICS/LABA Drug Class be added to the safety net program (Rapid Response Program).

The BAP voted:

Concur: 6	Non-concur: 1	Abstain: 0	Absent: 0

Additional Panel Comments:

The Panel member that non-concurred agrees with dissention of the 90 day implementation period.

UF CLASS REVIEWS—GASTROINTESTINAL (GI-1s) DRUG CLASS

P&T Comments

A. GI-1s: Oral Aminosalicylates Subclass—Relative Clinical Effectiveness and Conclusion

The P&T Committee evaluated the relative clinical effectiveness of the oral aminosalicylates, a subclass within the GI-1s Drug Class. The subclass is comprised of generic sulfasalazine and the 5-aminosalicylate (5-ASA) products [balsalazide (generic Colazal and Giazo), olsalazine (Dipentum), and mesalamine (Delzicol, Asacol HD, Pentasa, Lialda, and Apriso)].

The GI-1s were previously reviewed for UF placement in February 2011, and mesalamine delayed release (DR) tablets (Asacol), along with generic sulfasalazine, were recommended for BCF addition. Asacol was discontinued from the market in March 2013 due to safety concerns of dibutyl phthalate (DBP) present in the enteric coating of Asacol tablets. A new phthalate-free mesalamine DR formulation, Delzicol is now available. At the May 2013 meeting, Asacol was removed from the BCF, pending a re-review of the subclass.

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

1. Sulfasalazine remains the first-line oral aminosalicylate. For the induction of remission in active ulcerative colitis (UC). UC is inflammation and ulceration of the large intestine innermost lining, occurs, tiny open sores may form on the surface of the lining. Evidence from two systematic reviews found no clinically relevant differences in efficacy between sulfasalazine and the newer 5-ASA formulations.
2. For maintenance of remission in UC, another systematic review showed a therapeutic advantage of sulfasalazine over the 5-ASA formulations. This advantage was offset by an increase in adverse events observed with sulfasalazine, due to the sulfapyridine moiety.
3. The newer 5-ASA formulations employ different release mechanisms, which deliver the active drug to various sites in the GI tract. These differences in drug release and site of release do not confer additional benefits in terms of clinical response.
4. The mesalamine product Delzicol is the phthalate-free replacement for Asacol that is bioequivalent to its predecessor; no clinical trials were conducted to evaluate efficacy or safety.

5. Giazo is a new balsalazide product with a higher strength per unit than the other balsalazide formulations (1,100 mg versus 750 mg with Colazal). It is not approved for use in women, and it offers no compelling advantage to the other balsalazide products commercially available.
6. The safety profile is similar for the 5-ASA products, based on systematic reviews. In clinical trials, females treated with Giazo reported more adverse events than males.
7. Lialda and Apriso are dosed once daily, which provides patient convenience, but have not been shown to have clinically relevant benefits in terms of adherence compared to 5-ASAs dosed twice or three times daily. Lialda and Apriso also have the lowest tablet burden.
8. The 5-ASA products are highly therapeutically interchangeable for treating UC. The choice of 5-ASA for UC will depend on other factors, such as location and extent of disease, as well as patient preference in terms of tablet burden and frequency of dosing.

B. GI-1s: Oral Aminosalicylates Subclass—Relative Cost-Effectiveness Analysis and Conclusion

Cost minimization analysis (CMA) and BIA were performed to evaluate the GI-1s Aminosalicylate Subclass. The P&T Committee concluded (15 for, 0 opposed, 1 abstained, 0 absent) the following:

- CMA results showed that generic sulfasalazine was the most cost-effective agent in this subclass, followed by balsalazide 750 mg (Colazal, generics), olsalazine (Dipentum), and the branded mesalamine agents Apriso, Lialda, Delzicol, Asacol HD, and Pentasa. Giazo (branded balsalazide 1,100 mg) was not cost-effective relative to other agents in this class.

- BIA was performed to evaluate the potential impact of scenarios with selected agents designated formulary or NF on the UF. BIA results showed the scenario with Apriso, Delzicol, and Lialda designated as formulary on the UF, with Asacol HD and Pentasa designated as NF, was the most cost-effective for the MHS.

C. GI-1s: Oral Aminosalicylates Subclass—UF Recommendation

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

- UF: sulfasalazine, balsalazide 750 mg (Colazal, generics), olsalazine (Dipentum), and the mesalamine products Delzicol, Lialda, and Apriso
- NF: Pentasa, Asacol HD and the balsalazide 1,100 mg product (Giazo)

D. GI-1s: Oral Aminosalicylates Subclass—UF Implementation Plan

The P&T Committee recommended (15 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.

E. GI-1s: Oral Aminosalicylates Subclass – Physician's Perspective

The class review included the 5-aminosalicylate products; the entire class (GI steroids, and rectal products) had previously been reviewed in February 2011. Several of the products (Delzicol, Asacol HD, Pentasa, Lialda, and Apriso) all contain the same active ingredient – mesalamine. The drugs in the class are highly interchangeable, but there are some differences in the numbers of tablets administered daily, and the frequency of dosing.

Lialda, Apriso, Delzicol Colazol, and Dipentum were recommended for Uniform Formulary placement. Lialda and Apriso have the advantages of once daily dosing. Two mesalamine products, Asacol HD and Pentasa were recommended for non-formulary. Giazo was also recommended for non-formulary placement due to it's limited FDA approval for use only in men. Overall, there was no controversy in the Uniform Formulary recommendation, and the decision was unanimous.

F. GI-1s: Oral Aminosalicylates Subclass – Panel Questions and Comments:

The Panel members' questions and concerns focused on the methods used to determine whether the P&T Committee recommends and implementation date of 60, 90 or 180 days. More specifically, were there considerations about the doctor changing the prescription and the costs associated with the changes. Additionally, a Panel member commented that when compared to the previous class of drugs, the rational and logic regarding the implementation dates is unclear.

The costs associated with a doctor changing the prescription were taken in to considerations. Other factors are the impact on the member beneficiary; cost analysis; the ability for the contractor to get the information out; and the cost to delay something across the system for an extra 30 or 60 days.

G. GI-1s: Oral Aminosalicylates Subclass – Panel Vote on UF Recommendation

The P&T Committee recommended the following, based on the high degree of therapeutic interchangeability and cost-effectiveness:

- UF: sulfasalazine, balsalazide 750 mg (Colazal, generics), olsalazine (Dipentum), and the mesalamine products Delzicol, Lialda, and Apriso

- NF: Pentasa, Asacol HD and the balsalazide 1,100 mg product (Giazo)

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

H. 5-ARIs Subclass – Panel Vote on UF Implementation Plan

The P&T Committee recommended 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.

The BAP voted:

Concur: 7 Non-concur: 0 Abstained: 0 Absent: 0

UF CLASS REVIEWS—PANCREATIC ENZYME PRODUCTS (PEPs)

P&T Comments

A. PEPs—Relative Clinical Effectiveness and Conclusion

The P&T Committee evaluated the relative clinical effectiveness of the PEPs. The class was previously an extended core formulary class and last reviewed in February 2011. The PEPs were reviewed for the FDA-approved indication of exocrine pancreatic insufficiency (EPI) due to cystic fibrosis or other conditions; other uses (e.g., pain relief from pancreatitis) were not reviewed. Since the last review, three new products, Pertzye, Viokace, and Ultresa, have been marketed. The PEPs all contain various amounts of lipase, amylase, and protease.

The P&T Committee recommended (15 for, 1 opposed, 0 abstained, 0 absent) the following conclusions:

1. Based on clinical efficacy alone, Creon, Pancreaze, Zenpep, Viokace, Ultresa, and Pertzye are effective at increasing coefficient of fat absorption in patients with EPI, compared to placebo. Only limited clinical trial data is available.
2. Creon has the most indications and highest MHS utilization. Among the PEPs, Creon has an additional indication for EPI due to pancreatitis or pancreatectomy.
3. Zenpep has the most dosage strengths available, but it is solely approved for EPI due to cystic fibrosis.
4. Zenpep and Viokace have information for gastrostomy tube administration.

5. Viokace is an uncoated tablet that is not approved for use in pediatrics; it requires administration with a proton pump inhibitor, to prevent degradation in the stomach.
6. Creon, Pancreaze, and Zenpep have dosing recommendations for infants as young as 12 months of age while Pancreaze has dosing information in infants as young as 6 months.
7. Pertzye and Ultresa have limited data regarding efficacy in treating EPI and have limited dosage strengths available.
8. With regards to safety, the available evidence suggests there are no clinically relevant differences between any of the PEPs.
9. There is a high degree of therapeutic interchangeability among the class.

B. PEPs—Relative Cost-Effectiveness Analysis and Conclusion

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

- CMA results showed that Creon was the most cost-effective agent in this class, followed by Zenpep, Pancreaze, and Viokace. Ultresa and Pertzye were not cost-effective relative to other agents in this class.
- BIA was performed to evaluate the potential impact of scenarios with selected agents designated formulary or NF on the UF. BIA results showed the scenario with Creon, Zenpep, Pancreaze, and Viokace designated as formulary on the UF, with Ultresa and Pertzye designated as NF on the UF, was the most cost-effective for the MHS.

C. PEPs—UF Recommendation

The P&T Committee recommended (13 for, 2 opposed, 1 abstained, 0 absent) Creon, Pancreaze, Zenpep, and Viokace remain on the UF, and that Pertzye and Ultresa be designated as NF. Note error in handout

D. PEPs—UF Implementation Plan

The P&T Committee recommended (15 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.

E. PEPs—Physician's Perspective

The Pancreatic Enzyme products were reviewed, primarily because there are 3 new products on the market since the last review in Feb 2011, and also because the class is now a Basic Core Formulary class, rather than an Extended Core Formulary Class.

There are only minor differences between the products; they all contain the same active ingredient, with varying percentages of lipase, amylase, and protease. Overall, the Committee felt that this class was highly interchangeable.

Creon, Zenpep, Pancreaze, and Viokace were recommended for Uniform Formulary placement. Ultresa and Pertzye were recommended for non-formulary placement; these two product had only 65 prescriptions in the MHS. The two opposing votes for the Uniform Formulary recommendation were because the Committee members felt that Viokace should be non-formulary; Viokace has 0.7% of the market share, while Creon, Zenpep and Pancreaze together account for 99% of the market share for the class.

F. PEPs – Panel Questions and Comments:

The Panel members asked questions regarding the budget impact analysis (BIA) for Viokace and why committee members abstain.

As stated in the relative cost-effectiveness analysis and conclusions, a BIA was performed for Viokace and other agents. It did take into consideration that Viokace was an uncoated tablet.

The VA normally abstains because they do not provide comments on the formulary. They normally attend to provide information.

G. PEPs – Panel Vote on UF Recommendation

The P&T Committee recommended Creon, Pancreaze, Zenpep, and Viokace remain on the UF, and that Pertzye and Ultresa be designated as NF.

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

H. PEPs – Panel Vote on UF Implementaion Plan

The P&T Committee recommended 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.

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

RECENTLY APPROVED U.S. FDA AGENTS—ANTIDEPRESSANTS (AD-1s)

P&T Comments

A. AD-1s: Bupropion Extended Release (ER) 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)

The P&T Committee concluded (16 for, 0 against, 0 absent, 0 abstain) the following with regard to the clinical efficacy and safety of bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), levomilnacipran (Fetzima), and vortioxetine (Brintellix). All four drugs are indicated solely for the treatment of major depressive disorder (MDD).

1. Forfivo XL
    a) Forfivo XL is an extended-release 450 mg formulation of bupropion, a norepinephrine/dopamine reuptake inhibitor (NDRI). Several generic formulations of bupropion (Wellbutrin, Wellbutrin SR, and Wellbutrin XL) are on the BCF. There are no clinical trials with Forfivo XL; FDA approval was based on demonstrated bioequivalence to three tablets of 150 mg Wellbutrin XL.

    b) Limitations to the product include that patients must be titrated with another bupropion formulation first, and the dose cannot be adjusted in renal or hepatic impairment.

    c) Forfivo XL has similar safety and tolerability concerns as other bupropion agents.

    d) While Forfivo XL offers an alternative treatment option of one tablet administered once daily for patients requiring a high dose of bupropion, it offers no compelling clinical advantages over the other bupropion formulations on the BCF or UF.

2. Desvenlafaxine ER (Khedezla)
    a) Khedezla is a serotonin/norepinephrine reuptake inhibitor (SNRI) that is an extended-release form of desvenlafaxine (Pristiq). Khedezla differs from Pristiq in the salt form (desvenlafaxine base versus desvenlafaxine succinate). Generic desvenlafaxine formulations are now available.

    b) Khedezla has shown bioequivalence to Pristiq in three studies; there are no clinical trials available.

c) Khedezla offers no clinically relevant advantages over the venlafaxine products (Effexor, Effexor XR, generic) products on the UF.

3. Levomilnacipran (Fetzima)

   a) Levomilnacipran is a SNRI and is an extended-release stereoisomer of milnacipran (Savella). Fetzima is indicated for MDD whereas Savella is indicated for fibromyalgia.

   b) There are no head-to-head studies comparing levomilnacipran with other antidepressants.

   c) In the three placebo-controlled studies used to gain FDA approval, all levomilnacipran doses produced a statistically significant change from baseline in the Montgomery-Asberg Depression Rating Scale (MADRS). However, varying effects on response rates (e.g., a 50% reduction in the MADRS score from baseline) have been reported, depending on the dose and study design. There was no difference from placebo in remission rate at any Fetzima dose.

   d) The safety profile of levomilnacipran is similar to milnacipran (Savella) and carries the same warnings.

   e) Levomilnacipran offers no clinically compelling advantages over the other AD-1s on the UF.

4. Vortioxetine (Brintellix)

   a) There have been no head-to-head studies between vortioxetine and other antidepressants. In four of seven placebo-controlled studies, vortioxetine was superior to placebo in improving MADRS or HAMD (Hamilton Depression Rating Scale) scores from baseline.

   b) In active comparator studies using duloxetine (Cymbalta) or venlafaxine (Effexor), vortioxetine showed similar clinical results in the endpoints of MADRS, HAMD, response, or remission.

   c) The most common adverse events (AEs) with vortioxetine include nausea and vomiting. Vortioxetine has fewer known AEs and warnings compared to desvenlafaxine, duloxetine (Cymbalta), and levomilnacipran. However, vortioxetine is the newest AD-1 to reach the market and additional AEs may increase during post-marketing surveillance.

   d) Although vortioxetine offers additional serotonergic effects in its mechanism of action and has fewer AEs overall than some of the other AD-1s, this has not translated into greater efficacy in treating depression.

B. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Relative Cost-Effectiveness Analysis and Conclusion

CMA was performed to evaluate new antidepressants bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), levomilnacipran (Fetzima), and vortioxetine (Brintellix) compared with other AD-1 subclasses, including selective serotonin reuptake inhibitors (SSRIs), SNRIs, and NDRIs. Based on the CMA results, the P&T Committee concluded (16 for, 0 against, 0 absent, 0 abstain) the following:

- For the NDRIs, the current BCF drugs—generic bupropion immediate release (IR), sustained release and ER formulations—were the most cost-effective agents, followed by the new entrant Forfivo XL and then followed by the NF branded product bupropion hydrobromide (Aplenzin).

- For the SNRIs and SSRIs subclasses, the BCF drugs citalopram and sertraline were the most cost-effective drugs, followed by generic venlafaxine IR and ER, and then followed by generic desvenlafaxine, Khedezla, generic duloxetine (Cymbalta), levomilnacipran (Fetzima), vortioxetine (Brintellix), and branded duloxetine (Cymbalta), ranked in order from most to least cost effective.

C. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—UF Recommendation

The P&T Committee recommended (15 for, 0 against, 0 absent, 1 abstain) bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), levomilnacipran (Fetzima), and vortioxetine (Brintellix) be designated NF, based on clinical and cost effectiveness. Additionally, the P&T Committee recommended Khedezla, Fetzima, and Brintellix be non-step preferred ("behind the step"), which requires a trial of a formulary AD-1 prior to use in all current and new patients. See Prior Authorization section, below.

D. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—PA Criteria

The P&T Committee recommended (15 for, 0 against, 0 absent, 1 abstain) PA criteria should apply to Khedezla, Fetzima, and Brintellix.

1. Desvenlafaxine ER (Khedezla): For all new users of Khedezla, patients are required to try venlafaxine IR or ER (Effexor, Effexor XR; generics) first.

2. Levomilnacipran (Fetzima) and vortioxetine (Brintellix): For new users of Fetzima or Brintellix, patients are required to try a generic SSRI, duloxetine, SNRI (except milnacipran), tricyclic antidepressant (TCA), mirtazapine,

bupropion, serotonin antagonist reuptake inhibitor (trazodone or nefazodone), or mononamine oxidase inhibitor (MAOI) first.

- **Desvenlafaxine ER (Khedezla)—**PA criteria apply to all new users of Khedezla.

  Automated PA criteria

  - The patient has filled a prescription for venlafaxine IR or venlafaxine ER 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, Khedezla is approved in new users (e.g., trial of venlafaxine IR or venlafaxine ER is NOT required) if:

  - Use of the formulary SNRI (venlafaxine) is contraindicated (e.g., hypersensitivity to a dye or other inert ingredient) and use of any other formulary antidepressant is not clinically appropriate.
  - The patient has previously responded to Khedezla, and changing to a formulary medication would incur unacceptable risk (e.g., the patient is currently stabilized on therapy with Khedezla and changing to a formulary medication would present a risk of destabilization).
  - The patient is being treated for depression, requires treatment with a SNRI (e.g., due to failure of SSRI therapy), and has failed an adequate trial of venlafaxine. Note: an adequate trial is generally considered to be at least 4–8 weeks in duration, due to the delay in achieving maximal benefit.
  - The patient requires treatment with a SNRI (e.g., due to failure of SSRI therapy), and has been unable to tolerate venlafaxine.

- **Levomilnacipran (Fetzima) and vortioxetine (Brintellix)—**PA criteria apply to all new users of Fetzima and Brintellix.

  Automated PA criteria

  - The patient has filled a prescription for a formulary SSRI, duloxetine, SNRIs (except milnacipran), TCA, mirtazapine, buproprion, trazodone or nefazodone, or an MAOI at any MHS

pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

AND

Manual PA criteria—For new users, Fetzima or Brintellix is approved (e.g., trial of a formulary AD-1 listed above is NOT required) if:

- Use of a formulary antidepressant (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI) is contraindicated (e.g., hypersensitivity to a dye or other inert ingredient) and use of any other formulary antidepressant is not clinically appropriate.
- The patient has previously responded to Fetzima or Brintellix, and changing to a formulary medication would incur unacceptable risk (e.g., the patient is currently stabilized on therapy with Fetzima or Brintellix and changing to a formulary medication would present a risk of destabilization).
- The patient is being treated for depression and has failed therapy with the formulary antidepressants (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI). Note: an adequate trial is generally considered to be at least 4–8 weeks in duration, due to the delay in achieving maximal benefit.
- The patient is being treated for depression and has been unable to tolerate the formulary antidepressants (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI).

E. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—UF and PA Implementation Plan

The P&T Committee recommended (15 for, 0 against, 0 absent, 1 abstain) 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. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Physician's Perspective

There was no controversy in the non-formulary recommendations for the four new antidepressants; there is only limited clinical information available, and they are not cost-effective. There hasn't been a lot of utilization so far for these new products; there were

only 83 prescriptions dispensed. Three of the drugs, ForFivo, Khedezla and Fetzima are only minor variations of existing products.

The Uniform Formulary already has a wide selection of several drugs from the different sub-classes that are cost effective. The Committee did recommend step therapy for these four drugs, which is similar to what has been done previously in the class.

G. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Panel Questions and Comments

The Panel member asked questions regarding the number of formulary agents that patient has to try and fail prior to use for all current and new patients; specific PA requirement recommendations for Bupropion ER 450 mg (Forfivo XL); and if the system looks for 4-8 week trials in the automated PA criteria.

Current and new patients are only required to try one of the formulary agents, not all. There were no specific PA recommendations for Bupropion ER 450 (Forfivio XL) addressed by the committee but Dr. Meade will follow-up and confirm that there were none.

The systems will to confirm adequate 4-8 week trials in the automated PA criteria. It is assumed that the manual process with verify an adequate trial.

H. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Panel Vote on UF Recommenation

The P&T Committee recommended bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), levomilnacipran (Fetzima), and vortioxetine (Brintellix) be designated NF, based on clinical and cost effectiveness. Additionally, the P&T Committee recommended Khedezla, Fetzima, and Brintellix be non-step preferred ("behind the step"), which requires a trial of a formulary AD-1 prior to use in all current and new patients. See Prior Authorization section, below.

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

I. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Panel Vote on PA Criteria

The P&T Committee recommended PA criteria should apply to Khedezla, Fetzima, and Brintellix.

1. Desvenlafaxine ER (Khedezla): For all new users of Khedezla, patients are required to try venlafaxine IR or ER (Effexor, Effexor XR; generics) first.

2. Levomilnacipran (Fetzima) and vortioxetine (Brintellix): For new users of Fetzima or Brintellix, patients are required to try a generic SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, serotonin antagonist reuptake inhibitor (trazodone or nefazodone), or MAOI first.

- **Desvenlafaxine ER (Khedezla)—**PA criteria apply to all new users of Khedezla.

  Automated PA criteria

  - The patient has filled a prescription for venlafaxine IR or venlafaxine ER 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, Khedezla is approved in new users (e.g., trial of venlafaxine IR or venlafaxine ER is NOT required) if:

  - Use of the formulary SNRI (venlafaxine) is contraindicated (e.g., hypersensitivity to a dye or other inert ingredient) and use of any other formulary antidepressant is not clinically appropriate.
  - The patient has previously responded to Khedezla, and changing to a formulary medication would incur unacceptable risk (e.g., the patient is currently stabilized on therapy with Khedezla and changing to a formulary medication would present a risk of destabilization).
  - The patient is being treated for depression, requires treatment with a SNRI (e.g., due to failure of SSRI therapy), and has failed an adequate trial of venlafaxine. Note: an adequate trial is generally considered to be at least 4–8 weeks in duration, due to the delay in achieving maximal benefit.
  - The patient requires treatment with a SNRI (e.g., due to failure of SSRI therapy), and has been unable to tolerate venlafaxine.

- **Levomilnacipran (Fetzima) and vortioxetine (Brintellix)—**PA criteria apply to all new users of Fetzima and Brintellix.

  Automated PA criteria

  - The patient has filled a prescription for a formulary SSRI, duloxetine, SNRIs (except milnacipran), TCA, mirtazapine, buproprion, trazodone or nefazodone, or an MAOI at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

    AND

  Manual PA criteria—For new users, Fetzima or Brintellix is approved (e.g., trial of a formulary AD-1 listed above is NOT required) if:

  - Use of a formulary antidepressant (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI) is contraindicated (e.g., hypersensitivity to a dye or other inert ingredient) and use of any other formulary antidepressant is not clinically appropriate.
  - The patient has previously responded to Fetzima or Brintellix, and changing to a formulary medication would incur unacceptable risk

    (e.g., the patient is currently stabilized on therapy with Fetzima or Brintellix and changing to a formulary medication would present a risk of destabilization).
  - The patient is being treated for depression and has failed therapy with the formulary antidepressants (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI). Note: an adequate trial is generally considered to be at least 4–8 weeks in duration, due to the delay in achieving maximal benefit.
  - The patient is being treated for depression and has been unable to tolerate the formulary antidepressants (SSRI, duloxetine, SNRI (except milnacipran), TCA, mirtazapine, bupropion, trazodone or nefazodone, or MAOI).

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

J. AD-1s: Bupropion ER 450 mg (Forfivo XL), desvenlafaxine ER (Khedezla), Levomilnacipran (Fetzima), and Vortioxetine (Brintellix)—Panel Vote on UF and PA Implementation Plan

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

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

UTILIZATION MANAGEMENT

P&T Comments

A. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—PA Criteria

Mirabegron was FDA-approved for OAB in June 2012 and launched in October 2013. It will be reviewed as a new drug at an upcoming meeting. Mirabegron is a beta-3 agonist, which is a unique mechanism compared to the antimuscarinic OAB drugs. In placebo-controlled trials, the efficacy of mirabegron on OAB symptoms appears similar to that of the other OAB drugs; however, mirabegron causes less anticholinergic AEs (dry mouth, constipation). The OAB drugs were reviewed for UF placement in November 2012, and automated PA (step therapy) was implemented, requiring a trial of a generic OAB drug or Detrol LA in all new and current users of an OAB drug.

The P&T Committee recommended (13 for, 1 opposed, 1 abstained, 1 absent) PA criteria for all new users of mirabegron (Myrbetriq) for OAB.

- **Mirabegron (Myrbetriq)—**PA criteria apply to all new users of Myrbetriq.

  Automated PA criteria

  - The patient has filled a prescription for tolterodine ER (Detrol LA), oxybutynin ER, oxybutynin IR, or generic trospium IR (Sanctura) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

  - Coverage is only approved for the FDA-approved indication of OAB with symptoms of urge incontinence, urgency, and urinary frequency
  - Patient has failed a 12-week trial with at least one of the following step-preferred OAB drugs (Detrol LA, oxybutynin ER, oxybutynin IR, or trospium IR) due to a treatment failure or intolerable adverse effects.

- Patient has experienced central nervous system (CNS) adverse effects with oral OAB medications or is at increased risk for such CNS effects due to comorbid conditions or other medications.

B. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—PA Implementation

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 30-day implementation period in all POS.

C. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—Physician's Perspective

Mirabegron (Myrbetriq) – Myrbetriq is a new drug for treating overactive bladder that has a different mechanism of action than the anticholinergic drugs (Detrol LA, Ditropan, Vesicare, etc). The Committee will review Myrbetriq as a new drug at an upcoming meeting. However PA criteria were recommended because the other OAB drugs have PA criteria that require the use of Detrol LA or a generic drug first. The PA criteria for Myrbetriq will apply to new users of the drug. New users will be required to try Detrol LA or a generic first. However, the manual PA criteria for Myrbetriq is different from what is in place for the other OAB drugs; the PA criteria reflect that the product is better tolerated than the anticholinergic drugs.

The one opposing vote for the PA criteria was because the Committee member felt that the PA criteria should mention that Myrbetriq is not on the Beer's list, which is a list of drugs that should not be used in elderly patients, due to the risk of adverse events.

D. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetiq) – Panel Questions and Comments.

The Panel members asked questions about the Automated PA criteria and the method used to confirm that there was an adequate 12 week trial by the patient as well as the utilization of the IR and ER products for this particular class of drugs. More specifically, is a trial and fail of the ER product required.
There is no way to monitor whether a patient had an adequate 12 week trial of the medication. The manual form is used in an effort to make the physician check to confirm the trial.

The Panel made a recommendation to provide education and provider outreach to ensure that an adequate 12 week has occurred to for the generic and formulary OAB.

In response to the question regarding the utilization and possible trials for the IR and ER products, patients used the ER product more than the IR product.

E. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—Panel Vote on PA Criteria

The P&T Committee recommended PA criteria for all new users of mirabegron(Myrbetriq) for OAB.

Mirabegron (Myrbetriq)—PA criteria apply to all new users of Myrbetriq.

Automated PA criteria

- The patient has filled a prescription for tolterodine ER (Detrol LA), oxybutynin ER, oxybutynin IR, or generic trospium IR (Sanctura) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

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

- Coverage is only approved for the FDA-approved indication of OAB with symptoms of urge incontinence, urgency, and urinary frequency
- Patient has failed a 12-week trial with at least one of the following step-preferred OAB drugs (Detrol LA, oxybutynin ER, oxybutynin IR, or trospium IR) due to a treatment failure or intolerable adverse effects.
- Patient has experienced central nervous system (CNS) adverse effects with oral OAB medications or is at increased risk for such CNS effects due to comorbid conditions or other medications.

The BAP voted:

Concur: 6 Non-concur: 1 Abstain: 0 Absent: 0

Additional Panel Comments: It appears that there should be a step behind ER products, that the IR products wouldn't get them to where they want to be in the formulary.

F. Overactive Bladder (OAB) Drugs: Mirabegron (Myrbetriq)—Panel Vote on PA Implemenation

The P&T Committee recommended an effective date of the first Wednesday after a 30-day implementation period in all POS.

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

UTILIZATION MANAGEMENT

P&T Comments

A. Phosphodiesterase-5 (PDE-5) Inhibitor: Avanafil (Stendra)—PA Criteria

Avanafil is a new PDE-5 inhibitor approved by the FDA in April 2012, but not launched until January 2014. It is only approved for erectile dysfunction (ED). Currently, automated PA (step therapy) applies to the class for ED; Viagra is the step-preferred PDE-5 for ED.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) PA criteria for all users of Avanafil (Stendra) for ED. A trial of sildenafil (Viagra) for ED is required prior to using Stendra. Uses other than ED, including benign prostatic hypertrophy, following prostatectomy, pulmonary arterial hypertension, or Raynaud's phenomenon are not allowed.

- **Avanafil (Stendra)—**PA applies to all new and current users of avanafil (Stendra).

  Automated PA criteria

  - The patient has received a prescription for sildenafil (Viagra) at any MHS point of service (MTFs, Retail Network or Mail Order) during the previous 180 days.
  - The patient is a male, aged 40 years of older with ED.

  Manual PA criteria—if automated criteria are not met. Stendra is approved if:

  - The patient has tried sildenafil (Viagra) and has had an inadequate response or was unable to tolerate treatment due to adverse effects.
  - Treatment with Viagra is contraindicated.

  Note: Coverage is approved only for erectile dysfunction (ED). Use for benign prostatic hyperplasia (BPH), following prostatectomy, pulmonary arterial hypertension, and Raynaud's phenomenon is not allowed. Additionally, use is not allowed for treatment of ED in males younger than age 18, for ED due to psychogenic origin, or in women for female sexual dysfunction.

B. Phosphodiesterase-5 (PDE-5) Inhibitor: Avanafil (Stendra)—Physician's Prespective

This is the 4th PDE-5 inhibitor on the market. The other PDE-5 inhibitors (Viagra, Cialis and Levitra) have PA criteria. For Stendra, the recommendation was to have the same PA criteria for treating erectile dysfunction as the other products.

C. Phosphodiesterase-5 (PDE-5) Inhibitor: Avanafil (Stendra)—Panel Questions and Comments:

No questions or comments from the Panel.

D. Phosphodiesterase-5 (PDE-5) Inhibitor: Avanafil (Stendra)—Panel Vote on PA Criteria:

The P&T Committee recommended PA criteria for all users of Avanafil (Stendra) for ED. A trial of sildenafil (Viagra) for ED is required prior to using Stendra. Uses other than ED, including benign prostatic hypertrophy, following prostatectomy, pulmonary arterial hypertension, or Raynaud's phenomenon are not allowed.

Avanafil (Stendra)—PA applies to all new and current users of avanafil (Stendra).

Automated PA criteria

- The patient has received a prescription for sildenafil (Viagra) at any MHS point of service (MTFs, Retail Network or Mail Order) during the previous 180 days.
- The patient is a male, aged 40 years of older with ED.

Manual PA criteria—if automated criteria are not met. Stendra is approved if:

- The patient has tried sildenafil (Viagra) and has had an inadequate response or was unable to tolerate treatment due to adverse effects.
- Treatment with Viagra is contraindicated.

Note: Coverage is approved only for erectile dysfunction (ED). Use for benign prostatic hyperplasia (BPH), following prostatectomy, pulmonary arterial hypertension, and Raynaud's phenomenon is not allowed. Additionally, use is not allowed for treatment of ED in males younger than age 18, for ED due to psychogenic origin, or in women for female sexual dysfunction.

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

RE-EVALUATION OF NF AGENTS

P&T Comments

A. Duloxetine (Cymbalta)—UF Recommendation and Implementation

On an ongoing basis, the DHA Pharmacoeconomic Branch monitors changes in the clinical information, current costs, and utilization trends to determine whether the UF status of agents designated as NF needs to be readdressed. The P&T Committee's process for reevaluating NF agents was established at the May 2007 meeting and approved by the Director, TMA, on June 24, 2007.

The P&T Committee reevaluated the UF status of duloxetine (Cymbalta) in light of recent price reductions in generic formulations across all three POS. Additionally, automated PA (step therapy) requires a trial of a generic formulary antidepressant or generic non-opioid pain syndrome drug before receiving Cymbalta. As of the meeting, the generic duloxetine products were not cost-effective relative to the price of branded Cymbalta.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) maintaining Cymbalta as NF and continuing the current step therapy. When generic formulations of Cymbalta become cost-effective relative to the step-preferred agents, generic duloxetine will move to UF status, become step-preferred (e.g., "in front of the step"), and existing PA criteria will be removed 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 the generic agent's 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.

Meade says once that happened we would come back to you and let you know.

B. Duloxetine (Cymbalta)—Physician's Perspective

Generic formulations of Cymbalta were launched in the fall of 2013, however, the price of branded Cymbalta is still less expensive than the generics. We are closely watching the price of the generics, and wanted this section included in the minutes, so that when the generics become cost-effective, we can quickly act to designate Cymbalta as a Uniform Formulary product, and also remove the current Prior Authorization criteria.

C. Duloxetine (Cymbalta)—Panel Questions and Comments:

No questions or comments from the Panel.

D. Duloxetine (Cymbalta)—Panel Vote on UF Recommendation and Implementation

The P&T Committee recommended maintaining Cymbalta as NF and continuing the current step therapy. When generic formulations of Cymbalta become cost-effective relative to the step-preferred agents, generic duloxetine will move to UF status, become step-preferred (e.g., "in front of the step"), and existing PA criteria will be removed 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 the generic agent's 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.

The BAP voted:

Concur: 7 Non-concur: 0 Abstain: 0 Absent: 0

Col Spilker makes one additional comment that no private citizen comments were submitted.

He thanks the members of the panel for their service. The BAP adjourned at approximately 10:20am

Mr. R. Duane Tackitt, Interim Chair

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.

- 5 ASA – 5-Aminosalicylate
- AD-1 – Antidepressants
- AE – Adverse Events
- BAP – Beneficiary Advisory Panel
- BCF – Basic Core Formula
- BIA – Budget Impact Analysis
- BPH – Benign Prostatic Hyperplasia
- CFR – Code of Federal Regulations
- CMA – Cost Minimization Analysis
- CNS – Central Nervous System
- COPD – Chronic Obstructive Pulmonary Disease
- DBP – Dibutyl Phthalate
- DFO – Designated Federal Officer
- DHA – Defense Health Agency
- DoD – Department of Defense
- DR – Delayed Release
- ED – Erectile Dysfunction
- EPI – Exocrine Pancreatic Insufficiency
- ER – Extended Release
- FACA – Federal Advisory Committee Act
- FDA – Food and Drug Administration
- GI-1 – Gastrointestinal
- HAMD – Hamilton Depression Rating Scale
- HD – Delayed Release
- HFA – XXXX
- ICS/LABAs – Inhaled Corticosteroids/Long Acting Beta Agonist
- IR – Immediate Release
- LABA – Long Acting Beta Agonist
- MADRS – Montgomery-Asberg Depression Rating Scale
- MAOI – Mononamine Oxidase
- MTF – Military Treatment Facility
- NDRIs - Norepinephrine/Dopamine Reuptake Inhibitor
- NF – Non-formulary/Non-preferred

- OAB – Overactive Bladder
- P&T – DoD Pharmacy and Therapeutics Committee
- PA – Prior Authorization
- PDE-5 – Phosphodiesterase
- PEC – Pharmacoeconomic Branch
- PEP – Pancreatic Enzyme Product
- PORT – Pharmacy Outcomes Research Team
- POS – Point of Service
- SNRI – Seratonin/Norepinephrine Reuptake Inhibitor
- TCA – Tricyclic Antidepressant
- TMA – Tricare Management Activity
- TRICARE – Military Health Care System
- UC – Ulcerative Colitis
- UF – Uniform Formulary
- USC – United States Code
- XL – Extended Release