DEPARTMENT OF DEFENSE PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

INFORMATION FOR THE UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL

I. UNIFORM FORMULARY REVIEW PROCESS

Under 10 United States Code § 1074g, as implemented by 32 Code of Federal Regulations 199.21, the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee is responsible for developing the Uniform Formulary (UF). Recommendations to the Director, Defense Health Agency (DHA), on formulary status, pre-authorizations, and the effective date for a drug's change from formulary to nonformulary (NF) status receive comments from the Beneficiary Advisory Panel (BAP), which must be reviewed by the Director before making a final decision.

II. RECENTLY APPROVED U.S. FOOD AND DRUG ADMINISTRATION (FDA) AGENTS—ALZHEIMER'S DISEASE AGENTS

P&T Comments

A. Alzheimer's Disease Agents: Memantine Extended Release (Namenda XR) and Memantine Extended Release/Donepezil (Namzaric)—Relative Clinical Effectiveness and Conclusion

Memantine extended release (Namenda XR) is an N-methyl-D-aspartate (NMDA) receptor antagonist approved for once daily dosing in the treatment of moderate to severe Alzheimer's disease. The immediate release (IR) formulation of memantine (Namenda IR) is now available in a generic formulation. Namzaric is a fixed-dose combination product containing memantine extended release (ER) and donepezil (Aricept), the most commonly prescribed acetylcholinesterase inhibitor.

Although there are no well-conducted head-to-head studies that compare Namenda XR or Namzaric with other Alzheimer's drugs, the two new drugs appear similar to their IR and individual components in terms of efficacy and safety. Namenda XR and Namzaric provide a modest clinical benefit at best, and some efficacy endpoints in the clinical trials showed no benefit at all. While Namenda XR and Namzaric offer the convenience of once daily dosing, there is no data to support any additional clinical benefit of combining an NMDA receptor antagonist with an acetylcholinesterase inhibitor. There is no data available to support the fixed-dose combination improves adherence.

The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the main benefits for Namenda XR and Namzaric are their once daily dosing, which provides a convenience to caregivers or patients with swallowing difficulties. Aside from this factor, the memantine IR version and the individual components of memantine and donepezil are clinically interchangeable with the memantine ER version (Namenda XR) and combination product (Namzaric).

B. Alzheimer's Disease Agents: Memantine ER (Namenda XR) and Memantine ER/Donepezil (Namzaric)—Relative Cost-Effectiveness Analysis and Conclusion

Cost minimization analysis (CMA) was performed. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA results showed the following rankings from most to least cost-effective for the UF no-step scenario: donepezil (Aricept, generics), memantine IR (Namenda, generics), galantamine (Razadyne, generic), donepezil orally dissolving tablet (Aricept ODT, generic), rivastigmine (Exelon, generic), galantamine ER (Razadyne ER), memantine ER (Namenda XR), memantine ER/donepezil (Namzaric), rivastigmine transdermal system (Exelon Patch).

C. Alzheimer's Disease Agents: Memantine ER (Namenda XR) and Memantine ER/Donepezil (Namzaric)—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) memantine ER (Namenda XR) and memantine ER/donepezil (Namzaric) be designated NF. Manual PA criteria were recommended at the August 2015 DoD P&T Committee meeting, with an implementation date of February 3, 2016. Note that the P&T Committee also recommended maintaining the current Prior Authorization criteria for Namenda XR and Namzaric, which were approved by the Beneficiary Advisory Panel at the September 30, 2015 meeting.

D. Alzheimer's Disease Agents: Memantine ER (Namenda XR) and Memantine ER/Donepezil (Namzaric)—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; and, 2) DHA send a letter to beneficiaries affected by the UF decision.

III. RECENTLY APPROVED U.S. FDA AGENTS—ALZHEIMER'S DISEASE AGENTS

BAP Comments

A. Alzheimer's Disease Agents: Memantine ER (Namenda XR) and Memantine ER/Donepezil (Namzaric)—UF Recommendation

The P&T Committee recommended Namenda XR and Namzaric be designated NF.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. Alzheimer's Disease Agents: Memantine ER (Namenda XR) and Memantine ER/Donepezil (Namzaric)—UF Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

IV. UF CLASS REVIEWS—ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) STIMULANTS

P&T Comments

A. ADHD: Stimulants—Relative Clinical Effectiveness and Conclusion

The ADHD stimulants were reviewed for formulary placement. The full class, including the nonstimulants and wakefulness promoting agents, was previously reviewed in February 2012. New entrants to the class include amphetamine sulfate tablets (Evekeo), methylphenidate ER capsules (Aptensio XR), and dextroamphetamine tablets (Zenzedi). The only products that do not have generic equivalents include methylphenidate ER oral suspension (Quillivant XR), methylphenidate transdermal system (Daytrana), and lisdexamfetamine (Vyvanse).

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

- The new entrants to the class, Evekeo, Aptensio XR, and Zenzedi do not contain new chemical entities; they were approved by the FDA using data from previously approved drugs. There are no head-to-head studies between any of the new entrants and other ADHD stimulants. The active ingredients for the new drugs are available in generic formulations that are on the UF.
- Quillivant XR is the only long-acting methylphenidate oral suspension on the market and is approved for children as young as six years of age. Immediate release methylphenidate and dextroamphetamine oral solutions are therapeutic alternatives to Quillivant XR, but must be dosed twice daily.

- Daytrana is the only transdermal patch available for ADHD, but is associated with skin reactions.
- Vyvanse is currently designated NF and is approved for children and adults with ADHD. A review of Military Health System (MHS) prescribing habits shows that the vast majority of utilization for all the ADHD drugs, including Vyvanse, is in the population aged five to 14 years. Vyvanse has a new FDA-approved indication for binge eating disorder, but other therapies, including topiramate, zonisamide, and the selective serotonin reuptake inhibitors are also commonly used for this condition.
- For patients with swallowing difficulties, the following products can be used:
    - Vyvanse is dissolvable in water.
    - Ritalin LA, Metadate CD, Adderall XR, and Focalin XR capsules can be opened and their contents can be sprinkled on food.
- All the stimulants contain a black box warning for potential abuse and dependency.

Overall Relative Clinical Effectiveness Conclusion: There were no significant updates to the previous clinical conclusions from the February 2012 UF class review. The ADHD stimulants have a high degree of therapeutic interchangeability, although there are differences in the duration of action between products. The branded ADHD stimulants: Quillivant XR, Vyvanse, Daytrana, Zenzedi, Evekeo, and Aptensio XR offer no additional clinical advantages over the other stimulant agents on the UF.

B. ADHD: Stimulants—Relative Cost-Effectiveness Analysis and Conclusion

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

- CMA results for brand-only agents showed that methylphenidate XR capsules (Aptensio XR) was the most cost-effective agent, followed by methylphenidate transdermal system (Daytrana), lisdexamfetamine (Vyvanse), methylphenidate ER oral suspension (Quillivant XR), and amphetamine tablets (Evekeo).
- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating Aptensio XR, Quillivant XR, and Evekeo as formulary, with Daytrana and Vyvanse as NF, demonstrated the largest estimated cost avoidance for the MHS.

C. ADHD: Stimulants—UF Recommendation

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

- UF:
    - amphetamine sulfate tabs (Evekeo)
    - methylphenidate ER oral suspension (Quillivant XR suspension)
    - methylphenidate ER (Aptensio XR)
    - methamphetamine (Desoxyn, generic)

- dextroamphetamine (Dexedrine spansule, Dextrostat tabs, ProCentra solution, generics; Zenzedi tabs)
- mixed amphetamine salts ER (Adderall XR; generic)
- mixed amphetamine salts IR (Adderall, generic)
- methylphenidate osmotic controlled release oral delivery system (OROS) (Concerta; generic)
- methylphenidate CD (Metadate CD; generic)
- methylphenidate IR (Ritalin, generic)
- methylphenidate LA (Ritalin LA, generic)
- methylphenidate SR (Ritalin SR, generic)
- methylphenidate ER (Metadate ER, Methylin ER, generic)
- methylphenidate chewable tablets, solution (Methylin, generic)
- dexmethylphenidate IR (Focalin; generic)

- NF
  - lisdexamfetamine (Vyvanse)
  - methylphenidate transdermal system (Daytrana)
  - dexmethylphenidate ER (Focalin XR, generic)

D. ADHD: Stimulants—UF Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS.

V. UF CLASS REVIEWS—ADHD: STIMULANTS

BAP Comments

A. ADHD: Stimulants—UF Recommendation

The P&T Committee recommended the following:

- UF:
  - Evekeo
  - Quillivant XR suspension
  - Aptensio XR
  - Desoxyn, generic
  - Dexedrine spansule, Dextrostat tabs, ProCentra solution, generics; Zenzedi tabs
  - Adderall XR; generic
  - Adderall, generic
  - Concerta; generic
  - Metadate CD; generic
  - Ritalin, generic
  - Ritalin LA, generic
  - Ritalin SR, generic
  - Metadate ER, Methylin ER, generic

- Methylin, generic
- Focalin; generic

- NF
  - Vyvanse
  - Daytrana
  - Focalin XR, generic

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

B. ADHD: Stimulants—UF Implementation Plan

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

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

VI. UF CLASS REVIEWS—ANTIRHEUMATICS: INJECTABLE METHOTREXATE

P&T Comments

A. Antirheumatics: Injectable Methotrexate—Relative Clinical Effectiveness and Conclusion

Background—Methotrexate received FDA approval for the treatment of rheumatoid arthritis (RA) and psoriasis in 1959. Methotrexate is one of the most studied disease-modifying antirheumatic drugs (DMARD) and is a cornerstone of therapy for treating RA. Currently, injectable methotrexate is available in a generic 50 mg/2 mL vial formulation and two auto-injectors, Otrexup and Rasuvo. Injectable methotrexate products are administered subcutaneously.

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

- Methotrexate low-dose oral and injectable vial formulations:
  - Methotrexate absorption via the oral route is variable, especially at doses greater than 15 mg. In contrast, subcutaneous (SC) methotrexate injections are completely absorbed. Most patients prefer oral over SC methotrexate therapy.

- Anecdotal observations report that some gastrointestinal toxicities may be avoided by administering methotrexate subcutaneously.
- In 2008, a randomized controlled trial comparing the efficacy and safety of oral and SC methotrexate, reported SC administration was significantly more effective than oral administration at the same dosage, with no difference in tolerability profiles.

- Methotrexate low-dose injectable vials and auto-injector formulations:
  - There are no head-to-head trials or systematic reviews comparing the different types of injectable methotrexate formulations.
  - The two new auto-injectors, Otrexup and Rasuvo, were FDA approved through 505(b)(2) applications by demonstrating bioequivalence to the generic injectable methotrexate vial formulations.
  - There are no clinical trials that demonstrate Otrexup or Rasuvo auto-injectors provide greater benefit to patients over oral or conventionally injected methotrexate using vials. There is no comparative effectiveness, safety, or tolerability data.
  - There is a high degree of therapeutic interchangeability for the injectable methotrexate delivery options.

Overall Relative Clinical Effectiveness Conclusion: Except for patient convenience, the methotrexate pre-filled auto-injector formulations of Otrexup and Rasuvo offer no additional clinical advantages over generic methotrexate vials. The benefit of the new products may be limited to a niche group of patients with limited vision, decreased finger dexterity, or impaired cognition.

B. Antirheumatics: Injectable Methotrexate—Relative Cost-Effectiveness Analysis and Conclusion

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

- CMA results showed that injectable methotrexate in the vial formulation was the most cost-effective injectable agent, followed by Otrexup and Rasuvo.
- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating methotrexate injectable vials as formulary, with Otrexup and Rasuvo designated NF, demonstrated the largest estimated cost avoidance for the MHS.

C. Antirheumatics: Injectable Methotrexate—UF Recommendation

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

- UF:
  - Methotrexate 50 mg/2 mL vials

- NF:
    - Methotrexate auto-injector (Otrexup)
    - Methotrexate auto-injector (Rasuvo)

D. Antirheumatics: Injectable Methotrexate—Manual PA Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) PA criteria for the methotrexate auto-injectors (Otrexup and Rasuvo).

1. Otrexup and Rasuvo—Full PA Criteria

   Manual PA criteria apply to all new users of Otrexup and Rasuvo methotrexate auto-injectors.

   Manual PA criteria—Otrexup or Rasuvo are approved if:
   - The patient has experienced intolerance or significant adverse effects from generic injectable methotrexate vials
     OR
   - The patient has decreased finger dexterity, limited vision, or impaired cognition that results in the inability to utilize generic injectable methotrexate vials

   Prior authorization does not expire.

E. Antirheumatics: Injectable Methotrexate—UF and PA Implementation Plan

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 points of service (POS); and, 2) DHA send a letter to beneficiaries affected by the UF decision.

VII. UF CLASS REVIEWS—ANTIRHEUMATICS: INJECTABLE METHOTREXATE

BAP Comments

A. Antirheumatics: Injectable Methotrexate—UF Recommendation

The P&T Committee recommended the following:

- UF:
    - Methotrexate 50 mg/2 mL vials
- NF:
    - Otrexup
    - Rasuvo

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. Antirheumatics: Injectable Methotrexate—Manual PA Recommendation

The P&T Committee recommended PA criteria for Otrexup and Rasuvo.

The full prior authorization criteria were stated previously.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

C. Antirheumatics: Injectable Methotrexate—UF and PA Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

VIII. UF CLASS REVIEWS—ACNE DRUGS: ORAL ISOTRETINOINS

P&T Comments

A. Acne Drugs: Oral Isotretinoins—Relative Clinical Effectiveness and Conclusion

Background—All the products in the class have the same active ingredient, isotretinoin. The class is comprised of AB-rated generic formulations of Accutane, including Amnesteem, Claravis, Myorisan and Zenatane, and a branded product, Absorica.

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

- The oral isotretinoins, including Absorica, have the same FDA indication, labeling, efficacy, side effect profile, and drug interaction profile. As a subclass, the oral

isotretinoins are effective in achieving a ≥70% reduction in total nodular lesion count when taken with meals for up to 20 weeks of therapy.

- Absorica is an oral isotretinoin product specifically formulated to allow for absorption regardless of meals. Absorica has a higher bioavailability in fasting conditions than the other oral isotretinoins. To ensure adequate absorption, the generic formulations must be taken with meals.
- In one head-to-head comparison study of Absorica and generic isotretinoin, there was no difference in efficacy outcomes or adverse reactions between the two products when taken under feed conditions.
- Potential advantages of Absorica include patient convenience due to administration without regard to meals, and the availability of two additional dosage strengths (25 mg and 35 mg) compared to generic oral isotretinoins. However, there are no published head-to-head trials that indicate better compliance or reduced relapse rates with Absorica compared to other isotretinoins.
- The oral isotretinoins are reserved for treating severe nodular recalcitrant acne, due to their significant adverse effects, including teratogenicity, pseudotumor cerebri, and psychiatric problems including suicide risk.
- All the oral isotretinoins, including Absorica, are rated as pregnancy category X, require mandatory enrollment in the Risk Evaluation and Mitigation Strategies (REMS) program iPLEDGE, and are limited to dispensing of a 30-day supply at one time.
- There is a high degree of therapeutic interchangeability among the oral isotretinoins and Absorica.

Overall Relative Clinical Effectiveness Conclusion: Other than the convenience of taking Absorica without regard to meals, it offers no additional clinical advantages over the other oral isotretinoins. Based on clinical issues alone, only one isotretinoin product is required on the UF.

B. Acne Drugs: Oral Isotretinoins—Relative Cost-Effectiveness Analysis and Conclusion

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

- CMA results showed that Myorisan and Amnesteem were the most cost-effective oral isotretinoins, followed by Zenatane, Claravis, and Absorica.
- BIA was performed to evaluate the potential impact of designating selected oral isotretinoins as formulary or NF on the UF. BIA results showed that designating Myorisan, Amnesteem, Zenatane, and Claravis as formulary, with Absorica as NF, demonstrated the largest estimated cost avoidance for the MHS.

C. Acne Drugs: Oral Isotretinoins—UF Recommendation

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

- UF oral isotretinoins:
    - Myorisan
    - Amnesteem
    - Zenatane
    - Claravis

- NF oral isotretinoins:
    - Absorica

D. Acne Drugs: Oral Isotretinoins—Manual PA Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) manual PA criteria for Absorica.

1. Absorica—Full PA Criteria

   Manual PA criteria apply to all new users of Absorica.

   Manual PA criteria

   - Patient is unable to comply with the dietary requirements of an AB-rated generic oral isotretinoin

   Prior authorization does not expire.

E. Acne Drugs: Oral Isotretinoins—UF and PA 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.

IX. UF CLASS REVIEWS—ACNE DRUGS: ORAL ISOTRETINOINS

BAP Comments

A. Acne Drugs: Oral Isotretinoins—UF Recommendation

The P&T Committee recommended the following:

- UF oral isotretinoins:
    - Myorisan
    - Amnesteem
    - Zenatane

- Claravis

- NF oral isotretinoins:
  - Absorica

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

B. Acne Drugs: Oral Isotretinoins—Manual PA Recommendation

The P&T Committee recommended manual PA criteria for Absorica.

The full prior authorization criteria were stated previously.

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

C. Acne Drugs: Oral Isotretinoins—UF and PA 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.

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

X. UF CLASS REVIEWS—GASTROINTESTINAL-2 (GI-2) MISCELLANEOUS DRUGS

P&T Comments

A. GI-2 Miscellaneous Drugs—Relative Clinical Effectiveness and Conclusion

Background—The P&T Committee evaluated the GI-2 Miscellaneous Drugs. The drugs were previously reviewed for formulary placement in November 2012; there have been new additions to the class. Tegaserod (Zelnorm) has been discontinued from the market.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) the following for the GI-2 Miscellaneous agents:

- There are no updates or changes from the previous clinical conclusions made at the November 2012 UF drug class review for the treatment of hepatic encephalopathy, travelers' diarrhea, *clostridium difficile* associated diarrhea, and *clostridium difficile* infection (CDI). (The full conclusions from the November 2012 P&T Committee meeting minutes can be found online at http://www.health.mil/PandT.)
- There are no head-to-head studies among any of the drugs in the GI-2 miscellaneous subclass for the indications of diarrhea-predominant irritable bowel syndrome (IBS), constipation-predominant IBS, or chronic idiopathic constipation. All of the clinical trials for IBS studies showed a significant placebo effect.

Diarrhea-Predominant IBS (IBS-D)

- For rifaximin (Xifaxan), the studies for IBS-D are of moderate quality evidence. FDA approval for IBS-D was based on the unpublished TARGET 3 trial, which found that rifaximin was modestly more effective than placebo in relieving IBS-D symptoms but relapses were common. Rifaximin primarily relieves abdominal pain, but does not show a statistically significant improvement in stool consistency. It is also approved for travelers' diarrhea and to decrease the recurrence of hepatic encephalopathy.
- Use of alosetron (Lotronex) for IBS-D is restricted to women with severe refractory IBS-D. It is only available through an FDA-mandated REMS program due to the risk of severe adverse events, including death due to bowel obstruction.

Constipation-Predominant IBS (IBS-C)

- The FDA approved linaclotide (Linzess) for the treatment of IBS-C based on two placebo-controlled clinical trials. Linaclotide showed statistically significant improvements in both abdominal pain and an increase in number of bowel movements per week. The studies are rated as high quality evidence. It is generally well tolerated, although patients may experience diarrhea.
- The FDA approved lubiprostone (Amitiza) for the treatment of IBS-C based on two placebo-controlled trials that showed varying efficacy for IBS-C symptoms. The studies are of moderate quality evidence and were primarily conducted in Caucasian women.
    - The most common adverse events with lubiprostone (Amitiza) are nausea, headache, and diarrhea/abdominal pain. Limitations to use include its drug interaction profile and its FDA approval for use only in women for IBS.

Overall relative clinical effectiveness conclusion: At this time, comparative efficacy statements between the drugs approved for treating IBS cannot be made due to their differing mechanisms of action, lack of head-to-head studies, lack of consistent diagnostic criteria, and variable endpoints. The P&T Committee concluded that even though the studies showed statistically significant results for treating IBS symptoms,

whether the results are clinically meaningful remains to be determined due to the significant placebo response and lack of comparative studies.

B. GI-2 Miscellaneous Drugs—Relative Cost-Effectiveness Analysis and Conclusion

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

- CMA results for the branded products, for all FDA-approved indications, showed that lubiprostone (Amitiza) and linaclotide (Linzess) were the most cost-effective agents in the drug subclass, followed by alosetron (Lotronex), nitazoxanide (Alinia), rifaximin (Xifaxan), and fidaxomicin (Dificid).
- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF. BIA results showed that designating all agents in the GI-2 Miscellaneous Drug Subclass as formulary demonstrated the largest estimated cost avoidance for the MHS.

C. GI-2 Miscellaneous Drugs—UF Recommendation

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

- UF
  - alosetron (Lotronex)
  - fidaxomicin (Dificid)
  - linaclotide (Linzess)
  - lubiprostone (Amitiza)
  - nitazoxanide (Alinia)
  - rifaximin (Xifaxan)
  - tegaserod (Zelnorm)—discontinued
  - metronidazole (Flagyl, generic)
  - neomycin
  - vancomycin
- NF
  - None

D. GI-2 Miscellaneous Drugs—Manual PA Recommendation

Prior authorization was recommended for rifaximin, due to the potential for off-label uses for a wide range of conditions for which there is no supporting clinical data.

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

1. Rifaximin (Xifaxan) 550 mg Tablets—Full PA Criteria

All new users of rifaximin 550 mg tablets are required to undergo manual prior authorization criteria.

Manual PA criteria

- Hepatic Encephalopathy: No changes from November 2012
  - Patient is ≥18 years of age
  - Patient has a documented diagnosis of hepatic encephalopathy
  - Prior Authorization does not expire

- Irritable Bowel Syndrome-Diarrhea Predominant (IBS-D)
  - Patient has clinically documented moderate to severe IBS-diarrhea type, without constipation, and has symptoms of moderate abdominal pain and bloating.

    AND
  - The patient has had failure, intolerance, or contraindication to at least one antispasmodic agent; e.g., dicyclomine (Bentyl), Librax, hyoscyamine (Levsin), Donnatal, imodium (Loperamide),

    AND
  - The patient has had failure, intolerance, or contraindication to at least one tricyclic antidepressant (to relieve abdominal pain); e.g., amitriptyline, desipramine, doxepin, imipramine, nortriptyline, protriptyline
  - If yes to the above, then treatment will be approved for a single 14-day course of therapy (550 mg tablets, one tablet three times daily for 14 days)
  - For IBS-D, patients who experience recurrence of symptoms can be retreated up to two more times with the same regimen (total of three treatment courses in 6 months) if the following:
    - Patient has had a positive response to a previous 14-day course of rifaximin.
  - Prior authorization expires in 6 months

- Non-FDA approved uses, including use of the 200 mg rifaximin tablets for travelers' diarrhea, *C. difficile* infection, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, or any other non FDA-approved condition:
  - Prior Authorization is not approved

- Use of rifaximin 200 mg tablets for travelers' diarrhea is subject to automated prior authorization (step therapy), which requires a trial of a

fluoroquinolone first. See November 2012 P&T Committee meeting minutes.

E. GI-2 Miscellaneous Drugs—UF and PA Implementation Plan

P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS.

XI. UF CLASS REVIEWS—GI-2 MISCELLANEOUS DRUGS

BAP Comments

A. GI-2 Miscellaneous Drugs—UF Recommendation

The P&T Committee recommended the following:

- UF
  - Lotronex
  - Dificid
  - Linzess
  - Amitiza
  - Alinia
  - Xifaxan
  - Zelnorm—discontinued
  - Flagyl, generic
  - neomycin
  - vancomycin
- NF
  - None

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. GI-2 Miscellaneous Drugs—Manual PA Recommendation

Prior authorization was recommended for rifaximin, due to the potential for off-label uses for a wide range of conditions for which there is no supporting clinical data.

The P&T Committee recommended the following:

- Applying new manual PA criteria for new users of rifaximin (Xifaxan) 550 mg tablets for treating IBS-D at a dosage of one tablet three times daily for 14 days. Up to two re-treatment courses will be allowed in six months, for a total of three total treatment courses.
- Continuing the existing manual PA criteria for rifaximin (Xifaxan) 550 mg tablets, for hepatic encephalopathy at a dosage of one tablet twice daily. (See November 2012 DoD P&T Committee meeting minutes for full criteria.)
- Continuing the current step therapy for rifaximin 200 mg tablets for travelers' diarrhea, which requires a trial of a fluoroquinolone first. As part of this recommendation, the current quantity limits for rifaximin—200 mg tablets, one tablet three times daily for three days (a total of nine tablets), will be continued. (See November 2012 DoD P&T Committee meeting minutes for full criteria.)

The full prior authorization criteria were stated previously.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

C. GI-2 Miscellaneous Drugs—UF and PA Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

XII. UTILIZATION MANAGEMENT—TARGETED IMMUNOMODULATORY BIOLOGICS (TIBS)

P&T Comments

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

The TIBs were reviewed by the P&T Committee in August 2014 and automated PA (step therapy) and manual PA criteria were recommended for the class. Adalimumab (Humira) was selected as the UF step-preferred agent. In September 2015, adalimumab (Humira) received FDA approval for treatment of moderate to severe hidradenitis suppurativa. The

PA criteria were updated for Humira to reflect the new FDA indication.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) revised manual PA criteria for Humira in new patients, consistent with the new FDA-approved product labeling for hidradenitis suppurativa.

1. Adalimumab (Humira)—Full PA Criteria

   Manual PA Criteria applies to all new users of adalimumab (Humira).

   Coverage approved for patients ≥ 18 years with:

   - Moderate to severe active rheumatoid arthritis, active psoriatic arthritis, or active ankylosing spondylitis
   - Moderate to severe chronic plaque psoriasis who are candidates for systemic or phototherapy, and when other systemic therapies are medically less appropriate
   - Moderate to severely active Crohn's disease following an inadequate response to conventional therapy, loss of response to Remicade, or an inability to tolerate Remicade
   - Moderate to severely active ulcerative colitis following inadequate response to immunosuppressants
   - **Moderate to severe hidradenitis suppurativa (November 2015 new criteria)**

   Pediatric patients with:

   - Moderate to severe active polyarticular juvenile idiopathic arthritis (pediatric patients: 2–17 years)
   - Moderate to severely active Crohn's disease (≥ 6 years) who have had an inadequate response to corticosteroids, azathioprine, 6-mercaptopurine, or methotrexate

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

   Prior Authorization does not expire.

B. TIBs: Adalimumab (Humira)—PA Implementation Period

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) implementation of the PA for adalimumab become effective upon signing of the minutes.

XIII. UTILIZATION MANAGEMENT—TIBs

BAP Comments

A. TIBs: Adalimumab (Humira)—PA Criteria

The P&T Committee recommended revised manual PA criteria for Humira in new patients, consistent with the new FDA-approved product labeling for hidradenitis suppurativa.

The full prior authorization criteria were stated previously.

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

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

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

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

XIV. UTILIZATION MANAGEMENT—ANTIMALARIAL DRUGS

P&T Comments

A. Antimalarial Drugs: Mefloquine—Manual PA Criteria

The P&T Committee discussed recent changes to the package insert for the antimalarial drug mefloquine (Lariam, generic) due to the risk of serious psychiatric and neurologic side effects. Mefloquine is primarily utilized as malaria prophylaxis. The P&T Committee has not reviewed the antimalarial drug class; most of the agents are available in generic formulations, with variability in malaria resistance patterns across the world.

In April 2013, the Assistant Secretary of Defense for Health Affairs made changes to the malaria Force Health Protection program. Atovaquone-proguanil (Malarone, generic) and doxycycline are now first-line choices in areas other than Sub-Saharan Africa. In Sub-Saharan Africa, the first-line choice is atovaquone-proguanil, followed by doxycycline. Mefloquine is third line choice. In July 2013, the FDA added a black box warning due to risk of permanent adverse effects, including dizziness, loss of balance, and tinnitus. A Fiscal Year 2014 mefloquine drug utilization review revealed suboptimal documentation for contraindications and patient education in the available records.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) manual PA criteria for mefloquine in new users. The PA criteria are consistent with the FDA-approved product labeling to ensure safe and appropriate use of mefloquine.

1. Mefloquine—Full PA Criteria

   Manual PA Criteria apply to all new users of mefloquine.

   Coverage approved for patients with the following:
   - Patients requiring mefloquine for malaria chemoprophylaxis. The PA is not intended for patients requiring treatment of acute malaria infections.
   - Patients with a contraindication or intolerance to both atovaquone-proguanil (Malarone) and doxycycline (e.g., pregnancy)
   - Patients do NOT have a major psychiatric disorder to include but not limited to
     - Active or recent history of depression
     - Generalized anxiety disorder
     - Psychosis or schizophrenia
     - Post-Traumatic Stress Disorder (PTSD) or Traumatic Brain Injury (TBI)
   - Patients do NOT have a history of seizures or vestibular disorders
   - Patients do NOT have a cardiac conduction abnormality

   AND

   - The total treatment duration (months) must be documented on the PA form.

   AND
   - The above information is documented in the medical record and the patient has been educated on mefloquine adverse effects and dosing.

   Prior Authorization expires after one continuous treatment course.

B. Antimalarial Drugs: Mefloquine—PA Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS.

XV. UTILIZATION MANAGEMENT—ANTIMALARIAL DRUGS

BAP Comments

A. Antimalarial Drugs: Mefloquine—PA Criteria

The P&T Committee recommended manual PA criteria for mefloquine in new users. The PA criteria are consistent with the FDA-approved product labeling to ensure safe and appropriate use of mefloquine.

The full prior authorization criteria were stated previously.

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

B. Antimalarial Drugs: Mefloquine—PA Implementation Plan

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

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

XVI. UTILIZATION MANAGEMENT—HEPATITIS C VIRUS (HCV) DRUGS: DIRECT ACTING ANTIVIRALS (DAAs)

P&T Comments

A. HCV Drugs: DAAs—Manual PA Criteria

The HCV DAAs were reviewed by the P&T Committee in May 2015; manual PA criteria and QLs were recommended for the subclass. In July 2015, the FDA approved two new HCV DAAs for the treatment of HCV genotype 3 (GT3) and HCV genotype 4 (GT4): daclatasvir (Daklinza) and paritaprevir/ritonavir/ombitasvir (Technivie), respectfully. The P&T Committee reviewed the PA criteria and QLs for the DAAs due to the new entrants in the class, changes in the FDA package labeling, FDA drug safety communications, and updated treatment recommendations for HCV by the American Association for the Study of Liver Diseases/Infectious Diseases Society of America (AASLD/IDSA). Consult www.HCVguidelines.org for the most recent update from September 25, 2015.

1. The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) changes and/or new manual PA criteria for the following DAAs.

    a) Removing the hepatitis B virus (HBV) co-infection contraindication from all the current HCV DAA manual PA criteria.

b) Manual PA criteria for new users of paritaprevir/ritonavir/ombitasvir (Technivie). Technivie is contraindicated in patients with moderate and severe hepatic impairment (Child-Pugh Class B and C) and is not indicated for use in patients with cirrhosis. It can cause serious liver injury in patients with underlying advanced liver disease. Prior authorization will expire after 12 weeks, based on the treatment regimen.

(1) Paritaprevir/Ritonavir/Ombitasvir (Technivie)—New PA Criteria November 2015

- New users of paritaprevir/ritonavir/ombitasvir are required to undergo the PA process.
- Current users are not affected by PA; they can continue therapy uninterrupted.
- Consult the AASLD/IDSA HCV guidelines (www.hcvguidelines.org) for the most up-to-date and comprehensive treatment for HCV. Unique patient populations are also addressed, and treatment recommendations may differ from those for the general population.

Manual PA Criteria:

- Age ≥ 18
- Has laboratory evidence of chronic HCV genotype 4 infection
    - State the HCV genotype and HCV RNA viral load on the PA form
- Paritaprevir/ritonavir/ombitasvir (Technivie) is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
- Does not have moderate or severe hepatic impairment (Child-Pugh Class B & C), or cirrhosis

<u>Treatment Regimens and Duration of Therapy</u>

- Treatment and duration of therapy are approved for one of the following regimens outlined below, based on HCV genotype or unique population.
- Prior authorization will expire after 12 weeks, based on the treatment regimen selected.
- Regimen other than those listed above: Explain the rationale for treatment and duration of therapy. Consult the AASLD/IDSA HCV guidelines for new updates and guidelines.

c) Manual PA criteria for new users of daclatasvir (Daklinza). Prior authorization will expire after 12–24 weeks based on the treatment regimen.

(1) Daclatasvir (Daklinza)—New PA Criteria November 2015

- New users of daclatasvir are required to undergo the PA process.
- Current users are not affected by PA; they can continue therapy uninterrupted.
- Consult the AASLD/IDSA HCV guidelines (www.hcvguidelines.org) for the most up-to-date and comprehensive treatment for HCV. Unique patient populations are also addressed, and treatment recommendations may differ from those for the general population.

Manual PA Criteria:

- Age ≥ 18
- Has laboratory evidence of chronic HCV genotype 3 infection
  - State the HCV genotype and HCV RNA viral load on the PA form
- Daclatasvir (Daklinza) is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
- Daclatasvir (Daklinza) is not prescribed as monotherapy

<u>Treatment Regimens and Duration of Therapy</u>

- Treatment and duration of therapy are approved for one of the following regimens outlined below, based on HCV genotype or unique population.
- Prior authorization will expire after 12 to 24 weeks, based on the treatment regimen selected.
- Regimen other than those listed above: Explain the rationale for treatment and duration of therapy. Consult the AASLD/IDSA HCV guidelines for new updates and guidelines.

d) Revising the existing manual PA criteria for new users of sofosbuvir (Sovaldi). Prior authorization will expire after 12–48 weeks based on the treatment regimen.

e) Revising the existing manual PA criteria for new users of paritaprevir/ritonavir/ombitasvir with dasabuvir (Viekira Pak). Viekira Pak is contraindicated in patients with moderate and severe hepatic impairment (Child-Pugh Class B and C) and can cause serious liver injury in patients with underlying advanced liver disease. Prior authorization will expire after 12–24

weeks based on the treatment regimen.

f) Revising the existing manual PA criteria for new users of ledipasvir/sofosbuvir (Harvoni). Prior authorization will expire after 8–24 weeks based on the treatment regimen.

B. HCV Drugs: DAAs—PA Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) implementation for the manual PA criteria upon signing of the minutes.

XVII. UTILIZATION MANAGEMENT—HCV DRUGS: DAAs

BAP Comments

A. HCV Drugs: DAAs—Manual PA Criteria

The P&T Committee recommended changes and/or new manual PA criteria for the Hepatitis C Virus Drugs: Direct Acting Antivirals, as stated previously.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. HCV Drugs: DAAs—PA Implementation Plan

The P&T Committee recommended implementation for the manual PA criteria upon signing of the minutes.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

XVIII. UTILIZATION MANAGEMENT—FEMALE HYPOSEXUAL DESIRE DISORDER (HSDD) DRUGS

P&T Comments

A. HSDD Drugs: Flibanserin (Addyi)—Manual PA Criteria

Flibanserin is the first drug approved for treating HSDD in premenopausal women that is not due to a co-existing medical or psychiatric condition, problems within the relationship, or effects of a medication or other drug substance. The drug is available under a limited distribution program, requiring physician registration, due to the risk of adverse effects.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) manual PA criteria for flibanserin (Addyi) in all new and current users, due to the risk of severe hypotension, especially if used concomitantly with alcohol. Prior authorization will be limited to the FDA-approved indication. Discontinuation of treatment is warranted if there is no improvement in symptoms after eight weeks.

1. Flibanserin (Addyi)—Full PA Criteria

   Manual PA criteria apply to all new and current users of flibanserin (Addyi).

   Manual PA criteria—Flibanserin is approved if:

   - The drug is prescribed for a premenopausal female with HSDD not due to a co-existing medical or psychiatric condition, problems within the relationship, or effects of a medication or other drug substance,

   AND

   - The patient does not have current alcohol use,
   - The patient does not have hepatic impairment (Child-Pugh score ≥6),
   - The patient is not receiving concomitant therapy with a moderate or strong CYP3A4 inhibitor (e.g., ciprofloxacin, clarithromycin, diltiazem, fluconazole, itraconazole, ketoconazole, ritonavir, verapamil),

   AND

   - The prescription is written from a provider who is certified/enrolled in the flibanserin REMS program.
   - Note that contraindications to the use of flibanserin include concurrent alcohol, moderate or strong CYP3A4 inhibitors, and hepatic impairment

   Prior Authorization does not expire.

B. HSDD Drugs: Flibanserin (Addyi)—PA Implementation Plan

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

XIX. UTILIZATION MANAGEMENT—HSDD DRUGS

BAP Comments

A. HSDD Drugs: Flibanserin (Addyi)—Manual PA Criteria

The P&T Committee recommended manual PA criteria for Addyi in all new and current users, due to the risk of severe hypotension, especially if used concomitantly with alcohol. Prior

authorization will be limited to the FDA-approved indication. Discontinuation of treatment is warranted if there is no improvement in symptoms after eight weeks.

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

B. HSDD Drugs: Flibanserin (Addyi)—PA Implementation Plan

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

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

XX. UTILIZATION MANAGEMENT—BASAL INSULINS

P&T Comments

A. Basal Insulins: Insulin Glargine 300 U/mL (Toujeo)—Manual PA Criteria

Toujeo is a long-acting human insulin analog indicated for improvement of glycemic control in adults with type 1 or type 2 diabetes mellitus. It contains a concentrated solution of insulin glargine, 300 U/mL. Insulin glargine under the brand name of Lantus has been available since 2000, at a concentration of 100 U/mL. The hemoglobin A1c-lowering effect of Toujeo is similar to Lantus. Biosimilar formulations of insulin glargine are expected in 2016.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) manual PA criteria for Toujeo in all new and current users, to ensure appropriate use and to reduce the risk of insulin dosing errors.

1. Insulin Glargine 300 U/mL (Toujeo)—Full PA Criteria

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

   Manual PA criteria—Toujeo is approved if:

   - The patient is at least 18 years of age
     AND
   - The patient has diabetes and is using a minimum of 100 units of Lantus (insulin glargine) per day

AND

- The patient requires a dosage increase with Lantus and has experienced a clinically significant, severe hypoglycemia episode, despite splitting the Lantus dose
  AND
- The patient has been counseled regarding the risk of dosing errors.

- Note that the following are not acceptable reasons for Toujeo:
  - Non-adherence to previous insulin treatment
  - Patient or prescriber preference for the use of Toujeo
  - Patient or prescriber preference for a smaller injection volume

Prior Authorization does not expire.

B. Basal Insulins: Insulin Glargine 300 U/mL (Toujeo)—PA Implementation Plan

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS.

XXI. UTILIZATION MANAGEMENT—BASAL INSULINS

BAP Comments

A. Basal Insulins: Insulin Glargine 300 U/mL (Toujeo)—Manual PA Criteria

The P&T Committee recommended manual PA criteria for Toujeo in all new and current users, to ensure appropriate use and to reduce the risk of insulin dosing errors.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. Basal Insulins: Insulin Glargine 300 U/mL (Toujeo)—PA Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

XXII. UTILIZATION MANAGEMENT—CHRONIC HEART FAILURE DRUGS

P&T Comments

A. Chronic Heart Failure Drugs: Ivabradine (Corlanor)—Manual PA Criteria

Ivabradine (Corlanor) is approved to decrease the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure. The package insert states the drug should only be used in patients who have a left ventricular ejection fraction of less than 35%, who have a heart rate of at least 70 beats per minute, and who are receiving maximum tolerated doses of beta blockers, or who have a contraindication to beta blockers. Corlanor decreases heart rate without affecting ventricular repolarization or myocardial contractility.

The P&T Committee recommended (14 for, 0 opposed, 1 abstained, 1 absent) manual PA criteria for new users of Corlanor, consistent with the FDA-approved product labeling.

1. Ivabradine (Corlanor)—Full PA Criteria

   Manual PA criteria apply to all new users of Corlanor.

   Manual PA criteria—Corlanor is approved if:

   - The drug is prescribed by a cardiologist or heart failure specialist.
   - The patient has a diagnosis of stable, symptomatic heart failure with left ventricular ejection fraction ≤35%, is in sinus rhythm, and has a resting heart rate >70 beats per minute.
   - The patient has heart failure symptoms despite maximal therapy of a beta blocker therapy that has been shown to have survival benefit in heart failure.
     - Note that acceptable heart failure beta blockers and target doses include the following: metoprolol succinate ER 200 mg QD; carvedilol 25 mg BID, if 50 mg BID < 85 kg; carvedilol XR 80 mg QD; bisoprolol 10 mg QD (bisoprolol is not FDA-approved for heart failure but has proven efficacy in a large clinical trial)
   - **OR** the patient has a **contraindication to beta blocker use**
     - Note that the contraindication must be listed on the Prior Authorization form.

   Prior Authorization does not expire.

B. Chronic Heart Failure Drugs: Ivabradine (Corlanor)—PA Implementation Plan

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

XXIII. UTILIZATION MANAGEMENT—CHRONIC HEART FAILURE DRUGS

BAP Comments

A. Chronic Heart Failure Drugs: Ivabradine (Corlanor)—Manual PA Criteria

The P&T Committee recommended manual PA criteria for new users of Corlanor, consistent with the FDA-approved product labeling.

The full prior authorization criteria were stated previously.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. Chronic Heart Failure Drugs: Ivabradine (Corlanor)—PA Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

XXIV. INNOVATOR DRUGS—PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) INHIBITORS

P&T Comments

A. PCSK9 Inhibitors: Evolocumab (Repatha)—Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions

Section 702 of the FY15 NDAA established new authority for the P&T Committee's review process of FDA newly-approved innovator drugs. The P&T Committee is provided up to 120 days to recommend tier placement for innovator drugs on the UF. During this period, innovator drugs will be assigned a classification pending status; they will be available under terms comparable to NF drugs, unless medically necessary, in which case they would be available under terms comparable to formulary drugs. For additional information, see the August 2015 DoD P&T Committee meeting minutes at http://www.health.mil/PandT.

Drugs subject to the Innovator Rule are defined as new drugs that are approved by the FDA under a Biologic License Application (BLA) or New Drug Application (NDA). The NDA innovator drugs will be further defined by their chemical types to include, but

not limited to, new molecular entities, new active ingredients, and new combinations. The definition was further expanded to include new dosage formulations.

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

The PCSK9 inhibitors are a new class of biologic drugs that lower low-density lipoprotein (LDL) cholesterol and are administered by SC injection. The first product, alirocumab (Praluent), was approved on July 24, 2015, prior to implementation of the Innovator Rule on August 25, 2015. Evolocumab (Repatha) is the second PCSK9 inhibitor, and obtained FDA approval on August 27, 2015, after the Innovator Rule went into effect. An interim P&T Committee meeting held on September 3, 2015, recommended PA criteria for Repatha. (See August 2015 DoD P&T Committee meeting minutes, found at http://www.health.mil/PandT.)

The product labeling for Repatha is similar to Praluent, with the exception that, in addition to patients with heterozygous familial hypercholesterolemia (HeFH) and clinical atherosclerotic cardiovascular disease (ASCVD), Repatha is also approved for treating patients with homozygous familial hypercholesterolemia (HoFH), including pediatric patients from ages 13 to 17 years.

The PCSK9 inhibitors cause reductions in low-density lipoprotein cholesterol (LDL-C) ranging from 40% to 75%. Excluding the additional indication for HoFH, the LDL-lowering benefit for Repatha appears similar to Praluent, based on their individual trials.

The effect of the PCSK9 inhibitors on cardiovascular (CV) morbidity and mortality has not been determined. CV outcomes studies are expected in 2017, and will aid in defining the clinical benefit of this drug class.

Praluent is available on the UF and covers the same indication as Repatha. For patients with HoFH, patients can access Repatha via the previously approved PA and MN criteria.

Relative cost-effectiveness of Repatha was reviewed by the P&T Committee.

B. PCSK9 Inhibitors: Evolocumab (Repatha)—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) evolocumab (Repatha) be designated NF. No changes were recommended for the manual PA criteria, which were previously approved by the Beneficiary Advisory Panel at the September 30, 2015 meeting.

C. PCSK9 Inhibitors: Evolocumab (Repatha)—UF Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) an effective date upon signing of the minutes in all POS.

XXV. INNOVATOR DRUGS—PCSK9 INHIBITORS

BAP Comments

A. PCSK9 Inhibitors: Evolocumab (Repatha)—UF Recommendation

The P&T Committee recommended Repatha be designated NF.

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

B. PCSK9 Inhibitors: Evolocumab (Repatha)—UF Implementation Plan

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

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

XXVI. INNOVATOR DRUGS—ORAL ONCOLOGIC DRUGS

P&T Comments

A. Oral Oncologic Drugs: Trifluridine/Tipiracil (Lonsurf)—Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions

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

- Lonsurf is a last line, oral treatment for metastatic colorectal cancer. First line treatments are intravenously administered medications.
- Efficacy shows statistical significance for Lonsurf in terms of increased overall survival compared to placebo (7.1 months versus 5.3 months, respectively).
- Relative cost effectiveness of Lonsurf was reviewed by the Committee.

B. Oral Oncologic Drugs: Trifluridine/Tipiracil (Lonsurf)—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) tifluridine/tipiracil (Lonsurf) be designated formulary on the UF.

C. Oral Oncologic Drugs: Trifluridine/Tipiracil (Lonsurf)—UF Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) an effective date upon signing of the minutes in all POS.

XXVII. INNOVATOR DRUGS—PCSK9 INHIBITORS

BAP Comments

A. Oral Oncologic Drugs: Trifluridine/Tipiracil (Lonsurf)—UF Recommendation

The P&T Committee recommended Lonsurf be designated formulary on the UF.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. Oral Oncologic Drugs: Trifluridine/Tipiracil (Lonsurf)—UF Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

XXVIII. INNOVATOR DRUGS—NON-INSULIN DIABETES DRUGS: SODIUM-GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITORS

P&T Comments

A. SGLT2 Inhibitors: Empagliflozin/Metformin IR (Synjardy)—Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions

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

- The SGLT2 inhibitors were reviewed in August 2015. Empagliflozin (Jardiance) and empagliflozin/linagliptin (Glyxambi) were designated formulary and step-preferred, while the two other products and their combinations (canagliflozin and dapagliflozin with and without metformin) were designated NF and non step-preferred.
- Synjardy is the third available fixed-dose combination containing an SGLT2 inhibitor and metformin. There are no significant clinical differences between the three SGLT2 inhibitors in terms of effect on glycemic control, or changes in weight, blood pressure and lipid parameters.
- Empagliflozin/metformin offers the advantage of a fixed-dose combination with metformin. The parent compound is the step-preferred SGLT2 inhibitor.
- Relative cost effectiveness of Synjardy was reviewed by the Committee.

B. SGLT2 Inhibitors: Empagliflozin/Metformin IR (Synjardy)—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) empagliflozin/metformin IR (Synjardy) be designated formulary and step-preferred on the UF. No changes were recommended for the previously approved step-therapy and manual PA criteria, which were approved by the Beneficiary Advisory Panel at the September 30, 2015 meeting.

C. SGLT2 Inhibitors: Empagliflozin/Metformin IR (Synjardy)—UF Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) an effective date upon signing of the minutes in all POS.

XXIX. INNOVATOR DRUGS—NON-INSULIN DIABETES DRUGS: SGLT2 INHIBITORS

BAP Comments

A. SGLT2 Inhibitors: Empagliflozin/Metformin IR (Synjardy)—UF Recommendation

The P&T Committee recommended Synjardy be designated formulary and step-preferred on the UF.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. SGLT2 Inhibitors: Empagliflozin/Metformin IR (Synjardy)—UF Implementation Plan

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

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

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

P&T Comments

A. Section 703, NDAA FY08—UF Recommendation

The P&T Committee reviewed three drugs from pharmaceutical manufacturers that were not included on a DoD Retail Refund Pricing Agreement; these drugs were not in compliance with the FY08 NDAA, Section 703. The law stipulates that if a drug is not compliant with Section 703, it will be designated NF on the UF and will require pre-authorization prior to use in the Retail POS and medical necessity at military treatment facilities (MTFs). These NF drugs will remain available in the Mail Order POS without preauthorization.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) the following products be designated NF on the UF:

- Pari Respirator: tobramycin (Kitabis Pak), 300 mg/5 mL inhalation solution
- Libertas Pharm: doxycycline (Doryx), 200 mg delayed release tablet
- Gemini Labs: levothyroxine (Unithroid) 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 137 mcg, 150 mcg, 175 mcg, and 300 mcg tablets

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

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) the following preauthorization criteria for Kitabis Pak. Doryx, and Unithroid:

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

These preauthorization criteria do not apply to any other POS other than retail network pharmacies.

Note that the following drugs will not be available in the Mail Order Pharmacy:

- Kitabis Pak, 300 mg/5 mL inhalation solution, is only available in the Retail Network via a specialty distributor network of pharmacies.
- Unithroid 25 mcg and 100 mcg tablets are noncompliant with the Trade Agreements Act and, therefore, is only available in the retail network pharmacies.

C. Section 703, NDAA FY08—Implementation Plan for Pre-Authorization Criteria

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

XXXI. SECTION 703, NDAA FOR FY08

BAP Comments

A. Section 703, NDAA FY08—UF Recommendation

The P&T Committee recommended the following products be designated NF on the UF:

- Kitabis Pak, inhalation solution
- Doryx, 200 mg delayed release tablet
- Unithroid 25, 50, 75, 88, 100, 112, 137, 150, 175, and 300 microgram tablets

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

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

The P&T Committee recommended the following preauthorization criteria for Kitabis Pak. Doryx, and Unithroid:

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

These preauthorization criteria do not apply to any other POS other than retail network pharmacies.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

C. Section 703, NDAA FY08—Implementation Plan for Pre-Authorization Criteria

The P&T Committee recommended an effective date of the first Wednesday after a 90-day implementation period in the Retail Network and DHA send a letter to beneficiaries affected by this decision.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention