

DOD 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 DoD Pharmacy and Therapeutics (P&T) Committee is responsible for developing the Uniform Formulary (UF). Recommendations to the Director, TMA, 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. UF CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

P&T Comments

A. Non-Insulin Diabetes Drugs: Glucagon-Like Peptide-1 Receptor Agonists (GLP1RAs)—Relative Clinical Effectiveness Conclusion The GLP1RAs are a subclass of the Non-Insulin Diabetes Drug Class, which is comprised of exenatide twice daily (BID) injection (Byetta), liraglutide once daily injection (Victoza), and exenatide once weekly injection (Bydureon). Bydureon is the newest entrant to the class. The Pharmacy Outcomes Research Team (PORT) provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

The GLP1RA class was previously reviewed for UF placement in November 2010. Step therapy implemented in April 2011 requires that new GLP1RA users try metformin or sulfonylurea first, and that new GLP1RA users try exenatide twice daily (BID) (Byetta) before TRICARE® will cover the other agents in this drug subclass. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- Metformin is the most cost-effective agent and remains the first line treatment in all patients with type 2 diabetes mellitus, unless contraindications exist, due to positive outcomes data from the United Kingdom Prospective Diabetes Study.
- Exenatide BID injection (Byetta), liraglutide once daily injection (Victoza), and exenatide once weekly injection (Bydureon) all decrease hemoglobin A1c ~ 1%–2% from baseline when used as monotherapy or in combination with other oral agents.

- When compared head-to-head, overall there are no clinically relevant differences between the three GLP1RAs with regard to effect on glycemic control.
- Bydureon offers additional patient convenience given its once weekly dosing regimen and does not require titration compared to Byetta, but is not available in a pre-filled syringe.
- There are no studies evaluating adherence with the three GLP1RAs.

B. Non-Insulin Diabetes Drugs: GLP1RAs—Relative Cost-Effectiveness Analysis and Conclusion Pharmacoeconomic analyses were performed for the GLP1RA subclass, including cost minimization analysis (CMA) and budget impact analysis (BIA). For the BIAs, several of the model's key assumptions were varied, with corresponding sensitivity analyses conducted. Methods used for CMA and BIAs were based on current step therapy requiring a trial of metformin or a sulfonylurea prior to a patient receiving a GLP1RA.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that exenatide BID (Byetta) was the most cost-effective GLP1RA, based on the weighted average cost per day of treatment across all three points of service (POS), followed by exenatide once weekly (Bydureon) and liraglutide (Victoza). Results from the cost minimization and budget impact analyses showed scenarios where exenatide BID (Byetta), exenatide once weekly (Bydureon) and liraglutide (Victoza) are all designated UF presented a cost avoidance projection comparable to the current UF scenario where all GLP1RAs are UF. Data was not available to assess the potential pharmacoeconomic impact of longer-acting GLP1RA formulations on medication adherence and health-related outcomes in this cost-effectiveness evaluation.

C. Non-Insulin Diabetes Drugs: GLP1RAs—UF Recommendation The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) the following:

- Designating exenatide BID (Byetta), liraglutide once daily (Victoza), and exenatide once weekly (Bydureon) as formulary on the UF;
- Removing the current requirement for a trial of Byetta prior to the other GLP1RAs. As a result, there would no longer be a preferred GLP1RA product.

D. Non-Insulin Diabetes Drugs: GLP1RAs—Prior Authorization (PA) Criteria The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining the current PA requiring a trial of metformin or a sulfonylurea prior to the use of exenatide BID (Byetta), liraglutide once daily (Victoza), or exenatide once weekly (Bydureon) in new users. A trial of metformin or a sulfonylurea would not be required for patients with an adverse event, contraindication to, or inadequate response with metformin or sulfonylurea. Automated PA criteria (step-therapy) and manual PA criteria remain the

same as recommended at the November 2010 P&T Committee meeting, and implemented in April 2011.

Automated PA criteria: The patient has received a prescription for metformin or sulfonylurea (SU) at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria, if automated criteria are not met: Byetta, Bydureon, or Victoza is approved (e.g., trial of metformin or SU is NOT required) if:

- 1) The patient has a confirmed diagnosis of Type 2 Diabetes Mellitus
- 2) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.
- 3) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.
- 4) The patient has a contraindication to both metformin and a SU.
- 5) The patient has had an inadequate response to metformin and a SU.

E. Non-Insulin Diabetes Drugs: GLP1RAs—UF and PA Implementation Plan The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 30-day implementation period in all POS.

III. UF CLASS REVIEWS—NON-INSULIN DIABETES DRUGS

BAP Comments

A. Non-Insulin Diabetes Drugs: GLP1RAs—UF Recommendation The P&T Committee recommended the following:

- Designating Byetta, Victoza, and (Bydureon as formulary on the UF;
- Removing the current requirement for a trial of Byetta prior to the other GLP1RAs. As a result, there would no longer be a preferred GLP1RA product.

BAP Comment: Concur Non-concur

Additional Comments and Dissentions

A. Non-Insulin Diabetes Drugs: GLP1RAs—PA Criteria The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) maintaining the current PA requiring a trial of metformin or a sulfonylurea prior to the use of Byetta, Victoza, or Bydureon in new users. Automated PA criteria (step-therapy) and manual PA criteria remain the same as recommended at the November 2010 P&T Committee meeting, and implemented in April 2011.

Automated PA criteria: The patient has received a prescription for metformin or sulfonylurea (SU) at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria, if automated criteria are not met: Byetta, Bydureon, or Victoza is approved (e.g., trial of metformin or SU is NOT required) if:

- 1) The patient has a confirmed diagnosis of Type 2 Diabetes Mellitus
- 2) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.
- 3) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.
- 4) The patient has a contraindication to both metformin and a SU.
- 5) The patient has had an inadequate response to metformin and a SU.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

C. Non-Insulin Diabetes Drugs: GLP1RAs—UF and PA Implementation Plan The P&T Committee recommended an effective date of the first Wednesday after a 30-day implementation period in all POS.

BAP Comment: Concur Non-concur

IV. UF CLASS REVIEWS—OVERACTIVE BLADDER DRUGS

P&T Comments

A. Overactive Bladder Drugs (OABs)—Relative Clinical Effectiveness Conclusion

The Overactive Bladder (OAB) Drug Class is comprised of darifenacin (Enablex), fesoterodine (Toviaz), oxybutynin IR (Ditropan, generics), oxybutynin extended release (ER) (Ditropan XL, generics), oxybutynin transdermal delivery system (TDS) (Oxytrol), oxybutynin 10% gel (Gelnique), solifenacina (Vesicare), tolterodine IR (Detrol, generics), tolterodine ER (Detrol LA), trospium IR (Sanctura, generics), and trospium ER (Sanctura XR, generics). Generic formulations of Detrol IR, Sanctura IR and Sanctura XR recently entered the market. The OAB drug class has been previously reviewed for UF placement in August 2008, and May and November 2009.

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

- Review of the clinical literature for efficacy, safety, and tolerability data since the last P&T Committee UF decision in 2008 did not add substantial new information.
- The OAB agents are statistically superior to placebo, but the placebo response rates are high for the class, ranging from 30% to 50%.
- There is insufficient evidence to suggest whether one OAB drug is superior to another. Small studies of low quality evidence reported fesoterodine (Toviaz) was statistically superior to tolterodine, and solifenacina (Vesicare) was statistically superior to tolterodine, but the clinical effect is small, relating to a reduction in urge episodes/incontinent episodes of approximately one episode/day.
- No OAB agent has a superior safety profile. Oxybutynin TDS (Oxytrol) causes less dry mouth than tolterodine ER, but has higher withdrawal rates. There is scant safety data for the oxybutynin 10% gel (Gelnique) formulation, but the effects are likely to be similar to oxybutynin TDS with regards to dry mouth.
- Overall, adverse drug effects are lower with the ER formulations than IR formulations. The newer agents do not have significantly lower incidence of dry mouth or constipation than the older OAB drugs.
- Persistence rates within the Military Health System (MHS) remain low at 12% for all the OAB drugs. As needed use of the OAB drugs is 26% in the MHS.

- There are no studies evaluating clinical outcomes, such as reduced fall risk or delayed nursing home placement with the OAB drugs.

B. OABs—Relative Cost-Effectiveness Analysis and Conclusion

Pharmacoeconomic analyses were performed for the OABs, including CMA and BIA. For the BIAs, several of the model's key assumptions were varied, with corresponding sensitivity analyses conducted.

The P&T Committee concluded (17 for, 0 against, 0 abstained, 0 absent) that for preferred formulary placement status, oxybutynin immediate release (IR) (Ditropan, generics) was the least costly agent based on the weighted average cost per day of treatment across all three POS, followed by oxybutynin extended release (ER) (Ditropan XL, generics), tolterodine ER (Detrol LA), solifenacina (Vesicare), oxybutynin 10% gel (Gelnique), fesoterodine (Toviaz), oxybutynin transdermal delivery system (Oxytrol), trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), darifenacina (Enablex), and tolterodine IR (Detrol, generics).

Budget impact analysis (BIA) results were presented to the P&T Committee and indicated that step therapy scenarios were more cost-effective compared to the current baseline (non step therapy). Results from the cost minimization analysis (CMA) and BIA showed that among available formulary options examined, the scenario where oxybutynin IR, oxybutynin ER, and Detrol LA were designated as step-preferred, with step therapy applied to all current and new users of non-preferred OAB products, was most cost-effective.

C. OABs—UF Recommendation

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

- UF and step-preferred (“in front of the step”): tolterodine extended release (ER) (Detrol LA), oxybutynin IR (Ditropan, generics), and oxybutynin ER (Ditropan XL, generics). Automated prior authorization (step therapy) would require that all patients try Detrol LA, oxybutynin IR, or oxybutynin ER before TRICARE will cover the other agents in this drug class.
- UF and non step-preferred (“behind the step”): trospium IR (Sanctura, generics), trospium ER (Sanctura XR, generics), tolterodine IR (Detrol, generics) and solifenacina (Vesicare)
 - When the generics to Sanctura, Sanctura XR, and Detrol become cost-effective relative to the step-preferred agents, the generics will become step-preferred without further action by the P&T Committee, Beneficiary

Advisory Panel, or Director, TMA. 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.

- NF and non step-preferred: darifenacin (Enablex), fesoterodine (Toviaz), oxybutynin transdermal delivery system (Oxytrol), and oxybutynin 10% gel (Gelnique).
- Step therapy would apply to all users (current and new) of the OAB drugs.

B. OABs—PA Criteria

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) PA criteria for all current and new users of the OAB drugs, requiring a trial of Detrol LA, oxybutynin IR, or oxybutynin ER prior to the use of the other OAB drugs.

Automated PA Criteria: The patient has received a prescription for Detrol LA, oxybutynin IR or oxybutynin ER at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria, if automated criteria are not met (e.g., a trial of Detrol LA, oxybutynin IR, or oxybutynin ER is not required) if:

- 1) The patient has experienced any of the following issues while receiving Detrol LA, oxybutynin IR, or oxybutynin ER, which is not expected to occur with Detrol IR, Sanctura, Sanctura XR, Vesicare, Enablex, Toviaz, Oxytrol, or Gelnique 10%:
 - a. inadequate response;
 - b. intolerable adverse effects (e.g., the patient requires Sanctura due to intolerable dry mouth with Detrol LA); or,
 - c. contraindication.
- 2) Coverage is only approved for the following FDA-approved indications:
 - a. The patient has a confirmed diagnosis of OAB with symptoms of urge incontinence, urgency, and urinary frequency (for all 11 OAB drugs).
 - b. The patient is older than 6 years with symptoms of detrusor overactivity associated with a neurological condition (e.g., spina bifida), for oxybutynin ER.

Other uses, including stress incontinence, will not be approved.

E. OABs—UF and PA Implementation Plan

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

F. OABs—Addendum to UF Recommendation

Addendum to the UF recommendation: During a post meeting bid review, it was determined that after-step bids should not be accepted and modeled due to verbiage in the bid solicitation. As a result of this determination, the cost analysis was recalculated. This new cost model was presented to the DoD P&T committee via electronic means. An electronic vote was taken to determine a) whether to accept the new cost review, maintain the current scenario and maintain current UF recommendations, or b) withdraw the UF recommendation, rebid the class and present results at the Feb 2013 meeting.

COMMITTEE ACTION: ADDENDUM TO UF RECOMMENDATION

The P&T Committee recommended (9 for, 5 opposed, 0 abstained, 3 absent) to approve the current scenario, which maintains the UF recommendation, step therapy requirements for all new and current users of OAB drugs, and PA criteria.

V. UF CLASS REVIEWS—OVERACTIVE BLADDER DRUGS (OABs)

BAP Comments

A. OABs—UF Recommendation

The P&T Committee recommended the following:

- UF and step-preferred (“in front of the step”): Detrol LA, Ditropan, generics, and Ditropan XL, generics. Automated prior authorization (step therapy) would require that all patients try Detrol LA, Ditropan, generics, and Ditropan XL, generics before TRICARE will cover the other agents in this drug class.
- UF and non step-preferred (“behind the step”): (Sanctura, generics, (Sanctura XR, generics, Detrol, generics and Vesicare.
 - When the generics to Sanctura, Sanctura XR, and Detrol become cost-effective relative to the step-preferred agents, the generics will become step-preferred without further action by the P&T Committee, Beneficiary Advisory Panel, or Director, TMA. 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.

- NF and non step-preferred: Enablex, Toviaz, Oxytrol, and Gelnique 10%.
- Step therapy would apply to all users (current and new) of the OAB drugs.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

B. OABs—PA Criteria

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) PA criteria for all current and new users of the OAB drugs, requiring a trial of Detrol LA, Ditropan generics or Ditropan XL generics prior to the use of the other OAB drugs.

Automated PA Criteria: The patient has received a prescription for Detrol LA, Ditropan generics or Ditropan XL generics at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 180 days, AND

Manual PA criteria, if automated criteria are not met (e.g., a trial of Detrol LA, Ditropan generics or Ditropan XL generics is not required) if:

- 1) The patient has experienced any of the following issues while receiving Detrol LA, Ditropan generics or Ditropan XL generics, which is not expected to occur with Detrol IR, Sanctura, Sanctura XR, Vesicare, Enablex, Toviaz, Oxytrol, or Gelnique 10%:
 - a. inadequate response;
 - b. intolerable adverse effects (e.g., the patient requires Sanctura due to intolerable dry mouth with Detrol LA); or,
 - c. contraindication.
- 2) Coverage is only approved for the following FDA-approved indications:
 - a. The patient has a confirmed diagnosis of OAB with symptoms of urge incontinence, urgency, and urinary frequency (for all 11 OAB drugs).

- b. The patient is older than 6 years with symptoms of detrusor overactivity associated with a neurological condition (e.g., spina bifida), for Ditropan XL.

Other uses, including stress incontinence, will not be approved.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

C. OABs—UF and PA Implementation Plan

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

BAP Comment: Concur Non-concur

Additional Comments and Dissent

Addendum to the UF recommendation: During a post meeting bid review, it was determined that after-step bids should not be accepted and modeled due to verbiage in the bid solicitation. As a result of this determination, the cost analysis was recalculated. This new cost model was presented to the DoD P&T committee via electronic means. An electronic vote was taken to determine a) whether to accept the new cost review, maintain the current scenario and maintain current UF recommendations, or b) withdraw the UF recommendation, rebid the class and present results at the Feb 2013 meeting.

COMMITTEE ACTION: ADDENDUM TO UF RECOMMENDATION

The P&T Committee recommended (9 for, 5 opposed, 0 abstained, 3 absent) to approve the current scenario, which maintains the UF recommendation, step therapy requirements for all new and current users of OAB drugs, and PA criteria.

D. OABs—Addendum to UF Recommendation

The P&T Committee recommended to approve the current scenario, which maintains the UF recommendation, step therapy requirements for all new and current users of OAB drugs, and PA criteria.

BAP Comment: Concur Non-concur

Additional Comments and Dissentions

VI. UF CLASS REVIEWS—GASTROINTESTINAL-2 ORAL ANTIBIOTIC DRUGS

P&T Comments

A. Gastrointestinal-2 Oral Antibiotic Drugs (GI-2)—Relative Clinical Effectiveness Conclusion

The Gastrointestinal-2 Oral Antibiotics (GI-2) Drug Class includes metronidazole (Flagyl, generics), vancomycin (Vancocin, generics), rifaximin (Xifaxan), fidaxomicin (Dificid), nitazoxanide (Alinia) and neomycin (Neo-Fradin, generics). This review focused on clinical effectiveness with regard to hepatic encephalopathy, *Clostridium difficile* infection, travelers' diarrhea, and non FDA-approved (off-label) uses.

The class has not been previously reviewed for UF placement. The PORT provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following:

- For hepatic encephalopathy (HE), rifaximin is superior to lactulose in improving symptoms. While rifaximin (Xifaxan) is approved for monotherapy, it is commonly used in combination with lactulose, and is better tolerated than lactulose.
- For *Clostridium difficile* infection (CDI):
 - Metronidazole is equally effective as vancomycin in treating mild to moderate CDI, but for severe CDI vancomycin results in higher clinical cure rates.

- Fidaxomicin (Dificid) and vancomycin provide similar clinical cure rates for CDI; however, fidaxomicin decreases recurrence and increases global cure rates to a greater extent than vancomycin.
 - Comparative efficacy for nitazoxanide (Alinia) and rifaximin for CDI cannot be assessed, given the small numbers of trials.
- For travelers' diarrhea (TD), practice guidelines and a systematic review recommend fluoroquinolones (e.g., levofloxacin, ciprofloxacin) as first line treatment. Rifaximin is FDA-approved for TD but is limited to TD caused by noninvasive strains of *Escherichia coli*.
- Rifaximin is not FDA-approved for irritable bowel syndrome, and there is insufficient evidence to support its use for IBS. Other non-supportable uses of rifaximin include inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non FDA-approved indication.

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

Pharmacoeconomic analyses, including CMA, were performed for the GI-2 Drug Class. Cost analyses were based on the disease states discussed in the clinical section. Cost analyses were based on the disease states discussed in the clinical section. Comparative costs for agents from other drug classes were considered (e.g., lactulose, fluoroquinolones), due to the conclusions from the clinical effectiveness review.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) the following: for hepatic encephalopathy, lactulose was the least costly agent, followed by lactulose in combination with neomycin, and then rifaximin (Xifaxan). For CDI, metronidazole was the least costly agent, followed by vancomycin, with fidaxomicin (Dificid) as the most costly agent. For travelers' diarrhea, ciprofloxacin was the least costly agent followed by rifaximin (Xifaxan) and nitazoxanide (Alinia).

C. GI-2—UF Recommendation

The P&T Committee recommended (14 for, 2 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the MHS.

- UF: metronidazole, vancomycin, neomycin, rifaximin (Xifaxan), nitazoxanide (Alinia), and fidaxomicin (Dificid)
- Fidaxomicin (Dificid) is available solely in the retail network. Availability of Dificid from mail order is not recommended due to the time constraints for treating acute *C. difficile* infection. Additionally, due to noncompliance with the Trade Agreements Act, Dificid is excluded from mail order and military treatment

facilities (MTFs). Efforts to allow availability of Difid at the MTFs is ongoing at this time.

D. GI-2—PA Criteria

The P&T Committee recommended (15 for, 1 opposed, 1 abstained, 0 absent) PA criteria for rifaximin (Xifaxan) 200 mg for travelers' diarrhea, and recommended (14 for, 2 opposed, 1 abstained, 0 absent) PA criteria for rifaximin (Xifaxan) 550 mg for hepatic encephalopathy. Other uses of rifaximin are not covered, including *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, and rosacea.

Xifaxan 200 mg PA criteria: New users of Xifaxan 200 mg for travelers' diarrhea are required to undergo the PA process.

Automated PA Criteria: The patient has received a prescription for a fluoroquinolone at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 60 days, AND

Manual PA Criteria:

- 1) 200 mg tablets are approved for the following:
 - a. Documented use in travelers' diarrhea caused by noninvasive strains of *Escherichia coli*
 - b. Patient is between 12 and 18 years of age
 - c. Documented trial of a fluoroquinolone for patients > 18 years of age
 - d. Documented contraindication or allergy to fluoroquinolone antibiotics in last 60 days
 - e. Returning from area with high fluoroquinolone resistance
 - f. 200 mg tablets are being used to treat hepatic encephalopathy
- 2) 200 mg tablets are not approved for the following
 - a. Diarrhea complicated by fever or bloody stool
 - b. Treatment of dysentery
 - c. Diarrhea associated with use of antibiotics
 - d. Diarrhea caused by bacteria other than *E. coli*
 - e. *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved use

Xifaxan 500 mg PA criteria for hepatic encephalopathy: New users of Xifaxan 550 mg for hepatic encephalopathy are required to undergo the PA process. Prior authorization will expire after 365 days.

Manual PA Criteria:

- 1) 550 mg tablets are approved for the following:
 - a. Documented use in hepatic encephalopathy
- 2) 550 mg tablets are not approved for the following:
 - b. Travelers' diarrhea, *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved use

E. GI-2—UF and PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 90-day implementation period in all POS.

VII. UF CLASS REVIEWS—GASTROINTESTINAL-2 ORAL ANTIBIOTIC DRUGS (GI-2)

BAP Comments

A. GI-2—UF Recommendation

The P&T Committee recommended the following scenario for the UF, which is the most clinically and cost-effective option for the MHS.

- UF: metronidazole, vancomycin, neomycin, rifaximin (Xifaxan), nitazoxanide (Alinia), and fidaxomicin (Dificid)
- Fidaxomicin (Dificid) is available solely in the retail network. Availability of Dificid from mail order is not recommended due to the time constraints for treating acute *C. difficile* infection. Additionally, due to noncompliance with the Trade Agreements Act, Dificid is excluded from mail order and military treatment facilities (MTFs). Efforts to allow availability of Dificid at the MTFs is ongoing at this time.

<i>BAP Comment:</i>	<input type="checkbox"/> Concur	<input type="checkbox"/> Non-concur
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B. GI-2—PA Criteria

Xifaxan 200 mg PA criteria: New users of Xifaxan 200 mg for travelers' diarrhea are required to undergo the PA process.

Automated PA Criteria: The patient has received a prescription for a fluoroquinolone at any Military Health System pharmacy point of service (Military Treatment Facilities, retail network pharmacies, or mail order) during the previous 60 days, AND

Manual PA Criteria:

- 1) 200 mg tablets are approved for the following:
 - a. Documented use in travelers' diarrhea caused by noninvasive strains of *Escherichia coli*
 - b. Patient is between 12 and 18 years of age
 - c. Documented trial of a fluoroquinolone for patients > 18 years of age
 - d. Documented contraindication or allergy to fluoroquinolone antibiotics in last 60 days
 - e. Returning from area with high fluoroquinolone resistance
 - f. 200 mg tablets are being used to treat hepatic encephalopathy
- 2) 200 mg tablets are not approved for the following
 - a. Diarrhea complicated by fever or bloody stool
 - b. Treatment of dysentery
 - c. Diarrhea associated with use of antibiotics
 - d. Diarrhea caused by bacteria other than *E. coli*
 - e. *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved use

Xifaxan 500 mg PA criteria for hepatic encephalopathy: New users of Xifaxan 550 mg for hepatic encephalopathy are required to undergo the PA process. Prior authorization will expire after 365 days.

Manual PA Criteria:

- 1) 550 mg tablets are approved for the following:
 - a. Documented use in hepatic encephalopathy
- 2) 550 mg tablets are not approved for the following:
 - b. Travelers' diarrhea, *C. difficile* infection, irritable bowel syndrome, inflammatory bowel disease, chronic abdominal pain, hepatitis, diabetes, rosacea, and any other non-FDA approved use

BAP Comment: Concur Non-concur

Additional Comments and Dissent

C. GI-2—UF and 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 Dissent

VIII. UF CLASS REVIEWS—HEPATITIS C DRUGS

P&T Comments

A. Hepatitis C Drugs—Relative Clinical Effectiveness Conclusion

The Hepatitis C Drug Class includes the direct acting antiviral agents (DAAs) boceprevir (Victrelis) and telaprevir (Incivek); the interferon products PEG-interferon alfa-2a (Pegasys), PEG-interferon alfa-2b (PEG-Intron), and interferon alfacon-1(Infergen); and, various ribavirin products, including generics. Interferon alfa-2b (Intron A) is no longer used for treating hepatitis C virus infection and will not be discussed further. The PORT provided the P&T Committee detailed analyses of current MHS prescription patterns. The data presented were factored into the relative clinical and cost-effectiveness determinations.

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

- Triple therapy with a direct acting antiviral agent (boceprevir or telaprevir), PEG-interferon, and ribavirin increases sustained viral response (SVR) rates to a greater extent than dual therapy with PEG-interferon and ribavirin (PR).
- There is insufficient evidence to conclude whether boceprevir (Victrelis) or telaprevir (Incivek) is superior to the other, due to the lack of direct comparative trials. Telaprevir offers patient convenience due to its shorter treatment course than boceprevir (12 weeks versus 44 weeks), but this has not resulted in higher SVR rates.
- There is insufficient evidence to prefer Pegasys over PEG-Intron, but there do not appear to be clinically relevant differences in efficacy.
- Response-guided therapy for clinically appropriate patient populations maintains high levels of efficacy while shortening drug exposure times and treatment course duration.
- Compared with PR dual therapy, boceprevir triple therapy increases the risk for anemia and telaprevir triple therapy increases the risk for anemia and rash.

B. Hepatitis C Drugs—Relative Cost-Effectiveness Analysis and Conclusion

CMA was performed to compare each regimen for hepatitis C treatment (ribavirin, PEG-interferons, and DAAs). A cost-effectiveness analysis (CEA) was also performed comparing triple therapy (DAAs, PEG-interferon, and ribavirin) with dual therapy (PEG-interferon alfa and ribavirin). Additionally, a BIA was performed to compare competing formulary scenarios.

CMA results for the evaluated agents showed most dosage forms of ribavirin were generic and cost-effective. However, Ribapak was deemed not cost-effective compared with other ribavirin dosage forms. Both PEG-interferon alfa products (Pegasys and PEG-Intron) had comparable costs. Interferon alfacon-1 (Infergen) was identified as not cost-effective when compared with the PEG-interferon agents. CMA results for the DAAs showed response-guided therapy could be less costly with boceprevir than with telaprevir, based on current dosing recommendations. However, when each agent was taken over its full treatment duration, telaprevir was less costly than boceprevir.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that the most cost-effective scenario placed ribavirin (generics), PEG-interferon alfa-2a (Pegasys), interferon alfa-2b (Intron A), PEG-interferon alfa-2b (PEG-Intron),

boceprevir (Victrelis), and telaprevir (Incivek) as formulary on the UF, and ribavirin (Ribapak) and interferon alfacon-1 (Infergen) as NF on the UF.

C. Hepatitis C Drugs—UF Recommendation

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

- UF status for boceprevir (Victrelis), telaprevir (Incivek), PEG-interferon alfa-2a (Pegasys), PEG-interferon alfa-2b (PEG-Intron), interferon alfa-2b (Intron A), and ribavirin (except for the Ribapak formulation); and,
- NF status for interferon alfacon-1 (Infergen) and the ribavirin Ribapak formulation, due to the lack of compelling clinical advantages and cost disadvantages when compared to the UF products.

D. Hepatitis C Drugs—PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for boceprevir (Victrelis) and telaprevir (Incivek). New users of boceprevir or telaprevir are required to undergo the PA process. Prior authorization will expire after 12 weeks for telaprevir and 44 weeks for boceprevir.

Manual PA Criteria:

- 1) Age \geq 18
- 2) Has laboratory evidence of chronic hepatitis C—a quantified viral load (above undetectable)
- 3) Has laboratory evidence of genotype-1 hepatitis C infection
- 4) Is not co-infected with the human immunodeficiency virus (HIV) or Hepatitis B virus
- 5) Boceprevir or telaprevir will be co-administered with both a PEG-interferon alfa-2a or PEG-interferon alfa-2b product AND ribavirin
- 6) The patient has not previously used boceprevir or telaprevir.
- 7) For boceprevir, the patient will begin with a 4-week lead-in of both a PEG-Interferon alfa-2a or PEG-interferon alfa-2b product and ribavirin.

E. Hepatitis C Drugs—UF and PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in all

POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

IX. UF CLASS REVIEWS—HEPATITIS C DRUGS

BAP Comments

A. Hepatitis C Drugs—UF Recommendation

The P&T Committee recommended the following:

- UF status for Victrelis, Incivek, Pegasys, PEG-Intron, Intron A, and ribavirin (except for the Ribapak formulation); and,
- Non-formulary status for Infergen and the ribavirin Ribapak formulation, due to the lack of compelling clinical advantages and cost disadvantages when compared to the UF products.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

B. Hepatitis C Drugs—PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for boceprevir (Victrelis) and telaprevir (Incivek). New users of boceprevir or telaprevir are required to undergo the PA process. Prior authorization will expire after 12 weeks for telaprevir and 44 weeks for boceprevir.

Manual PA Criteria:

- 1) Age \geq 18
- 2) Has laboratory evidence of chronic hepatitis C—a quantified viral load (above undetectable)
- 3) Has laboratory evidence of genotype-1 hepatitis C infection
- 4) Is not co-infected with the human immunodeficiency virus (HIV) or Hepatitis B virus
- 5) Boceprevir or telaprevir will be co-administered with both a PEG-interferon alfa-2a or PEG-interferon alfa-2b product AND ribavirin

- 6) The patient has not previously used boceprevir or telaprevir.
- 7) For boceprevir, the patient will begin with a 4-week lead-in of both a PEG-Interferon alfa-2a or PEG-interferon alfa-2b product and ribavirin.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

C. Hepatitis C 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, and 2) TMA send a letter to beneficiaries affected by this UF decision.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

X. RECENTLY APPROVED U.S. FDA AGENTS

P&T Comments

A. High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—Relative Clinical Effectiveness Conclusion

Oxecta is a formulation of oxycodone IR that is tamper resistant but not tamper proof. FDA approval was based on demonstrated bioequivalence to the Roxycodone proprietary formulation of oxycodone IR. One small “drug liking” study showed a reduced “liking” for Oxecta versus Roxycodone, but the widespread clinical applicability of these results is unknown. The Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Oxecta is the first

abuse deterrent IR oxycodone formulation marketed. There is no evidence to suggest oxycodone IR (Oxecta) has a compelling clinical advantage over the other high potency narcotic analgesics included on the UF.

B. High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—Relative Cost-Effectiveness Analysis and Conclusion

A pharmaco-economic analysis was performed. The weighted average cost per tablet at all three points of service (POS) was evaluated for oxycodone IR (Oxecta) in relation to the other drugs in the high potency narcotic subclass. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that oxycodone IR (Oxecta) was not cost-effective when compared to other high potency narcotic analgesics included on the UF.

C. High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—UF Recommendation

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

D. High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—UF Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

XI. RECENTLY APPROVED U.S. FDA AGENTS

BAP Comments

A. High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—UF Recommendation

The P&T Committee recommended Oxecta be designated non-formulary due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

B. High Potency Narcotic Analgesics: Oxycodone IR (Oxecta)—UF Implementation Plan

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60-day implementation period in all POS, and 2) TMA send a letter to beneficiaries affected by this UF decision.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

XII. RE-EVALUATION OF NF AGENTS

P&T Comments

On an ongoing basis, the DoD Pharmacoeconomic Center 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 the re-evaluation of NF agents established at the May 2007 meeting was approved by the Director, TMA on June 24, 2007, and is outlined in Appendix A on page 28.

The P&T Committee reevaluated the UF status of Lexapro (escitalopram) and pantoprazole (Protonix) in light of recent price reductions in the generic formulations across all three POS.

A. Escitalopram—UF Recommendation and Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) reclassification of escitalopram (Lexapro, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

B. Pantoprazole—UF Recommendation and Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) reclassification of pantoprazole (Protonix, generic) as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

XIII. RE-EVALUATION OF NF AGENTS

BAP Comments

A. Escitalopram—UF Recommendation and Implementation Plan

The P&T Committee recommended reclassification of Lexapro, generic as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

B. Pantoprazole—UF Recommendation and Implementation Plan

The P&T Committee recommended reclassification of Protonix, generic as formulary on the UF, as cost-effective generic formulations are now available in all three POS. Implementation will occur upon signing of the minutes.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

XIV. UTILIZATION MANAGEMENT

P&T Comments

A. Phosphodiesterase-5 (PDE-5) Inhibitors—PA Criteria

The PA criteria for the PDE-5 Inhibitors Drug Class was reviewed. Prior authorization allows use of a PDE-5 inhibitor following prostatectomy for preservation/restoration of erectile function for one year. There is no published evidence suggesting benefit if the PDE-5 inhibitor is initiated beyond one year after surgery. Recommendations were to clarify the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed.

The additional recommendations were:

- For Cialis: that existing criteria that apply to patients with benign prostatic hyperplasia (BPH) also apply to patients with BPH and erectile dysfunction (ED); and,
- For sildenafil used for primary pulmonary hypertension (PPH): that the sildenafil dosage formulation specifically state 20 mg tablets to discourage use of sildenafil 20 mg tablets for ED.

The P&T Committee recommended (14 for, 1 opposed, 2 abstained, 0 absent) PA criteria for the PDE-5 inhibitors (1) clarifying the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed; (2) for Cialis, that the existing criteria also apply to patients with BPH and ED; and, (3) for sildenafil for PPH, that the sildenafil dosage formulation will specifically state 20 mg tablets.

XV. UTILIZATION MANAGEMENT

BAP Comments

A. PDE-5 Inhibitors—PA Criteria

The P&T Committee recommended PA criteria for the PDE-5 inhibitors (1) clarifying the existing PA criteria to state that prostatectomy surgery must have occurred less than 365 days from the date the PA form is signed; (2) for Cialis, that the existing criteria also apply to patients with BPH and ED; and, (3) for sildenafil for PPH, that the sildenafil dosage formulation will specifically state 20 mg tablets.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

XVI. UTILIZATION MANAGEMENT

P&T Comments

A. Testosterone Replacement Therapy (TRT)—TRT Use in Women PA Criteria

PA criteria for the TRT Drug Class were developed at the August 2012 meeting and signed by the Director, TMA on November 8, 2012. The P&T Committee reviewed

the PA criteria for use of TRT in women, which was based on level A evidence from the American College of Obstetrics and Gynecology, as outlined in a 2011 Clinical Bulletin. The Clinical Bulletin specifically mentions that there is little evidence to support long-term TRT use (longer than 6 months) in women.

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the PA criteria for use of TRT in women to limit use to six months.

XVII. UTILIZATION MANAGEMENT

BAP Comments

A. TRT—TRT Use in Women PA Criteria

The P&T Committee recommended revising the PA criteria for use of TRT in women to limit use to six months.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

XVIII. UTILIZATION MANAGEMENT

P&T Comments

A. PAs

Injectable Gonadotropins—PA criteria currently apply to the injectable gonadotropins (fertility agents). Injectable gonadotropins are not covered under the TRICARE pharmacy benefit if they are being used in conjunction with a noncoital reproductive technology. In 2010, the Assistant Secretary of Defense for Health Affairs (ASD(HA)) authorized in vitro fertilization services for the benefit of severely or seriously ill/injured active duty service members.

Implementation guidance for these services was developed in an April 2012 ASD(HA) policy.

COMMITTEE ACTION: INJECTABLE GONADOTROPINS PA

CRITERIA—The P&T Committee recommended (15 for, 0 opposed, 2 abstained, 0 absent) revising the PA criteria for the injectable gonadotropins

(fertility agents), to allow for use in conjunction with a noncoital reproductive technology, as outlined in the ASD(HA) April 2012 “Policy for Assisted Reproductive Services for the Benefit of Seriously or Severely Ill/Injured (Category II or III) Active Duty Service Members.” A Signed Authorization Memorandum from TMA must be included with the prescription.

XIX. UTILIZATION MANAGEMENT

BAP Comments

A. PAs

Injectable Gonadotropins—PA criteria currently apply to the injectable gonadotropins (fertility agents). Injectable gonadotropins are not covered under the TRICARE pharmacy benefit if they are being used in conjunction with a noncoital reproductive technology. In 2010, the Assistant Secretary of Defense for Health Affairs (ASD(HA)) authorized in vitro fertilization services for the benefit of severely or seriously ill/injured active duty service members. Implementation guidance for these services was developed in an April 2012 ASD(HA) policy.

COMMITTEE ACTION: INJECTABLE GONADOTROPINS PA

CRITERIA—The P&T Committee recommended (15 for, 0 opposed, 2 abstained, 0 absent) revising the PA criteria for the injectable gonadotropins (fertility agents), to allow for use in conjunction with a noncoital reproductive technology, as outlined in the ASD(HA) April 2012 “Policy for Assisted Reproductive Services for the Benefit of Seriously or Severely Ill/Injured (Category II or III) Active Duty Service Members.” A Signed Authorization Memorandum from TMA must be included with the prescription.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

XX. UTILIZATION MANAGEMENT

P&T Comments

A. Adalimumab (Humira)—PA Criteria

The FDA recently approved a new indication for Humira, the designated Extended Core Formulary agent in the targeted immunomodulatory biologics (TIBs) Drug Class.

Humira is now indicated for the treatment of moderately to severely active ulcerative colitis following inadequate response to immunosuppressants such as corticosteroids, azathioprine, and 6-mercaptopurine.

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) revising the existing PA criteria for Humira to incorporate the new indication for ulcerative colitis, consistent with the FDA-approved product labeling.

XXI. UTILIZATION MANAGEMENT

BAP Comments

A. Adalimumab (Humira)—PA Criteria

The P&T Committee recommended revising the existing PA criteria for Humira to incorporate the new indication for ulcerative colitis, consistent with the FDA-approved product labeling.

BAP Comment: Concur Non-concur

Additional Comments and Dissent

XXII. UTILIZATION MANAGEMENT

P&T Comments

A. Enzalutamide (Xtandi) and Abiratone (Zytiga)—PA Criteria

Two new drugs for metastatic castration-resistant prostate cancer were recently approved. Xtandi and Zytiga are costly agents with specific FDA-indications, requiring use of prior docetaxel-containing regimens.

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) PA criteria for enzalutamide (Xtandi), and abiratone (Zytiga), consistent with the FDA-approved product labeling.

1) Xtandi PA Criteria: Coverage approved for treatment of patients:

- a. With a documented diagnosis of metastatic castration-resistant prostate cancer, AND

- b. Previous treatment with docetaxel
- 2) Zytiga PA Criteria: Coverage approved for treatment of patients:
- a. With a documented diagnosis of metastatic castration-resistant prostate cancer, AND
 - b. Prior chemotherapy with docetaxel, AND
 - c. Patient is receiving concomitant therapy with prednisone

XXIII. UTILIZATION MANAGEMENT

BAP Comments

A. Enzalutamide (Xtandi) and Abiratone (Zytiga)—PA Criteria

The P&T Committee recommended PA criteria for enzalutamide (Xtandi), and abiratone (Zytiga), consistent with the FDA-approved product labeling.

- 1) Xtandi PA Criteria: Coverage approved for treatment of patients:
- a. With a documented diagnosis of metastatic castration-resistant prostate cancer, AND
 - b. Previous treatment with docetaxel
- 2) Zytiga PA Criteria: Coverage approved for treatment of patients:
- a. With a documented diagnosis of metastatic castration-resistant prostate cancer, AND
 - b. Prior chemotherapy with docetaxel, AND
 - c. Patient is receiving concomitant therapy with prednisone

BAP Comment: Concur Non-concur

Additional Comments and Dissent

Appendix A—Criteria for Re-evaluation of Nonformulary Drugs for Uniform Formulary Status

The P&T Committee's process for the re-evaluation of nonformulary (NF) agents established at the May 2007 meeting was approved by the Director, TMA on June 24, 2007, according to the criteria below:

- 1) The NF agent becomes generically available and
 - a) The generic product is “A-rated” as therapeutically equivalent to the brand name product according to the FDA’s classification system.
 - b) The generic market supply is stable and sufficient to meet the DoD Military Health System supply demands.
- 2) The NF agent is cost-effective relative to similar agents on the Uniform Formulary (UF). A NF agent becomes cost-effective when:
 - a) The NF 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 UF class to which they were compared.
 - b) The NF agent’s total weighted average cost based on an alternate measure used during the previous review is less than or equal to that for the UF class to which they were compared. For example, antibiotics may be compared on the cost per course of therapy used to treat a particular condition.