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—ANDROGENS ANABOLIC STEROIDS

P&T Comments

A. Androgens Anabolic Steroids—Transdermal and Buccal Testosterone Replacement Therapies

Background and Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the transdermal and buccal testosterone replacement therapies (TRTs), which are used for treating adult male hypogonadism. The TRT class is comprised of the following formulations of topical or buccal testosterone: transdermal patch (Androderm), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), transdermal solution (Axiron), transdermal 2% gel pump (Fortesta), buccal tablets (Striant), and transdermal gel tubes (Testim).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) the following concerning the TRT agents:

1. Although high-quality comparative data is lacking, there appear to be no clinically relevant differences in efficacy between products.
2. Transdermal and buccal testosterone replacement products effectively raise testosterone levels in hypogonadal men to the normal range when used in accordance with product labeling.
3. Skin-to-skin transfer of transdermal testosterone to women and children should be minimized due to risk of virilization or premature onset of puberty. Testosterone buccal tablets (Striant) carry the lowest risk while the topically applied products carry the highest risk.

4. Transdermal and buccal TRTs have a low overall incidence of systemic adverse events, which are not considered to differ clinically across products.
5. The most frequent adverse events are dermal application site reactions for the transdermal products and oral application site reactions for buccal tablets; most are mild or transient in nature.

B. Androgens Anabolic Steroids: TRTs—Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion

Pharmacoeconomic analyses were performed for the topical and buccal testosterone class, including cost minimization analysis (CMA) and budget impact analysis (BIA). The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that transdermal 2% gel pump (Fortesta) was the least costly agent, followed by transdermal solution (Axiron), transdermal patch (Androderm), transdermal 1.62% gel pump (Androgel 1.62%), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal gel tubes (Testim), and testosterone buccal tablets (Striant).

The analyses also evaluated the potential budgetary impact of cost scenarios where selected TRTs were designated with preferred product status (step therapy) on the UF; i.e., a trial of a preferred TRT would be required before using other TRTs. BIA results showed scenarios implementing step therapy were more cost-effective than scenarios without step therapy. The scenario where transdermal 2% gel (Fortesta) is step-preferred on the UF, all other TRTs are designated non-preferred on the UF or NF, and step therapy is applied to all current and new users of TRTs, was determined to be the most cost-effective scenario.

C. Androgens Anabolic Steroids: TRTs—UF Recommendation

The P&T Committee recommended (13 for, 3 opposed, 1 abstained, 0 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the Military Health System (MHS):

1. testosterone transdermal 2% gel pump (Fortesta) be designated step-preferred and formulary on the UF;
2. testosterone transdermal patch (Androderm), testosterone transdermal gel tubes (Testim), and testosterone buccal tablets (Striant) be designated non-preferred and formulary on the UF; and
3. testosterone transdermal 1% gel pump and gel packets (Androgel 1%), testosterone transdermal 1.62% gel pump (Androgel 1.62%), and testosterone transdermal solution (Axiron) be designated non-preferred and NF on the UF.
4. This recommendation includes step therapy, which requires a trial of testosterone transdermal 2% gel pump (Fortesta) prior to using other transdermal and buccal TRTs.

D. Androgens Anabolic Steroids: TRTs—Prior Authorization (PA) Criteria

The P&T Committee recommended (12 for, 0 opposed, 1 abstained, 4 absent) that the following manual PA criteria should apply to all current and new users of the testosterone replacement therapies. Coverage would be approved if the patient met any of the following criteria:

1. Manual PA criteria for all transdermal and buccal testosterone replacement products:
   a) Patient is male and has a diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism.
   b) Patient is a female and receiving testosterone for the following uses:
   c) Treatment of hypoactive sexual desire in menopausal women (whether natural or surgical); or
   d) Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone).
   e) Note that coverage of transdermal or buccal testosterone replacement therapies is not approved for osteoporosis or urinary incontinence.
   f) Note that coverage for use in women will be by appeal only.
   g) Note that use in adolescents under the age of 17 is not approved and will be by appeal only.

2. In addition to the above criteria, the following PA criteria would apply specifically to transdermal gel tubes (Testim), transdermal patch (Androderm), buccal tablets (Striant), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), and transdermal solution (Axiron):
   a) The patient requires a testosterone replacement therapy that has a low risk of skin-to-skin transfer between family members (for Striant and Androderm only).
   b) The patient has tried transdermal 2% gel pump (Fortesta) for a minimum of 90 days AND failed to achieve total testosterone levels above 400ng/dL (lab must be drawn 2 hours after Fortesta application) AND denied improvement in symptoms.
   c) The patient has a contraindication or relative contraindication to Fortesta (e.g., hypersensitivity to a component [including alcohol]; concomitant disulfiram use) that does not apply to Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

d) The patient has experienced a clinically significant skin reaction to Fortesta that is not expected to occur with Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

E. Androgens Anabolic Steroids: TRTs—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.

III. UF CLASS REVIEWS—ANDROGENS ANABOLIC STEROIDS

BAP Comments

A. Androgens Anabolic Steroids: TRTs—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:

1. testosterone transdermal 2% gel pump (Fortesta) be designated step-preferred and formulary on the UF;
2. testosterone transdermal patch (Androderm), testosterone transdermal gel tubes (Testim), and testosterone buccal tablets (Striant) be designated non-preferred and formulary on the UF; and
3. testosterone transdermal 1% gel pump and gel packets (Androgel 1%), testosterone transdermal 1.62% gel pump (Androgel 1.62%), and testosterone transdermal solution (Axiron) be designated non-preferred and NF on the UF.
4. This recommendation includes step therapy, which requires a trial of testosterone transdermal 2% gel pump (Fortesta) prior to using other transdermal and buccal TRTs.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. Androgens Anabolic Steroids: TRTs—PA Criteria

The P&T Committee recommended that the following manual PA criteria should apply to all current and new users of the testosterone replacement therapies. Coverage would be approved if the patient met any of the following criteria:

1. Manual PA criteria for all transdermal and buccal testosterone replacement products:
2. Patient is male and has a diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism.
3. Patient is a female and receiving testosterone for the following uses:
    a Treatment of hypoactive sexual desire in menopausal women (whether natural or surgical); or
    b Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone).
    c Note that coverage of transdermal or buccal testosterone replacement therapies is not approved for osteoporosis or urinary incontinence.
    d Note that coverage for use in women will be by appeal only.
4. Note that use in adolescents under the age of 17 is not approved and will be by appeal only.

5. In addition to the above criteria, the following PA criteria would apply specifically to transdermal gel tubes (Testim), transdermal patch (Androderm), buccal tablets (Striant), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), and transdermal solution (Axiron):
6. The patient requires a testosterone replacement therapy that has a low risk of skin-to-skin transfer between family members (for Striant and Androderm only).
7. The patient has tried transdermal 2% gel pump (Fortesta) for a minimum of 90 days AND failed to achieve total testosterone levels above 400ng/dL (lab must be drawn 2 hours after Fortesta application) AND denied improvement in symptoms.
8. The patient has a contraindication or relative contraindication to Fortesta (e.g., hypersensitivity to a component [including alcohol]; concomitant disulfiram use) that does not apply to Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

9. The patient has experienced a clinically significant skin reaction to Fortesta that is not expected to occur with Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

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

C. Androgens Anabolic Steroids: TRTs—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 Dissention

IV. UF CLASS REVIEWS—ANTICOAGULANTS

P&T Comments

A. Anticoagulants—Heparin and Related Products

Background and Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the Heparin and Related Products subclass of the anticoagulants. (The newer oral anticoagulants, including the Factor Xa inhibitors and direct thrombin inhibitors will be discussed at a later date.) The drugs in this subclass include unfractionated heparin, which is available in many generic formulations and will not be discussed further, enoxaparin (Lovenox), dalteparin (Fragmin), and fondaparinux (Arixtra). Two products, tinzaparin (Innohep) and ardeparin (Normiflow), were voluntarily discontinued by their manufacturers due to nonsafety reasons. The subclass has not previously been

reviewed for UF placement. Generic biologic formulations of enoxaparin and fondaparinux are available; both are FDA AP-rated (therapeutically equivalent parenteral products) to Lovenox and Arixtra, respectively.

Relative Clinical Effectiveness Conclusion—The P&T Committee agreed (15 for, 0 opposed, 0 abstained, 2 absent) on the following clinical effectiveness conclusions:

1. Enoxaparin has the widest clinical utility of the subclass, due to its long history of use, largest number of FDA-approved indications, availability in several dosage strengths, and recommendations by the American College of Chest Physicians for use in special populations (pregnancy, pediatrics). The package labeling cautions against use in patients with a history of heparin-induced thrombocytopenia (HIT).
2. Fondaparinux has fewer FDA-approved indications than enoxaparin. It has a therapeutic niche for patients with a history of HIT. The risk of bleeding is increased in patients with low body weight (<50 kg), the elderly, and in patients with decreased renal function.
3. The major limitation with dalteparin is the lack of an FDA-approved indication for treating deep venous thrombosis and pulmonary embolism. The package insert also cautions against use in patients with a history of HIT.

B. Anticoagulants: Heparin and Related Products—Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion

CMA and BIA were used to evaluate the drugs in this subclass, with corresponding sensitivity analyses. Due to recent availability of generic fondaparinux (Arixtra), an estimated generic drug price was used in the cost analyses. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that generic enoxaparin was the most cost-effective agent based on a weighted average cost per unit across all three POS, followed by branded dalteparin (Fragmin), and generic fondaparinux (ranked in order from most cost-effective to least cost-effective). BIA results showed that, among currently available formulary options, scenarios where generic enoxaparin is included on the Basic Core Formulary (BCF) and dalteparin (Fragmin) and generic fondaparinux are included on the UF generated the greatest cost-avoidance projection.

C. Anticoagulants: Heparin and Related Products—UF Recommendation

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) enoxaparin, dalteparin (Fragmin), and fondaparinux remain designated as formulary on the UF.

D. Anticoagulants: Heparin and Related Products—UF Implementation Plan: Not applicable (no changes in formulary status).

V. UF CLASS REVIEWS—ANTICOAGULANTS

BAP Comments

A. Anticoagulants: Heparin and Related Products—UF Recommendation

The P&T Committee recommended enoxaparin, dalteparin (Fragmin), and fondaparinux remain designated as formulary on the UF.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissention

B. Anticoagulants: Heparin and Related Products— UF and Implementation Plan

Not applicable (no changes in formulary status).

VI. RECENTLY APPROVED U.S. FDA AGENTS

P&T Comments

A. Targeted Immunomodulatory Biologics (TIBs)—Abatacept Subcutaneous (SC) Injection (Orencia SC)

Background and Relative Clinical Effectiveness—Abatacept (Orencia) inhibits the activation of T-cells and is approved for treating moderate to severe active rheumatoid arthritis (RA) in adults. It was first marketed in 2005 as an intravenous (IV) infusion, which is only available through the TRICARE medical benefit. A new subcutaneous (SC) abatacept formulation intended for self-injection is now available. FDA-approval of abatacept SC was based on its demonstrated non-inferiority to abatacept IV. Prior authorization criteria and quantity limits apply to the TIBs and were placed on abatacept SC in November

2011, which are consistent with the FDA-approved package labeling.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that although abatacept SC (Orencia SC) provides an alternative to the tumor necrosis factor (TNF) alpha inhibitors used for treatment of RA and offers patient convenience over the abatacept IV formulation, there is currently insufficient data to conclude that Orencia SC offers improved efficacy, safety, or tolerability compared to the TNF alpha inhibitors in the TIBs class.

B. TIBs: Abatacept SC Injection (Orencia SC)—Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion

A pharmacoeconomic analysis was performed. The weighted average cost per month at all three points of service (POS) was evaluated for abatacept SC (Orencia SC) in relation to the other drugs in the TIBs class indicated for treatment of RA. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Orencia SC was not cost-effective when compared to other TIBs included on the UF.

C. TIBs: Abatacept SC Injection (Orencia SC)—UF Recommendation

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

D. TIBs: Abatacept SC Injection (Orencia SC)—UF 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.

VII. RECENTLY APPROVED U.S. FDA AGENTS

BAP Comments

A. TIBs: Abatacept SC Injection (Orencia SC)—UF Recommendation

The P&T Committee recommended abatacept SC (Orencia SC) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. TIBs: Abatacept SC Injection (Orencia SC)—UF 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 Dissentions:

VIII. RECENTLY APPROVED U.S. FDA AGENTS

P&T Comments

A. Glaucoma Drugs: Prostaglandin Analogs—Tafluprost Ophthalmic Solution (Zioptan)

Relative Clinical Effectiveness—Tafluprost ophthalmic solution (Zioptan) is a preservative-free prostaglandin analog indicated for the reduction of elevated intraocular pressure (IOP) in patients with glaucoma or ocular hypertension. In one head-to-head comparison, tafluprost proved inferior to latanoprost in lowering IOP, failing to meet the pre-specified margin for non-inferiority. Whether preservative-free tafluprost is associated with decreased adverse events compared to preservative-containing tafluprost remains to be determined.

Relative Clinical Effectiveness Conclusion—The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 0 absent) that tafluprost (Zioptan) offers no compelling clinical advantages over the other prostaglandins available on the UF.

B. Glaucoma Drugs: Prostaglandin Analogs—Tafluprost Ophthalmic Solution (Zioptan)—Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion

A pharmacoeconomic analysis was performed. The weighted average cost per day at all three POS was evaluated for tafluprost (Zioptan) in relation to the other ophthalmic prostaglandin analogues. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Zioptan was not cost-effective when compared to the other ophthalmic prostaglandins currently included on the UF.

C. Glaucoma Drugs: Prostaglandin Analogs: Tafluprost Ophthalmic Solution (Zioptan)—UF Recommendation

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) tafluprost (Zioptan) be designated NF because it has no compelling clinical advantages over the other ophthalmic prostaglandin analogues and is not cost-effective compared to latanoprost, the most utilized drug in the MHS.

D. Glaucoma Drugs: Prostaglandin Analogs: Tafluprost Ophthalmic Solution (Zioptan)—UF 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.

IX. RECENTLY APPROVED U.S. FDA AGENTS

BAP Comments

A. Glaucoma Drugs: Prostaglandin Analogs: Tafluprost Ophthalmic Solution (Zioptan)—UF Recommendation

The P&T Committee recommended tafluprost (Zioptan) be designated NF because it has no compelling clinical advantages over the other ophthalmic prostaglandin analogues and is not cost-effective compared to latanoprost, the most utilized drug in the MHS.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Glaucoma Drugs: Prostaglandin Analogs: Tafluprost Ophthalmic Solution (Zioptan)—UF 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 Dissentions:

X. RECENTLY APPROVED U.S. FDA AGENTS

P&T Comments

A. Oral Non-steroidal Anti-inflammatory Drugs (NSAIDs)—Ibuprofen/Famotidine (Duexis)

Relative Clinical Effectiveness—Ibuprofen/famotidine (Duexis) is the first fixed-dose combination of a non-selective NSAID with an H2 antagonist. Ibuprofen and famotidine are currently on the BCF and UF, respectively, and are available over-the-counter. Other combination NSAID/gastroprotective agents on the UF include esomeprazole/enteric-coated naproxen (Vimovo), diclofenac/misoprostol (Arthrotec), and the COX-2 inhibitor celecoxib (Celebrex). No studies with Duexis have evaluated clinically important upper gastrointestinal (GI) events (bleeding, perforation, obstruction). Although the fixed-dose combination of famotidine and ibuprofen offers the convenience of a gastroprotective agent with an NSAID**,** the three-times daily dosing regimen may affect patient compliance. Systematic reviews and national professional guidelines state a preference for NSAID with proton pump inhibitor or NSAID with misoprostol versus an NSAID with H2 antagonist for reducing GI ulcers.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) ibuprofen/famotidine (Duexis) offers no distinct clinical advantages to the combination NSAID/gastroprotective agents already on the UF.

B. Oral NSAIDs: Ibuprofen/Famotidine (Duexis)—Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion

A pharmacoeconomic analysis was performed. The weighted average cost per day at all three POS was evaluated for ibuprofen/famotidine (Duexis) in relation to the other oral gastroprotective NSAIDs. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that Duexis was not cost-effective when compared to other oral NSAIDs agents included on the UF; it was also more costly than the individual components, ibuprofen and famotidine.

C. Oral NSAIDs: Ibuprofen/Famotidine (Duexis)—UF Recommendation

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

D. Oral NSAIDs: Ibuprofen/Famotidine (Duexis)—UF 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.

XI. RECENTLY APPROVED U.S. FDA AGENTS

BAP Comments

A. Oral NSAIDs: Ibuprofen/Famotidine (Duexis)—UF Recommendation

The P&T Committee recommended ibuprofen/famotidine (Duexis) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Oral NSAIDs: Ibuprofen/Famotidine (Duexis)—UF 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 Dissentions:

XII. RECENTLY APPROVED U.S. FDA AGENTS

P&T Comments

A. Oral NSAIDs—Ketorolac Nasal Spray (Sprix)

Relative Clinical Effectiveness—Ketorolac nasal spray (Sprix) is the first NSAID administered by the intranasal route. There is no direct comparative data with ketorolac nasal spray or other oral NSAIDs or low potency narcotic analgesics. The studies used to obtain FDA-approval were conducted using a placebo control in the in-patient setting where concomitant morphine or rescue analgesia was administered. Reduced morphine requirements were seen at 24 hours in some studies with Sprix—whether these results are clinically relevant is difficult to determine. Opioid-sparing drugs on the UF include other NSAIDs and tramadol. Sprix is limited by a five-day duration of use, and warnings not seen with other NSAIDs, including contraindications for use in patients with a history of GI bleeding or renal dysfunction.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) there is no evidence to suggest ketorolac nasal spray (Sprix) has a compelling clinical advantage over the other oral NSAIDs already on the BCF and UF.

B. Oral NSAIDs: Ketorolac Nasal Spray (Sprix)—Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion

A pharmacoeconomic analysis was performed. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 0 absent) that ketorolac nasal spray (Sprix) was more costly, based on an average weighted cost per day of therapy at all three POS, than the other oral NSAIDs and low-potency narcotic analgesics currently on the BCF and UF.

C. Oral NSAIDs: Ketorolac Nasal Spray (Sprix)—UF Recommendation

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 0 absent) ketorolac nasal spray (Sprix) be designated NF due to the lack of compelling

clinical advantages and cost disadvantages compared to the UF products.

D. Oral NSAIDs: Ketorolac Nasal Spray (Sprix)—UF 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.

XIII. RECENTLY APPROVED U.S. FDA AGENTS

BAP Comments

A. Oral NSAIDs: Ketorolac Nasal Spray (Sprix)—UF Recommendation

The P&T Committee recommended ketorolac nasal spray (Sprix) be designated NF due to the lack of compelling clinical advantages and cost disadvantages compared to the UF products.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Oral NSAIDs: Ketorolac Nasal Spray (Sprix)—UF 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 Dissentions:

XIV. RECENTLY APPROVED U.S. FDA AGENTS

P&T Comments

A. Non-Insulin Diabetes Drugs: Dipeptidyl Dipeptidase-4 (DPP-4) Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)

Relative Clinical Effectiveness—Janumet XR and Jentadueto are fixed-dose combination products containing metformin in either an extended release (ER) formulation with sitagliptin (Janumet XR) or an immediate release (IR) formulation with linagliptin (Jentadueto). Sitagliptin is also available in a fixed-dose combination product with metformin IR (Janumet).

Both Janumet XR and Jentadueto were approved via the FDA 505(b)(2) process, requiring only proof of bioequivalence to their respective individual components. There are no efficacy studies with either agent. The combination of sitagliptin with metformin IR reduces hemoglobin A1c by 0.51% to 0.67%, while the combination of linagliptin with metformin IR decreases A1c by 0.4% to 0.5%. No studies evaluating clinical outcomes (e.g., cardiovascular death, myocardial infarction, and stroke) are available for the DPP-4 inhibitors, but trials are underway.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) there is no evidence to suggest either sitagliptin/metformin ER (Janumet XR) or linagliptin/metformin (Jentadueto) have a compelling clinical advantage over the other DPP-4 inhibitor/metformin fixed-dose combinations included on the UF.

B. Non-Insulin Diabetes Drugs: DPP-4 Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)—Relative Cost-Effectiveness Analysis and Relative Cost-Effectiveness Conclusion

A pharmacoeconomic analysis was performed. The weighted average cost per day at all three POS was evaluated for sitagliptin/metformin ER (Janumet XR) and linagliptin/metformin (Jentadueto) in relation to the other drugs in the DPP-4 inhibitors subclass. The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 1 absent) that Janumet XR and Jentadueto were cost-effective when compared to other DPP-4 inhibitors included on the UF.

C. Non-Insulin Diabetes Drugs: DPP-4 Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)—UF Recommendation

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

1. sitagliptin/metformin ER (Janumet XR) be designated step-preferred and formulary on the UF; and

2. linagliptin/metformin (Jentadueto) be designated non-preferred and formulary on the UF.

3. This recommendation includes step therapy, which requires a trial of sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/simvastatin (Juvisync), or sitagliptin/metformin ER (Janumet XR) (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors also requires a trial of metformin or sulfonylurea for new patients.

D. Non-Insulin Diabetes Drugs: DPP-4 Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)—PA Criteria

Existing automated prior authorization (step therapy) requires a trial of metformin or a sulfonylurea prior to use of a DPP-4 inhibitor. Additionally, sitagliptin-containing products (Januvia, Janumet, Janumet XR, and Juvisync) are the preferred agents in the DPP-4 inhibitors subclass. New users must try a preferred product before trying linagliptin or saxagliptin-containing products.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to the DPP-4 inhibitors subclass. Coverage would be approved if the patient met any of the following criteria:

1. Automated PA criteria:

   a) The patient has filled a prescription for metformin or a sulfonylurea at any MHS pharmacy POS [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

   b) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, Juvisync, Janumet XR, Tradjenta, Jentadueto, Onglyza, or Kombiglyze XR) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual PA criteria, if automated criteria are not met:

The fixed-dose combination product Janumet XR or Jentadueto is approved (e.g., a trial of sulfonylurea is not required if):

   a) The patient has had an inadequate response to metformin or sulfonylurea.

   b) The patient has experienced the following adverse event while receiving a sulfonylurea: hypoglycemia requiring medical treatment.

c) The patient has a contraindication to a sulfonylurea.

1. In addition to the above criteria regarding metformin and sulfonylurea, the following PA criteria would apply specifically to linagliptin/metformin metformin (Jentadueto):

   a) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with linagliptin-containing products.

   b) The patient has had an inadequate response to a sitagliptin-containing product.

   c) The patient has a contraindication to sitagliptin.

E. Non-Insulin Diabetes Drugs: DPP-4 Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)—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.

XV. RECENTLY APPROVED U.S. FDA AGENTS

BAP Comments

A. Non-Insulin Diabetes Drugs: DPP-4 Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)—UF Recommendation

The P&T Committee recommended the following:

1. sitagliptin/metformin ER (Janumet XR) be designated step-preferred and formulary on the UF; and

2. linagliptin/metformin (Jentadueto) be designated non-preferred and formulary on the UF.

3. This recommendation includes step therapy, which requires a trial of sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/simvastatin (Juvisync), or sitagliptin/metformin ER (Janumet XR) (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors also requires a trial of metformin or sulfonylurea for new patients.

4.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. Non-Insulin Diabetes Drugs: DPP-4 Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)—PA Criteria

Existing automated prior authorization (step therapy) requires a trial of metformin or a sulfonylurea prior to use of a DPP-4 inhibitor. Additionally, sitagliptin-containing products (Januvia, Janumet, Janumet XR, and Juvisync) are the preferred agents in the DPP-4 inhibitors subclass. New users must try a preferred product before trying linagliptin or saxagliptin-containing products.

The P&T Committee recommended the following PA criteria should apply to the DPP-4 inhibitors subclass. Coverage would be approved if the patient met any of the following criteria:

1. Automated PA criteria:

   a) The patient has filled a prescription for metformin or a sulfonylurea at any MHS pharmacy POS [Military Treatment Facilities (MTFs), retail network pharmacies, or mail order] during the previous 180 days.

   b) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, Juvisync, Janumet XR, Tradjenta, Jentadueto, Onglyza, or Kombiglyze XR) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual PA criteria, if automated criteria are not met:

The fixed-dose combination product Janumet XR or Jentadueto is approved (e.g., a trial of sulfonylurea is not required if):

   a) The patient has had an inadequate response to metformin or sulfonylurea.

   b) The patient has experienced the following adverse event while receiving a sulfonylurea: hypoglycemia requiring medical treatment.

c) The patient has a contraindication to a sulfonylurea.

3. In addition to the above criteria regarding metformin and sulfonylurea, the following PA criteria would apply specifically to linagliptin/metformin metformin (Jentadueto):

   a) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with linagliptin-containing products.

   b) The patient has had an inadequate response to a sitagliptin-containing product.
   c) The patient has a contraindication to sitagliptin.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. Non-Insulin Diabetes Drugs: DPP-4 Inhibitors—Sitagliptin/Metformin ER (Janumet XR) and Linagliptin/Metformin (Jentadueto)—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 Dissentions