

**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, prior authorization (PA), pre-authorizations, and the effective date for a drug's change from formulary to nonformulary (NF) status are received 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: GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS (GLP1RA) SUBCLASS

P&T Comments

A. Non-Insulin Diabetes Drugs: Glucagon-Like Peptide-1 Receptor Agonists (GLP1RA) Subclass—Relative Clinical Effectiveness Analysis and Conclusion

Background— The GLP1RAs were most recently reviewed in August 2015, with exenatide once weekly (Bydureon) and albiglutide (Tanzeum) selected as Uniform Formulary (UF) and step-preferred status, with all the other GLP1RAs designated as non formulary (NF) and non step-preferred. Since the last review, two new products have been approved, an exenatide once weekly autoinjector (Bydureon BCise), and semaglutide (Ozempic). The GLP1RA combinations with insulin were not included in this review.

Voluntary market discontinuation of Tanzeum is expected in August 2018.

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

- Metformin remains the first-line treatment in all patients with type 2 diabetes mellitus (T2DM) unless there are contraindications.
- The new Bydureon BCise autoinjector formulation is easier to self-administer than the Bydureon pen. It is comparable to Bydureon in lowering A1c.
- When used as monotherapy or in combination with other oral agents, the GLP1RAs decrease hemoglobin A1c (A1c) on average approximately 1% to 2% from baseline. Overall, differences in A1c between the GLP1RAs are not clinically relevant.
 - However, in one study (SUSTAIN-3), semaglutide (Ozempic) was statistically and clinically superior to exenatide once weekly (Bydureon) in glycemic control, as semaglutide lowered A1c by 1.5% from baseline compared to 0.9% with exenatide. Limitations to the SUSTAIN-3 study include its open label, active comparator design; it was not designed to show superiority.

- In the open-label, active comparator SUSTAIN-7 study, semaglutide was statistically superior to dulaglutide (Trulicity) in glycemic control, as it reduced A1c by 1.5-1.8% from baseline compared to 1.1-1.4% with dulaglutide. However, the differences in change in A1c between semaglutide and dulaglutide were not considered clinically relevant, as the change in A1c between the two drugs was less than 0.5%.
- Patients are likely to experience weight loss with use of any GLP1RA.
- Cardiovascular outcomes trials (CVOTs) evaluating the effects on endpoints, including CV mortality, non-fatal myocardial infarction, and stroke, have been completed with four of the products: liraglutide (Victoza) in the LEADER trial, Ozempic in SUSTAIN-6, Bydureon in the EXSCEL trial, and lixisenatide (Adlyxin) in the ELIXA trial. Trials are currently ongoing with dulaglutide (Trulicity) in the REWIND trial and Tanzeum in the HARMONY-OUTCOME trial.
- Liraglutide (Victoza) is the only GLP1RA that has an additional indication to reduce CV risk in patients with established CV disease, based on the LEADER trial. However, given the differences in patient populations in the CVOTs, it is difficult to directly compare one GLP1RA to another in terms of CV benefit.
- In the four CVOTs the association of GLP1RAs with retinopathy has been a concern, however this was a secondary outcome, and the trials were underpowered to adequately assess worsening retinopathy. Additional studies are needed to definitively determine the long-term effects of GLP1RAs on diabetic retinopathy.
- Gastrointestinal (GI) effects of nausea, vomiting, and diarrhea are the most commonly reported adverse effects with the class. The incidence of nausea varies based on dosing, with higher doses resulting in more nausea. Bydureon has the lowest incidence of nausea at 14%, compared to Ozempic (16-20%), Trulicity (12-21%), Victoza (23%), Adlyxin (29%), and exenatide twice daily (Byetta) (35%).
- Victoza, Adlyxin, and Ozempic have an advantage in offering a smaller needle size for patient convenience. One disadvantage of Bydureon and Bydureon BCise is the larger needle size.
- Bydureon, Bydureon BCise, Trulicity, and Ozempic, have the advantage of once weekly dosing, while Victoza and Adlyxin are dosed once daily, and Byetta is dosed twice daily. Potential advantages of Bydureon and Bydureon BCise include that they are the only GLP1RAs that do not require dosage titration.
- Trulicity, Victoza, and Ozempic require no dose adjustment in renal insufficiency.

B. GLP1RA Subclass—Relative Cost-Effectiveness Analysis and Conclusion

Cost-minimization analysis (CMA) and budget impact analysis (BIA) were performed to evaluate the GLP1RAs. The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA results showed that exenatide once weekly (Bydureon and Bydureon BCise) were the most cost-effective agents, followed by dulaglutide (Trulicity), exenatide twice daily (Byetta), semaglutide (Ozempic), liraglutide (Victoza), and lixisenatide (Adlyxin).
- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating exenatide (Bydureon and Bydureon BCise) and dulaglutide (Trulicity) as formulary and step-preferred, with exenatide twice daily (Byetta), semaglutide (Ozempic), liraglutide (Victoza), and lixisenatide (Adlyxin) as NF and non step-preferred demonstrated the largest estimated cost avoidance for the Military Health System (MHS).

C. GLP1RA Subclass—UF Recommendation

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

- UF and step-preferred
 - exenatide once weekly (Bydureon and Bydureon BCise)
 - dulaglutide (Trulicity)
- NF and non step-preferred
 - albiglutide (Tanzeum)
 - exenatide twice daily (Byetta)
 - liraglutide (Victoza)
 - lixisenatide (Adlyxin)
 - semaglutide (Ozempic)
- This recommendation includes step therapy which requires a trial of exenatide once weekly (Bydureon or Bydureon BCise) and dulaglutide (Trulicity) prior to use of the NF, non step-preferred GLP1RA drugs in all new and current users.

D. GLP1RA Subclass—Manual Prior Authorization (PA) Criteria

PA criteria currently apply to the GLP1RAs subclass. Currently, a trial of metformin or a sulfonylurea is required prior to use of a GLP1RA, and use of the step-preferred GLP1RAs are also required prior to the non step-preferred products. The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) removing the requirement for a trial of a sulfonylurea, and maintaining the metformin step, based on the treatment guidelines from several diabetes associations where metformin is preferred due to its positive effects on glycemic control, safe adverse effect profile, and minimal cost. Additionally sulfonylureas are no longer considered first line therapy for diabetes.

The Committee also recommended updating the existing manual PA criteria so that new and current GLP1RA users must try the step-preferred products, Bydureon or Bydureon BCise and Trulicity, prior to using Tanzeum, Byetta, Victoza, Adlyxin, or Ozempic. Use of the non step-preferred products is allowed if the patient has had an inadequate response to the step-preferred GLP1RAs.

PA Criteria:

All new users of a GLP1RA are required to try metformin before receiving a GLP1RA. Patients currently taking a GLP1RA must have had a trial of metformin first.

Bydureon/Bydureon BCise, Trulicity, Tanzeum, Byetta, Victoza, Adlyxin, or Ozempic is approved (i.e., a trial of metformin is NOT required) if:

- The patient has a confirmed diagnosis of Type 2 diabetes mellitus.
- The patient has experienced any of the following issues on metformin:
 - impaired renal function precluding treatment with metformin
 - history of lactic acidosis
- The patient has had inadequate response to metformin
- The patient has a contraindication to metformin

In addition to the above criteria regarding metformin the following PA criteria would apply specifically to new and current users of Tanzeum, Byetta, Victoza, Adlyxin, and Ozempic:

- The patient has had an inadequate response to Bydureon/Bydureon BCise and Trulicity.

Off-label uses are not approved.
Prior Authorization does not expire.

E. GLP1RA Subclass—PA Criteria UF and PA Implementation Plan

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

1) an effective date of the first Wednesday after a 90-day implementation period in all points of service and, 2) DHA send letters to beneficiaries who are affected by the UF decision.

III. UF CLASS REVIEWS—GLP1RA SUBCLASS

BAP Comments

A. Non-Insulin Diabetes Drugs: GLP1RA Subclass—UF Recommendation

The P&T Committee recommended the following:

- UF and step-preferred
 - Bydureon and Bydureon BCise
 - Trulicity
- NF and non step-preferred
 - Tanzeum
 - Byetta
 - Victoza
 - Adlyxin

- Ozempic

BAP Comment: Concur Non-concur

Additional Comments and Dissension

B. GLP1RA Subclass—Manual PA Criteria

The P&T Committee recommended removing the requirement for a sulfonylurea prior to use of a GLP1RA inhibitor. The recommendation also includes step therapy, which requires a trial of Bydureon or Bydureon BCise and Trulicity prior to use of the non formulary, non step-preferred GLP1RA drugs in all new and current users

The full PA criteria were stated previously.

BAP Comment: Concur Non-concur

Additional Comments and Dissension

C. GLP1RAs—UF and PA Implementation Plan

The P&T Committee recommended an effective date of the first Wednesday after a 90-day implementation in all points of service, and DHA send letters to beneficiaries who are affected by the UF decision

BAP Comment: Concur Non-concur

Additional Comments and Dissension

IV. ANTI-INFLAMMATORY IMMUNOMODULATORY OPHTHALMICS: OPHTHALMIC IMMUNOMODULATORY AGENTS SUBCLASS

P&T Comments

A. Anti-Inflammatory Immunomodulatory Ophthalmics: Ophthalmic Immunomodulatory Agents Subclass—Relative Clinical Effectiveness Analysis and Conclusion

Cyclosporine ophthalmic emulsion (Restasis) and lifitegrast 5% ophthalmic solution (Xiidra) are the two products in this subclass, which are both approved to treat dry eye disease. Prior authorization criteria currently apply to both drugs.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) the following for the ophthalmic immunomodulatory drugs:

- Ocular surface inflammation and damage are characteristic of moderate to severe dry eye disease. Restasis and Xiidra are both approved for dry eye disease, but their mechanisms of action differ.
- Both drugs are dosed twice daily. Xiidra's onset of action can occur as soon as two weeks following initiation of therapy, however peak effect will not likely occur until after 12 weeks of therapy. In contrast, Restasis' onset of action may take up to six months. Over-the-counter (OTC) ocular lubricants can be used concomitantly with both Restasis and Xiidra.
- Both Xiidra and Restasis in individual placebo-vehicle controlled trials have shown reductions in signs and symptoms of dry eye disease using different endpoints. There are no head-to-head trials between Restasis and Xiidra. It is difficult to determine the clinical relevance of these changes, and dry eye disease is a progressive condition that waxes and wanes. Recent treatment guidelines for dry eye disease do not favor one product over another (American Academy of Ophthalmology 2017; Dry Eye Workshop II 2017).
- There are no published studies evaluating efficacy when patients are switched from one product to another.
- While the clinical studies that led to FDA approval had low patient dropout rates, most trials were of short duration. An analysis of MHS prescription claims showed that approximately 70% of patients fill prescriptions for less than six months of therapy.
- The safety profiles of Restasis and Xiidra are most commonly associated with ocular burning and stinging. Lifitegrast causes dysgeusia in 16% of patients. There are no apparent serious concerns.
- There is a moderate degree of therapeutic interchangeability with Restasis and Xiidra, as there is a variable response to these drugs in practice. To meet the needs of DoD beneficiaries, at least one ophthalmic immunomodulatory agent is needed to treat the majority of patients with dry eye syndrome.

B. Ophthalmic Immunomodulatory Agents Subclass—Relative Cost-Effectiveness Analysis and Conclusion

CMA, and BIA were performed. The P&T Committee concluded (15 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA showed that Restasis and Xiidra were cost effective in the various formulary scenarios.

- BIAs with corresponding sensitivity analyses were performed on all formulary scenarios.

C. Ophthalmic Immunomodulatory Agents Subclass—UF Recommendation

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

- UF:
 - cyclosporine 0.05% ophthalmic emulsion (Restasis)
 - lifitegrast 5% ophthalmic solution (Xiidra)
- NF: None

D. Ophthalmic Immunomodulatory Agents Subclass—Manual PA Criteria

The P&T Committee recommended (15 for, 0 opposed, 0 abstained, 1 absent) revising the existing manual PA criteria for both Restasis and Xiidra. The drugs must be prescribed by an ophthalmologist or optometrist, the diagnosis of dry eye disease must be documented, and a trial of two OTC ocular lubricants is now required. The revised PA criteria will apply to new patients and existing users who have not filled a prescription for Restasis or Xiidra in the past 120 days.

PA Criteria: Coverage is approved if all the criteria are met:

- The drug is prescribed by an ophthalmologist or optometrist
- The patient is ≥ 18 years old
- A diagnosis of Moderate to Severe Dry Eye Disease is supported by both of the criteria below:
 - Positive symptomology screening for moderate to severe dry eye disease from an appropriate measure AND
 - At least one positive diagnostic test (e.g., Tear Film Breakup Time, Osmolarity, Ocular Surface Staining, Schirmer Tear Test) AND
- Patient must have tried and failed the following:
 - At least 1 month of one ocular lubricant used at optimal dosing and frequency (e.g., carboxymethylcellulose, polyvinyl alcohol, etc.)
 - Followed by at least 1 month of a different ocular lubricant that is preservative-free at optimal dosing and frequency (e.g., carboxymethylcellulose, polyvinyl alcohol, etc.) AND
- Concomitant use of Restasis and Xiidra is NOT allowed.
- Restasis is also approved for the following conditions: graft rejection/graft versus host disease (GvHD), corneal transplant, atopic keratoconjunctivitis (AKC) / vernal keratoconjunctivitis (VKC), and LASIK associated dry eye (limited to 3 months of therapy)

Off-label uses for Xiidra are not approved.
Off-label uses for Restasis, other than those listed above, are not approved.
PA expires in 365 days.

Renewal PA Criteria: Coverage will be approved indefinitely if all criteria are met:

- The drug is prescribed by an ophthalmologist or optometrist.
- The patient must have documented improvement in ocular discomfort.
- The patient must have documented improvement in signs of dry eye disease.

E. Ophthalmic Immunomodulatory Agents Subclass—UF and PA Implementation Plan

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

**V. ANTI-INFLAMMATORY IMMUNOMODULATORY OPHTHALMICS:
OPHTHALMIC IMMUNOMODULATORY AGENTS SUBCLASS**

BAP Comments

A. Ophthalmic Immunomodulatory Agents Subclass—UF Recommendation

The P&T Committee recommended the following based on clinical and cost effectiveness:

- UF:
 - Restasis
 - Xiidra
- NF: None

BAP Comment:

Concur

Non-concur

Additional Comments and Dissension

B. Ophthalmic Immunomodulatory Agents Subclass— Manual PA Criteria

The P&T Committee recommending revising the existing manual PA criteria to include diagnosis by a specialist, and a requirement for a trial of two over-the-counter artificial tears products. PA will be required for patients who have not filled a prescription for Restasis or Xiidra in the past 120 days. Renewal PA criteria are also required. The Full PA criteria were stated previously.

BAP Comment:

Concur

Non-concur

Additional Comments and Dissension

C. Ophthalmic Immunomodulatory Agents Subclass—UF and PA Implementation

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

BAP Comment:

Concur

Non-concur

Additional Comments and Dissension

VI. OSTEOPOROSIS DRUGS: PARATHYROID HORMONE (PTH) ANALOGS

P&T Comments

A. Osteoporosis Drugs: Parathyroid Hormone (PTH) Analogs—Relative Clinical Effectiveness Analysis and Conclusion

The P&T Committee evaluated the PTH analogs for treatment of osteoporosis; this subclass has not previously been reviewed for formulary status, although the full class was reviewed in 2008. The subclass consists of two injectable products, teriparatide (Forteo) and abaloparatide (Tymlos), which are both approved for the treatment (and not for the prevention) of osteoporosis in postmenopausal women at high risk for fracture.

Relative Clinical Effectiveness Analysis and Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 0 absent) the following:

- Both abaloparatide (Tymlos) and teriparatide (Forteo) have potential benefit in reducing fracture risk in high-risk patients or those with a history of fragility fractures, regardless of whether they were treated with bisphosphonates or not.
- With regard to fracture risk reduction, both Tymlos and Forteo have comparable efficacy for vertebral and non-vertebral fracture risk reduction in patients at high risk for fractures, compared to placebo. A 2016 trial (ACTIVE) reported the risk difference of new vertebral fractures with abaloparatide versus placebo was 3.6%, with a number needed to treat (NNT) of 28, compared to a risk difference of 3.4% with teriparatide versus placebo (NNT 29).

- In terms of changes in bone mineral density, both Tymlos and Forteo produced a statistically significant increase in bone mineral density at 18 months compared to placebo at the hip, femoral neck, and lumbar spine (ACTIVE trial).
- Both PTH analogs have similar adverse drug reaction profiles. Both drugs are limited to cumulative lifetime use of two years based on findings of osteosarcoma associated with use of teriparatide in rodent studies. However, a 2017 meta-analysis from the Institute for Clinical and Economic Review reported extensive real world clinical experience with teriparatide (Forteo) in postmenopausal women without identification of any new adverse events.
- In terms of other factors, Tymlos does not require refrigeration, while Forteo must be kept refrigerated. Forteo has additional indications for men with high fracture risk and for treatment of glucocorticoid-induced osteoporosis in patients at high risk for fracture.
- There is a high degree of interchangeability between Forteo and Tymlos.

B. Osteoporosis Drugs: Parathyroid Hormone (PTH) Analogs—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 showed that Forteo was the more cost-effective PTH analog, followed by Tymlos.
- BIA was performed to evaluate the potential impact of designating selected agents as formulary or NF on the UF. BIA results showed that designating Forteo as formulary and step-preferred, with Tymlos as NF and non step-preferred demonstrated the largest estimated cost avoidance for the MHS.

C. Osteoporosis Drugs: Parathyroid Hormone (PTH) Analogs—UF Recommendation

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

- UF and step-preferred: teriparatide (Forteo)
- NF and non step-preferred: abaloparatide (Tymlos)
- This recommendation includes step therapy, which requires a trial of teriparatide in new patients, prior to use of abaloparatide.

D. Osteoporosis Drugs: Parathyroid Hormone (PTH) Analogs— Manual PA Criteria

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 0 absent) manual PA criteria for new users of Forteo and Tymlos, consistent with the package labeling for indications and safety. Additionally, the step therapy requirements will be included in the manual PA.

Manual PA criteria

1. teriparatide (Forteo)

Forteo is approved if **ALL** of the following criteria are met:

- The patient is ≥ 18 years old
- The drug is prescribed for treatment of osteoporosis, and not for prevention of osteoporosis.
- The patient has one of the following diagnoses:
 - Patient is a postmenopausal female with osteoporosis, OR
 - The patient is male with primary or hypogonadal osteoporosis, OR
 - The patient has osteoporosis associated with sustained systemic glucocorticoid therapy (e.g., > 6 months use of >7.5 mg/day prednisone or equivalent) AND
- Patient has one of the following:
 - The patient is at high risk for fracture, defined as one of the following:
 - history of osteoporotic fracture
 - multiple risk factors for fracture (e.g., a history of vertebral fracture or low-trauma fragility fracture of the hip, spine or pelvis, distal forearm or proximal humerus)
 - documented bone mineral density (BMD) T-score of -2.5 or worse
 - has one of the following: has tried and experienced an inadequate response to, therapeutic failure with, is intolerant to (unable to use or absorb), or has contraindications to at least one formulary osteoporosis therapy (e.g., alendronate, ibandronate) AND
- The patient will continue to take calcium and vitamin D supplementation during PTH analog therapy if dietary intake is inadequate AND
- Cumulative treatment with Forteo will not exceed 24 months during the patient's lifetime AND
- Patient is not at increased risk for osteosarcoma (e.g., Paget's disease, unexplained elevations of alkaline phosphatase, patients with open epiphyses, prior external beam or implant radiation therapy involving the skeleton)

Off-label uses are not approved unless supporting documentation is provided.

Prior Authorization expires in 24 months.

Prior Authorization may not be renewed.

2. Abaloparatide (Tymlos)

The PA criteria for Tymlos are similar to that of Forteo, with the exception that Tymlos is only approved for postmenopausal females with osteoporosis at high risk for fracture, and the patient cannot comply with the refrigeration requirements for Forteo

E. Osteoporosis Drugs: Parathyroid Hormone (PTH) Analogs—UF and 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 points of service.

VII. OSTEOPOROSIS DRUGS: PARATHYROID HORMONE (PTH) ANALOGS

BAP Comments

A. PTH Analogs—UF Recommendation

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

- UF and step-preferred: teriparatide (Forteo)
- NF and non step-preferred: abaloparatide (Tymlos)

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

B. PTH Analogs— Manual PA Criteria

The P&T Committee recommend manual PA criteria for new users of a PTH analog, consistent with the individual package insert indications and safety warnings. Additionally, a trial of Forteo is required before Tymlos unless the patient cannot comply with the refrigeration requirements of Forteo.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

C. Osteoporosis Drugs: Parathyroid Hormone (PTH) Analogs—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 points of service.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

VIII. CORTICOSTEROIDS-IMMUNE MODULATORS: ADRENOCORTICOTROPIC HORMONES (ACTH)

P&T Comments

A. Adrenocorticotropin Hormones (ACTH)—Relative Clinical Effectiveness Analysis and Conclusion

The P&T Committee evaluated the ACTH subclass, which is comprised of injectable corticotropin. Injectable corticotropin has been commercially available since 1952, but now is only marketed as a proprietary product, H.P. Acthar Gel. This is the first formulary review of the subclass, but manual PA criteria have applied to H.P. Acthar Gel since December 2013.

H.P. Acthar Gel is a highly purified natural product of adrenocorticotropin derived from porcine pituitary gland. H. P. Acthar gel carries FDA indications for treatment of infantile spasms (West Syndrome) and treatment of exacerbations of multiple sclerosis (MS). The label also states that H.P. Acthar Gel “may” be used for a wide variety of other disorders, but does not explicitly state that it is indicated for those disorders. This language is in the context of the drug’s initial approval in 1952, prior to the higher standards demonstrating clinical effectiveness mandated by the Kefauver-Harris Amendment in 1962.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (14 for, 0 opposed, 0 abstained, 2 absent) the following for H.P. Acthar Gel:

- Infantile Spasms
 - Optimal treatment of infantile spasms involves early hormonal therapy.
 - Evidence supports both glucocorticoid-dependent as well as glucocorticoid-independent pathways in the treatment of infantile spasms.
 - A comprehensive review of the evidence in infantile spasms suggests that the clinical effectiveness of high-dose oral corticosteroids (e.g., prednisone) is non-

inferior to that of ACTH. Evidence also supports that some patients refractory to high-dose oral corticosteroids will respond to ACTH.

- Trial evidence is supported by numerous Level 1 systematic reviews and meta-analyses with low to moderate quality evidence.
- The most common adverse effects of ACTH in infantile spasms leading to intervention, dose-reduction, or discontinuation include infection and irritability. The adverse effects are typically transitory in relation to treatment duration.
- MS Exacerbation
 - Professional treatment guidelines clearly and unanimously define the standard of care for treating MS exacerbations with intravenous (IV) methylprednisolone.
 - A comprehensive review of the evidence in MS suggests that the clinical effectiveness of high-dose oral corticosteroids is equivalent to or superior to that of ACTH.
 - A 2013 Cochrane review concluded that onset of treatment in an MS exacerbation is irrelevant to the exacerbation outcome. The evidence is insufficient to determine the impact of hormonal therapies on future exacerbation prevention and is also insufficient to determine the impact of hormonal therapies on long-term disability.
 - There is limited evidence to delineate adverse event profiles between ACTH and methylprednisolone. Head-to-head clinical trials have shown that the adverse reactions with ACTH and methylprednisolone are equivalent. Methylprednisolone is associated with a higher propensity for GI and psychiatric effects, while ACTH has a higher propensity for causing weight gain and edema.
 - Clinical trial evidence is supported by numerous Level 1 systematic reviews and meta-analyses with low to moderate quality evidence.

- Other Uses

A comprehensive review of the evidence for all of the disease states where H.P. Acthar Gel “may” be used failed to identify well-controlled studies of clinically meaningful endpoints that substantively determined H.P. Acthar Gel’s efficacy, maximum-tolerated dose, toxicity, and safety as compared with standard means of treatment. Therefore, the evidence for H.P. Acthar Gel failed to establish clinical effectiveness for those conditions. H.P. Acthar Gel is unsupported by the literature in the following conditions:

- Rheumatologic disorders: systemic lupus erythematosus, inflammatory myopathies (including dermatomyositis and polymyositis), psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis, and ankylosing spondylitis
- Dermatologic diseases: erythema multiforme (of any severity), Stevens-Johnson syndrome, and Toxic Epidermal Necrolysis (TEN) syndrome
- Allergic states: serum sickness
- Ophthalmic diseases: severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as keratitis, iritis, iridocyclitis,

diffuse posterior uveitis and choroiditis, birdshot choroiditis, chorioretinitis, anterior segment inflammation, scleritis, conjunctivitis, and Opsoclonus Myoclonus syndrome

- Respiratory diseases: sarcoidosis
- Nephrotic syndromes, including focal segmental glomerulosclerosis (FSGS), idiopathic membranous nephropathy, IgA nephropathy, membranoproliferative glomerulonephritis (MPGN), and monoclonal diffuse proliferative glomerulonephritis, and any other non-nephrotic edematous state
- Other neurologic disease: amyotrophic lateral sclerosis (ALS), MS (not related to exacerbation of MS), optic neuritis (not related to exacerbation of MS), and neurosarcoidosis
- Any other indication outside of the medically necessary indications of infantile spasms and MS exacerbation

B. Adrenocorticotrophic Hormones (ACTH)—Relative Clinical Effectiveness Analysis and Conclusion

CMA was performed. The P&T Committee concluded (14 for, 0 opposed, 0 abstained, 2 absent) that H.P. Acthar Gel was significantly more costly than its clinical comparators.

C. Adrenocorticotrophic Hormones (ACTH)—UF Recommendation

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) the following, based on clinical and cost effectiveness:

- UF: injectable corticotropin (H.P. Acthar Gel)
- NF: None

D. Adrenocorticotrophic Hormones (ACTH)—Manual PA Criteria

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) manual PA criteria for new and current users of H.P. Acthar Gel for treatment of infantile spasms (West Syndrome) in infants less than 24 months of age who are unresponsive to high-dose steroids. Manual PA criteria are also recommended for new and current users of H.P. Acthar Gel with MS exacerbation who have failed or who are intolerant to an adequate trial of IV or oral corticosteroids. PA renewal will be allowed for infantile spasms; however, PA review will be required for each occurrence of MS exacerbation.

H.P. Acthar Gel is not approved for use of any other condition outside of infantile spasms or MS exacerbation. H.P. Acthar Gel's efficacy for the other indications listed above in the clinical effectiveness conclusion has not been established and/or remains unproven. Experimental and investigational use of H.P. Acthar Gel for these other conditions is not medically necessary and is therefore excluded from TRICARE coverage.

Manual PA criteria

Manual PA criteria apply to all new and current users of H.P. Acthar Gel.

H.P. Acthar Gel PA will be approved if all of the following criteria are met for either treatment of infantile spasms or treatment of exacerbation in patients with multiple sclerosis.

1) Infantile Spasms (West Syndrome):

- The patient is < 24 months old
- The patient is diagnosed with infantile spasms with electroencephalogram-confirmed hypsarrhythmia
- The patient has tried a 2-week course of high-dose (40-60 mg/day) prednisone/prednisolone for any episode of infantile spasms and has failed therapy as evidenced by continued signs/symptoms of either spasms or hypsarrhythmia on EEG
- H.P. Acthar Gel is prescribed by or in consultation with a pediatric neurologist with expertise in the management of infantile spasm.

Prior Authorization expires in 30 days.

Renewal Criteria for infantile spasms: Coverage will be approved for an additional 365 days for infantile spasms if all criteria are met:

- The patient is < 24 months old
- The patient has demonstrated a clinical response to H.P. Acthar Gel as defined by cessation of both previous characteristic spasms AND hypsarrhythmia on EEG within 2 weeks of starting H.P. Acthar Gel
- The patient has not previously demonstrated intolerance to H.P. Acthar Gel, defined as the patient requiring discontinuation of H.P. Acthar Gel therapy.

2) Multiple Sclerosis Exacerbation:

- The patient is an adult diagnosed with multiple sclerosis
- The patient is diagnosed with an exacerbation of multiple sclerosis OR optic neuritis as a specific exacerbation of multiple sclerosis
- The patient has failed or is intolerant to an adequate trial of IV/PO corticosteroids (e.g., 1000 mg methylprednisolone IV x 5-14 days OR oral equivalent) for the present exacerbation.
 - Note that anticipated hypercortisolism and other non-emergent side effects (e.g., non-emergent hyperglycemia, weight gain, non-urgent/emergent hypertension, edema, paresthesias, insomnia, constipation, diarrhea, hyperphagia, anorexia, nasal/sinus congestion, acne, and menstrual irregularities, etc.) do not meet the threshold for authorization of this PA. Similarly, if the patient has had emergent or life-threatening adverse effects to high-dose corticosteroids, H.P. Acthar gel is contraindicated.

- H.P. Acthar Gel is prescribed by or in consultation with a neurologist.

Prior Authorization expires in 30 days.

PA Renewal is not authorized for multiple sclerosis exacerbation.

- 3) Other uses: PA will be not be approved for any condition other than infantile spasms in infants less than 24 months of age or MS exacerbation, including, but not limited to the following: optic neuritis not related to MS exacerbation, Rheumatoid Arthritis, Systemic Lupus Erythematosus, Psoriatic Arthritis, Ankylosing Spondylitis, Dermatomyositis, Polymyositis, Juvenile Idiopathic Arthritis, Erythema Multiforme (any severity), Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis Syndrome, Serum Sickness, Keratitis, Iritis, Iridocyclitis, Uveitis, Choroiditis, Birdshot choroiditis, Chorioretinitis, anterior segment inflammation, Nephrotic Syndrome including focal segmental glomerulosclerosis (FSGS), idiopathic membranous nephropathy, IgA nephropathy, membranoproliferative glomerulonephritis (MPGN), and monoclonal diffuse proliferative glomerulonephritis, non-nephrotic edematous states, sarcoidosis, gout, scleritis, or conjunctivitis.

E. Adrenocorticotrophic Hormones (ACTH)—UF and PA Implementation Period

The P&T Committee recommended (14 for, 0 opposed, 0 abstained, 2 absent) an effective date of the first Wednesday after a 60-day implementation period in all points of service and that DHA send letters to beneficiaries who are affected by the UF decision

IX. ADRENOCORTICOTROPIC HORMONES (ACTH)

BAP Comments

A. ACTH—UF Recommendation

The P&T Committee recommended that Acthar Gel be designated as formulary on the Uniform Formulary.

BAP Comment: Concur Non-concur

Additional Comments and Dissension

B. Adrenocorticotrophic Hormones (ACTH)—Manual PA Criteria

The P&T Committee recommended manual PA criteria for new and current users of Acthar Gel for treatment of infantile spasms (West Syndrome) in infants, and for patients with MS

exacerbation who have failed or can't tolerate steroids. PA renewal will be allowed for infantile spasms; however, PA review will be required for each occurrence of MS exacerbation. All other users of Acthar gel are unsupported and excluded from TRICARE coverage.

The full PA criteria were stated above.

BAP Comment: Concur Non-concur

Additional Comments and Dissension

C. Adrenocorticotrophic Hormones (ACTH)—UF and PA Implementation Period

The P&T Committee recommended a 60-day implementation period and that DHA send letters to beneficiaries who are affected by the UF decision.

BAP Comment: Concur Non-concur

Additional Comments and Dissension

X. NEWLY-APPROVED DRUGS PER 32 CFR 199.21(g)(5)

P&T Comments

A. Newly-Approved Drugs per CFR 199.21(g)(5)—Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions

The P&T Committee agreed (Part 1: 16 for, 0 opposed, 0 abstained, 0 absent; Part 2: 15 for, 0 opposed, 0 abstained, 1 absent) with the relative clinical and cost-effectiveness analyses presented for the newly-approved drugs reviewed according to 32 CFR 199.21(g)(5).

B. Newly-Approved Drugs per CFR 199.21(g)(5)—UF Recommendation

The P&T Committee recommended (Part 1: 15 for, 0 opposed, 1 abstained, 0 absent; Part 2: 15 for, 0 opposed, 0 abstained, 1 absent) the following:

- UF:
 - acalabrutinib (Calquence) – Oral Oncologic Agent for Mantle Cell Lymphoma
 - benznidazole – Miscellaneous Anti-Infective for Chagas Disease
 - dolutegravir/rilpivirine (Juluca) – Antiretrovirals for Human Immunodeficiency Virus (HIV)
 - emicizumab-kxwh (Hemlibra) – Antihemophilic Factors
 - letermovir (Prevymis) Antivirals

- NF:
 - coagulation factor IX, recombinant (Rebinyn) – Antihemophilic Factors
 - dapagliflozin/saxagliptin (Qtern) – Non-Insulin Diabetes Drugs – Sodium Glucose Co-Transporter-2 (SGLT2) Inhibitor
 - fluticasone propionate 93 mcg nasal spray (Xhance) – Nasal Allergy Drugs – Corticosteroids
 - house dust mite allergen extract (Odactra) – Immunological Agents
Miscellaneous: Oral Agents
 - latanoprostene bunod ophthalmic solution (Vyzulta) – Glaucoma Drugs
 - minocycline ER (Ximino) – Antibiotics: Tetracyclines
 - sodium picosulfate/magnesium oxide/anhydrous citric acid (Clenpiq) – Laxatives-Cathartics-Stool Softeners
 - spironolactone 25 mg/5 mL oral suspension (CaroSpir) – Diuretics

C. Newly-Approved Drugs per CFR 199.21(g)(5)—PA Criteria

The P&T Committee recommended (Part 1: 15 for, 0 opposed, 1 abstained, 0 absent; Part 2: 15 for, 0 opposed, 0 abstained, 1 absent) the following:

- Applying the same manual PA criteria for dapagliflozin/saxagliptin (Qtern) in new and current users, as is currently in place for the other non step-preferred SGLT2 inhibitors and dipeptidyl peptidase-4 (DPP-4) inhibitors. Patients must first try the step-preferred SGLT1 inhibitor empagliflozin (Jardiance).
- Applying the same manual PA criteria for minocycline ER (Ximino) in new and current users, as is currently in place for the other non step-preferred tetracyclines. Patients must first try formulary step-preferred agents.
- Applying manual PA criteria to new users of Odactra, Hemlibra, and Calquence, and for new users of CaroSpir who are over 12 years old.

- Applying manual PA criteria to new and current users of Xhance and Vyzulta.

Full PA Criteria for the Newly-Approved Drugs per CFR 199.21(g)(5)

1. **acalabrutinib (Calquence)**

Manual PA criteria apply to all new users of Calquence. Coverage will be approved if all criteria are met:

- The patient is ≥ 18 years
- The patient has pathologically confirmed mantle cell lymphoma, with documentation of monoclonal B cells that have a chromosome translocation t(11;14)(q13;q32) and/or overexpress cyclin D1
- The patient must not have significant cardiovascular disease such as uncontrolled or symptomatic arrhythmias, congestive heart failure, or myocardial infarction within 6 months of screening, or any Class 3 or 4 cardiac disease as defined by the New York Heart Association Functional Classification, or corrected QT interval (QTc) > 480 msec

Off-label uses are not approved.

Prior authorization does not expire.

2. **dapagliflozin/saxagliptin (Qtern)**

Manual PA criteria apply to all new and current users of Qtern. Coverage will be approved if all criteria are met:

- The patient must have had an inadequate response or experienced significant ADRs, or have a contraindication to metformin AND
- The patient must have tried one of the preferred SGLT2 inhibitors (Jardiance, Glyxambi, Synjardy, and Synjardy XR) and had an inadequate response or experienced significant ADRs, or have a contraindication to empagliflozin AND
- The patient must have tried one of the preferred DPP-4 inhibitors (Januvia, Janumet, and Janumet XR) and had inadequate response or experienced significant ADRs, or have a contraindication to sitagliptin.

Off-label uses are not approved.

Prior authorization does not expire.

3. **emicizumab-kxwh (Hemlibra)**

Manual PA criteria apply to all new users of Hemlibra. Coverage will be approved if all criteria are met:

- The patient must have a documented diagnosis of Hemophilia A AND
- The patient must have a history of a high titer of factor VIII inhibitor (greater than or equal to 5 Bethesda units per mL) AND
- The patient must NOT have been treated within the last 12 months for thromboembolic disease, or have current signs of, thromboembolic disease AND
- Hemlibra must be prescribed by or in consultation with a hematologist.

Off-label uses are not approved.
Prior authorization does not expire.

4. fluticasone propionate 93 mcg nasal spray (Xhance)

Manual PA criteria apply to all new users and current users of Xhance. Coverage will be approved if all criteria are met:

- Patient has nasal polyps AND
- Patient must have tried and failed at least two of the following: azelastine 137 mcg nasal spray (generic Astelin), flunisolide nasal spray, fluticasone propionate 50 mcg nasal spray (generic Flonase), or ipratropium nasal spray (Atrovent nasal spray) AND
- Patient has tried and failed mometasone (Nasonex) OR beclomethasone (Beconase)

Off-label uses are not approved.
Prior authorization does not expire.

5. house dust mite allergen extract (Odactra)

Manual PA criteria apply to all new users of Odactra. Coverage will be approved if all criteria are met:

- Odactra is prescribed by an allergist/immunologist AND
- The patient is between the ages of 18 and 65 years AND
- The patient has a diagnosis of house dust mite (HDM) allergic rhinitis confirmed with either a positive skin test or an in vitro testing pollen-specific for IgE antibodies to *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* house dust mites AND
 - The patient's symptoms of allergic rhinitis have not been controlled with a nasal corticosteroid (e.g., fluticasone) AND at least one of the following: oral antihistamine, nasal antihistamines, or a leukotriene receptor antagonist (montelukast) OR
 - The patient has a diagnosis of HDM-related allergic rhinitis and allergic asthma that has not responded to an adequate trial of inhaled steroids, and the patient's FEV₁ >70% AND
- The patient has received the first dose in the office setting and was observed for 30 minutes with no allergic reactions noted AND
- The patient has a prescription for self-administered SC epinephrine AND

- The patient does not have a history of severe local allergic reaction to sublingual immunotherapy AND
- Patient is not receiving co-administered SC immunotherapy AND
- Patient does not have severe, uncontrolled, unstable asthma

Other off-label uses other than allergic asthma are not approved.
PA expires in 6 months.

Renewal Criteria: Coverage will be approved indefinitely if the patient has responded positively to treatment and is not receiving co-administered SC immunotherapy and does not have severe, uncontrolled, unstable asthma.

6. latanoprostene bunod ophthalmic solution (Vyzulta)

Manual PA criteria apply to all new and current users of Vyzulta. Coverage will be approved if all criteria are met:

- Patient must have a diagnosis of open angle glaucoma OR ocular hypertension
- Patient is ≥ 16 years old
- Patient has tried and failed at least two ophthalmic prostaglandin glaucoma agents (e.g., latanoprost, bimatoprost)

Off-label uses are not approved.
Prior authorization does not expire.

7. minocycline ER (Ximino)

PA criteria apply to all new and current users of Ximino.

Automated PA Criteria:

- Patient has filled a prescription for one generic IR doxycycline (either hyclate or monohydrate salt; does not include doxycycline monohydrate 40 mg IR/DR) AND one generic minocycline IR product at any Military Treatment Facility (MTF), retail network pharmacy, or the mail order pharmacy in the previous 180 days

Manual PA Criteria—If automated PA criteria are not met, Ximino is allowed if:

- The patient has acne with inflammatory lesions AND
- The patient cannot tolerate generic minocycline IR due to gastrointestinal adverse events

Off-label uses are not approved.
Prior authorization expires in 365 days.

Renewal criteria: Ximino will be approved for an additional 365 days, if:

- The patient's therapy has been re-evaluated within the last 12 months

- The patient is tolerating treatment and there continues to be a medical need for the medication
- The patient has disease stabilization or improvement in disease while on therapy

8. spironolactone 25 mg/5 mL oral suspension (CaroSpir)

Manual PA criteria apply to all new users of CaroSpir who are over 12 years old. Coverage will be approved if all criteria are met.

- The patient has heart failure, hypertension or edema from cirrhosis AND
- The provider must write in why the patient requires CaroSpir and cannot take an aldosterone blocker / potassium-sparing diuretic in a tablet formulation
 - Acceptable responses: patient cannot swallow tablets due to some documented medical condition – dysphagia, etc., and not due to convenience

Off-label uses are not approved.
Prior authorization does not expire.

D. Newly-Approved Drugs per CFR 199.21(g)(5)—UF and PA Implementation Plan

The P&T Committee recommended (Part 1: 15 for, 0 opposed, 1 abstained, 0 absent; Part 2: 15 for, 0 opposed, 0 abstained, 1 absent) an effective date upon the first Wednesday two weeks after the signing of the minutes in all points of service.

XI. NEWLY-APPROVED DRUGS PER 32 CFR 199.21(g)(5)

BAP Comments

A. Newly-Approved Drugs per CFR 199.21(g)(5)—UF Recommendation

The P&T Committee recommended the following:

- UF:
 - Calquence
 - benznidazole
 - Juluca
 - Hemlibra
 - Prevyomis
- NF:

- Rebinyn
- Qtern
- Xhance
- Odactra
- Vyzulta
- Ximino
- Clenpiq
- CaroSpir

BAP Comment: Concur Non-concur

Additional Comments and Dissension

B. Newly-Approved Drugs per CFR 199.21(g)(5)—PA Criteria

The P&T Committee recommended the PA criteria for the new drugs as stated previously. The recommendations are as follows:

- The same PA criteria for the drugs where there is existing step therapy would apply for Qtern (SGLT-2 inhibitors) and Ximino (oral tetracyclines for acne).
- Applying manual PA criteria to new users of Odactra, Hemlibra, and Calquence, and for new users of CaroSpir who are over 12 years old.
- Applying manual PA criteria to new and current users of Xhance and Vyzulta.

BAP Comment: Concur Non-concur

Additional Comments and Dissension

C. Newly-Approved Drugs per CFR 199.21(g)(5)—UF and PA Implementation

The P&T Committee recommended the first Wednesday two weeks after the signing of the minutes as the implementation date.

BAP Comment: Concur Non-concur

XII. UTILIZATION MANAGEMENT CORTICOSTEROIDS-IMMUNE MODULATOR AGENTS—CORTICOSTEROID SUBCLASS

P&T Comments

A. Corticosteroids-Immune Modulator Agents—Corticosteroid Subclass: Prednisone Delayed Release (Rayos)—New Manual PA Criteria

Rayos is a branded formulation of delayed release (DR) prednisone that has the same indications as immediate release (IR) prednisone, which was approved in 1955. It is dosed once daily, similar to IR prednisone, and has the same safety profile. Cost-effective generic formulations of prednisone and other glucocorticoids are available on the UF without PA required.

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) manual PA criteria for Rayos due to the significant cost differences and lack of clinically compelling benefits between Rayos and generic prednisone. New and current users of Rayos are required to try generic prednisone IR and a second corticosteroid first.

Full PA Criteria:

Manual PA criteria apply to all new and current users of Rayos. Note that PA is not required for generic prednisone; providers are encouraged to consider changing the prescription to generic prednisone. Coverage for Rayos will be approved if:

- The provider writes in why the patient requires delayed release prednisone and why patient cannot take immediate release prednisone
- Acceptable responses are approved if ALL of the criteria are met:
 - The patient has a diagnosis of rheumatoid arthritis AND
 - The patient medical history includes trial and failure of both:
 - generic prednisone AND
 - at least one generic oral corticosteroid (e.g., dexamethasone, methylprednisolone, etc.)

Off-label uses are not approved.

Prior Authorization does not expire.

B. Corticosteroids-Immune Modulator Agents—Corticosteroid Subclass: Prednisone Delayed Release (Rayos)—New Manual PA Implementation Date

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) new manual PA for Rayos become effective on the first Wednesday after a 90-day implementation period in all points of service. Additionally, the P&T Committee recommended DHA send letters to the beneficiaries affected by this decision.

XIII. UTILIZATION MANAGEMENT CORTICOSTEROIDS-IMMUNE MODULATOR AGENTS—CORTICOSTEROID SUBCLASS

BAP Comments

A. Prednisone Delayed Release (Rayos)—New Manual PA Criteria

The P&T Committee recommended manual PA criteria for Rayos due to the significant cost differences and lack of clinically compelling benefits between Rayos and generic prednisone.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

B. Prednisone Delayed Release (Rayos)—New Manual PA Implementation Plan

The P&T Committee recommended the new manual PA for Rayos become effective on the first Wednesday after a 90-day implementation period , and that DHA send letters to the beneficiaries affected by this decision.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

XIV. UTILIZATION MANAGEMENT ANTIVIRALS

P&T Comments

A. Antivirals: Acyclovir/Hydrocortisone 5%/1% Cream (Xerese), Penciclovir 1% Cream (Denavir), and Acyclovir 50 mg buccal tablet (Sitavig)—New Manual PA Criteria

The committee reviewed three treatments for herpes labialis (cold sores). Xerese is a branded combination of acyclovir/hydrocortisone cream that has an equivalent efficacy and safety profile as the separate ingredients applied individually. Denavir is a branded penciclovir 1% cream that is indicated for treatment of recurrent cold sores, while Sitavig is a buccal tablet formulation of acyclovir. Cost-effective generic formulations of acyclovir cream and the oral antiviral agents (e.g., acyclovir, valacyclovir) used for treating herpes labialis are available on the UF without PA required.

The P&T Committee recommended (11 for, 0 opposed, 0 abstained, 5 absent) manual PA criteria for Xerese, Denavir, and Sitavig due to the significant cost differences and lack of clinically compelling benefits compared with generic topical and oral antivirals. New and current users of these products are required to try generic acyclovir cream and oral antiviral agents first.

Full PA Criteria

1. acyclovir 5%/hydrocortisone 1% cream (Xerese)

Note: DoD Formulary products include topical or oral antiviral agents. Consider alternate agents first, such as acyclovir oral/topical or valacyclovir oral tablets. This PA is only approved for treatment of immunocompetent patients 6 years and older with recurrent herpes labialis (not approved for prophylaxis).

Manual PA criteria apply to all new and current users of Xerese. Coverage for Xerese is approved if:

- The provider writes in why the patient requires Xerese and why they cannot take oral antivirals or cannot use acyclovir 5% cream and hydrocortisone 1% cream separately.
- Acceptable responses are approved if ALL of the criteria are met:
 - Tried and failed topical acyclovir 5% cream and hydrocortisone 1% cream separately AND
 - Treatment failure of one of the following: oral acyclovir, valacyclovir, or famciclovir

Off-label uses are not approved.
Prior authorization does not expire.

2. Penciclovir 1% cream (Denavir) and acyclovir 50 mg buccal tablet (Sitavig)

Note: DoD Formulary products include topical or oral antiviral agents. Consider alternate agents first, such as acyclovir oral/topical or valacyclovir oral tablets. This PA is only approved for treatment of immunocompetent patients 12 years and older with recurrent herpes labialis (not approved for prophylaxis).

Manual PA criteria apply to all new and current users of Denavir or Sitavig. Coverage is approved if:

- The provider writes in why the patient requires Denavir or Sitavig and why they cannot take oral antivirals or cannot use acyclovir 5% cream.
- Acceptable responses are approved if ALL of the criteria are met:
 - Tried and failed topical acyclovir 5% cream AND
 - Treatment failure of one of the following: oral acyclovir, valacyclovir, or famciclovir

Off-label uses are not approved.
 Prior authorization does not expire.

B. Antivirals: Acyclovir/Hydrocortisone 5%/1% Cream (Xerese), Penciclovir 1% Cream (Denavir), and Acyclovir 50 mg buccal tablet (Sitavig)—New Manual PA Implementation Plan

The P&T Committee recommended the new manual PA for Xerese, Denavir and Sitavig become effective on the first Wednesday after a 90-day implementation period, and that DHA send letters to the beneficiaries affected by this decision.

XV. ANTIVIRALS

BAP Comments

A. Antivirals: Xerese, Denavir and Sitavig—New Manual PA Criteria

The P&T Committee recommended manual PA criteria for Xerese, Denavir and Sitavig, due to the significant cost differences and lack of clinically compelling benefits compared with generic topical and oral antivirals.

<i>BAP Comment:</i>	<input type="checkbox"/> Concur	<input type="checkbox"/> Non-concur	
Additional Comments and Dissension			

B. Antivirals: Xerese, Denavir and Sitavig—New Manual PA Implementation Plan

The P&T Committee recommended the new manual PA for Xerese, Denavir, and Sitavig become effective on the first Wednesday after a 90-day implementation period, and that DHA send letters to the beneficiaries affected by this decision.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

XVI. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA AND STEP THERAPY

P&T Comments

A. Updated Manual PA Criteria and PA Renewal Criteria

Updates to the step therapy and manual PA criteria for several drugs were recommended by the P&T Committee due to a variety of reasons, including expanded FDA indications and safety. The updated manual PAs outlined below will apply to new users.

The P&T Committee recommended (12 for, 0 opposed, 0 abstained, 4 absent) updates to the manual PA criteria for Xeljanz, Xeljanz XR, Taltz, Trulance, Addyi, and Lyrica; and updated PA renewal criteria for the tetracyclines.

- 1. Targeted Immunomodulatory Biologics (TIBs): Tofacitinib (Xeljanz/Xeljanz XR) and Ixekizumab Injection (Taltz)**—The TIBs were most recently reviewed in August 2014, with step therapy requiring a trial of adalimumab (Humira) first. Xeljanz was originally approved for treating rheumatoid arthritis, while Taltz was originally approved for plaque psoriasis and was reviewed as a new drug in May 2016. PA criteria were updated to add the additional indication for active psoriatic arthritis in adults for Xeljanz, Xeljanz XR, and Taltz.
- 2. GI-2 Miscellaneous Agents: Plecanatide (Trulance)**—Trulance was reviewed as a new drug in May 2017 and indicated for chronic idiopathic constipation, with manual PA criteria recommended. The PA criteria were updated to add the additional FDA indication for treatment of irritable bowel syndrome with constipation (IBS-C), with the requirement for a trial of linaclotide (Linzess) before approval of plecanatide for IBS-C.
- 3. Female Hypoactive Sexual Desire Disorder Agents: Flibanserin (Addyi)**—Addyi was reviewed in November 2015 with manual PA criteria recommended. The PA

criteria were updated to add an expiration date of three months, with renewal PA criteria ensuring efficacy and safety.

4. **Antidepressants and Non-Opioid Pain Syndrome Agents: Pregabalin (Lyrica) PA and MN Criteria**—Step therapy and manual PA criteria have applied to Lyrica since it was originally reviewed for formulary placement in November 2011, with the most recent update occurring in May 2017. The additional indication for treatment of neuropathic pain associated with spinal cord injury after a trial of gabapentin and duloxetine was added to the PA criteria.
5. **Antibiotics: Tetracyclines**—The PA criteria for the tetracyclines, which were originally reviewed in February 2017, was updated to include renewal criteria, that ensure the patient has been re-evaluated within the past 12 months, that the patient is tolerating therapy, and continues to need the medication and that the disease has stabilized or improved while on therapy. The PA renewal will expire in 365 days.

B. Updated Manual PA Criteria and PA Renewal Criteria—PA Implementation Plan

The P&T Committee recommended the following updates to the current PAs for Taltz, Xeljanz/Xeljanz XR, Addyi, Trulance, and Lyrica, and the renewal criteria for the tetracyclines become effective on the first Wednesday two weeks after the signing of the minutes in all points of service.

XVII. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA AND STEP THERAPY

BAP Comments

A. Updated Manual PA Criteria and PA Renewal Criteria

The P&T Committee recommended updates to the manual PA criteria for Xeljanz, Xeljanz XR, Taltz, Trulance, Addyi, and Lyrica; and updated PA renewal criteria for the tetracyclines, as stated above.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

B. Updated Manual PA Criteria and PA Renewal Criteria—PA Implementation Plan

The P&T Committee recommended the updates to the PA criteria for the drugs discussed above become effective on the first Wednesday two weeks after the signing of the minutes.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

XVIII. BRAND OVER GENERIC AUTHORIZATION FOR SILDENAFIL TABLETS (VIAGRA)

P&T Comments

A. Viagra—Brand over Generic Requirement and Manual PA Criteria

TRICARE Policy requires dispensing of generic products at the Retail Network and Mail Order Pharmacy. However, pricing for the branded Viagra product is more cost effective than the AB-rated generic formulations for sildenafil, which were launched in December 2017. The manufacturer of Viagra has offered a Distribution and Pricing Agreement (DAPA). Therefore, the branded Viagra product will continue to be dispensed, and the generic will only be available with prior authorization (i.e., the reverse of the current brand to generic policy). The Tier 1 (generic) copayment will apply to Viagra. The “brand over generic” requirement for Viagra will be removed administratively when it is no longer cost effective compared to the AB-rated generics.

The P&T Committee recommended (12 for, 0 opposed, 0 abstained, 4 absent) implementing the requirement to prefer the branded Viagra product over generic formulations. Manual PA criteria are required for generic sildenafil in the Retail Network and Mail Order Pharmacy. The prescriber will provide patient-specific justification as to why the branded Viagra product cannot be used.

PA Criteria

Manual PA criteria apply to all new users of generic Viagra. Note that brand Viagra is the preferred PDE5 product in DoD.

Manual PA Criteria: Coverage for generic sildenafil is approved if the following criteria is met:

- The provider has provided patient-specific justification as to why the brand Viagra product cannot be used.
- Acceptable reasons include the following, which have occurred or are likely to occur with the branded Viagra product: allergy to the branded Viagra; contraindication; sub-therapeutic response; physical restriction (e.g., swallowing issues); and brand availability issues.

B. Viagra—Brand Copayment Change

The P&T Committee recommended (12 for, 0 opposed, 0 abstained, 4 absent) that the brand (Tier 2) formulary cost share for Viagra in the TRICARE Mail Order Pharmacy and the TRICARE Retail Network Pharmacy be lowered to the generic (Tier 1) formulary cost share.

XIX. BRAND OVER GENERIC AUTHORIZATION FOR SILDENAFIL TABLETS (VIAGRA)

BAP Comments

A. Viagra—Brand over Generic Requirement and Manual PA Criteria

The P&T Committee recommended implementing the requirement to prefer the branded Viagra product over generic formulations. Manual PA criteria are required for generic Viagra in the Retail Network and Mail Order Pharmacy. The prescriber will provide patient-specific justification as to why the branded Viagra product cannot be used.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

B. Viagra—Brand Copayment Change

The P&T Committee recommended that the brand (Tier 2) formulary cost share for Viagra in the TRICARE Mail Order Pharmacy and the TRICARE Retail Network Pharmacy be lowered to the generic (Tier 1) formulary cost share.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p> <p style="text-align: right;">Additional Comments and Dissension</p>

Table of Implementation Status of UF Recommendations/Decisions Summary

Date	DoD PEC Drug Class	Type of Action	UF Medications	Nonformulary Medications	Implement Date	Notes and Unique Users Affected
Feb 2018	Non-Insulin Diabetes Drugs: Glucagon-Like Peptide-1 Receptor Agonists (GLP1RA) Subclass	UF Class Review Class previously reviewed Nov 2010 Nov 2012 Aug 2015	<u>UF Step-Preferred</u> <ul style="list-style-type: none"> ▪ exenatide once weekly (Bydureon, Bydureon BCise) ▪ dulaglutide (Trulicity) 	<u>NF Non Step-Preferred</u> <ul style="list-style-type: none"> ▪ albiglutide (Tanzeum) ▪ exenatide twice daily (Byetta) ▪ liraglutide (Victoza) ▪ lixisenatide (Adlyxin) ▪ semaglutide (Ozempic) 	90 days	<ul style="list-style-type: none"> ▪ Must try metformin first in all new users of any GLP1RA unless a contraindication exists ▪ Manual PA criteria required for all new and current users of a GLP1RA ▪ Must try Bydureon/BCise and Trulicity first before use of a nonformulary, non step-preferred GLP1RA ▪ Tanzeum market D/C in Aug 2018 <p><u>Unique Users Affected</u> 9,412 affected by NF status Affected by PA Mail 21,215 MTF 13,827 Retail 1,949 Total 32,321</p>
Feb 2018	Anti-Inflammatory Immunomodulatory Ophthalmic Drugs: Ophthalmic Immunomodulatory Subclass	UF Class review Class previously reviewed Feb 2016	<u>UF</u> <ul style="list-style-type: none"> ▪ cyclosporine 0.05% ophthalmic emulsion (Restasis) ▪ lifitegrast 5% ophthalmic solution (Xiidra) 	None	90 days	<ul style="list-style-type: none"> ▪ Manual PA criteria applies to all new patients defined as not having filled Xiidra or Restasis in the last 180 days ▪ A trial of two different artificial tears products required first <p><u>Unique Users Affected</u> Not applicable - no products selected for nonformulary status.</p>

Date	DoD PEC Drug Class	Type of Action	UF Medications	Nonformulary Medications	Implement Date	Notes and Unique Users Affected
Feb 2018	Osteoporosis Drugs: Parathyroid Hormone Analogs Subclass	UF Class Review Subclass not reviewed; Class Reviewed June 2013	<u>UF Step-Preferred</u> ▪ teriparatide injection (Forteo)	<u>NF Non Step-Preferred</u> ▪ abaloparatide injection (Tymlos)	60 days	<ul style="list-style-type: none"> Manual PA apply to all new users of Forteo and Tymlos Additionally, a trial of Forteo is required in all new patients prior to use of Tymlos <u>Unique Users Affected:</u> Not applicable; PA applies to new patients
Feb 2018	Corticosteroids-Immune Modulators: Adrenocorticotropic Subclass	UF Class Review Not previously reviewed	▪	▪ repository corticotropin injection (H.P. Acthar Gel)	60 days	<ul style="list-style-type: none"> Prior Authorization applies new and current users for infantile spasms and multiple sclerosis exacerbation; other uses not covered <u>Unique Users Affected:</u> 86

February 2018 Drugs with New Prior Authorization Criteria—Unique Utilizers Affected Per Drug

Drug	MTF	Mail Order	Retail	Total
Corticosteroids-Immune Modulator Agents—Corticosteroid Subclass: Prednisone Delayed Release (Rayos)	1	143	101	245
Antivirals: Acyclovir/Hydrocortisone 5%/1% Cream (Xerese), Penciclovir 1% Cream (Denavir), and Acyclovir 50 mg buccal tablet (Sitavig)	79	319	586	984