

**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 or Tier 4/not covered status, prior authorization (PA), pre-authorizations, and the effective date for a drug's change from formulary to nonformulary (NF) or Tier 4 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—PROTON PUMP INHIBITORS (PPIS) – CAPSULES AND TABLETS AND ALTERNATIVE DOSAGE FORM SUBCLASSES

P&T Comments

A. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses

Background—The P&T Committee evaluated the relative clinical effectiveness of the Proton Pump Inhibitors (PPIs), including omeprazole (Prilosec), pantoprazole (Protonix), rabeprazole (Aciphex), dexlansoprazole (Dexilant), lansoprazole (Prevacid), omeprazole/sodium bicarbonate (Zegerid), esomeprazole (Nexium), and esomeprazole strontium. Generic formulations of all the products are marketed, except for Dexilant and esomeprazole strontium. Over-the-counter (OTC) formulations of Nexium, Prevacid, Prilosec, and their generics are also available.

The Alternative Dosage Form subclass was also evaluated for UF status and is comprised of 6 products: Prilosec, Protonix, Nexium, and Zegerid packets for oral suspension, Aciphex sprinkle, and Prevacid orally dissolving tablet (ODT). There are no generic PPI alternative dosage forms.

The Committee reviewed new clinical data available since the original class review in May 2007. Nexium was designated NF at the most recent class review in February 2017.

The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

- The May 2007 drug class review concluded that PPIs have similar efficacy in treating a wide range of acid-related disorders and are highly therapeutically interchangeable. The P&T Committee did not find new clinical efficacy data that would change the original conclusion.
- The 2013 American College of Gastroenterology (ACG) Gastroesophageal Reflux Disease (GERD) Guidelines also support the May 2007 conclusion in their

statement that there are no major differences in efficacy between the different PPIs for symptom relief and healing of erosive esophagitis.

- Several recent meta-analyses and systematic reviews state the PPIs do not have clinically significant differences in efficacy (e.g., 2009 Oregon Health & Science University Drug Effectiveness Review Project; 2018 Utah Medicaid P&T Committee).
- A recent network meta-analysis evaluated the comparative efficacy of PPIs for erosive esophagitis and concluded that at equipotent doses the PPIs do not exhibit superiority of one product over the other (Medicine 2017).
- Head-to-head trials between the PPIs are limited in that comparisons of equipotent doses are not always included.
- Differences in pharmacokinetic properties between the PPIs, such as release mechanism (e.g., delayed release or dual release), salt form (e.g., magnesium strontium or sodium bicarbonate), and chirality (e.g., R- vs. R- and S-enantiomers) have little to no clinical impact.
- With regard to the individual PPIs, the P&T Committee concluded the following:
 - Dexlansoprazole (Dexilant) contains the R enantiomer of lansoprazole.
 - Although dexlansoprazole provides two releases of medication with peak concentrations at 2 and 5 hours, the link between dual release and therapeutic benefit is not known. Dexlansoprazole is only approved for patients 12 years and older and is not manufactured in an alternative dosage form.
 - FDA approval for dexlansoprazole was based on two Phase 3 randomized controlled trials showing non-inferiority to lansoprazole. Dexlansoprazole displayed a higher discontinuation rate due to adverse effects in comparison to lansoprazole.
 - The 2009 FDA Review noted that although dexlansoprazole was effective for the requested indications, there was no convincing evidence of additional benefit over existing therapies, and the benefit-to-risk profile for dexlansoprazole was unfavorable.
 - The 2017 network meta-analysis also found that dexlansoprazole was the PPI with the highest discontinuation rate in comparison to all other products.
 - There is no new data to change the May 2009 conclusion that Dexilant does not have a significant clinically meaningful therapeutic advantage in terms of effectiveness, safety, and clinical outcomes compared to other PPI drugs currently included on the UF.
- Esomeprazole strontium contains a different salt formulation from esomeprazole magnesium (Nexium) and is not available in an alternative dosage form.
 - FDA approval was based on the data with Nexium, and no clinical trials were conducted with this formulation. Strontium is incorporated into bone

and is not recommended for use in children or during pregnancy due to safety. Esomeprazole strontium is also not recommended in patients with severe renal impairment.

- Esomeprazole strontium offers no clinically compelling advantages in comparison to esomeprazole magnesium (Nexium) or the other PPIs.
- Omeprazole/sodium bicarbonate (Zegerid) is only approved for adults. FDA approval was granted based on the original omeprazole studies. Due to the sodium bicarbonate component, it is contraindicated in patients with metabolic alkalosis, hypocalcemia, respiratory alkalosis or those on salt restricted diets (it contains 300 to 400 mg of sodium per tablet). Zegerid offers no compelling clinical advantages over the other PPIs.
- Lansoprazole (Prevacid, generic) has the largest number of FDA-approved indications; however, there is robust evidence for off-label use for all PPIs for all indications. The alternative dosage form of Prevacid ODT contains phenylalanine and should be avoided in patients with phenylketonuria. Lansoprazole is approved for patients as young as 12.
- Pantoprazole (Protonix, generic) provides an option for flexible mealtime dosing and does not require dosage adjustment for hepatic impairment. It has an alternative dosage form for treating patients down to the age of 5.
- Rabeprazole (Aciphex, generic) also provides an option for those who require flexible mealtime dosing but is not available in a formulation for use in PEG or NG tubes. The Aciphex sprinkle formulation is approved for children down to the age of 12 years.
- Esomeprazole (Nexium, generic) and omeprazole (Prilosec, generic) have a long history of use, are available OTC, are compatible with NG/PEG tube administration, and the alternative dosage forms carry the youngest FDA-approved age range down to 1 month.
- The 2013 ACG GERD Guidelines and 2017 American Gastroenterological Association (AGA) Best Practices agree that high-quality evidence recommend 4 weeks to 8 weeks of PPI therapy for GERD. Patients with uncomplicated GERD who respond to short-term PPIs should subsequently attempt to stop or reduce PPI use.
- Unless otherwise clinically necessary, PPIs should be used for the shortest period possible per label indication. Indications for longer-term PPI use include refractory GERD, erosive esophagitis, Zollinger-Ellison syndrome, NSAID-induced ulcer history, Barrett's Esophagus, and chronic anticoagulation after an Upper GI Bleed.
- With the exception of high discontinuation rates associated with dexlansoprazole (Dexilant), there are no important safety differences in long-term findings between PPI agents, but studies are observational in nature.
- Studies have shown PPIs are not benign and long-term use has been associated with adverse events. FDA safety alerts in 2011, 2012 and 2016 reported that prescription PPIs may cause nutrient malabsorption (vitamin B12, iron, magnesium, calcium) resulting in osteoporosis, hypomagnesemia, vitamin B12 deficiency, and increased

infection risk (*Clostridium. difficile* infections, salmonella, campylobacter, and pneumonia) and drug-induced cutaneous and systemic lupus erythematosus.

- The updated Beers Criteria published by the American Geriatrics Society in January 2019 reaffirms the 2015 recommendation to avoid prolonged use of PPIs beyond 8 weeks in adults age 65 years or older, unless there is a justified reason to continue use.
- PPI deprescribing campaigns suggest tapering patients, emphasizing therapeutic lifestyle modification, using rescue therapy such as calcium carbonate antacids or histamine blockers (e.g., ranitidine, famotidine), or attempting on-demand or de-escalation of dosing.

B. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—Relative Cost-Effectiveness Analysis and Conclusion

Cost-minimization analysis (CMA) and budget impact analysis (BIA) were performed to evaluate the PPIs. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

Tablets and Capsules Subclass

- CMA results for the Tablets and Capsules subclass showed that esomeprazole strontium, dexlansoprazole, and omeprazole/bicarbonate were substantially less cost-effective than the remainder of the class.
- BIA was performed for the Tablets and Capsules subclass to evaluate the potential impact of designating selected agents as formulary, NF, or Tier 4 on the UF. BIA results showed that designating omeprazole (Prilosec, generics) and pantoprazole (Protonix, generics) as formulary and step-preferred, esomeprazole (Nexium, generics) and rabeprazole (Aciphex, generics) as UF and non-step-preferred, lansoprazole (Prevacid, generics) and omeprazole/sodium bicarbonate (Zegerid, generics) as NF and non-step-preferred, and dexlansoprazole (Dexilant) and esomeprazole strontium as Tier 4 demonstrated significant cost avoidance for the Military Health System (MHS).

Alternative Dosage Form Subclass

- CMA results for the Alternative Dosage Form subclass showed that the 6 PPIs available in these formulations were relatively similar in cost-effectiveness when adjusted for utilization.
- BIA results for the PPI Alternative Dosage Forms showed that designating Nexium packets, Prilosec packets, Protonix packets, and Aciphex sprinkles as UF, and Prevacid ODT and Zegerid packets as NF demonstrated significant cost avoidance for the MHS.

C. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—UF/Tier 4/Not Covered Recommendation

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following formulary recommendations for the Proton Pump Inhibitors as outlined below, based on clinical and cost-effectiveness.

When considering the PPI candidates for Tier 4/not covered status, the P&T Committee considered the information outlined in the interim rule, Section 702(b)(10) of the NDAA 2018 published on December 11, 2018, and found at: <https://www.federalregister.gov/documents/2018/12/11/2018-26562/tricare-pharmacy-benefits-program-reforms>. The interim rule allows for complete exclusion of drugs from TRICARE pharmacy benefit coverage when certain criteria are met. Tier 4 status will apply to all users of the recommended candidates.

Capsules and Tablets Subclass

- UF and step-preferred
 - omeprazole 20 mg and 40 mg capsules (Prilosec, generics)
 - pantoprazole tablets (Protonix, generics)
- UF and non-step-preferred
 - rabeprazole tablets (Aciphex, generics)
 - esomeprazole capsules (Nexium, generics)
- NF and non-step-preferred
 - lansoprazole capsules (Prevacid, generics)
 - omeprazole/sodium bicarbonate capsules (Zegerid, generics)
- This recommendation includes step therapy, which requires a trial of omeprazole or pantoprazole before esomeprazole and rabeprazole and a trial of all the UF step-preferred and non-step preferred products (omeprazole, pantoprazole, rabeprazole and esomeprazole) before lansoprazole or omeprazole/sodium bicarbonate. See PA section below.
- Tier 4/Not Covered
 - dexlansoprazole (Dexilant)—The P&T Committee concluded that dexlansoprazole provides very little to no additional clinical effectiveness relative to the other PPIs; that the risk of use may outweigh any potential benefit including a higher discontinuation rate; and that the FDA reviewer expressed concerns regarding the benefit to risk profile. Overall the P&T Committee felt that that the needs of TRICARE beneficiaries can be met by the other PPIs.
 - esomeprazole strontium—The P&T Committee concluded that the esomeprazole strontium has little clinical data to support its use; has very little or no additional clinical effectiveness relative to the other PPIs and that the needs of TRICARE beneficiaries can be met by the other PPIs.

Alternative Dosage Form Subclass

- UF
 - esomeprazole (Nexium) packet for suspension
 - omeprazole (Prilosec) packet for suspension
 - pantoprazole (Protonix) packet for suspension

- rabeprazole (Aciphex) Sprinkle
- NF
 - lansoprazole ODT (Prevacid ODT)
 - omeprazole/sodium bicarbonate (Zegerid) packet for suspension
- Note that step therapy does not apply to the PPI Alternative Dosage Forms.

D. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—Manual Prior Authorization (PA) Criteria

The PPI class currently has step therapy requirements. The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updated PA criteria for the PPIs. PA criteria are not required for omeprazole or pantoprazole. Updated manual and automated step therapy PA criteria were recommended in new users for rabeprazole and esomeprazole, requiring a trial of either of the preferred products (omeprazole or pantoprazole) first. Additionally, the manual PA criteria for new users of lansoprazole and omeprazole/sodium bicarbonate were updated to require a trial of all of the UF products (omeprazole, pantoprazole, rabeprazole, and esomeprazole) first. Use of the non-preferred PPI is allowed if there is a contraindication, inadequate response, or adverse reaction to the preferred PPI.

The current PA criteria for the Alternative Dosage Forms were also updated. PA criteria are not required for the packets for oral suspension formulations of Prilosec, Nexium, or Protonix, or the Aciphex sprinkles. Manual PA criteria are recommended for Prevacid ODT and Zegerid packets for oral suspension in all new and current users older than age 18. The provider must state why the patient needs an alternative dosage form and why they cannot take all of the formulary alternative dosage forms.

The PA criteria are as follows:

1. Nexium capsules, Aciphex tablets, and generics

Note that prior authorization is not required for omeprazole capsules or pantoprazole tablets.

Manual and Automated PA criteria apply to all new users of esomeprazole (Nexium, generics) and rabeprazole (Aciphex, generics).

Automated PA Criteria: The patient has filled an Rx for generic omeprazole OR generic pantoprazole product at any Military Treatment Facility (MTF), retail network pharmacy, or the mail order pharmacy in the previous 365 days.

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

- Provider acknowledges that omeprazole and pantoprazole are the DoD's preferred agents
 - Provider acknowledges that omeprazole and pantoprazole are Uniform Formulary and do not require prior authorization
 - The patient has a contraindication to omeprazole and pantoprazole
- OR

- The patient has had an inadequate response or had an adverse reaction to omeprazole OR
- The patient has had an inadequate response or had an adverse reaction to pantoprazole

Non-FDA-approved uses are not approved.
PA does not expire.

2. Prevacid capsules and Zegerid capsules

Manual PA and Automated PA criteria apply to all new users of lansoprazole (Prevacid, generics) and omeprazole/sodium bicarbonate (Zegerid, generics).

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

- Provider acknowledges that omeprazole and pantoprazole are the DoD's preferred agents
- Provider acknowledges that omeprazole and pantoprazole are Uniform Formulary and do not require prior authorization
- And the patient meets all four of the following criteria:
 - Has a contraindication, had an inadequate response, or had an adverse reaction to omeprazole

AND

- Has a contraindication, had an inadequate response, or had an adverse reaction to pantoprazole

AND

- Has a contraindication, had an inadequate response, or had an adverse reaction to esomeprazole

AND

- Has a contraindication, had an inadequate response, or had an adverse reaction to rabeprazole

Non-FDA-approved uses are not approved.
PA does not expire.

3. Prevacid ODT and Zegerid packet for suspension

Age edit applies: Patients 18 years and older will be subject to the PA.

Manual PA criteria apply to all new and current users of Prevacid ODT and Zegerid packet for suspension.

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

- Provider acknowledges that omeprazole and pantoprazole tablets and capsules are Uniform Formulary and do not require prior authorization

- Provider acknowledges that omeprazole, esomeprazole, and pantoprazole packets for suspension and rabeprazole sprinkles are Uniform Formulary and do not require prior authorization
- Provider must document patient-specific clinical rationale of why the patient cannot take ALL alternative PPI agents

Non-FDA-approved uses are not approved.
PA does not expire.

E. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—OTC Omeprazole UF Recommendation

OTC omeprazole and omeprazole magnesium tablets and capsules have been included on the TRICARE Pharmacy benefit since the August 2015 DoD P&T Committee meeting, under provisions of 32 CFR 199.21(h)(5). The P&T Committee reviewed the cost and utilization of the OTC PPIs, including omeprazole, at the three points of service (POS). OTC omeprazole is not cost-effective compared to generic prescription formulations of omeprazole and pantoprazole. Low-cost OTC omeprazole is readily available for purchase at several venues (retail pharmacies, commissary, grocery stores, etc.).

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) removing OTC omeprazole and omeprazole magnesium capsules and tablets from the UF, based on cost-effectiveness.

F. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—UF/Tier 4/Not Covered and PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 2 absent) 1) an effective date of the first Wednesday 120 days after signing of the P&T minutes at all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/not covered recommendations and those affected by the removal of PTC omeprazole and omeprazole magnesium from the UF.

III. UF CLASS REVIEWS—PPIS – CAPSULES AND TABLETS AND ALTERNATIVE DOSAGE FORM SUBCLASSES

BAP Comments

A. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—UF/Tier 4/Not Covered Recommendation

The P&T Committee recommended the formulary status for the PPI agents as discussed above.

Capsules and Tablets Subclass

- UF and step-preferred
 - Prilosec capsules, generics
 - Protonix tablets, generics
- UF and non-step-preferred
 - Aciphex tablets, generics

- Nexium capsules, generics
- NF and non-step-preferred
 - Prevacid capsules, generics
 - Zegerid capsules, generics
- This recommendation includes step therapy, which requires a trial of Prilosec or Protonix (for Nexium and Aciphex) and all the UF products (for Prevacid or Zegerid).
- Tier 4/Not Covered
 - Dexilant
 - esomeprazole strontium

Alternative Dosage Forms Subclass

- UF
 - Nexium packet for suspension
 - Prilosec packet for suspension
 - Protonix packet for suspension
 - Aciphex sprinkle
- NF
 - Prevacid ODT
 - Zegerid packet for suspension
- Note that step therapy does not apply to the PPI Alternative Dosage Forms.

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

B. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—Manual PA Criteria

The P&T Committee recommended updates to the current manual PA criteria for new users of Nexium capsules, Aciphex tablets, Prevacid capsules, and Zegerid capsules and new and current users of Prevacid ODT and Zegerid packets for suspension, as discussed previously.

BAP Comment: Concur Non-concur

C. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—OTC Omeprazole UF Recommendation

The P&T Committee recommended removing OTC omeprazole and omeprazole magnesium capsules and tablets from the UF, as discussed above.

BAP Comment: Concur Non-concur

D. PPIs – Capsules and Tablets and Alternative Dosage Form Subclasses—UF/Tier 4/Not Covered and PA Implementation Plan

The P&T Committee recommended 1) an effective date of the first Wednesday 120 days after signing of the P&T minutes at all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/not covered recommendations and OTC omeprazole removal from the UF.

BAP Comment: Concur Non-concur

IV. PULMONARY ARTERIAL HYPERTENSION (PAH) AGENTS – PROSTACYCLINS, ENDOTHELIN RECEPTOR ANTAGONISTS (ERAS), AND NITRIC OXIDE DRUGS

P&T Comments

A. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—Relative Clinical Effectiveness Analysis and Conclusion

Background—The P&T Committee reviewed the clinical effectiveness of the PAH agents, which are divided into the three subclasses outlined below. The class was last reviewed in February 2015. The intravenous prostacyclins (e.g., Flolan and Remodulin) and PDE-5 inhibitors indicated for erectile dysfunction (e.g., Viagra and Cialis) were not included in the review.

- **Endothelin Receptor Antagonists (ERAs):** bosentan (Tracleer), ambrisentan (Letairis, generics), and macitentan (Opsumit);
- **Prostacyclins:** treprostinil nebulized solution (Tyvaso), iloprost nebulized solution (Ventavis), treprostinil extended-release oral tablets (Orenitram ER), and selexipag tablets (Uptravi);
- **Nitric Oxide Drugs:** the soluble guanylate cyclase stimulator, riociguat (Adempas) and the PDE-5 inhibitors sildenafil (Revatio, generics) and tadalafil (Adcirca, Alyq, generics).

The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

Guidelines

- Guidelines from the 6th World Symposium on PAH were updated in 2019. Key findings include the following:
 - Utilizing risk assessment to determine whether to start initial monotherapy or combination therapy in treatment-naïve patients.
 - Initial combination therapy is recommended for most patients with World Health Organization (WHO) Group 1 PAH; however, initial monotherapy may be considered for select patients.
 - Clinical trial design in PAH is shifting primary endpoints from a short-term correlate such as six-minute walk distance (6MWD) to long-term clinical efficacy measures such as clinical worsening or clinical failure.
- There are no head-to-head studies between the PAH agents in the individual drug subclasses. Comparative efficacy is limited to indirect comparisons, systematic reviews, and meta-analyses.

Endothelin Receptor Antagonists (ERAs)

- There is insufficient evidence to suggest one ERA is superior to another in terms of efficacy.
- Ambrisentan (Letairis) and macitentan (Opsumit) have the advantage of once daily dosing, while bosentan is dosed twice daily.
- Generic formulations of ambrisentan (Letairis) are available.
- Data supporting combination therapy with an ERA and a PDE-5 inhibitor is available with Letairis in treatment-naïve patients (AMBITION trial) and Opsumit in treatment-experienced patients (SERAPHIN trial). Benefits of combination therapy include an improvement in the composite endpoint of time to clinical failure (AMBITION trial), and reduced morbidity/mortality versus placebo or reduced hospitalization versus background therapy (SERAPHIN trial).
- Letairis may cause peripheral edema, while bosentan (Tracleer) has a higher risk of hepatic impairment and requires liver function test (LFT) monitoring.
- All of the ERAs require a Risk Evaluation and Mitigation Strategies (REMS) program for embryo-fetal toxicity (pregnancy category X rating).

Prostacyclins

- There is insufficient evidence to suggest one oral prostacyclin is superior to another in terms of efficacy. The oral prostacyclins (Uptravi and Orenitram) have advantages over the inhaled agents (Tyvaso and Ventavis), including ease of administration and less frequent dosing, which has resulted in reduced MHS utilization of the inhaled agents.
- Oral selexipag (Uptravi) in the GRIPHON trial showed a 40% reduction in the occurrence of the primary composite endpoint, which included mortality.
- Results from the FREEDOM-EV study showed that early addition of oral treprostinil (Orenitram ER) in patients receiving one oral background PAH agent significantly delayed disease progression.
- An Agency for Healthcare Research and Quality (AHRQ) systematic review (2013) evaluated the association of adverse reactions (ADRs) with the various PAH drug classes. Inhaled prostacyclins are likely to be associated with ADRs such as headaches, cough, jaw pain, and flushing. With the exception of cough, similar ADRs are seen with the oral prostacyclins.

Nitric Oxide Drugs

- The PAH nitric oxide agents differ in indication, dosing frequency, and pregnancy risk.
- Riociguat (Adempas) is the only soluble guanylate cyclase stimulator, is dosed three times daily, has an additional indication for chronic thromboembolic pulmonary hypertension (CTEPH), and requires a REMS due to a pregnancy category X rating.
- For the PDE-5 inhibitors, sildenafil 20 mg is dosed three times daily and tadalafil is dosed as two 20 mg tablets once daily.
- A Cochrane review (2016) of riociguat (Adempas) showed improved 6MWD; however, the results were not statistically significant. Riociguat did reduce pulmonary artery pressures. No significant differences were seen in the endpoints of mortality, change in functional class, or clinical worsening.
- Concomitant use of riociguat (Adempas) and the PDE-5 inhibitors should be avoided due to additive adverse reactions.

Overall Conclusion

- The choice of the PAH drug depends on a variety of factors including FDA-approved indication, labeling, mechanism of action, route of administration, side effect profile, drug interactions, patient preference, and physician experience.

B. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—Relative Cost-Effectiveness Analysis and Conclusion

The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA results by formulary subclass showed that ambrisentan (Letairis) was the most cost-effective ERA followed by macitentan (Opsumit) and bosentan (Tracleer); riociguat (Adempas) was the least cost-effective nitric oxide drug; treprostinil (Tyvaso) was the most cost-effective nebulized prostacyclin, followed by iloprost

(Ventavis); and treprostinil (Orenitram ER) was the most cost-effective oral prostacyclin followed by selexipag (Uptravi).

- BIA was performed to evaluate the potential impact of designating selected agents as formulary or non-formulary on the uniform formulary. BIA results found that designating all the PAH drugs as formulary on the uniform formulary demonstrated cost avoidance for the MHS.

C. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—UF Recommendation

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following for the PAH agents, as outlined below, based on clinical and cost-effectiveness:

Endothelin Receptor Antagonists (ERAs)

- UF
 - bosentan (Tracleer)
 - ambrisentan (Letairis, generics)
 - macitentan (Opsumit)

Prostacyclins

- UF
 - treprostinil nebulized solution (Tyvaso)
 - iloprost nebulized solution (Ventavis)
 - treprostinil extended-release oral tablets (Orenitram ER)
 - selexipag (Uptravi)

Nitric Oxide Drugs

- UF and step-preferred
 - sildenafil 20 mg tablets (Revatio, generics)
- UF and non-step-preferred
 - tadalafil 20 mg (Adcirca, Alyq, generics)
 - riociguat (Adempas)
- For the nitric oxide drugs, note that this recommendation includes step therapy, which requires a trial of sildenafil 20 mg generic in all new users of tadalafil (Adcirca, Alyq, generics) or riociguat (Adempas).
- Note that sildenafil 10 mg/mL oral suspension is also UF, but not part of the step therapy requirements for the other nitric oxide drugs.
- Note that for all the PAH drugs, no products were recommended for NF status.

D. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—Manual PA Criteria

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) new manual PA criteria in new users for the ERAs (bosentan [Tracleer], ambrisentan [Letairis], and macitentan [Opsumit]) and the prostacyclins (inhaled iloprost [Ventavis], inhaled treprostinil [Tyvaso], oral treprostinil [Orenitram ER], and selexipag [Uptravi]). Updated step therapy and manual PA criteria were recommended in new users for riociguat (Adempas) and tadalafil (Adcirca, Alyq, and generics) requiring a trial of sildenafil 20 mg.

1. Letairis brand and Opsumit

Manual PA criteria apply to new users of Letairis or Opsumit.

Manual PA Criteria: Letairis or Opsumit is approved if all criteria are met:

- Prescribed by or in consultation with a cardiologist or a pulmonologist
- Patient has documented diagnosis of WHO group 1
 - Patient has had a right heart catheterization (documentation required)
 - Results of the right heart catheterization confirm the diagnosis of World Health Organization (WHO) group 1 PAH
- Patient and provider are enrolled in the Letairis or Opsumit REMS program
- Patient is not pregnant
- Women of childbearing potential must use adequate contraception
- Patient has no history of liver function test (LFT) elevations on previous endothelin receptor antagonist (ERA) therapy accompanied by signs or symptoms of liver toxicity or increases in bilirubin greater than two times the upper limit of normal
- Patient does not have moderate or severe liver impairment (e.g., Child-Pugh Class B or C)

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

2. Generic ambrisentan

Manual PA criteria apply to new and current users of generic ambrisentan.

Manual PA Criteria: Ambrisentan generics are approved if all criteria are met:

- The brand Letairis formulation is the preferred product over generic Letairis (ambrisentan) and is covered at the lowest copayment, which is the generic formulary copayment for non-Active Duty patients and at no cost-share for Active Duty patients. Although Letairis is a branded product, it will be covered at the generic formulary copayment or cost-share.
 - The provider must document a patient-specific justification as to why the brand Letairis product cannot be used in this patient:
-

- AND the patient must meet the criteria for Letairis:
- Prescribed by or in consultation with a cardiologist or a pulmonologist
- Patient has documented diagnosis of WHO group 1 PAH
 - Patient has had a right heart catheterization (documentation required)
 - Results of the right heart catheterization confirm the diagnosis of WHO group 1
- Patient and provider are enrolled in the ambrisentan REMS program
- Patient is not pregnant
- Women of childbearing potential must use adequate contraception
- Patient has no history of liver function test (LFT) elevations on previous endothelin receptor antagonist (ERA) therapy accompanied by signs or symptoms of liver toxicity or increases in bilirubin greater than two times the upper limit of normal.
- Patient does not have moderate or severe liver impairment (e.g., Child-Pugh Class B or C)

Non-FDA-approved uses are not approved.
Prior authorization does not expire.

3. Tracleer

Manual PA criteria apply to new users of Tracleer.

Manual PA Criteria: Tracleer is approved if all criteria are met:

- Prescribed by or in consultation with a cardiologist or a pulmonologist
- Patient has diagnosis of WHO group 1 or 4 (see below)
- Patient has documented diagnosis of WHO group 1
 - Patient has had a right heart catheterization (documentation required)
 - Results of the right heart catheterization confirm the diagnosis of WHO group 1 OR
- Patient has documented diagnosis of Chronic Thromboembolic Pulmonary Hypertension (CTEPH) (WHO group 4) and the patient has tried Adempas or has a contraindication to Adempas
- Patient and provider are enrolled in the Tracleer REMS program
- Patient is not pregnant
- Women of childbearing potential must use adequate contraception
- Patient does not have baseline elevated aminotransferases greater than three times the upper limit of normal due to difficulty in monitoring for hepatotoxicity
- Patient does not have moderate or severe liver impairment (e.g., Child-Pugh Class B or C)

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

4. Ventavis and Tyvaso

Manual PA criteria apply to new users of Ventavis or Tyvaso.

Manual PA Criteria: Ventavis or Tyvaso is approved if all criteria are met:

- Prescribed by or in consultation with a cardiologist or a pulmonologist
- Patient has documented diagnosis of WHO group 1 PAH
 - Patient has had a right heart catheterization (documentation required)
 - Results of the right heart catheterization confirm the diagnosis of WHO group 1 PAH

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

5. Uptravi and Orenitram ER

Manual PA criteria apply to new users of Uptravi or Orenitram ER.

Manual PA Criteria: Uptravi or Orenitram ER is approved if all criteria are met:

- Prescribed by or in consultation with a cardiologist or a pulmonologist
- Patient has documented diagnosis of WHO group 1 PAH
 - Patient has had a right heart catheterization (documentation required)
 - Results of the right heart catheterization confirm the diagnosis of WHO group 1 PAH
- Patient meets one of the following criteria
 - The patient has tried one oral therapy for PAH from one of the three following different categories (either alone or in combination) each for ≥ 60 days: one PDE-5 inhibitor (tadalafil or sildenafil), one ERA (Letairis, Opsumit, or Tracleer), or Adempas; OR
 - The patient has tried one prostacyclin therapy (oral, IV, or nebulized)

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

6. Adempas

Manual PA criteria apply to new users of Adempas.

Manual PA Criteria: Adempas is approved if all criteria are met:

- Prescribed by or in consultation with a cardiologist or a pulmonologist
- Patient has a documented diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) WHO Group 4 PAH

- OR
- Patient has documented diagnosis of WHO group 1 PAH
 - Patient has had a right heart catheterization (documentation required)
 - Results of the right heart catheterization confirm the diagnosis of WHO group 1 PAH
- Patient has had an adequate trial of sildenafil 20 mg (Revatio, generics) and failed or did not respond to therapy AND
- Patient has had an adequate trial of tadalafil 40 mg (Adcirca, generics) and failed or did not respond to therapy AND
- Patient is not receiving PDE-5 inhibitors or nitrates concomitantly

Non-FDA-approved uses are not approved.
Prior authorization does not expire.

7. Adcirca, Alyq, and generics

Manual PA criteria apply to new users of tadalafil 20 mg (Adcirca, generics) and Alyq.

Manual PA Criteria: Tadalafil 20 mg (Adcirca, generics) or Alyq is approved if all criteria are met:

- Prescribed by or in consultation with a cardiologist or a pulmonologist
- Patient has documented diagnosis of WHO group 1 PAH
 - Patient has had a right heart catheterization (documentation required)
 - Results of the right heart catheterization confirm the diagnosis of WHO group 1 PAH
- Patient has had an adequate trial of sildenafil 20 mg (Revatio, generics) and failed or did not respond to therapy and
- Patient is not receiving other PDE-5 inhibitors, nitrates, or riociguat (Adempas) concomitantly

Non-FDA-approved uses are not approved.
Prior authorization does not expire.

E. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—Brand over Generic Requirement for ambrisentan (Letairis) and PA Criteria

TRICARE Policy requires dispensing of generic products at the Retail Network and Mail Order Pharmacy. However, pricing for the branded Letairis is more cost-effective than the AB-rated generic formulations for ambrisentan, which were launched in March 2019. Therefore, branded Letairis 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 P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) requiring brand Letairis over generic ambrisentan in all new and current users, based on cost effectiveness. The prescriber will provide patient-specific justification as to why branded Letairis cannot be used. The Tier 1 (generic) copayment will apply to brand Letairis. The “brand over generic” requirement will be removed administratively when it is no longer cost-effective compared to the AB-rated generics.

F. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—Brand Letairis Copayment Change

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) lowering the current cost-share for the endothelin receptor antagonist Letairis to the generic Tier 1 cost-share.

The authority for this recommendation is codified in 32 CFR 199.21(j)(3), which states that "when a blanket purchase agreement, incentive price agreement, Government contract, or other circumstances results in a brand pharmaceutical agent being the most cost effective agent for purchase by the Government, the P&T Committee may also designate that the drug be cost-shared at the generic rate."

G. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—UF and PA Implementation Plan

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) an effective date of the first Wednesday 90 days after the signing of the minutes in all points of service (POS).

V. PAH AGENTS – PROSTACYCLINS, ERAS, AND NITRIC OXIDE DRUGS

BAP Comments

A. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—UF Recommendation

The P&T Committee recommended the formulary status, as stated above.

Prostacyclins

- UF
 - Tyvaso nebulized solution
 - Ventavis nebulized solution
 - Orenitram ER tablets
 - Upravi tablets

Endothelin Receptor Antagonists (ERAs)

- UF
 - Tracleer tablets
 - Letairis tablets, generics
 - Opsumit tablets

Nitric Oxide Drugs

- UF and step-preferred
 - Revatio tablets, generics
- UF and non-step-preferred
 - Adcirca tablets, Alyq tablets, generics
 - Adempas tablets

BAP Comment: Concur Non-concur

B. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—Manual PA Criteria

The P&T Committee recommended updates to manual PA criteria for Letairis, Opsumit, generic ambrisentan, Tracleer, Ventavis, Tyvaso, Uptravi, Orenitram ER, Adempas, Adcirca, Alyq, and tadalafil generics, as discussed above.

BAP Comment: Concur Non-concur

C. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—Brand over Generic Requirement for ambrisentan (Letairis) and PA Criteria

The P&T Committee recommended requiring brand Letairis over generic ambrisentan in all new and current users, as discussed above.

BAP Comment: Concur Non-concur

D. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—Brand Letairis Copayment Change

The P&T Committee recommended lowering the current cost-share for Letairis to the generic Tier 1 cost-share.

BAP Comment: Concur Non-concur

E. PAH Agents – Prostacyclins, ERAs, and Nitric Oxide Drugs—UF and PA Implementation Plan

The P&T Committee recommended an effective date of the first Wednesday 90 days after the signing of the minutes in all points of service (POS).

BAP Comment: Concur Non-concur

VI. NEWLY APPROVED DRUGS PER 32 CFR 199.21(G)(5)

P&T Comments

A. Newly Approved Drugs per 32 CFR 199.21(g)(5)—Relative Clinical Effectiveness and Relative Cost-Effectiveness Conclusions

The P&T Committee agreed (17 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 32 CFR 199.21(g)(5)—UF Recommendation

The P&T Committee recommended (group 1: 17 for, 0 opposed, 0 abstained, 1 absent; group 2: 18 for, 0 opposed, 0 abstained, 0 absent; Tirosint-SOL: 10 for, 7 opposed, 1 abstained, 0 absent) the following:

- UF:
 - cladribine (Mavenclad) – Multiple Sclerosis Agents: Oral Agents
 - epinephrine injection (Symjepi) – Respiratory Agents Miscellaneous
 - levodopa inhalation powder (Inbrija) – Parkinson’s Agents
 - levothyroxine sodium oral solution (Tirosint-SOL) – Thyroid and Antithyroid Agents
 - loteprednol etabonate 0.38% ophthalmic gel (Lotemax SM) – Anti-inflammatory Immunomodulatory Ophthalmic Agents: Ophthalmic Anti-inflammatory Agents
 - netarsudil 0.02%/latanoprost 0.005% ophthalmic solution (Rocklatan) – Glaucoma Agents

- siponimod (Mayzent) – Multiple Sclerosis Agents: Oral Miscellaneous
- stiripentol (Diacomit) – Anticonvulsants-Antimania Agents
- tacrolimus oral suspension (Prograf) – Immunosuppressives
- NF:
 - benzhydrocodone/acetaminophen (Apadaz) – Narcotic Analgesics and Combinations
 - estradiol 1 mg/progesterone 100 mg capsules (Bijuva) – Gynecological Agents Miscellaneous
 - meloxicam ODT (Qmiiz ODT) – Pain Agents: NSAID
 - prucalopride (Motegrity) – Gastrointestinal-2 Agents: Chronic Idiopathic Constipation (CIC) and Irritable Bowel Syndrome Constipation-Predominant (IBS-C)

C. Newly Approved Drugs per 32 CFR 199.21(g)(5)—PA Criteria

The P&T Committee recommended (group 1: 17 for, 0 opposed, 0 abstained, 1 absent; group 2: 18 for, 0 opposed, 0 abstained, 0 absent; Tirosint-SOL: 10 for, 7 opposed, 1 abstained, 0 absent) the following:

- Applying the same manual PA criteria for Rocklatan in new users as is currently in place for Rhopressa.
- Applying manual PA criteria to new and current users of Mavenclad, Mayzent, Motegrity, and Qmiiz ODT.
- Applying manual PA criteria to new users of Inbrija.
- Applying an automated age edit to new and current users of Tirosint-SOL and new users of Prograf solution. Patients younger than 6 years for Tirosint solution and younger than 12 years for Prograf solution will not be subject to the PA.

Full PA Criteria for the Newly Approved Drugs per 32 CFR 199.21(g)(5)

1. cladribine (Mavenclad)

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

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

- Prescribed by a neurologist
- Patient has a documented diagnosis of one of the following:
 - Relapsing-Remitting Multiple Sclerosis
 - Active Secondary Progressive Multiple Sclerosis
- Patient is not currently using a disease-modifying therapy (DMT)
- Patient has failed another DMT
- Mavenclad is not used in patients with:

- Current malignancy
- Pregnant women or breastfeeding
- Men and women of reproductive potential who do not plan to use effective contraception during treatment and 6 months after the last dose
- Active chronic infection (e.g., hepatitis, tuberculosis, or HIV infection)
- Monitoring for hematological and lymphocytic parameters will occur before, during, and after treatment

Non-FDA-approved uses are not approved.
Prior authorization does not expire.

2. levodopa inhalation powder (Inbrija)

Manual PA criteria apply to all new users.

Manual PA Criteria: Inbrija will be approved if all criteria are met:

- Age \geq 18 years
- Patient has a diagnosis of Parkinson's disease
- Inbrija is prescribed by or in consultation with a neurologist
- Patient continues to experience wearing off periods, despite optimizing carbidopa/levodopa therapy (e.g., increasing the dose or increasing the frequency of dosing)
- Patient is currently taking and will continue taking carbidopa-levodopa therapy
- Inbrija is not being used concomitantly with, or within 2 weeks of, a non-selective monoamine oxidase (MAO) inhibitor (e.g., phenelzine, tranylcypromine, isocarboxazid, hydracarbazine)
- Patient does not have chronic underlying pulmonary disease (e.g., asthma, COPD)

Non-FDA-approved uses are not approved.
Prior authorization expires in one year.

Renewal Criteria: PA will be renewed indefinitely if the patient:

- Has had a documented reduction in motor symptoms associated with "off" periods of Parkinson's disease, and
- Is not taking an MAO inhibitor, and does not have a chronic underlying pulmonary disease (e.g., asthma, COPD).

3. levothyroxine sodium solution (Tirosint-SOL)

PA does not apply to patients younger than 6 years of age (age edit)

PA criteria apply to all new and current users of Tirosint-SOL 6 years of age and older.

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

- Patient is not able to chew a levothyroxine tablet
- Patient is not able to swallow a capsule or tablet
- Drug is prescribed by or in consultation with an endocrinologist

Non-FDA-approved uses are not approved.

PA expires after 12 months. No renewal allowed; must fill out a new PA.

4. meloxicam orally disintegrating tablets (ODT) (Qmiiz ODT)

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

Manual PA Criteria: Coverage for Qmiiz will be approved if:

- Note: Multiple formulary NSAIDs, including meloxicam oral tablets, are available for DoD beneficiaries without a PA.
- The provider must state the clinical rationale of why patient cannot take any of the formulary NSAIDs: _____

Non-FDA-approved uses are not approved.

Prior authorization expires in one year.

Renewal criteria – No renewal criteria. PA will be renewed for an additional year if a new PA form is completed.

5. netarsudil 0.02%/latanoprost 0.005% ophthalmic solution (Rocklatan)

Manual PA criteria apply to all new users of Rocklatan.

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

- Written by an ophthalmologist or an optometrist
- Patient has had a trial of appropriate duration of 2 different formulary options from different drug classes in combination or separately and has not reached intraocular pressure (IOP) target goals
 - Prostaglandin analogs
 - Beta-blockers
 - Alpha 2-adrenergic agonists
 - Topical carbonic anhydrase inhibitors

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

6. prucalopride (Motegrity)

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

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

- Patient is ≥ 18 years of age
- Patient has tried and failed all formulary agents including Amitiza, Linzess, and Trulance
- Patient has documented symptoms for ≥ 3 months
- Patient has diagnosis of chronic idiopathic constipation (CIC)
- Patient does not have a GI obstruction
- Patient has no history of suicidal ideation
- Patient has low cardiovascular risk
- Patient has documentation of failure of an increase in dietary fiber/dietary modification
- Patient has tried at least 2 standard laxative classes or has an intolerance or FDA-labeled contraindication to at least 2 standard laxative classes defined as
 - osmotic laxative (e.g., lactulose, sorbitol, magnesium [Mg] citrate, Mg hydroxide, glycerin rectal suppositories)
 - bulk forming laxative (e.g., psyllium, oxidized cellulose, calcium polycarbophil) with fluids;
 - stool softener (e.g., docusate);
 - stimulant laxative (e.g., bisacodyl, sennosides)
- Patient is not taking any of these agents concomitantly (Amitiza, Linzess, Trulance, Symproic, Relistor, Movantik)

Non-FDA-approved uses are not approved.

Initial Expiration date: 1 year; Renewal PA (continuation): 1 year

Renewal PA Criteria: Motegrity will be approved for an additional 12 months if the following are met:

- Patient has had improvement in constipation symptoms
- Patient is not taking any of these agents concomitantly (Amitiza, Linzess, Trulance, Symproic, Relistor, Movantik)
- Patients are monitored for suicidal risk

7. siponimod (Mayzent)

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

Manual PA criteria: Coverage will be approved if all criteria are met:

- Prescribed by a neurologist
- A documented diagnosis of one of the following:
 - Clinically Isolated Syndrome
 - Relapsing-Remitting Multiple Sclerosis
 - Active Secondary Progressive Multiple Sclerosis
- Patient is not currently using another disease-modifying therapy (DMT)
- Patient has not failed an adequate course of fingolimod (Gilenya)
- All recommended Mayzent monitoring has been completed, and patient will be monitored throughout treatment as recommended in the label. Monitoring includes complete blood count (CBC), liver function tests (LFT), varicella zoster virus (VZV) antibody serology, genotyping of CYP2C9, electrocardiogram (ECG), and macular edema screening.
- In patients with CYP2C9 *1/*3 or *2/*3 maintenance dosing will be 1 mg daily
- Mayzent will not be used in patients with a CYP2C9 *3/*3 genotype
- Mayzent will not be used in patients with significant cardiac history, including:
 - Patients with a recent history (within the past 6 months) of class III/IV heart failure, myocardial infarction, unstable angina, stroke, transient ischemic attack, or decompensated heart failure requiring hospitalization
 - Patients with a history or presence of Mobitz type II second-degree or third-degree atrioventricular (AV) block or sick sinus syndrome, unless a functioning pacemaker is inserted

Non-FDA-approved uses are not approved.
Prior authorization does not expire.

8. tacrolimus oral suspension (Prograf)

PA does not apply to patients younger than 12 years of age (age edit).

PA criteria apply to all new users of Prograf solution 12 years of age and older.

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

- Prescribed by or in consultation with a transplant specialist AND
- Has severe dysphagia (e.g., severe esophagitis, mucositis) or is completely unable to swallow (e.g., has G-tube) OR
- Patient is < 18 years old and has difficulty swallowing tablets/capsules

Applies to new users (grandfathering allowed).
PA does not expire.

D. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF and PA Implementation Plan

The P&T Committee recommended (group 1: 17 for, 0 opposed, 0 abstained, 1 absent; group 2: 18 for, 0 opposed, 0 abstained, 0 absent) an effective date upon the first Wednesday two weeks after the signing of the minutes in all points of service.

VII. NEWLY APPROVED DRUGS PER 32 CFR 199.21(G)(5)

BAP Comments

A. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF Recommendation

The P&T Committee recommended the formulary status for the new drugs as stated previously.

- UF:
 - Mavenclad
 - Symjepi
 - Inbrija
 - Tirosint-SOL
 - Lotemax SM
 - Rocklatan
 - Mayzent
 - Diacomit
 - Prograf
- NF:
 - Apadaz
 - Bijuva
 - Qmiiz ODT
 - Motegrity

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

B. Newly Approved Drugs per 32 CFR 199.21(g)(5)—PA Criteria

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

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

C. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF and PA Implementation Plan

The P&T Committee recommended an effective date upon the first Wednesday two weeks after the signing of the minutes in all points of service.

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

VIII. UTILIZATION MANAGEMENT—NEW MANUAL PA CRITERIA

P&T Comments

A. New PA Criteria

New manual PA criteria were recommended for the following drugs, which will be discussed below.

- 1. NEWLY APPROVED DRUGS NOT SUBJECT TO 32 CFR 199.21(g)(5):
Antihistamine-1: First generation and combinations – Carbinoxamine maleate 6 mg tablets (Ryvent, generics) and Carbinoxamine maleate 4 mg/5 mL ER oral suspension (Karbinal ER)**

Carbinoxamine 6 mg tablets and 4 mg/5 mL ER oral suspension are new drugs approved via the Abbreviated New Drug Application (ANDA) pathway and thus do not qualify for review by the DoD P&T Committee under the innovator program or new drug reviews. These ANDA-approved products contain ingredients that are currently available in generic products or were included in formulations previously removed from the market.

Carbinoxamine maleate is a first-generation antihistamine and is available in 4 mg and 6 mg generic tablets, 6 mg brand tablets (Ryvent), 4 mg/5 mL immediate release oral solution, and a 4 mg/5 mL ER suspension (Karbinal ER). The 6 mg brand and generic

tablets and 4 mg/5 mL ER suspension are not cost-effective relative to the generic 4 mg tablets and 4 mg/5 mL IR oral solution. Cost-effective generic formulations of carbinoxamine 4 mg oral tablets and IR solution are available on the UF without a PA required, and low-cost OTC tablet formulations for diphenhydramine, fexofenadine, or dimenhydrinate tablets and low-cost OTC liquid formulations for diphenhydramine, fexofenadine, or loratadine are widely available.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for carbinoxamine 6 mg tablets (Ryvent and generics) and carbinoxamine 4 mg/5 mL ER oral suspension (Karbinal ER) in new and current users, due to the significant cost differences and lack of clinically compelling benefits over generic alternatives.

The manual PA criteria are as follows:

Manual PA criteria apply to all new and current users of carbinoxamine 6 mg tablets (Ryvent brand and generics) and 4 mg/5 mL ER oral suspension (Karbinal ER).

Note: Carbinoxamine generic IR liquid and 4 mg tablets are available without a PA; providers are encouraged to consider changing the prescription to generic IR liquid or 1 or 2 of the 4 mg tablets.

Coverage for carbinoxamine 6 mg tablets (Ryvent brand and generics) or Karbinal ER suspension will be approved if:

- This agent has been identified as having cost-effective alternatives. Please describe why this drug is required as opposed to available alternatives.
_____ (blank write in)

Non-FDA-approved uses are not approved.
Prior authorization does not expire.

2. Insulins: Rapid Acting Agents: generic insulin lispro (authorized generic for Humalog)

An authorized generic for Humalog entered the market in April 2019. An “authorized generic” is the brand company's own product repackaged and marketed as a generic drug. An authorized generic is considered therapeutically equivalent to the name brand drug because it is the same drug. The FDA does not consider authorized generics as AB-rated generic formulations.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for the authorized generic insulin lispro in new and current users, requiring a trial of branded Humalog, due to cost-effectiveness. The PA requirement will be removed when it is no longer cost advantageous.

The manual PA criteria are as follows:

Manual PA criteria apply to all new and current users of insulin lispro (authorized generic for Humalog). Coverage is approved if all criteria are met:

- Note: Brand Humalog is the preferred insulin lispro product in the DoD. If the prescription is for Humalog, prior authorization is not required.
- Please provide a patient-specific justification as to why the brand Humalog product cannot be used _____ (blank write in)

Non-FDA-approved uses are not approved.
PA does not expire.

3. Oral Oncologic Agents: niraparib (Zejula), olaparib (Lynparza), and rucaparib (Rubraca)

PA criteria have not previously been required for the ovarian cancer drugs (PARP inhibitors). The P&T Committee reviewed three oral oncologic agents, Zejula, Lynparza, and Rubraca. PA criteria were recommended for these three products in new users, in order to assure prescribing in accordance with FDA-approved indications or a National Comprehensive Cancer Network (NCCN) Guideline-endorsed indication.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) manual PA criteria for new users.

a) niraparib (Zejula)

Manual PA criteria apply to all new users of Zejula.

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

- Zejula is prescribed by or in consultation with a hematologist/oncologist
- Patient is 18 years of age or older
- Patient has a deleterious or suspected deleterious BRCA mutation as detected by an FDA-approved test
- Zejula will be prescribed as a maintenance therapy for one of the following diagnoses:
 1. Recurrent epithelial ovarian cancer, fallopian tube or primary peritoneal cancerAND
 2. Patient has received 2 or more lines of platinum-based chemotherapy AND
 3. Patient was in objective response (either complete or partial) to most recent treatment regimen AND
 4. Zejula will not be combined with bevacizumab (Avastin)OR

- The diagnosis is NOT listed above but is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, the provider must list the diagnosis: _____.
- Female patients are not pregnant or planning to become pregnant and will take highly effective contraception while taking Zejula and for 6 months after the last dose.

Other non-FDA-approved uses are not approved.
Prior authorization does not expire.

b) olaparib (Lynparza)

Manual PA criteria apply to all new users of Lynparza.

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

- Lynparza is prescribed by or in consultation with a hematologist/oncologist
- Patient is 18 years of age or older
- Patient has a deleterious or suspected deleterious BRCA mutation as detected by an FDA-approved test
- Patient will use Lynparza as either treatment or maintenance therapy for one or more of the following diagnoses:
 - a) Recurrent or Stage IV Triple negative breast cancer OR
 - b) Recurrent or Stage IV hormone receptor (+) (ER, PR, or both) HER2 (-) breast cancer AND the patient was either:
 - Previously treated with prior endocrine therapy OR
 - The patient was not an appropriate candidate for endocrine therapy OR
 - c) Recurrent advanced ovarian cancers (either platinum-sensitive or platinum-resistant), fallopian tube or primary peritoneal cancers AND
 - Patient has received at least 3 prior lines of therapy
 - Lynparza will be used as a single agent
- Lynparza will be prescribed as maintenance therapy for one of the following diagnoses:
 - a) Platinum-sensitive, relapsed, epithelial ovarian cancer, fallopian tube or primary peritoneal cancer AND
 - Patient has received 2 or more lines of platinum-based chemotherapy
 - Patient was in objective response (either complete or partial) to most recent treatment regimen

- Lynparza will not be combined with bevacizumab (Avastin) OR

b) Newly diagnosed, advanced, high-grade, epithelial ovarian cancer, fallopian tube or primary peritoneal cancer AND

- Patient has had a complete or partial response to primary therapy with a platinum-based therapy
- Lynparza will not be combined with bevacizumab (Avastin)

OR

- The diagnosis is NOT listed above but is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, the provider must list the diagnosis: _____.

- Female patients are not pregnant or planning to become pregnant and will take highly effective contraception while taking Lynparza and for 6 months after the last dose.

Other non-FDA-approved uses are not approved.
Prior authorization does not expire.

c) rucaparib (Rubraca)

Manual PA criteria apply to all new users of Rubraca.

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

- Rubraca is prescribed by or in consultation with a hematologist/oncologist
- Patient is 18 years of age or older
- Patient has a deleterious BRCA mutation as detected by an FDA-approved test
- Rubraca will be prescribed for one of the following:
 - a) Treatment of recurrent, high-grade, epithelial ovarian cancer (platinum-sensitive or platinum-resistant), fallopian tube or primary peritoneal cancer AND
 - Patient has received at least 2 prior lines of therapy
 - Rubraca will be used as a single agent
 - b) Maintenance of relapsed platinum-sensitive ovarian cancer, fallopian tube or primary peritoneal cancer AND
 - Patient has received 2 or more lines of platinum-based chemotherapy

- Patient was in objective response (either complete or partial) to most recent treatment regimen
- Rubraca will not be combined with bevacizumab (Avastin)

c) Newly diagnosed, advanced, high-grade, ovarian cancer, fallopian tube or primary peritoneal cancer AND

- Patient has had a complete or partial response to primary therapy with a platinum-based therapy
- Rubraca will not be combined with bevacizumab (Avastin)

OR

- The diagnosis is NOT listed above but is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. If so, please list the diagnosis: _____.

- Female patients are not pregnant or planning to become pregnant and will take highly effective contraception while taking Rubraca and for 6 months after the last dose.

Other non-FDA-approved uses are not approved.
Prior authorization does not expire.

B. New PA Criteria—PA Implementation

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) new PAs for carbinoxamine 6 mg tablets (Ryvent, generics), Karbinal ER suspension, Rubraca, Lynparza, and Zejula become effective 90 days after the signing of the minutes. DHA will send letters to beneficiaries affected by the new PA requirements for carbinoxamine 6 mg tablets (Ryvent, generics) and Karbinal ER if applicable, as new and current users will be subject to the PA.

IX. UTILIZATION MANAGEMENT—NEW MANUAL PA CRITERIA

BAP Comments

A. New Manual PA Criteria

The P&T Committee recommended new manual PA criteria for the drugs discussed above.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p>
--

B. New Manual PA Criteria—PA Implementation Plan

The P&T Committee recommended the new PA criteria for the drugs discussed above become effective 90 days after the signing of the minutes.

BAP Comment: Concur Non-concur

X. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA

P&T Comments

A. Updated PA 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. The updated manual PAs outlined below will apply to new users.

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) updates to the manual PA criteria for Qsymia, the weight loss agents, Dupixent, Xeljanz/Xeljanz XR, Cimzia, Humira, and Imbruvica. All updated PA criteria apply to new users of these agents.

The updates are as follows:

- 1. Corticosteroids: Immune Modulators – Atopic Dermatitis Subclass – dupilumab (Dupixent)**—Manual PA criteria were originally recommended for Dupixent for atopic dermatitis during the May 2017 P&T Committee meeting. The Dupixent PA was then updated to reflect the additional FDA-approved indication for asthma in November 2018. In February and May 2019, the FDA lowered the age for both asthma and atopic dermatitis down to 12 years. The P&T Committee updated the PA to reflect the lower age allowance and also lowered the baseline eosinophils requirement from 300 cells/mcL to 150 cells/mcL, as some benefit was seen at the lower range in the clinical trial.
- 2. Oral Oncologic Agents**—Ibrutinib (Imbruvica) is an oral oncology agent that was designated as UF prior to the Innovator Rule established in August 2015. In May 2018, the P&T Committee recommended PA criteria for both the tablets and capsules. The committee reviewed the NCCN Guidelines and updated the PA to include an allowance for an additional indication that carries a Grade 1, 2A, or 2B recommendation from the NCCN Guidelines.
- 3. Targeted Immunomodulatory Biologics (TIBs): certolizumab (Cimzia) and adalimumab (Humira)**—Cimzia was granted a new FDA indication in March 2019 for non-radiographic axial spondyloarthritis with objective signs of inflammation (nr-ax SpA). Nr-ax SpA is a subtype of spondyloarthritis, a spectrum of disease that also

includes ankylosing spondylitis. Guidelines from the Assessment of SpondyloArthritis international Society (ASAS)/European League Against Rheumatism (EULAR) recommend the TNF inhibitors adalimumab (Humira), certolizumab (Cimzia), etanercept (Enbrel), and golimumab (Simponi) for nr-ax SpA, and state that the price of the TNF inhibitor should influence therapy. The P&T Committee updated the Cimzia PA for this additional indication. Although Humira is not approved for treating nr-ax SpA in the United States, clinical trial data is available and it carries this approval by foreign agencies. Based on the ASAS/EULAR guidelines and clinical trial data, the Humira PA was also updated to allow treatment for nr-ax SpA. Patients with nr-ax SpA will still be required to try Humira prior to Cimzia.

- 4. Targeted Immunomodulatory Biologics (TIBs): tofacitinib citrate (Xeljanz/Xeljanz XR)**—Xeljanz was originally approved for treating rheumatoid arthritis; the indication was later expanded to include psoriatic arthritis and ulcerative colitis in adults. The committee reviewed the new FDA safety alert for increased risk for pulmonary embolism and death in patients taking a 10 mg twice daily dose for rheumatoid arthritis. This dosage is only approved for patients with ulcerative colitis. The P&T Committee updated the PA to limit the 10 mg twice daily dose for the labeled indication of ulcerative colitis.
- 5. Weight Loss Agents**—The P&T Committee recommended updates to the manual PA criteria for the branded weight loss agents to provide additional clarity regarding step therapy. Patients must first try generic phentermine before use of any of the non-phentermine branded drugs for weight loss. All updated PA criteria apply to new users.
- 6. Weight Loss Agents: topiramate extended-release/phentermine (Qsymia)**—The P&T Committee recommended updates to the manual PA criteria for Qsymia to include safety concerns regarding pregnancy risk and the REMS program.

B. Updated PA Criteria—Implementation Plan

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) updates to the current PA criteria for Qsymia, the weight loss agents, Dupixent, Xeljanz/Xeljanz XR, Cimzia, Humira, and Imbruvica in new users become effective 30 days after the signing of the minutes.

XI. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA

BAP Comments

A. Updated Manual PA Criteria

The P&T Committee recommended updates to the manual PA criteria for the drugs discussed above.

<p><i>BAP Comment:</i> <input type="checkbox"/> Concur <input type="checkbox"/> Non-concur</p>
--

B. Updated Manual PA Criteria—PA Implementation Plan

The P&T Committee recommended the updates to the PA criteria for the drugs discussed above become effective 30 days after the signing of the minutes.

BAP Comment: Concur Non-concur

XII. BRAND OVER GENERIC AUTHORIZATION FOR FLUTICASONE/SALMETEROL (ADVAIR DISKUS)

P&T Comments

Pricing for the branded Advair Diskus product is more cost-effective than the AB-rated generic formulations for fluticasone/salmeterol, which were launched in March 2019. Therefore, the branded Advair Diskus 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 Advair Diskus as outlined in Section IV E on page 17. The “brand over generic” requirement for Advair Diskus will be removed administratively when it is no longer cost-effective compared to the AB-rated generics.

A. Advair Diskus Brand over Generic Requirement and PA Criteria

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) implementing the requirement to prefer the branded Advair product over generic formulations. Manual PA criteria are required for generic fluticasone/salmeterol in the Retail Network and Mail Order Pharmacy. The prescriber will provide patient-specific justification as to why the branded fluticasone/salmeterol product cannot be used.

B. Advair Diskus Brand Copayment

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) that the brand (Tier 2) formulary cost-share for Advair Diskus in the TRICARE Mail Order Pharmacy and the TRICARE Retail Network Pharmacy be lowered to the generic (Tier 1) formulary cost-share.

XIII. BRAND OVER GENERIC AUTHORIZATION FOR FLUTICASONE/SALMETEROL (ADVAIR DISKUS)

BAP Comments

A. Advair Diskus Brand over Generic Requirement and PA Criteria

The P&T Committee recommended brand over generic preference for Advair Diskus and manual PA criteria for generic fluticasone/salmeterol.

BAP Comment: Concur Non-concur

B. Advair Diskus Brand Copayment

The P&T Committee recommended that the brand (Tier 2) formulary cost-share for Advair Diskus be lowered to the generic (Tier 1) formulary cost-share.

BAP Comment: Concur Non-concur

XIV. INFORMATIONAL ITEM—SUMMARY OF RECOMMENDATIONS AND BENEFICIARY IMPACT MAY 2019

Table of Implementation Status of UF Recommendations/Decisions Summary

DoD PEC Drug Class	UF Drugs	NF Drugs	Tier 4/Not Covered Drugs	Implement Date	Notes and Unique Users Affected
Proton Pump Inhibitor Agents: Capsule and Tablet Subclass	<p><i>Step-preferred</i></p> <ul style="list-style-type: none"> ▪ omeprazole 20 mg and 40 mg capsules (Prilosec, generics) ▪ pantoprazole tablets (Protonix, generics) <p><i>Non-step-preferred</i></p> <ul style="list-style-type: none"> ▪ esomeprazole (Nexium, generics) ▪ rabeprazole (Aciphex, generics) 	<p><i>Non-step-preferred</i></p> <ul style="list-style-type: none"> ▪ lansoprazole (Prevacid, generics) ▪ omeprazole/ sodium bicarbonate (Zegerid, generics) 	<ul style="list-style-type: none"> ▪ dexlansoprazole (Dexilant) ▪ esomeprazole strontium 	Pending signing of the minutes / 120 days	<ul style="list-style-type: none"> ▪ No PA required for omeprazole or pantoprazole ▪ Manual PA required for non-step-preferred products in new users; current users are grandfathered ▪ New Tier 4/Not Covered recommendation for Dexilant and esomeprazole strontium applies to both new and current users <p><u>Unique Users Affected (Dexilant and esomeprazole strontium)</u> Mail –14,263 MTF – 2,802 Retail – 1,790 Total – 18,855</p>

DoD PEC Drug Class	UF Drugs	NF Drugs	Tier 4/Not Covered Drugs	Implement Date	Notes and Unique Users Affected
Proton Pump Inhibitor Agents: Alternative Dosage Form Subclass	<ul style="list-style-type: none"> ▪ omeprazole packet for oral suspension (Prilosec) ▪ pantoprazole packet for oral suspension (Protonix) ▪ esomeprazole packet for oral suspension (Nexium) ▪ rabeprazole sprinkle (Aciphex) 	<ul style="list-style-type: none"> ▪ lansoprazole orally dissolving tablet (Prevacid ODT) ▪ omeprazole/bicarbonate packet for oral suspension (Zegerid) 	<ul style="list-style-type: none"> ▪ None 	<p>Pending signing of the minutes / 120 days</p>	<ul style="list-style-type: none"> ▪ Note that step-therapy does not apply to the alternative dosage forms ▪ Manual PA required for Prevacid ODT and Zegerid in all new and current users. Patients 18 years and under are not subject to the PA. <p><u>Unique Users Affected (Prevacid ODT and Zegerid packets)</u> Mail – 465 MTF – 137 Retail – 123 Total – 725</p>
Pulmonary Arterial Hypertension: Prostacyclin Subclass, Endothelin Receptor Antagonists Subclass, and Nitric Oxide Subclass	<p><u>Prostacyclins</u></p> <ul style="list-style-type: none"> ▪ treprostinil nebulized solution (Tyvaso) ▪ iloprost nebulized solution (Ventavis) ▪ treprostinil oral tablets (Orenitram extended release [ER] tablets) ▪ selexipag tablets (Uptravi) <p><u>Endothelin Receptor Antagonists (ERAs)</u></p> <ul style="list-style-type: none"> ▪ bosentan tablets (Tracleer, generics) ▪ ambrisentan tablets (Letairis) ▪ macitentan tablets (Opsumit) <p><u>Nitric Oxide Drugs</u> <i>Step-preferred</i></p> <ul style="list-style-type: none"> ▪ sildenafil 20 mg tablets (Revatio generics) <p><i>Non-step-preferred</i></p> <ul style="list-style-type: none"> ▪ tadalafil 20 mg tablets (Adcirca, Alyq, generics) ▪ riociguat tablets (Adempas) 	<ul style="list-style-type: none"> ▪ None 	<ul style="list-style-type: none"> ▪ None 	<p>Pending signing of the minutes / 90 days</p>	<ul style="list-style-type: none"> ▪ Brand Letairis preferred over generics <p><u>Unique Users Affected</u> Not applicable</p>

Drugs with New Prior Authorization Criteria—Unique Utilizers Affected

Drug	MTF	Mail Order	Retail	Total
Antihistamine-1: First Generation and Combinations – carbinoxamine maleate 6 mg tablets (Ryvent, generics) and carbinoxamine maleate 4 mg/5 mL ER oral suspension (Karbinal ER)	15	47	205	267