DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS FROM THE MAY 2021 MEETING

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) or their designee, 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 non-formulary (NF) or Tier 4 status are received from the Beneficiary Advisory Panel (BAP), which must be reviewed by the Director or their designee before making a final decision.

II. UF CLASS REVIEWS—Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass

P&T Comments

A. Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Subclass Relative Clinical Effectiveness Analysis and Conclusion

Background—The Menopausal Hormone Therapy (MHT) class has not previously been reviewed for formulary placement. Estradiol vaginal insert (Imvexxy) and estradiol/micronized progesterone (Bijuva) were reviewed as innovators in 2018 and 2019, respectively, and both were designated nonformulary, with Imvexxy also requiring prior authorization (PA) criteria. Three MHT subclasses, Oral Single Agents, Oral Combination Agents, and Vaginal Agents, are the subject of this review.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

Oral Single Agents Subclass

- The subclass is made up of three drugs, estradiol (Estrace and generics), conjugated equine estrogens (Premarin), and esterified estrogens (Menest).
- Estradiol and esterified estrogens are plant-derived. The conjugated equine estrogens (CEE) found in Premarin products are derived from pregnant mares' urine. While potency and doses differ among the drugs in this subclass, there is little difference in efficacy for treating

vasomotor symptoms of menopause (hot flashes). (North American Menopause Society (NAMS) 2017 Position Statement)

- Data from one randomized controlled trial included in the 2016 Cochrane Review does not suggest a safety difference between estradiol and CEE; however, small observational trials suggest cardiovascular and cognitive benefits with estradiol over CEE.
- Estradiol is preferred over CEE in transgender patients due to ease of monitoring.

Oral Combination Agent Subclass

- The oral combination subclass is primarily used to treat vasomotor symptoms of menopause. The class is comprised of estrogen/progestogen combinations and estrogen/testosterone combinations.
- The purpose of adding a progestin to an estrogen for the combination products is to prevent endometrial hyperplasia and cancer in women who have a uterus. Uterine cancer can develop in as little as 6 months with use of unopposed estrogen therapy in women who have not had a hysterectomy.
- There is conflicting data regarding the relative endometrial protection provided with different progestogens (i.e., norethindrone acetate, medroxyprogesterone acetate, progesterone). (American Association of Clinical Endocrinologists and American College of Endocrinology [AACE/ACE] 2017)
- The 2017 AACE/ACE guidelines state that micronized progesterone is considered the safer alternative when progesterone is necessary.
- Compared to medroxyprogesterone acetate, micronized progesterone appears to have better outcomes for cardiovascular effects, blood pressure, venous thromboembolism, stroke, and breast cancer. However, safety risks with medroxyprogesterone acetate are diminished if used for 5 years or less.
- Bijuva is the only combination product that contains estradiol and micronized progesterone.
- Estradiol/drospirenone (Angeliq) has additional contraindications (renal impairment and adrenal insufficiency) and drug interactions (NSAIDs, ACEIs, ARBs) compared to the other oral combination agents. However, it is the only product that contains the progestin drospirenone, which has anti-mineralocorticoid activity, and may cause small reductions in blood pressure.

- Combination products containing methyltestosterone (i.e., Covaryx, generics) may be used in menopausal women with sexual interest/arousal disorder.

Vaginal Agents Subclass

- The subclass is further divided into vaginal creams, inserts, and rings. With the exception of Femring, which is a systemically acting hormone therapy, all other drugs in this subclass are locally acting.
- The Vaginal Agents are almost exclusively used to treat the genitourinary syndrome of menopause (GSM). There are no significant differences in efficacy between the various estrogen creams, inserts, and rings for the treatment of GSM, including urogenital atrophy (Cochrane 2016).
- Overall, there are little to no differences in safety between the various vaginal estrogens when used at typical doses and dosing frequencies.
- Estradiol acetate vaginal ring (Femring) bypasses the GI tract and thus has a less anticipated impact on lipids and blood clotting and is not associated with an increased risk of venous thromboembolism compared to oral products.
- Vaginal rings (Estring, Femring) are convenient as they last for three months, but they can become dislodged and may not initially be used in patients with significant vaginal stenosis.
- Vaginal creams (Premarin, Estrace) allow for dose titration and for application directly to external tissues, but are messier than the other vaginal dosage forms.
- Vaginal inserts (Yuvafem vaginal tablets and Imvexxy vaginal capsules) are less messy than the creams, but cannot be titrated. Imvexxy capsules are available in a lower estradiol strength of 4 mcg in addition to 10 mcg.
- Some patients may prefer the vaginal rings and tablets over the vaginal creams, as they may be easier to administer, are less messy, and some patients consider these formulations more comfortable.

Overall Clinical Conclusion

- In order to meet the needs of Military Health System (MHS) beneficiaries, a variety of menopausal hormone therapy products are needed on the formulary. The formulation, dose, and route of administration should be determined individually and reassessed periodically. Inclusion of multiple agents in each subclass on the uniform formulary is beneficial in supporting differences in patient and provider preferences.

B. Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass—Relative Cost-Effectiveness Analysis and Conclusion

A cost-minimization analysis (CMA) and budget impact analysis (BIA) were performed. The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

- CMA results showed that generic formulations in each subclass were the most cost-effective, followed by the branded products, which are ranked from least to most costly, as outlined below:
  - **For the oral single agents**, generic estradiol tablets were the most cost-effective agent followed by conjugated equine estrogens tablets (Premarin), and esterified estrogens (Menest).
  - **For the oral combination agents,** the generics (e.g., generic Femhrt, Activella, Eemt) were most cost effective, followed by conjugated equine estrogens/medroxyprogesterone acetate tablet (Prempro), conjugated equine estrogens plus medroxyprogesterone acetate tablets (Premphase), estradiol/progesterone caps (Bijuva), estradiol/norgestimate (Prefest) and estradiol/drospirenone (Angeliq).
  - **For the vaginal agents**: Generic estradiol vaginal cream and vaginal tablets were the most cost effective products, followed by estradiol vaginal ring (Estring), estradiol vaginal insert (Imvexxy), conjugated equine estrogens vaginal cream (Premarin cream), and estradiol acetate vaginal ring (Femring).
- BIA was performed to evaluate the potential impact of designating selected agents as formulary, NF, or Tier 4 on the UF. BIA results showed that designating all oral single, oral combination and vaginal agents as UF and none as NF or Tier 4 demonstrated significant cost avoidance for the MHS.

C. Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass—UF/Tier 4/Not Covered Recommendation

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

Oral Single Agents Subclass

- UF
  - conjugated equine estrogens tablets (Premarin)

- estradiol tablets (Estrace, generics)
- esterified estrogens tablets (Menest)

- NF
  - None

- Tier 4/Not Covered
  - None

Oral Combination Agents Subclass

- UF
  - conjugated equine estrogens/medroxyprogesterone acetate tablets (Prempro)
  - conjugated equine estrogens plus medroxyprogesterone acetate tablets (Premphase)
  - ethinyl estradiol/norethindrone acetate tablets (Jinteli, Femhrt, Fyavolv, generics)
  - estradiol/norethindrone acetate tablets (Activella, Amabelz, Jinteli, Mimvey, Mimvey Lo, generics)
  - esterified estrogens/methyltestosterone (Covaryx, Covaryx HS, Eemt, Eemt HS, generics)
  - estradiol/drospirenone (Angeliq)
  - estradiol/norgestimate (Prefest)
  - estradiol/progesterone capsules (Bijuva) *(moves from NF to UF)*

- NF – None

- Tier 4/Not Covered - None

Vaginal Agents Subclass

- UF
  - conjugated equine estrogens vaginal cream (Premarin)
  - estradiol vaginal cream (Estrace, generics)
  - estradiol vaginal ring (Estring)
  - estradiol acetate vaginal ring (Femring)

- estradiol vaginal tablet (Yuvafem, generics)
- estradiol vaginal insert (Imvexxy) *(moves from NF to UF)*

- NF – None
- Tier 4/Not Covered - None

D. Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass—Manual PA Criteria

Existing PA criteria currently apply to estradiol vaginal insert (Imvexxy). The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) removing the PA for Imvexxy. As a result, there are no PA requirements in any of the three MHT subclasses reviewed.

E. Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass—UF, PA Removal, and Implementation Plan

The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent): an effective date of the first Wednesday 30 days after signing of the P&T minutes at all points of service.

III. UF CLASS REVIEWS—Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass

BAP Comments

A. Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass—UF/Tier 4/Not Covered Recommendation

The P&T Committee recommended the formulary status for the Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass as discussed above:

Oral Single Agents Subclass

- UF
  - Premarin
  - Estrace, generics
  - Menest

- NF - None
- Tier 4/Not Covered- None

Oral Combination Agents Subclass

- UF
  - Prempro
  - Premphase
  - Jinteli, Femhrt, Fyavolv, generics
  - Activella, Amabelz, Jinteli, Mimvey, Mimvey Lo, generics
  - Covaryx, Covaryx HS, Eemt, Eemt HS, generics
  - Angeliq
  - Prefest
  - Bijuva *(moves from NF to UF)*
- NF - None
- Tier 4/Not Covered - None

Vaginal Agents Subclass

- UF
  - Premarin
  - Estrace, generics
  - Estring
  - Femring
  - Yuvafem, generics
  - Imvexxy *(moves from NF to UF)*
- NF - None
- Tier 4/Not Covered - None

BAP Comment: ☐ Concur ☐ Non-concur

B. Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass—Manual PA Criteria

The P&T Committee recommended removing the PA criteria for Imvexxy, as outlined above.

BAP Comment: ☐ Concur ☐ Non-concur

C. Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents Subclass—UF, PA and Implementation Plan

The P&T Committee recommended the implementation plan of the first Wednesday 30 days after signing of the minutes in all points of service.

BAP Comment: ☐ Concur ☐ Non-concur

IV. UF CLASS REVIEWS—Sleep Disorders: Insomnia Agents Subclass

P&T Comments

A. Sleep Disorders: Insomnia Agents Subclass Relative Clinical Effectiveness Analysis and Conclusion

Background—The P&T Committee evaluated the relative clinical effectiveness of the drugs used to treat insomnia. This class was last reviewed in May 2012. Drugs in the class include numerous formulations of zolpidem (immediate-release, extended-release, oral spray, and sublingual), eszopiclone, zaleplon, and doxepin, melatonin agonists (ramelteon and tasimelteon), and the newer dual orexin receptor antagonists (DORAs) suvorexant (Belsomra) and lemborexant (Dayvigo). The DORAs were previously reviewed as individual new drugs in May 2015 and August 2020, respectively.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

Guidelines and Therapies

- Non-pharmacological therapies including sleep hygiene, relaxation, and cognitive behavioral therapy for insomnia (CBT-I) are recommended as first-line treatment of chronic insomnia.
- Pharmacologic treatment can be used in addition to non-pharmacologic therapies for patients who continue to have insomnia.
- Guidelines recommend treating insomnia with pharmacologic therapies for the shortest possible treatment course.
- Options for sleep onset insomnia include zolpidem IR (Ambien, generics), zaleplon (Sonata, generics), and the melatonin agonist ramelteon (Rozerem, generics). Agents approved for both sleep onset and sleep maintenance include zolpidem ER (Ambien CR, generics), eszopiclone (Lunesta, generics), and the DORAs suvorexant (Belsomra) and lemborexant (Dayvigo).

Older Agents

- All the older agents improve sleep latency (the time to fall asleep) by approximately 10 to 15 minutes, compared to placebo.
- For the older insomnia drugs, there was no new data to change the conclusions from the May 2012 meeting, which stated that there are no clinically relevant differences between the drugs.
- Doxepin tablets (Silenor, generics) improve insomnia due to sleep maintenance problems; no comparative data exists with doxepin and the other drugs in the class. One advantage is that doxepin is not a controlled substance.
- Other than providing an alternative dosage formulation for patients with swallowing difficulties, zolpidem oral spray (Zolpimist), and zolpidem sublingual (Edluar and Intermezzo) do not offer clinically compelling advantages over other insomnia drugs.

DORAs

- Suvorexant (Belsomra) and lemborexant (Dayvigo) competitively inhibit the wakefulness promoting neuropeptides orexin A and B.
- No direct comparative data are available between Belsomra and Dayvigo, and indirect comparisons are confounded due to the different endpoints used. An indirect comparison showed both DORAs decrease the time to fall asleep by approximately 15 minutes and increase the total time asleep by about 30 minutes.
- Both agents have efficacy and safety data in older adults and in patients with dementia related to Alzheimer's disease who have insomnia. There is

currently no evidence to support that one DORA is better than another when treating elderly patients.

- More data is needed to determine comparative effectiveness in patients experiencing middle of the night awakenings.
- Both DORAs have drug-drug interactions that should be considered when treating patients. Lemborexant (Dayvigo) has a longer half-life (17-19 hours) compared to suvorexant (12 hours). Adverse events with lemborexant and suvorexant are generally similar and dose-related.
- Warnings and precautions for the DORAs include daytime somnolence (patients using higher doses are cautioned against driving the next day); sleep paralysis, hallucinations, and cataplexy-like symptoms; and complex sleep behaviors. The DORAs should be used with caution in patients with compromised respiratory function; and worsening of depression.

Melatonin Agonists

- Ramelteon (Rozerem, generics) is a melatonin agonist that improves sleep onset and is not a controlled substance.
- Tasimelteon (Hetlioz) is another prescription melatonin agonist, and has been designated as NF with PA criteria since February 2015. It was originally indicated for blind patients with non-24 hour sleep-wake disorder.
- The prescription products ramelteon (Rozerem generics) and tasimelteon (Hetlioz) have similar chemical compositions to the dietary supplement melatonin.
- Since the last formulary review, tasimelteon is now indicated for use in Smith-Magenis Syndrome (SMS), a rare condition. A liquid formulation (Hetlioz LQ) specifically approved for children aged 3 to 15 years with SMS was recently marketed. Use of tasimelteon in SMS is based on one unpublished study with poor efficacy results and numerous limitations.
- Other than its unique indications, tasimelteon (Hetlioz) offers no compelling clinical advantages over other melatonin agonists.

B. Sleep Disorders: Insomnia Agents Subclass—Relative Cost-Effectiveness Analysis and Conclusion

CMA and BIA were performed. The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) the following:

- CMA results showed that doxepin tablets (Silenor, generics), eszopiclone (Lunesta, generics), ramelteon (Rozerem, generics), zaleplon (Sonata,

generics), and zolpidem IR and ER tablets (Ambien, Ambien CR, and generics) are more cost-effective than lemborexant (Dayvigo) and suvorexant (Belsomra). Intermezzo, Zolpimist, Edluar, Hetlioz and Hetlioz LQ are not cost-effective relative to the other insomnia drugs.

- BIA was performed to evaluate the potential impact of designating selected agents as formulary, NF, or Tier 4 on the UF. BIA results showed that designating generic doxepin, eszopiclone, ramelteon, zaleplon, and zolpidem IR/ER as UF , with lemborexant (Dayvigo) and suvorexant (Belsomra) as UF and step-preferred branded products, and branded tasimelteon (Hetlioz, Hetlioz LQ), zolpidem spray (Zolpimist), and zolpidem tablets (Edluar, Intermezzo, and generics) as NF and non-step-preferred demonstrated significant cost avoidance for the MHS.

C. Sleep Disorders: Insomnia Agents Subclass—UF Recommendation

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

- UF
  - eszopiclone (Lunesta, generics)
  - zaleplon (Sonata, generics)
  - zolpidem IR (Ambien, generics)
  - zolpidem ER (Ambien CR, generics)
  - doxepin 3 mg, 6 mg (Silenor, generics)
  - ramelteon (Rozerem, generics) *(moves from NF to UF)*

- UF and step-preferred brands
  - lemborexant (Dayvigo)
  - suvorexant (Belsomra) *(moves from NF to UF)*
  - Note that as part of the formulary recommendation for Belsomra and Dayvigo, a trial of zolpidem ER or eszopiclone is required
- NF and non-step-preferred brands
  - zolpidem oral spray (Zolpimist)
  - zolpidem 5 mg, 10 mg sublingual tabs (Edluar)
  - zolpidem 1.75 mg, 3.5 mg sublingual tabs (Intermezzo)
  - tasimelteon capsules (Hetlioz)
  - tasimelteon oral suspension (Hetlioz LQ)

- Note that as part of this formulary recommendation for Zolpimist, Edluar, and Intermezzo, a trial of zolpidem IR or zaleplon and Belsomra or Dayvigo are required in new and current users
- Note that as part of this formulary recommendation for Hetlioz and Hetlioz LQ, a trial of ramelteon and melatonin are required in new users

- Tier 4/Not Covered – None

D. Sleep Disorders: Insomnia Agents Subclass—Manual PA Criteria

PA has applied to the older insomnia drugs since 2010, the DORA Belsomra since 2015, the DORA Dayvigo since 2020, and to Hetlioz since 2014. The P&T Committee recommended (16 for, 1 opposed, 0 abstained, 1 absent) updates to the manual PA criteria as outlined below.

- Ramelteon (Rozerem generics) and doxepin 3 mg, 6 mg (Silenor generics): The existing PA criteria will be removed. Use of these agents will be monitored for inappropriate use and consideration will be given to reinstating PA criteria if necessary.
- Edluar, Intermezzo and Zolpimist: The updated PA criteria in new and current users will include a trial of cognitive behavioral therapy for insomnia (CBT-I) as part of the non-pharmacologic therapy options. In addition to a trial of a generic zolpidem IR or zaleplon first, the PA will also require a trial of a DORA (Belsomra or Dayvigo). The current automation setup will be removed and replaced with manual criteria. Renewal criteria will now be required. The PA criteria are as follows, with all updates from the May 2021 P&T meeting in bold:

  1. **zolpidem sublingual (Edluar), zolpidem sublingual (Intermezzo), and zolpidem oral spray (Zolpimist)**
     Note that the current automation will be removed.

     Manual PA criteria apply to all new and current users of Intermezzo, Edluar, and Zolpimist and will be approved if all the following criteria are met:

     - **The provider acknowledges that the following agents are available without prior authorization: zolpidem IR, zolpidem ER, zaleplon, eszopiclone**
     - Patient has documented diagnosis of insomnia characterized by difficulties with **sleep onset**
     - Non-pharmacologic therapies have been inadequate in improving functional impairment, including but not limited to relaxation therapy, **cognitive behavioral therapy for insomnia (CBT-I),**

sleep hygiene and the patient will continue with non-pharmacologic therapies throughout treatment

- Patient has tried and failed or had clinically significant adverse effects to **zolpidem immediate-release or zaleplon**
- **Patient has tried and failed or had clinically significant adverse effects with an orexin antagonist (i.e., Belsomra or Dayvigo)**
- Patient has documented swallowing difficulties

Non-FDA-approved uses are not approved.
Prior authorization expires after 1 year.

Renewal criteria: Initial TRICARE PA approval is required for renewal. PA will be renewed for an additional 1 year if the renewal criteria are met.

- **Patient has not adequately responded to non-pharmacologic therapies**
- **Patient agrees to continue with non-pharmacologic therapies including but not limited to relaxation therapy, cognitive behavioral therapy for insomnia (CBT-I), and/or sleep hygiene**
- **Patient continues to respond to the drug**

- Dayvigo and Belsomra: The updated PA criteria in new users will include a trial of CBT-I as a non-pharmacologic therapy option and require renewal criteria. The PA criteria are as follows, with all updates from the May 2021 P&T meeting in bold:

2. suvorexant (Dayvigo) and lemborexant (Belsomra)

Manual PA criteria apply to all new users of Belsomra and Dayvigo and will be approved if all the following criteria are met:

- **The provider acknowledges that the following agents are available without prior authorization: zolpidem IR and ER, zaleplon, eszopiclone**
- Patient has documented diagnosis of insomnia characterized by difficulties with sleep onset and/or sleep maintenance
- Non-pharmacologic therapies have been inadequate in improving functional impairment, including but not limited to relaxation therapy, **cognitive behavioral therapy for insomnia (CBT-I),** sleep hygiene and the patient will continue with non-pharmacologic therapies throughout treatment
- Patient has tried and failed or had clinically significant adverse effects to zolpidem extended-release OR eszopiclone

- Patient does not have a current or previous history of narcolepsy
- Patient does not have a current or previous history of drug abuse

Non-FDA-approved uses are not approved.
Prior authorization expires in 1 year.

<u>Renewal criteria:</u> Initial TRICARE PA approval is required for renewal. PA will be renewed for an additional 1 year if the renewal criteria are met.

- **Patient has not adequately responded to non-pharmacologic therapies**
- **Patient agrees to continue with non-pharmacologic therapies including but not limited to relaxation therapy, cognitive behavioral therapy for insomnia (CBT-I), and/or sleep hygiene**
- **Patient continues to respond to the drug**

- Hetlioz and Hetlioz LQ: The updated PA criteria in new users will include a trial of ramelteon in addition to OTC melatonin. The PA criteria are as follows, with all updates from the May 2021 P&T meeting in bold:

3. tasimelteon (Hetlioz/Hetlioz LQ)

Manual PA criteria apply to all new users of Hetlioz/Hetlioz LQ, and will be approved if all the following criteria are met:

- The provider acknowledges that Hetlioz capsules are not approved for pediatrics or adolescents and are not approved for treating SMS; and that Hetlioz LQ liquid is only approved for pediatrics with SMS and is not approved for Non-24 sleep wake disorder or for use in adults
- For the Hetlioz capsule formulation, the patient is 18 years of age or older and is totally blind and has a documented diagnosis of non-24 sleep wake disorder OR
- For the Hetlioz LQ liquid formulation, the patient is 3 years of age up to 15 years of age and has a documented diagnosis of Smith-Magenis Syndrome (SMS)
- The patient has had a trial of melatonin and either failed or had an adverse event
- **The patient has tried and failed ramelteon**
- The patient is not taking a drug that will interact with tasimelteon (i.e., beta blockers or strong CYP3A4 inducers)

Non-FDA-approved uses are not approved including insomnia, jet lag disorder, or other circadian rhythm disorders.

PA Criteria will expire after 6 months (if patient has not responded after 6 months, they will be deemed a non-responder)

<u>Renewal criteria</u>: Initial TRICARE PA approval is required for renewal. PA will be renewed for an additional 6 months if the renewal criteria are met.

- **The patient has been receiving Hetlioz/Hetlioz LQ for 6 months and has had a documented response to therapy.**

E. Sleep Disorders: Insomnia Agents Subclass—UF Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 2 absent) an effective date of the first Wednesday 60 days after signing of the minutes in all points of service; 2) DHA send letters to beneficiaries who are affected by the updated PA requirements for Edluar, Intermezzo and Zolpimist.

V. UF CLASS REVIEWS—Sleep Disorders: Insomnia Agents Subclass

BAP Comments

A. Sleep Disorders: Insomnia Agents Subclass—UF Recommendation

The P&T Committee recommended the formulary status for Sleep Disorders: Insomnia Agents Subclass as discussed above:

- UF
    - eszopiclone (Lunesta, generics)
    - zaleplon (Sonata, generics)
    - zolpidem IR (Ambien, generics)
    - zolpidem ER (Ambien CR, generics)
    - doxepin 3 mg, 6 mg (Silenor, generics)
    - ramelteon (Rozerem, generics) *(moves from NF to UF)*
- UF and step-preferred brands
    - Dayvigo
    - Belsomra *(moves from NF to UF)*
    - Note that as part of the formulary recommendation for Belsomra and Dayvigo, a trial of zolpidem ER or eszopiclone is required

- NF and non-step-preferred brands
    - Zolpimist
    - Edluar
    - Intermezzo
    - Hetlioz
    - Hetlioz LQ
    - Note that as part of this formulary recommendation for Zolpimist, Edluar, and Intermezzo, a trial of zolpidem IR or zaleplon and Belsomra or Dayvigo are required in new and current users
    - Note that as part of this formulary recommendation for Hetlioz and Hetlioz LQ, a trial of ramelteon and melatonin are required in new users
- Tier 4/Not Covered – None

BAP Comment:	☐ Concur	☐ Non-concur

B. Sleep Disorders: Insomnia Agents Subclass—Manual PA Criteria

The P&T Committee recommended updates to the PA criteria as outlined above.

BAP Comment:	☐ Concur	☐ Non-concur

C. Sleep Disorders: Insomnia Agents Subclass—UF and Implementation Period

The P&T Committee recommended an effective date of the first Wednesday 60 days after signing of the minutes in all points of service; and that DHA send letters to beneficiaries who are affected by the updated PA requirements for Edluar, Intermezzo and Zolpimist.

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/Tier 4/Not Covered Recommendation

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

- UF
    - cabotegravir (Vocabria) – Integrase strand transfer inhibitor antiretroviral for HIV
    - ponesimod (Ponvory) – Oral miscellaneous multiple sclerosis (MS) agent for relapsing forms of MS
    - tepotinib (Tepmetko) – Oral oncologic agent for non-small cell lung cancer (NSCLC)
    - tivozanib (Fotivda) – Oral oncologic agent for renal cell carcinoma (RCC)
    - umbralisib (Ukoniq) – Oral oncologic agent for marginal zone lymphoma (MZL) and follicular lymphoma (FL)
    - vericiguat (Verquvo) – Miscellaneous cardiovascular agent for reducing risk of cardiovascular death in adults with chronic heart failure
    - vibegron (Gemtesa) – Overactive Bladder (OAB) drug

- NF

- ethinyl estradiol (EE) 20 mcg/ levonorgestrel 0.1 mg chewable tablet (Tyblume) – Monophasic combination oral contraceptive with 20 mcg estrogen
- levothyroxine sodium 100 mcg/5 mL oral solution (Thyquidity) – Thyroid Agent
- mannitol inhalation powder (Bronchitol) – Miscellaneous Respiratory Agent for Cystic Fibrosis
- methotrexate injection (Reditrex) – Antirheumatic
- solifenacin oral suspension (Vesicare LS) – Antimuscarinic Overactive Bladder Agent for pediatric neurogenic detrusor overactivity (NDO)
- tirbanibulin 1% ointment (Klisyri) – Antineoplastic for actinic keratosis
- voclosporin (Lupkynis) – Calcineurin inhibitor immunosuppressive for active lupus nephritis (LN)

- Tier 4/Not Covered
  - levetiracetam 1,000 mg and 1,500 mg extended-release tablets (Elepsia XR) – Anticonvulsant Agent
    - Elepsia XR was recommended for Tier 4 status as it has little to no additional clinical effectiveness relative to other levetiracetam products and similar agents in the class, and the needs of TRICARE beneficiaries are met by available alternative anticonvulsant agents. Alternatives include levetiracetam 500 mg and 750 mg ER tablets (Keppra generics), lamotrigine XR, and topiramate ER.

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

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

- OAB Drugs: Applying manual criteria to new users of vibegron (Gemtesa), requiring a trial of two formulary generic OAB drugs first.
- Antirheumatics: Applying manual criteria to new users of Reditrex, requiring a trial of oral methotrexate first.
- Oncologic drugs: Applying manual PA criteria to new users of Fotivda, Tepmetko, and Ukoniq.
- Applying manual PA criteria to new users of Bronchitol, Klisyri, Lupkynis, Ponvory, Thyquidity, Tyblume, and Verquvo.
- Applying manual PA criteria to new users of Vesicare LS.

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

1. **ethinyl estradiol (EE) 20 mcg/levonorgestrel 0.1 mg chewable tablets (Tyblume)**

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

   Manual PA criteria apply to all new users of Tyblume and will be approved if all criteria are met:

   - Provider acknowledges that other formulations of EE 20 mcg/levonorgestrel 0.1 mg (e.g., Sronyx, Lutera, or equivalent) do not require prior authorization.
   - Patient has been counseled that this medication needs to be taken on an empty stomach with a full glass of water
   - Patient requires chewable tablets and cannot swallow due to some documented medical condition – dysphagia, oral candidiasis, systemic sclerosis, developmental disability, etc. and not due to convenience

   Non-FDA approved uses are not approved.

   PA does not expire

2. **levothyroxine sodium 100 mcg/5 mL oral solution (Thyquidity)**

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

   Manual PA is required for all new users of Thyquidity and is approved if all criteria are met:

   - The patient is not able to chew a levothyroxine tablet
   - The patient is not able to swallow a levothyroxine capsule or tablet
   - Thyquidity is prescribed by or in consultation with an endocrinologist

   Non-FDA-approved uses are not approved

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

3. **mannitol inhalation powder (Bronchitol)**

Manual PA criteria apply to all new users of Bronchitol and is approved if all criteria are met:

- The provider is aware and acknowledges that dornase alfa (Pulmozyme) and hypertonic saline 7% inhalation (sodium chloride) are formulary alternatives available to DoD beneficiaries without the need of PA. Providers are encouraged to consider changing the prescription to Pulmozyme or hypertonic saline 7%.
- The patient is 18 years of age or older
- The patient has a diagnosis of cystic fibrosis (CF)
- Bronchitol is prescribed by or in consultation with a pulmonologist
- The provider has performed a Bronchitol Tolerance Test (BTT) AND the patient did not have a severe reaction
- The patient has been counseled on how to appropriately use Bronchitol
- The patient has or will be prescribed a short-acting bronchodilator (i.e., ProAir is TRICARE's formulary short-acting beta agonist) to use before treatment with Bronchitol
- The patient has tried and had an inadequate response to dornase alfa (Pulmozyme) and hypertonic saline OR has a contraindication to both products
- The patient will not use Bronchitol in combination with hypertonic saline

Non-FDA-approved uses are not approved

Prior authorization does not expire.

4. methotrexate subcutaneous injection (Reditrex)

Manual PA is required for all new users of Reditrex, and is approved if the following are met:

- The patient has a diagnosis of active rheumatoid arthritis, polyarticular juvenile idiopathic arthritis or severe, recalcitrant, disabling psoriasis in adults
- The patient has tried and failed ORAL methotrexate
- The patient has experienced intolerance or significant adverse effects from generic injectable methotrexate

  OR

- Patient has decreased finger dexterity, limited vision or impaired cognition resulting in the inability to utilize generic injectable methotrexate.

Non-FDA-approved uses are not approved including neoplastic diseases.

Prior authorization does not expire.

5. ponesimod (Ponvory)

Manual PA is required for all new users of Ponvory and is approved if all criteria are met:

- Prescribed by a neurologist
- Patient has a documented diagnosis of relapsing forms of multiple sclerosis (MS)
- Patient is not concurrently using a disease-modifying therapy (e.g., beta interferons [Avonex, Betaseron, Rebif, Plegridy, Extavia], glatiramer [Copaxone, Glaptopa], dimethyl fumarate [Tecfidera], diroximel fumarate [Vumerity], monomethyl fumarate [Bafiertam], cladribine [Mavenclad], teriflunamide [Aubagio])
- Patient has not previously failed a treatment course of fingolimod (Gilenya), siponimod (Mayzent), and ozanimod (Zeposia)
- Provider acknowledges that all recommended Ponvory monitoring has been completed and the patient will be monitored throughout treatment as recommended in the package insert. Monitoring includes complete blood count (CBC); liver function tests (LFT), varicella zoster virus (VZV) antibody serology, electrocardiogram (ECG), pulmonary function tests (PFTs), blood pressure, skin assessments and macular edema screening as indicated.
- Ponvory 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 they have a functioning pacemaker

Non-FDA-approved uses are NOT approved.

PA does not expire

6. solifenacin oral suspension (Vesicare LS)

Manual PA criteria apply to all new users of solifenacin oral suspension (Vesicare LS).

Automated PA Criteria: PA does not apply to patients younger than 12 years of age (age edit) AND if the patient has filled a prescription for oxybutynin tablets oral syrup at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 720 days.

If automated criteria are not met: Manual PA Criteria apply and Vesicare LS is approved if all criteria are met:

- The provider acknowledges that oxybutynin oral syrup is available for patients with neurogenic detrusor overactivity and does not require prior authorization
- Prescribed by or in consultation with a urologist or nephrologist
- Patient has a diagnosis of neurogenic bladder secondary to detrusor overactivity and/or myelomeningocele
- Patient cannot swallow due to some documented medical condition – dysphagia, oral candidiasis, systemic sclerosis, etc. and not due to convenience OR
- Patient requires a dose that cannot be achieved without splitting a solifenacin tablet
- Patient has tried and failed or has a contraindication to oxybutynin

Non-FDA-approved uses are not approved including for overactive bladder.

Prior authorization does not expire.

7. tepotinib (Tepmetko)

Manual PA is required for all new users of Tepmetko, and is approved if all criteria are met

- The patient is 18 years of age or older

- Tepmetko is prescribed by or in consultation with a hematologist/oncologist
- The patient has metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to laboratory-confirmed mesenchymal-epithelial transition (MET) exon 14 skipping.
- The provider will monitor for interstitial lung disease (ILD)/pneumonitis and hepatotoxicity
- Female patients of childbearing age are not pregnant confirmed by (-) HCG.
- Female patients will not breastfeed during treatment
- Both male and female patients of childbearing potential agree to use effective contraception during treatment and for at least 1 week after cessation of therapy
- 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: _____.

Non-FDA-approved uses are not approved, except as noted above

PA does not expire

8. Tirbanibulin 1% ointment (Klisyri)

Manual PA is required for all new users of Klisyri and is approved if all criteria are met.

- Klisyri is prescribed by or in consultation with a dermatologist
- The patient is 18 years of age or older
- The patient has a diagnosis of actinic keratosis of the face or scalp
- The patient has tried and failed or has a contraindication to fluorouracil and imiquimod

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

9. tivozanib (Fotivda)

Manual PA is required for all new users of Fotivda and is approved if all criteria are met:

- The patient is 18 years of age or older
- The patient has laboratory evidence of relapsed or refractory advanced renal cell carcinoma with clear cell histology following two or more prior systemic therapies including at least one VEGFR kinase inhibitor other than sorafenib (Nexavar) (e.g., Sutent, Votrient, Cabometyx, or Lenvima).
- The patient will be monitored for hypertensive crisis, cardiac ischemia, arterial and venous thromboembolism, hemorrhage, proteinuria, thyroid dysfunction, and reversible posterior leukoencephalopathy syndrome
- Fotivda is prescribed by or in consultation with a hematologist/oncologist
- Female patients of childbearing age are not pregnant confirmed by (-) HCG
- Female patients will not breastfeed during treatment and for at least 1 month after the cessation of treatment
- Both male and female patients of childbearing potential agree to use effective contraception during treatment and for at least 1 month after cessation of therapy
- 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: _____.

Non-FDA-approved uses are not approved, except as noted above.

Prior authorization does not expire.

10. umbralisib (Ukoniq)

Manual PA is required for all new users of Ukoniq and is approved if all criteria are met:

- The patient is 18 years of age or older
- Ukoniq is prescribed by a hematologist/oncologist
- The patient has a diagnosis of:

- Relapsed or refractory marginal zone lymphoma (MZL) AND has received at least one prior anti-CD20-based regimen [e.g., rituximab (Rituxan), obinutuzumab (Gazyva)] OR
- Relapsed or refractory follicular lymphoma (FL) AND has received at least three prior lines of systemic therapy including an anti-CD20 based regimen and an alkylating agent

- Female patients of childbearing age are not pregnant confirmed by (-) HCG
- Female patients will not breastfeed during treatment and for at least 1 month after the cessation of treatment
- Female patients of childbearing potential and male patients with female partners of childbearing potential agree to use contraception during treatment and for at least 1 month after the cessation of treatment
- Male patients are aware that Ukoniq may cause male infertility
- 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: _____

Other Non-FDA-approved uses are not approved.

Prior authorization does not expire.

11. vericiguat (Verquvo)

Manual PA is required for all new users of Verquvo and is approved if all criteria are met:

- Patient is 18 years of age or older
- Initial prescription is written by or in consultation with a cardiologist
- Patient has a documented diagnosis of chronic HF (NYHA II-IV)
- Patient has a left ventricular ejection fraction (LVEF) < 45%
- Patient has worsening heart failure symptoms defined as one of the following:
  - History of previous heart failure hospitalization within the past 6 months OR

- Outpatient IV diuretics for heart failure (without hospitalization) within the past 3 months

- Patient's systolic blood pressure is at least 100 mmHg
- Patient is receiving appropriate guideline-directed medical therapy (GDMT), including the following: ACE/ARB/ARNI, BB, MRA, SGLT2 inhibitor, hydralazine plus nitrate, Corlanor, and/or diuretic
  - Unless contraindicated or unable to tolerate due to adverse effects
- Patient is not receiving concomitant treatment with long-acting nitrates, other sGC stimulators (riociguat [Adempas], or PDE5 inhibitors (sildenafil [Viagra, Revatio], tadalafil [Cialis, Adcirca])
- For women of childbearing age:
  - Patient is not pregnant AND
  - Provider is aware and the patient has been counseled on the teratogenicity risks with Verquvo and will comply with the contraceptive requirements listed in the package insert.

Non-FDA-approved uses are not approved including HFpEF, acute decompensated HF, PAH

Prior authorization does not expire.

12. vibegron (Gemtesa)

Manual PA is required for all new users of Gemtesa and is approved if all criteria are met:

- The patient has a confirmed diagnosis of overactive bladder (OAB) with symptoms of urge incontinence, urgency, and urinary frequency
- The patient has tried and failed behavioral interventions to include pelvic floor muscle training in women, and bladder training,
- The patient has had a 12-week trial with 2 formulary step-preferred products (oxybutynin IR, oxybutynin ER, tolterodine ER) and had therapeutic failure OR
- The patient has experienced central nervous system adverse events with at least one oral OAB medication OR is at increased risk for such central nervous system effects due to comorbid conditions or other medications,

- The patient's creatinine clearance (CrCl) is greater than 15 mL/min

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

13. voclosporin (Lupkynis)

Manual PA is required for all new users of Lupkynis and is approved if all criteria are met:

- The patient is 18 years of age or older
- Lupkynis is prescribed by or in consultation with a nephrologist
- The patient has a documented diagnosis of active lupus nephritis (LN)
- The patient has tried and failed previous therapy with mycophenolate (generic Cellcept)
- The patient has tried and failed previous therapy with either tacrolimus or cyclosporine
- Lupkynis will not be used concomitantly with cyclophosphamide, as evidence for this combination has not been established
- Due to drug interactions, the patient agrees to avoid eating grapefruit or drinking grapefruit juice while taking Lupkynis
- The patient will not receive live vaccines
- The provider agrees to monitor renal function, blood pressure, ECG, electrolytes, and monitor for neurotoxicity including risk of posterior reversible encephalopathy syndrome (PRES)
- The provider is aware and patient is informed of the increased risk for developing malignancies and serious infections with Lupkynis or other immunosuppressants that may lead to hospitalization or death
- For women of childbearing age: the provider is aware and patient is informed of the risk of fetal harm

Non-FDA-approved uses are not approved including kidney transplantation.

Prior authorization does not expire.

D. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF, Tier 4/Not Covered AND PA IMPLEMENTATION PLAN

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) with an effective date of the following:

- **New Drugs Recommended for UF or NF Status:** An effective date of the first Wednesday two weeks after signing of the minutes in all points of service.

- **New Drugs Recommended for Tier 4/Not Covered Status:** 1) An effective date 120 days after signing of the minutes in all points of service, and 2) DHA send letters to beneficiaries who are affected by the Tier 4/Not Covered recommendation at 30 days and 60 days prior to implementation.

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/Tier 4 Recommendation

The P&T Committee recommended the formulary status for the newly approved drugs as discussed above:

- **UF**
  - Vocabria
  - Ponvory
  - Tepmetko
  - Fotivda
  - Ukoniq
  - Verquvo
  - Gemtesa

- **NF**
  - Tyblume
  - Thyquidity
  - Bronchitol
  - Reditrex
  - Vesicare LS
  - Klisyri

- Lupkynis

- **Tier 4/Not Covered**
  - Elepsia XR

BAP Comment: ☐ Concur ☐ 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.

BAP Comment: ☐ Concur ☐ Non-concur

C. Newly Approved Drugs per 32 CFR 199.21(g)(5)—UF, Tier 4/Not Covered and PA Implementation Plan

The P&T Committee recommended the implementation plan as outlined above, of 2 weeks for the new drugs recommended for UF or NF status, and 120 days for the drug recommended for Tier 4/Not Covered status.

BAP Comment: ☐ Concur ☐ Non-concur

VIII. UTILIZATION MANAGEMENT—NEW MANUAL PA CRITERIA

P&T Comments

A. New Manual PA Criteria

1) Attention Deficit/Hyperactivity Disorder (ADHD) Stimulants – Methylphenidate Extended Release 72 mg tablets (Relexxii, generics)

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) manual PA criteria for methylphenidate 72 mg extended release tablets in new and current users, to ensure that more cost-effective methylphenidate ER products are tried first.

Relexxii 72 mg ER tablets use the same technology as found in Concerta, which is available in 18 mg, 27 mg, 36 mg, and 54 mg tablets. FDA approval for Relexxii was based on the data for Concerta. Several cost-effective extended release methylphenidate formulations are available on the UF without PA. Relexxii and its generics are not cost effective relative to other formulary long-acting methylphenidate formulations including generic Concerta and methylphenidate ER/CD/LA, Quillivant XR, and Aptensio XR.

Methylphenidate Extended Release 72 mg tablets (Relexxii, generics): The manual PA criteria apply to all new and current users of methylphenidate extended release 72 mg tablets (Relexxii) and is approved if all the following are met:

- Provider is aware and acknowledges that several other long-acting methylphenidate ER formulations, including generic Concerta, generic Metadate CD, generic Methylin ER, generic Aptensio XR, generic Ritalin, and Quillivant XR are available to DoD beneficiaries without requiring prior authorization
- The provider must explain why the patient requires Relexxii 72 mg ER tablets and cannot take the available alternatives.

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

2) Targeted Immunomodulatory Biologics – Rilonacept injection (Arcalyst)

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) manual PA criteria for rilonacept (Arcalyst) in current users, to ensure that guideline recommended therapies for recurrent pericarditis are tried first.

The targeted immunomodulatory biologic rilonacept (Arcalyst) was originally approved in 2008 for the treatment of cryopyrin-associated

periodic syndrome (CAPS), and for maintenance of remission of deficiency of interleukin-1 receptor antagonist (DIRA), which are rare conditions. In March 2021, Arcalyst received a new indication for treatment of recurrent pericarditis.

The 2015 European Society of Cardiology treatment guidelines for pericardial disease recommend aspirin or NSAIDs plus colchicine for six months as first-line therapy to improve remission rates and prevent recurrences of pericarditis. Corticosteroids may be added if there is an incomplete response to first-line therapies. MHS provider input supported PA to require a trial of conventional therapies for recurrent pericarditis.

Rilonacept injection (Arcalyst): The manual PA criteria apply to all new and users of Arcalyst and is approved if all the following are met

- Patient has one of the following diagnoses:
  - Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS), and Muckle-Wells Syndrome (MWS)
    - Patient is 12 years of age of older
  - Recurrent pericarditis
    - Patient is 12 years of age of older
    - Prescription is written by or in consultation with a cardiologist
    - Patient has a contraindication to colchicine and at least ONE of the following drug classes: aspirin, NSAIDs OR
    - Patient has tried and failed a treatment course of at least 6 months with colchicine and at least ONE of the following drug classes: aspirin, NSAIDs, corticosteroids
  - Deficiency of Interluekin-1 Receptor Antagonist (DIRA)
    - The patient weighs at least 10 kg (22 pounds)
- The patient is not concurrently receiving a TNF-inhibitor (e.g., Humira, Enbrel, Cimzia, and Simponi) due to the increased risk of serious infections.

Non-FDA-approved uses are not approved, including rheumatoid arthritis, neonatal-onset multisystemic inflammatory disease (NOMID), cardiovascular disease other than pericarditis (MI, acute coronary syndrome, atherosclerosis, heart failure, and Kawasaki disease), and gout.

Prior authorization does not expire.

B. New Manual PA Criteria—Implementation Plan

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the new PA for methylphenidate 72 mg extended release tablets (Relexxii) will become effective in new and current users the first Wednesday 90 days after the signing of the minutes and DHA will send letters to affected patients.

The P&T Committee also recommended (16 for, 0 opposed, 1 abstained, 1 absent) the new PA for Arcalyst will become effective in new users the first Wednesday 30 days after the signing of the minutes.

IX. UTILIZATION MANAGEMENT—NEW MANUAL PA CRITERIA

BAP Comments

A. New Manual PA Criteria

The P&T Committee recommended manual PA criteria for Relexxii and Arcalyst in new users, as outlined above.

BAP Comment: ☐ Concur ☐ Non-concur

B. New Manual PA Criteria—Implementation Plan

The P&T Committee recommended the new PA criteria for Relexxii become effective at 90 days and the new PA criteria for Arcalyst become effective at 30 days.

BAP Comment: ☐ Concur ☐ Non-concur

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

P&T Comments

A. Updated Manual PA Criteria

Updates to the manual PA criteria and step therapy were recommended due to availability of cost-effective alternative treatments, clinical trial data, clinical practice guideline updates, or provider recommendation. The updated PAs and step therapy outlined below will apply to new users.

1) Gastrointestinal-2 Agents: Chronic Idiopathic Constipation/Irritable Bowel Syndrome Constipation predominant (CIC/IBS-C) — lubiprostone (Amitiza)

The CIC/IBS-C class was reviewed in November 2018. Amitiza, linaclotide (Linzess), and plecanatide (Trulance) were made uniform formulary, with prucalopride (Motegrity) designated non-formulary and tegaserod (Zelnorm) designated as Tier 4/Not covered. As of November 2018, the drugs in the class all require PA, with a trial of standard laxatives required first. A generic to Amitiza has recently entered the market; however, it is markedly more expensive than Linzess. The manual PA criteria for Amitiza was updated to require a trial of linaclotide (Linzess) prior to use of Amitiza for all new users.

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updates to the manual PA criteria for Amitiza.

lubiprostone (Amitiza): Manual PA criteria apply to all new users of Amitiza and is approved if all criteria are met:

- The patient is 18 years of age or older OR is prescribed in consultation with a pediatric gastroenterologist for pediatric patients
- Patient has documented symptoms for ≥ 3 months
- Patient has diagnosis of constipation predominant irritable bowel syndrome (IBS-C) or chronic idiopathic constipation (CIC) or opioid induced constipation (OIC) in adults with chronic, non-cancer pain
    - Patient is currently taking an opioid if used for OIC
    - Patient is female if used for IBS-C
- Patient has documentation of failure of an increase in dietary fiber/dietary modification to relieve symptoms
- Patient has absence of GI obstruction

- 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 has tried and failed linaclotide (Linzess)**
- Patient is not taking any of these agents concomitantly (Linzess, Amitiza, Trulance, Symproic, Relistor, or Movantik)

Non-FDA-approved uses are not approved

Prior authorization expires after 1 year.

Renewal PA Criteria: Initial TRICARE PA approval is required for renewal. Coverage will be approved for 1 year for continuation of therapy if the following are met:

- Patient has had improvement in constipation symptoms
- Patient is not taking any of these agents concomitantly (Linzess, Amitiza, Trulance, Symproic, Relistor, or Movantik)

2) Antirheumatics: Injectable methotrexate—Otrexup and Rasuvo

The injectable methotrexate agents were reviewed in November 2015. Generic methotrexate injectable solution is uniform formulary while both methotrexate autoinjector formulations (Otrexup and Rasuvo) are NF. The manual PA criteria for Otrexup and Rasuvo were updated to require oral methotrexate in addition to generic injectable methotrexate prior to use of these less cost-effective autoinjector formulations for all new users. The updated PA criteria are the same as the PA criteria recommended in the new drug section for Reditrex on page 20.

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updates to the manual PA criteria for Otrexup and Rasuvo

Injectable methotrexate—Otrexup and Rasuvo: Manual PA criteria apply to all new users of Otrexup, and Rasuvo, and is approved if the following are met (with the updates from the May 2021 in bold)

- The patient has a diagnosis of active rheumatoid arthritis, polyarticular juvenile idiopathic arthritis or severe, recalcitrant, disabling psoriasis in adults

- **The patient has tried and failed ORAL methotrexate.**
- The patient has experienced intolerance or significant adverse effects from generic injectable methotrexate OR
- Patient has decreased finger dexterity, limited vision or impaired cognition resulting in the inability to utilize generic injectable methotrexate.

Non-FDA-approved uses are not approved, including neoplastic diseases

Prior authorization does not expire.

3) OAB Drugs – mirabegron (Myrbetriq)

Manual PA criteria for Myrbetriq have been in place since 2014. Vibegron (Gemtesa) is a new beta-3 adrenergic receptor agonist also approved for OAB, which was recommended for UF status in the new drug section. Vibegron is a therapeutic alternative to mirabegron, and is more cost effective. New users of Myrbetriq will now be required to try Gemtesa first, in addition to the existing PA requirements. *Note that Myrbetriq tablets received an additional indication for neurogenic detrusor overactivity (NDO, which were discussed at the August 2021 P&T meeting.)*

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updates to the manual PA criteria for Myrbetriq.

mirabegron (Myrbetriq): Manual PA criteria apply to all new users of Myrbetriq, and is approved if all criteria are met, with updates from the May 2021 meeting in bold.

- The patient has a confirmed diagnosis of overactive bladder (OAB) with symptoms of urge incontinence, urgency, and urinary frequency
- The patient has tried and failed behavioral interventions to include pelvic floor muscle training in women, and bladder training,
- The patient has had a 12-week trial with 2 formulary step-preferred products (oxybutynin IR, oxybutynin ER, tolterodine ER) and had therapeutic failure OR
- The patient has experienced central nervous system adverse events with oral OAB medications OR is at increased risk for such central nervous system effects due to comorbid conditions or other medications,

- **Patient has tried and failed or has a contraindication to vibegron (Gemtesa)**
- The patient does not have a CrCl < 15 mL/min
- If the CrCl is between 15-29 mL/min, the dosage does not exceed 25 mg QD

Non-FDA-approved uses are not approved.

Prior authorization does not expire.

4) Renin-Angiotensin Antihypertensives: Combinations – sacubitril/valsartan (Entresto)

Sacubitril/valsartan is an angiotensin receptor-neprilysin inhibitor (ARNI) approved for treating patients with chronic heart failure (HF). Entresto was reviewed and recommended for UF status with a manual PA in May 2016. Current PA criteria requires the patient to have been stabilized on an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) first, and to have a left ventricular ejection fraction (LVEF) ≤ 35%, based on the inclusion criteria of the PARADIGM clinical trial, which was used to gain FDA approval.

The Committee reviewed the February 2021 American College of Cardiology (ACC) Expert Consensus Decision Pathway for Optimization of HF, which now recommends ARNI therapy as preferred for first line treatment of chronic HF. Earlier this year, the FDA expanded the Entresto package insert, which now states the drug is indicated to decrease the risk of cardiovascular death and HF hospitalization in adults with chronic heart failure, with the benefits most evident in patients with LVEF below normal. The PARAGON trial results in patients with heart failure and preserved ejection fraction (HFpEF) were also reviewed. MHS cardiology providers have requested expanded access to Entresto.

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) removing the current PA criteria for sacubitril/valsartan, recognizing that guideline directed medical therapies (GDMT) for chronic HF, including Entresto are underutilized, and also acknowledging the 2021 ACC consensus pathway recommendations and updated FDA package labeling. Follow-up monitoring for Entresto utilization will be ongoing to evaluate usage patterns.

B. Updated Manual PA Criteria—Implementation Plan

The P&T Committee recommended the following implementation periods:

- The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updates to the current PA criteria in new users for Amitiza, the updates to the Rasuvo and Otrexup PA criteria for new users, updates to the PA for Myrbetriq for new users, and the removal of the Entresto PA criteria will become effective the first Wednesday 30 days after the signing of the minutes.

XI. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA

BAP Comments

A. Updated PA Criteria

The P&T Committee recommended updates to the manual PA criteria for the Amitiza, Otrexup Rasuvo, and Myrbetriq, and removing the Entresto PA as discussed above.

BAP Comment: □ Concur □ Non-concur

B. Updated PA Criteria—Implementation Plan

The P&T Committee recommended the PA updates for Amitiza, Rasuvo, Otrexup and Myrbetriq, and the removal of the Entresto PA criteria become effective the first Wednesday 30 days after the signing of the minutes

BAP Comment: □ Concur □ Non-concur

XII. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA FOR NEW FDA-APPROVED INDICATIONS, NCCN GUIDELINE UPDATES, OR

AGE RANGES

P&T Comments

A. Updated Manual PA Criteria

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updates to the PA criteria for several drugs due to new FDA-approved indications and expanded age ranges. The updated PA criteria outlined below will apply to new users.

Note that since these types of updates expand the patient population eligible for the drug, only a summary of the PA criteria is provided here; the current full PA criteria can be found on the TRICARE Formulary Search Tool at https://www.express-scripts.com/frontend/open-enrollment/tricare/fst/#/.

1) **Oncological Agents**
   - **Lung Cancer – crizotinib (Xalkori)—**The manual PA criteria were updated to allow for the new indication for treatment of relapsed or refractory systemic anaplastic large cell lymphoma (ALCL) that is anaplastic lymphoma kinase-positive (ALK+) in pediatric patients one year of age and older, and young adults. There is a limitation of use in older adults for this new indication as safety and efficacy of Xalkori is not established in older adults with relapsed or refractory, systemic ALK+ ALCL.
   - **Lung Cancer – lorlatinib (Lorbrena)—**Manual PA criteria now allow use as first-line treatment of adults with ALK+ metastatic non-small cell lung cancer (NSCLC) when tumors are ALK+ as detected by an FDA-approved test.

2) **Targeted Immunomodulatory Biologics (TIBs)**
   - **adalimumab (Humira)—**Manual PA criteria now allow use in pediatric patients 5 years of age and older as well as adults for moderately to severely active ulcerative colitis (UC).
   - **tocilizumab subcutaneous (Actemra SQ)—**Includes the new FDA-approved indication for slowing the rate of decline in pulmonary function in systemic sclerosis-associated interstitial lung disease (SSc-ILD) in adults.

3) **Parkinson's Agents – amantadine (Gocovri)—**Includes the new indication for use as adjunctive treatment to levodopa/carbidopa for add-on therapy for "off" episodes of Parkinson's Disease (PD).

4) **Pulmonary Arterial Hypertensions: prostacyclin nebulized – treprostinil (Tyvaso)—**Includes the new FDA-approved indication for treatment of pulmonary hypertension associated with interstitial lung disease (WHO Group 3) to improve exercise ability.

B. Updated PA Criteria—Implementation Plan

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the updates to the current PA criteria in new users for the oncology drugs Xalkori and Lorbrena; the TIBs Humira and Actemra SQ; the Parkinson's Disease Agent Gocovri; the pulmonary arterial hypertension drug Tyvaso will become effective the first Wednesday 60 days after the signing of the minutes. *Note that due to the BAP meeting delay and subsequent delay of the signing of the May 2021 P&T Committee meeting minutes, and the fact that the PA updates expand the potential patient eligible to receive the drugs listed above, the PAs were updated in September 2021.*

XIII. UTILIZATION MANAGEMENT—UPDATED MANUAL PA CRITERIA FOR NEW FDA-APPROVED INDICATIONS, NCCN GUIDELINE UPDATES, OR AGE RANGES

BAP Comments

A. Updated PA Criteria

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) updates to the PA criteria for several drugs due to new FDA-approved indications and expanded age ranges. The updated PA criteria outlined below will apply to new users.

BAP Comment: ☐ Concur ☐ Non-concur

B. Updated PA Criteria—Implementation Plan

The P&T Committee recommended the updates to the PA criteria for the drugs discussed above become effective at 60 days. Note that implementation occurred in September 2021.

BAP Comment:	☐ Concur	☐ Non-concur

XIV. RE-EVALUATION OF NONFORMULARY GENERICS: CALCIUM CHANNEL BLOCKERS (CCBs)

P&T Comments

Calcium Channel Blockers (CCBs) – Relative Clinical Effectiveness and Cost Analysis, Formulary Status and Implementation Plan

Background—The DHA Pharmacy Operations Division (POD) Formulary Management Branch (FMB) monitors changes in clinical information, current costs, and utilization trends to determine whether the formulary status of NF drugs that are now available in generic formulations needs to be readdressed. The P&T Committee's process for the reevaluation of NF agents was established at the May 2007 meeting and approved by the Director, of the then TRICARE Management Agency (now DHA), on July 24, 2007. A summary of the criteria is available in Appendix E of the November 2012 P&T Committee minutes, available online at https://health.mil/About-MHS/OASDHA/Defense-Health-Agency/Operations/Pharmacy-Division/DoD-Pharmacy-and-Therapeutics-Committee-2021/Meeting-Minutes.

The P&T Committee re-evaluated the UF status of the six NF CCBs, all of which are now available in generic formulations: verapamil capsule 24 hr (Verelan PM); verapamil capsule (Verelan); diltiazem tablet ER 24h (Cardizem LA); isradipine capsule (generic only); nicardipine (generic only); and nisoldipine tablet ER 24h (Sular).
Verelan PM has been designated as NF since the CCB drug class review in August 2005. The P&T Committee re-evaluated the formulary status of Verelan PM due to price reductions in generic verapamil capsule 24 hour formulations available across all three points of service (POS). There was no new clinical data to change the conclusion that the CCBs are highly therapeutically interchangeable.

Current utilization trends, numbers of generic products on the market by different manufactures, and relative cost-effectiveness, including the weighted average cost per unit for generic verapamil capsule 24 hour were also reviewed. The unit cost of generic verapamil capsule 24 hour formulations has dropped significantly

from the previous generic and brand cost, and the generic supply appears stable. The other NF CCB products have not shown a significant decline in cost.

The P&T Committee recommended (17 for, 0 opposed, 0 abstained, and 1 absent) returning generic verapamil capsule 24 hour (Verelan PM) to formulary status, effective the first Wednesday 30-days after signing of the minutes. The remaining nonformulary CCBs (Verelan, Cardizem LA, isradipine, nicardipine and nisoldipine) will remain NF.

XV. RE-EVALUATION OF NONFORMULARY GENERICS: CALCIUM CHANNEL BLOCKERS (CCBs)

BAP Comments

Calcium Channel Blockers (CCBs) – Relative Clinical Effectiveness and Cost Analysis, Formulary Status and Implementation Plan

The P&T Committee recommended returning generic Verelan PM to formulary status, as noted above, effective 30-days after signing of the minutes.

BAP Comment: ☐ Concur ☐ Non-concur

XVI. INFORMATION ITEM—SUMMARY OF RECOMMENDATIONS AND BENEFICIARY IMPACT

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
Menopausal Hormone Therapy: Single Agents, Combination Agents, and Vaginal Agents	*Vaginal Agents* ▪ conjugated equine estrogens vaginal cream (Premarin) ▪ estradiol vaginal cream (Estrace, generics) ▪ estradiol vaginal ring (Estring) ▪ estradiol acetate vaginal ring (Femring) ▪ estradiol vaginal tablet (Vagifem, generics) ▪ estradiol vaginal insert (Imvexxy) *moves from NF to UF* *Oral Single Agents* ▪ conjugated equine estrogens tablets (Premarin) ▪ estradiol tablets (Estrace, generics) ▪ esterified estrogens (Menest *Oral Combination Agents* ▪ conjugated equine estrogens/medroxyprogesterone acetate tablets (Prempro) ▪ conjugated equine estrogens plus medroxyprogesterone acetate tablets (Premphase) ▪ ethinyl estradiol/norethindrone acetate tablets (Jinteli, Femhrt, Fyavolv, generics) ▪ estradiol/norethindrone acetate tablets (Activella, Amabelz, Jinteli, Mimvey, Mimvey Lo, generics) ▪ esterified estrogens/ methyltestosterone (Covaryx, Covaryx HS, Eemt, Eemt HS, generics) ▪ estradiol/drospirenone (Angeliq) ▪ estradiol/norgestimate (Prefest) ▪ estradiol/progesterone caps (Bijuva)	▪ None	▪ None	Pending signing of the minutes / 30 days.	▪ No drugs designated as NF ▪ Imvexxy and Bijuva move from NF to UF ▪ No PAs for any agents in any of the three subclasses ▪ Current PA for Imvexxy was removed

DoD PEC Drug Class	UF Drugs	NF Drugs	Tier 4/Not Covered Drugs	Implement Date	Notes and Unique Users Affected
Sleep Disorders: Insomnia	UF step-preferred generics ▪ zolpidem IR (Ambien, generics) ▪ zolpidem ER (Ambien CR, generics) ▪ eszopiclone (Lunesta, generics) ▪ zaleplon (Sonata, generics) ▪ ramelteon (Rozerem, generics) *moves from NF to UF* ▪ doxepin 3 mg, 6 mg tablets (Silenor, generics) UF step-preferred brands ▪ suvorexant (Belsomra) *moves from NF to UF* ▪ lemborexant (Dayvigo)	NF and non-step-preferred brands ▪ zolpidem IR 1.75 mg, 3.5 mg sublingual tabs (Intermezzo, generics) ▪ zolpidem IR 5 mg, 10 mg sublingual tabs (Edluar) ▪ zolpidem oral spray (Zolpimist) ▪ tasimelteon capsules (Hetlioz) ▪ tasimelteon oral suspension (Hetlioz LQ)	▪ None	Pending signing of the minutes: 60 days.	▪ No changes made to the current NF drugs ▪ PAs updated as discussed on pp 12-14

Table of Newly Approved New Drugs Designated Tier 4—Unique Utilizers Affected

Drug	Total
levetiracetam 1,000 mg and 1,500 mg extended-release table (Elepsia XR)	0

Drugs with New Prior Authorization Criteria—Unique Utilizers Affected

Drug	MTF	Mail Order	Retail	Total
Methylphenidate extended release 72 mg tablets (Relexxii, generics)	1	24	155	180