

PRESCRIPTION MONOGRAPH

Compounded Active Ingredients: Progesterone/Estradiol

Form: Topical Cream

Drug Class:

- Progesterone: Progestin (Natural Steroid Hormone)
 - Estradiol (E2): Estrogen; agonist at estrogen receptors
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Mechanism of Action^{1,2,3:}

When compounded together, Progesterone/Estradiol can recreate ovarian function to reduce menopausal symptoms while minimizing progestin-related adverse effects. It is intended to:

- Bind estrogen receptors (ER α /ER β) in reproductive tissues, brain, bone, and vasculature, alleviating hot flashes, vaginal dryness, and mood changes.
 - Provide endometrial protection by opposing estrogen-induced hyperplasia.
 - Convert to allopregnanolone, a GABA-A modulator, improving sleep quality and anxiety.
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Indications Commonly Prescribed for:

- Prevention of endometrial hyperplasia in postmenopausal women receiving estrogen therapy
 - Treatment of secondary amenorrhea
 - Assisted reproductive technology (ART) for infertile women with progesterone deficiency
 - Prevention of postmenopausal osteoporosis
 - Treatment of vulvovaginal atrophy
 - Menopausal hormone therapy (MHT)
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Before Use: Let your healthcare provider know if you have any medication allergies before you take this compounded preparation. Let your healthcare provider know if you have any liver or kidney problems. Let your healthcare provider know of all supplements you are currently taking.

Contraindications:

- Known hypersensitivity to components
 - Undiagnosed abnormal genital bleeding
 - Hormone-sensitive malignancies
 - Thromboembolic disorders or recent events (e.g., DVT, PE, stroke, MI)
 - Liver dysfunction or disease
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Cautions: Let your Healthcare provider know if you experience any adverse side effects.

How to Use: This compounded preparation is in the form of a topical cream. The cream is a special container that will administer 0.25ml dose. Clean desired area prior to use. To administer remove the protective covering on the top of the dispenser. Place the jar on a flat surface. Using clean, dry hands, gently press down on the top of the pump. This will dispense a measured amount of cream through the center opening. Confirm the cream has exited the holes at the top of the dispenser. Apply the cream onto the desired area. Continue to rub the area until the cream is evenly dispersed over the desired area. Replace the protective cover and store the device until next dose. If you miss a dose apply as soon as you remember, but not at the time for the next dose. The desired results may take up to several weeks.

Compounded medications are not FDA-approved and may differ in risks, benefits, and side effects from FDA-approved products. These statements have not been evaluated by the FDA and are not intended to diagnose, treat or cure any disease or condition and do not indicate any claims of safety or efficacy. Individual results may vary.

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Warnings and Precautions:

- Cardiovascular Risks: Potential increased risk of heart attack and stroke; monitor patients.
 - Use cautiously/avoid in patients with hormone-sensitive malignancies.
 - Fluid Retention: Exercise caution in patients with conditions that may be exacerbated by fluid retention, such as epilepsy, migraine, asthma, cardiac or renal dysfunction.
 - Sedation/dizziness: Take at bedtime; caution driving/operating machinery.
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Adverse Reactions: If you experience any side effects or adverse reactions, including those not listed, please contact your healthcare provider. Seek emergency care if symptoms are severe

Common:

- Breast tenderness
- Bloating, fluid retention
- Mood swings
- Drowsiness, Dizziness, Headache

Serious:

- Thromboembolic events
 - Cardiovascular events
 - Breast/endometrial cancer risk
 - Gallbladder disease
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Interactions:

- Potential interaction with thyroid hormones (may affect binding globulins)
 - CYP3A4 modulators: May alter hormone levels
 - Anticoagulants: Estrogen may reduce anticoagulant efficacy
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Use in Specific Populations:

- Pregnancy: Use only if clearly needed and prescribed by a healthcare provider.
 - Lactation: Progesterone is excreted in breast milk; caution is advised.
 - Pediatrics: Safety and efficacy have not been established in pediatric patients.
 - Geriatrics: Use with caution; increased sensitivity in some older individuals cannot be ruled out.
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Storage:

- Store in original container at room temperature (up to 30°C or 86°F)
 - Store in a cool dry place away from heat, sunlight, and moisture
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Monitoring Parameters:

- Regular physical examinations, including breast and pelvic exams
 - Hormone and thyroid panels
 - Routine labs: Lipid profile, liver function, and blood pressure
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Citations:

1. Cable JK, Grider MH. Physiology, Progesterone. [Updated 2022 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK558960/>
 2. Goletiani NV, Keith DR, Gorsky SJ. Progesterone: review of safety for clinical studies. *Exp Clin Psychopharmacol*. 2007 Oct;15(5):427-44. doi: 10.1037/1064-1297.15.5.427. PMID: 17924777.
 3. Kovács T, Szabó-Meleg E, Ábrahám IM. Estradiol-Induced Epigenetically Mediated Mechanisms and Regulation of Gene Expression. *International Journal of Molecular Sciences*. 2020; 21(9):3177. <https://doi.org/10.3390/ijms21093177>
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