

# PRESCRIPTION MONOGRAPH

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**Compounded Active Ingredients:** Estradiol/Estriol

**Form:** Topical Cream

**Drug Class:**

- Estradiol (E2): Estrogen; agonist at estrogen receptors
  - Estriol (E3): Estrogen; agonist at estrogen receptors
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**Mechanism of Action**<sup>1,2</sup>: When compounded together, Estradiol/Estriol is intended to offer a balanced formulation aimed at restoring estrogen. It is intended to:

- Bind to nuclear ER $\alpha$  and ER $\beta$ , regulating gene expression across tissues
  - Activate non-genomic pathways via membrane estrogen receptors (e.g., GPER), providing rapid cellular signaling.
  - Exhibit antigonadotropic effects by suppressing LH and FSH through negative feedback on the hypothalamic-pituitary axis.
  - Exert local mucosal and urethral effects, enhancing lubrication and elasticity.
  - Reduce hypothalamic thermoregulatory instability.
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**Indications Commonly Prescribed for:**

- Menopausal hormone therapy (MHT)
  - Hypogonadism and delayed puberty in adolescent females (e.g., Turner syndrome).
  - Feminizing hormone therapy in transgender women and non-binary individuals.
  - Adjunctive support in bioidentical hormone regimens.
  - Infertility and IVF protocols: For endometrial preparation and cervical mucus modulation.
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**Before Use:** Let your health care provider know if you have any medication allergies before you take this compounded preparation. Let your health care provider know if you have any liver or kidney problems. Let your healthcare provider know of all supplements you are currently taking.

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**Contraindications:**

- Undiagnosed vaginal bleeding
  - Hormone-sensitive malignancies
  - Thromboembolic disorders or recent events (e.g., DVT, PE, stroke, MI)
  - Active liver disease or liver dysfunction
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**Cautions:** Let your Healthcare provider know if you experience any adverse side effects.

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**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. Turn the dosing knob in the direction marked for the number of prescribed clicks. Confirm the cream has exited the holes at the top of the dispenser. Apply the cream by rubbing the dispenser (where cream exited the holes) onto the desired area. Continue to rub the area until the cream is evenly dispersed over the desired area. Replace the protective cover with a light push 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.

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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:

- Endometrial hyperplasia and cancer risk when used without progestin in women with a uterus.
  - Venous thromboembolism (VTE) and cardiovascular risks are higher with oral administration due to first-pass hepatic effects; lower with transdermal routes.
  - Breast cancer risk: Elevated with prolonged estrogen ± progestin use.
  - Cardiovascular Risks: Potential increased risk of heart attack and stroke; monitor patients.
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## Adverse Reactions:

### Common:

- Breast tenderness
- Bloating, nausea
- Headache
- Fluid retention
- Irregular bleeding

### Serious, but Rare:

- Cardiovascular events
  - Gynecomastia
  - Myocardial infarction
  - Breast/endometrial cancer risk
  - Gallbladder disease
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## Interactions:

- Anticoagulants: monitor closely.
  - CYP3A4 modulators: May alter metabolism.
  - Insulin: may impact glucose tolerance; watch glycemic control.
  - Potential interaction with thyroid hormones (may affect binding globulins).
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## Use in Specific Populations:

- Postmenopausal women: Relief of menopausal symptoms.
  - Pregnancy and lactation: Contraindicated.
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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:

- Hormone and thyroid panels
  - Clinical monitoring: Vasomotor symptoms, bleeding, breast changes.
  - Routine labs: Lipid profile, liver function, and blood pressure.
  - Screening exams: Annual mammography and endometrial surveillance as clinically indicated.
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## Citations:

1. 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>
  2. Postmenopausal estrogen therapy: route of administration and risk of venous thromboembolism. *ACOG Committee Opinion No. 556. Obstet Gynecol*. 2013;121(4):887–889.
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