RonanRx
PERSONALIZED MEDICINE

CLINICAL MONOGRAPH · HORMONE OPTIMIZATION

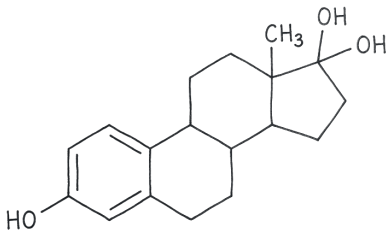
# Estriol

*Weaker estrogen often combined with estradiol (Bi-Est)*

Estriol (E3) is one of three human estrogens (alongside estradiol/E2 and estrone/E1) [kuhl2005]. It is a weaker estrogen than estradiol and is the dominant estrogen circulating during pregnancy, where it is made by the placenta.

Outside the US, estriol has been used for decades as a prescription medicine for menopausal vaginal atrophy and related symptoms; brands such as Ovestin are sold in Europe [pinkerton2022]. In the United States, estriol is not FDA-approved as a drug, no branded estriol product is marketed in the US, and the only legal way to obtain it is via 503A compounding pharmacies on a patient-specific prescription.

Major US menopause societies (NAMS, the Endocrine Society, NASEM, and ACOG) have raised concerns about how compounded estriol, especially in Bi-Est and Tri-Est combinations, is marketed to consumers as a 'safer' or 'natural' alternative to FDA-approved estradiol [nams2017; nasem2020; acog2012]. The available evidence does not support those marketing claims. RonanRx prepares estriol only on a patient-specific prescription written by a licensed doctor for an identified patient and does not promote cBHRT marketing language [head1998].




EVIDENCE POSTURE WELL STUDIED EMERGING

REVIEWED **2026-05-11**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State-licensed 503A


Pharmacist reviewed


Doctor led


Cold-chain ready


Patient choice preserved


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## Why Personalized Estriol

Estriol has no FDA-approved single-agent product in the United States. There is no branded estriol dose to anchor on, no US manufacturer schedule, no average trial patient to titrate toward. The European literature was built around vaginal pessaries and oral tablets at fixed strengths, and even those studies were not picked for your baseline E2, your age at menopause, your endometrial history, whether your symptoms are predominantly vaginal and urogenital or systemic, or whether you respond to estradiol the way the average study participant did.

That is the work a compounding pharmacy does. Estriol in the US exists almost entirely as a compounded preparation: vaginal cream and suppositories for GSM at strengths the European brands do not cover, oral troches and capsules for systemic symptoms, and Bi-Est blends (estriol plus estradiol) where the ratio is chosen for that patient rather than fixed by a manufacturer. A prescriber who knows your chart can shift the E3:E2 ratio, drop the systemic dose, swap route from oral to vaginal when only urogenital tissue needs treatment, and leave out preservatives or excipients you do not tolerate. Estriol's well studied evidence base is in vaginal use for genitourinary symptoms; systemic and Bi-Est dosing rests on lower-tier evidence and individual response, which is exactly the situation a patient-specific prescription is built for.

This is what pharmacy looked like before mass manufacturing. A doctor wrote the prescription, a pharmacist prepared it for that patient, and the label named them both. Compounded estriol is that older arrangement, kept honest by modern oversight.

## Quick Facts About Estriol

**Category:** Endogenous human estrogen (weak; E3)

**Common aliases:** E3, oestriol, 16α-hydroxy-estradiol, 1,3,5(10)-estratrien-3,16α,17β-triol

**Biological role:** Dominant estrogen during pregnancy (placental product); minor circulating estrogen outside pregnancy

**Receptor preference:** Binds both ERα and ERβ but with markedly lower affinity than estradiol; short residence time on the receptor gives it weak agonist behavior at usual physiologic concentrations

**FDA-approval status (United States):** NOT FDA-approved. No branded estriol product is marketed in the US. Estriol is available in the US only through 503A compounding.


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**Approval outside the US:** Marketed in many European countries as Ovestin and similar brands for vaginal atrophy and menopausal symptoms; available in the United Kingdom, Netherlands, Germany, and elsewhere

**Compounded under:** 503A, patient-specific prescription only

**Common compounded forms:** Vaginal cream, vaginal suppository / pessary, oral tablet, troche, and compounded combinations such as Bi-Est (estriol + estradiol) or Tri-Est (estriol + estradiol + estrone)

**cBHRT context:** Major US menopause and endocrine bodies (NAMS, Endocrine Society, NASEM, ACOG) have specifically criticized marketing of compounded bioidentical hormone therapy, including Bi-Est and Tri-Est, that claims estriol-containing preparations are 'safer' than FDA-approved estradiol products. Evidence does not support that claim.

**SPECIALS: PATIENT-SPECIFIC PRESCRIPTION ONLY**

Estriol described in this monograph is a 503A compounded preparation. Every dose is made on a prescription, for a named patient, by a licensed pharmacist. It is not a stocked, mass-manufactured product.

- **Made to order, not off a shelf.** No batch sits in a warehouse waiting for buyers. Your prescription triggers the prep.
- **Named-patient label.** The bottle carries one patient's name. The batch records carry one prescription.
- **Dose, strength, and route chosen for the patient.** A prescriber decides what gets compounded, not a manufacturer who set the strength for a trial population.
- **Licensed pharmacist on the hook.** A real person, with a license that can be pulled, signs off on every prep. State inspectors check the facility.
- **Compounded drugs are not FDA-approved.** They should not be evaluated using branded-drug trial data alone. Availability varies by state and prescribed medication.

## How This Differs from a Research-Use-Only Website

A research-use-only website ships a vial from a warehouse. There is no prescription, no pharmacist, no facility inspection, and no way to recall the product if something is wrong with it. If the vial is mislabeled, contaminated, or under-potent, there is nobody whose license is at stake.

A 503A compounding pharmacy is the other thing. The doctor writes the prescription. A licensed pharmacist, whose name is on the label, prepares the medicine in a facility the state inspects. If something goes wrong, there is a person and a license on the hook, and a documented chain of custody on every lot. That accountability is what makes it safe.

## What is Estriol?

Estriol (E3) is a steroid hormone produced naturally in the human body. Chemically it is 16α-hydroxy-estradiol, a metabolite of estradiol with an additional hydroxyl group at position 16α [kuhl2005]. Outside pregnancy, plasma estriol concentrations are low (typically <80 pg/mL), and most circulating E3 is derived from peripheral conversion of estradiol and estrone [head1998].


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During pregnancy estriol becomes the dominant circulating estrogen. The placenta synthesizes large amounts of estriol from dehydroepiandrosterone sulfate (DHEAS) produced by the fetal adrenal gland and 16α-hydroxylated in the fetal liver, so maternal serum estriol rises from picograms per milliliter to nanograms per milliliter over the course of gestation [kuhl2005]. Maternal unconjugated estriol was historically used in clinical practice as a marker of fetoplacental well-being and remains a component of the second-trimester triple/quadruple screen for fetal aneuploidy.

Outside pregnancy, estriol is sometimes referred to as a 'weak' estrogen because its affinity for the estrogen receptor, and especially its receptor residence time, is much lower than estradiol's [head1998, kuhl2005]. Pharmacologically it is still an estrogen agonist; with continuous exposure at therapeutic doses, its biological effects are qualitatively similar to those of other estrogens, just less potent.

## How Estriol Works

Estriol binds the two classical nuclear estrogen receptors, ERα and ERβ, and triggers the same general transcriptional machinery as estradiol. The difference is quantitative: estriol's binding affinity for ER is roughly one order of magnitude lower than estradiol's, and its receptor residence time is much shorter [kuhl2005, head1998]. At physiologic non-pregnant concentrations this short residence translates into weaker estrogenic effect. At sustained therapeutic doses, estriol behaves as a full estrogen agonist on target tissues.

Selectivity between ERα and ERβ is modest and concentration-dependent [head1998]. Marketing claims that estriol is a clean 'ERβ-selective' estrogen and therefore inherently safer than estradiol have not been supported in the controlled clinical literature [nams2017, nasem2020].

Vaginal estriol acts predominantly on local ER in the vaginal epithelium, urethra, trigone, and vulvar tissues, the targets of genitourinary syndrome of menopause (GSM). At low vaginal doses, systemic absorption is small relative to oral therapy, which is why low-dose vaginal estriol has been adopted in European practice as a local therapy for GSM with limited systemic estrogenic exposure [lethaby2016, cardozo1998, head1998].

## Biological Role of Estriol

Estriol is the dominant circulating estrogen during human pregnancy. The placenta cannot synthesize estriol on its own; it depends on a fetoplacental unit in which the fetal adrenal gland makes DHEA-sulfate, the fetal liver 16α-hydroxylates it, and the placenta then aromatizes that substrate to estriol [kuhl2005]. This anatomical dependency made maternal serum unconjugated estriol a useful historical marker of fetal-placental function, low maternal estriol can indicate fetal compromise, placental insufficiency, or anencephaly. In current US obstetric practice, unconjugated estriol remains a component of the second-


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trimester multiple-marker screen for trisomy 21, trisomy 18, and open neural-tube defects, where low maternal E3 is one of the contributing markers.

Outside pregnancy, estriol is a minor circulating estrogen. Most estriol in non-pregnant adults derives from peripheral metabolism of estradiol and estrone rather than from de novo ovarian secretion [head1998]. Endogenous postmenopausal estriol concentrations are very low.

The clinical relevance of estriol outside pregnancy is therefore almost entirely pharmacologic, exogenous administration for menopausal symptoms (predominantly vaginal atrophy / GSM in European practice), for compounded combination 'Bi-Est' and 'Tri-Est' menopausal hormone therapy preparations in the US, and as an investigational adjunct in autoimmune disease.

## Detailed Mechanism of Estriol

Mechanistically, estriol's short ER residence time means that, at low circulating levels, it occupies the receptor briefly and dissociates before completing the full transcriptional response that estradiol would. This kinetic difference, not a fundamentally different receptor, is the basis for its 'weak estrogen' classification [kuhl2005, head1998]. When estriol is administered continuously at higher doses, occupancy is sustained and the agonist response approaches that of other estrogens, including endometrial and breast tissue effects.

Some preclinical and older clinical work suggested that estriol given in a pulsed, brief-occupancy fashion might antagonize estradiol's effect on breast tissue [head1998]; this hypothesis underpinned mid-century 'estriol therapy as breast protection' claims. Larger controlled clinical work has not confirmed that estriol is preferentially safe or protective at the breast at clinically used dosing schedules, and the 2017 NAMS position statement, the 2020 NASEM report on cBHRT, and ACOG Committee Opinion 532 all explicitly caution against marketing estriol-containing compounded products as 'safer' than FDA-approved estradiol [nams2017, nasem2020, acog2012].

Mechanism studies relevant to multiple sclerosis (a non-classical indication for estriol) found that pregnancy-range estriol exposure is anti-inflammatory in experimental autoimmune encephalomyelitis (EAE), the principal MS animal model. Estrogen-receptor-α expression on astrocytes is required for the protective effect [spence2011, spence2012], and ERβ ligands are independently neuroprotective in disease-onset models [wisdom2013]. These mechanisms are biologically interesting and underpin the Voskuhl clinical program, but they describe MS biology rather than a 'safety' advantage for menopausal use.


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## Estriol Research History

Estriol was characterized as a third human estrogen in the 1930s [pinkerton2014]. European clinical use for menopausal symptoms began in the 1960s and 1970s under brand names such as Ovestin (Organon) and continued through subsequent decades in oral and vaginal formulations [head1998, kuhl2005].

Schiff and colleagues' work in the 1980s and a sequence of European and Japanese trials in the 1990s and 2000s established the dose ranges used clinically for oral and vaginal estriol in menopausal symptoms [takahashi2000a, takahashi2000b] [pinkerton2014]. A line of work culminating in Granberg 2002 documented that oral estriol at typical European doses does not appear to stimulate the endometrium meaningfully when used as monotherapy at low dose [granberg2002] [murina2016; hirschberg2020].

The vaginal estriol literature accelerated in the 2000s and 2010s with multiple randomized trials and head-to-head comparisons in postmenopausal vaginal atrophy and GSM, including ultra-low-dose 50 µg vaginal gel formulations [pinkerton2014] [caruso2016; caruso2017]. The 2016 Cochrane review by Lethaby and colleagues [lethaby2016] consolidated this evidence and concluded that low-dose vaginal estrogens (including vaginal estriol) are effective for GSM with limited systemic absorption [buchholz2015].

Outside menopausal medicine, the most consequential modern estriol literature is Rhonda Voskuhl's multiple sclerosis program at UCLA [pinkerton2014]. The original 2002 open-label pilot in 10 women with relapsing-remitting or secondary-progressive MS reported a substantial reduction in gadolinium-enhancing brain lesions during pregnancy-range estriol dosing [sicotte2002]. Mechanistic follow-up [soldan2003] documented immunologic shifts. The 2016 placebo-controlled phase 2 trial of oral estriol 8 mg/day added to glatiramer acetate in 158 women with RRMS [voskuhl2016] demonstrated a modest reduction in annualized relapse rate at 12 months that did not persist at 24 months, and follow-on neuroimaging [mackenzie2018] and neurofilament-light-chain [voskuhl2022] analyses described subgroup signals. To date this remains the only well-controlled trial of high-dose oral estriol for an autoimmune disease, and the effect is best characterized as modest.

On the regulatory and societal side, the 2010s and 2020s saw a sequence of major US position statements specifically addressing compounded bioidentical hormone therapy: ACOG Committee Opinion 532 (2012) [acog2012], the NAMS 2017 hormone therapy position statement [nams2017], Pinkerton & Pickar 2016 [pinkerton2016], the 2020 NASEM consensus report on cBHRT [nasem2020], and Pinkerton 2022 [pinkerton2022] [pinkerton2014]. All of these explicitly addressed estriol-containing compounded preparations and concluded that marketing claims of superior safety or 'natural' advantage are not supported by the evidence and that prescribing should be patient-specific rather than driven by direct-to-consumer marketing.


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## Estriol Timeline

**1930s** • Estriol characterized as a third human estrogen alongside estradiol and estrone

**1960s, 1980s** • European clinical use of oral and vaginal estriol (Ovestin, Synapause) for menopausal symptoms; foundational pharmacology and dose-finding work [head1998; kuhl2005]

**1994** • Henriksson et al [henriksson1994]. publish multicenter comparison of estradiol vaginal ring vs estriol vaginal pessaries for urogenital atrophy

**1998** • Head publishes 'Estriol: safety and efficacy' review in Alternative Medicine Review, summarizing European estriol literature for North American audience [head1998]

**2000** • Takahashi et al [takahashi2000a; takahashi2000b]. publish two reports on oral estriol for postmenopausal symptoms (Maturitas; Human Reproduction)

**2002** • Sicotte et al. publish open-label pilot of oral estriol 8 mg/day in 10 women with multiple sclerosis (Annals of Neurology); Granberg et al [sicotte2002; granberg2002]. publish endometrial-safety study of oral estriol

**2003** • Soldan et al [soldan2003]. publish immune-modulation mechanism data from the Sicotte pilot population

**2005** • Kuhl publishes comprehensive review 'Pharmacology of estrogens and progestogens: influence of different routes of administration' (Climacteric) [kuhl2005]

**2012** • ACOG Committee Opinion 532 on compounded bioidentical menopausal hormone therapy [acog2012]

**2016** • Voskuhl et al. publish phase 2 trial of estriol + glatiramer acetate in relapsing-remitting MS (Lancet Neurology); Caruso et al [voskuhl2016]. publish ultra-low-dose vaginal estriol gel quality-of-life trial; Lethaby et al [caruso2016; lethaby2016]. Cochrane review of local vaginal estrogen for atrophy

**2017** • NAMS 2017 hormone therapy position statement explicitly addresses cBHRT including estriol-containing preparations; Caruso 2017 ultralow topical estriol in pelvic-organ-prolapse population [nams2017; caruso2017]

**2018** • MacKenzie-Graham et al [mackenzie2018]. publish voxel-based morphometry analysis of estriol-treated MS patients showing localized neuroprotection signal

**2020** • NASEM publishes 'The Clinical Utility of Compounded Bioidentical Hormone Therapy' consensus report; Hirschberg et al [nasem2020; hirschberg2020]. publish ultra-low-dose vaginal estriol gel in breast-cancer survivors on aromatase inhibitors


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**2022** • Pinkerton publishes 'Concerns About Compounded Bioidentical Menopausal Hormone Therapy' (Cancer Journal); Voskuhl et al [pinkerton2022; voskuhl2022]. report decreased neurofilament-light-chain in estriol-treated MS

**2023** • Crandall et al [crandall2023]. JAMA review 'Management of Menopausal Symptoms' summarizes evidence for vaginal estrogens including estriol in GSM

## Clinical Contexts for Estriol

### Genitourinary syndrome of menopause (GSM) / vulvovaginal atrophy WELL STUDIED

*Well studied outside the US; vaginal estriol is a first-line local therapy in European practice.*

Multiple randomized trials and a 2016 Cochrane systematic review [lethaby2016] support low-dose vaginal estriol (cream, suppository/pessary, ring, or ultra-low-dose gel) for the symptoms of postmenopausal vaginal atrophy, dryness, dyspareunia, urgency, and recurrent UTI [henriksson1994; cardozo1998]. Ultra-low-dose 50 µg estriol vaginal gel has been studied in healthy postmenopausal women [caruso2016], in women after surgery for pelvic-organ prolapse [caruso2017], in coital pain populations [murina2016], and in breast-cancer survivors on aromatase inhibitors [hirschberg2020]. Vaginal estriol combined with lactobacilli has been studied for quality of life in endocrine-treated breast cancer [buchholz2015]. Systemic absorption from low-dose vaginal estriol is limited, and endometrial stimulation appears minimal at standard dosing [granberg2002, lethaby2016]. In the US, vaginal estriol is available only through 503A compounding because no FDA-approved estriol product exists [crandall2023].

### Menopausal vasomotor symptoms (oral estriol) WELL STUDIED

*Studied in European and Japanese trials; less effective than estradiol; not first-line in current US guidelines.*

Oral estriol has been studied for menopausal symptoms including hot flushes and mood disturbance, predominantly in European and Japanese populations [takahashi2000a, takahashi2000b]. Typical European oral doses (1, 8 mg/day) reduce some menopausal symptoms but are generally considered less potent than oral estradiol [kuhl2005, head1998] [crandall2023]. Endometrial safety at standard European oral doses appears acceptable [granberg2002], although high or sustained oral dosing reaches receptor occupancies comparable to other estrogens and conventional unopposed-estrogen risks should be assumed unless specifically refuted [nams2017]. US menopause guidelines do not recommend oral estriol as a first-line vasomotor therapy.


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### Bi-Est / Tri-Est compounded menopausal hormone therapy EMERGING

*Common compounded use in US practice; major US menopause and endocrine bodies have specifically criticized claims that estriol-containing combinations are 'safer' than FDA-approved estradiol.*

In the United States, where no FDA-approved estriol product is marketed, compounded combinations of estriol with estradiol (Bi-Est, typically 80% estriol / 20% estradiol) or estriol + estradiol + estrone (Tri-Est) are commonly prepared as menopausal hormone therapy in topical creams, troches, or pellets [boothby2004; files2011]. The pharmacologic rationale offered in cBHRT marketing, that estriol is a uniquely 'safe' or 'natural' estrogen, has been specifically and repeatedly criticized by ACOG (Committee Opinion 532) [acog2012], NAMS (2017 position statement) [nams2017], the Endocrine Society / Pinkerton & Pickar 2016 [pinkerton2016, pinkerton2014], the 2020 NASEM consensus report [nasem2020], and Pinkerton 2022 [pinkerton2022]. The consensus across these bodies is that compounded estriol-containing menopausal HT should be reserved for patient-specific clinical needs that an FDA-approved estradiol product cannot meet (e.g., true documented allergy to a non-active ingredient, dose that is not commercially available), not used as a direct-to-consumer 'safer alternative.'

### Multiple sclerosis (relapsing-remitting) EMERGING

*Investigational adjunctive use; one well-designed phase 2 trial with modest effect.*

The Voskuhl program at UCLA has been the principal source of MS evidence. The 2002 open-label pilot [sicotte2002] in 10 women reported reduction in gadolinium-enhancing lesions on oral estriol 8 mg/day. Mechanistic immune studies [soldan2003] and preclinical EAE studies [spence2011, spence2012, wisdom2013] supported plausibility. The 2016 randomized, placebo-controlled phase 2 trial added oral estriol 8 mg/day to glatiramer acetate in 158 women with RRMS [voskuhl2016] and reported a modest reduction in annualized relapse rate at 12 months that did not persist at 24 months [confavreux1998]. Follow-up MRI [mackenzie2018] and neurofilament-light-chain [voskuhl2022] analyses describe additional subgroup signals. No pivotal trial has been completed. The clinical context is one well-designed phase 2 trial with modest effect; estriol is not an FDA-approved MS therapy.

### Recurrent urinary tract infection in postmenopausal women WELL STUDIED

*Local vaginal estrogen (including estriol) reduces recurrent UTI in postmenopausal women.*

Postmenopausal genitourinary atrophy is associated with recurrent UTI, and local vaginal estrogen reduces the recurrence rate in placebo-controlled trials. The Lethaby 2016 Cochrane review and follow-up reviews of postmenopausal UTI management identify local vaginal estrogens, including estriol formulations in European studies, as effective for UTI recurrence reduction [lethaby2016, gupta2011]. The mechanism is restoration of vaginal epithelial maturation, vaginal pH, and lactobacillus colonization [buchholz2015].


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## Off-Label Uses of Estriol

**Pregnancy fetal-monitoring marker (historical clinical use)** WELL STUDIED

*Historical use, now largely superseded.*

Maternal serum or urinary unconjugated estriol was used historically as a marker of fetoplacental well-being. In current US obstetric practice it remains a component of the second-trimester multiple-marker (triple/quad) screen for fetal aneuploidy and open neural-tube defects, but cell-free fetal DNA and other markers have largely replaced E3 monitoring for routine fetal-well-being assessment. This is a diagnostic use of endogenous estriol, not a therapeutic use of exogenous estriol [kuhl2005].

## Compounded Estriol (503A)

Because no FDA-approved estriol product is marketed in the US, every estriol prescription in the US is filled either via importation from Europe under specific conditions or, far more commonly, by a 503A compounding pharmacy [acog2012, nasem2020, pinkerton2022]. This is structurally different from many other compounded substances, where compounding is an alternative to an FDA-approved product. For estriol, compounding is the primary route of legal US availability.

RonanRx prepares compounded estriol on a patient-specific prescription written by a licensed prescribing physician for an identified patient, consistent with section 503A of the Federal Food, Drug, and Cosmetic Act [fda503a]. Common preparations include vaginal cream, vaginal suppository, oral tablet or troche, and combination products such as Bi-Est and Tri-Est.

RonanRx does not market compounded estriol-containing menopausal hormone therapy as 'safer' or 'more natural' than FDA-approved estradiol products [pinkerton2016]. The major US menopause and endocrine bodies, ACOG, NAMS, the Endocrine Society, and the National Academies (NASEM), have explicitly stated that such marketing claims are not supported by the available evidence [nams2017]. Compounded estriol is appropriate when the prescribing physician documents a patient-specific clinical need (excipient sensitivity, dose not commercially available, vaginal formulation not commercially available in the US), not as a direct-to-consumer substitute for FDA-approved therapy [pinkerton2014].

## Estriol Formulations and Routes

| Form | Concentration | Description |
|---|---|---|
| Vaginal cream | | |


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| Form | Concentration | Description |
|---|---|---|
| | 0.5, 1 mg per gram (typical European labeling); ultra-low-dose 50 µg/g formulations studied in clinical trials | Applied intravaginally for GSM / vulvovaginal atrophy; the route with the strongest controlled evidence base |
| Vaginal suppository / pessary | 0.5 mg per pessary in the European literature (e.g., Henriksson 1994 used 0.5 mg estriol pessaries) | Single-use intravaginal pessary for GSM |
| Oral tablet | 1, 2 mg per tablet in European labeling; trial doses 1, 8 mg/day depending on indication | Used in European practice for menopausal symptoms; 8 mg/day used in the Voskuhl MS phase 2 trial |
| Compounded topical cream (Bi-Est / Tri-Est) | — | Compounded blend of estriol with estradiol (Bi-Est, typically 80/20) or with estradiol and estrone (Tri-Est); applied to skin |
| Troche | — | Sublingual or buccal troche compounded form; pharmacokinetic data are limited compared with oral and vaginal routes |

**Routes used in published literature:** vaginal, oral, topical, troche.

## Estriol Dosing

| Route | Population | Range | Duration | Study type |
|---|---|---|---|---|
| vaginal cream | postmenopausal women, GSM | 0.5, 1 mg per application; ultra-low-dose 50 µg per application in newer gel trials | daily for 2, 3 weeks for symptom induction, then twice weekly maintenance is a typical European pattern | randomized controlled trials and Cochrane review |
| vaginal pessary / suppository | postmenopausal women, urogenital atrophy | 0.5 mg per pessary | varied (daily induction to twice-weekly maintenance) | randomized comparative trial |
| oral | postmenopausal women, menopausal symptoms | 1, 8 mg/day in European and Japanese trials | weeks to months | randomized and open-label clinical trials |
| oral | women with relapsing-remitting MS (investigational) | 8 mg/day | 24 months in the phase 2 trial | randomized, double-blind, placebo-controlled phase 2 |


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Doses listed reflect published clinical-trial protocols and European labeling for products that are not FDA-approved in the United States. They are not RonanRx prescribing recommendations. The prescribing doctor selects route, dose, and frequency based on the patient's clinical context, indication, and goals.

Doses listed should not be presented to patients as instructions. Patient instructions originate from the prescribing physician's prescription, not from this educational page.

## Estriol Safety

Estriol is an estrogen. Its safety profile shares the class-level considerations of other systemic estrogens, venous thromboembolism, stroke, gallbladder disease, breast and endometrial effects with sustained systemic exposure, and these should be assumed at therapeutic systemic doses unless directly refuted by trial data [25][2] [30]. Marketing claims that estriol is intrinsically 'safer' or 'natural' relative to FDA-approved estradiol are not supported by the available evidence and have been specifically rejected by ACOG, NAMS, the Endocrine Society, and NASEM [27][29][26].

Low-dose vaginal estriol delivers limited systemic absorption and is generally well tolerated in the published trials. Even at low vaginal doses, current US guidance treats vaginal estrogens in women with a history of breast cancer as a shared-decision discussion with the treating oncologist [19] [16][17]. Endometrial safety at low-dose vaginal estriol monotherapy appears acceptable in the published literature [14][21], although the lack of a US-labeled product means there is no FDA-approved endometrial-monitoring schedule for the formulations actually dispensed in the US [28].

### Contraindications

By class, contraindications are those that apply to all systemic estrogen therapy: known or suspected estrogen-dependent malignancy (notably breast cancer, treated as a relative contraindication requiring oncology involvement), known or suspected pregnancy outside the specific obstetric context, active or recent venous thromboembolism, active arterial thromboembolic disease (recent stroke, MI), undiagnosed abnormal genital bleeding, severe active hepatic disease, and known hypersensitivity to a component of the preparation [25][2]. The absence of a US-approved product means there is no FDA-labeled US contraindications list for estriol specifically; the prescribing physician applies the class-level considerations.

### Drug interactions

Estriol shares the metabolic and binding considerations of other estrogens: hepatic CYP3A4-mediated metabolism (and therefore interactions with CYP3A4 inducers such as rifampin, phenytoin, carbamazepine, and St John's wort, and CYP3A4 inhibitors), competition with thyroid binding globulin and corticosteroid binding globulin that can alter free hormone levels, and modest effects on coagulation factors at systemic exposure. The clinical magnitude of these interactions for low-dose vaginal estriol is small but not zero [2]. The prescribing physician's interaction review applies.


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### Adverse events

In the published vaginal estriol trials, reported adverse events have been mild and predominantly local, vaginal irritation, application-site discomfort, transient discharge, with low rates of systemic estrogenic symptoms [16][17]. In oral estriol trials at European menopausal doses, breast tenderness, headache, and breakthrough bleeding have been reported at frequencies comparable to other oral estrogens [12][13] [18]. In the Voskuhl MS phase 2 trial at 8 mg/day, irregular menses was the most commonly reported adverse event [5].

Serious estrogen-class adverse events, venous thromboembolism, stroke, endometrial hyperplasia / cancer with sustained unopposed systemic dosing, breast effects, should be assumed possible at any systemic dose absent direct evidence to the contrary [25][26] [19]. The low-dose-vaginal-estriol literature reports endometrial safety at standard dosing [14][21] but is not the same as long-term high-dose oral data.

## Monitoring Estriol Therapy

Monitoring follows the prescribing physician's plan and the indication. For low-dose vaginal estriol used for GSM, routine biochemical monitoring is not required; symptom response and any unexpected vaginal bleeding are the principal clinical signals, with prompt evaluation of any postmenopausal bleeding [lethaby2016, nams2017].

For systemic (oral or compounded transdermal) estriol-containing menopausal HT, prescribers typically apply the monitoring framework of FDA-approved estradiol HT, periodic blood pressure, breast and pelvic examination per usual care guidelines, mammography per age-appropriate screening, evaluation of any abnormal bleeding, and reassessment of the risk/benefit balance at least annually [nams2017, crandall2023]. Compounded preparations do not relieve any of these monitoring expectations.

Patients should report any unexpected vaginal bleeding, breast lump, leg swelling or pain (potential VTE), sudden severe headache or visual disturbance, or sudden weakness/numbness (potential stroke) to the prescribing physician promptly.

## Estriol in Special Populations

## Estriol Evidence Quality

Evidence quality varies sharply by indication. For low-dose vaginal estriol in GSM, the evidence is well developed: multiple randomized trials, a Cochrane systematic review [lethaby2016], and a comprehensive JAMA narrative review [crandall2023] all support efficacy with limited systemic absorption [caruso2016].

For oral estriol in menopausal vasomotor symptoms, the evidence base is older and predominantly European/Japanese [takahashi2000a, takahashi2000b, granberg2002], with limited US replication and no


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head-to-head superiority over FDA-approved oral or transdermal estradiol. US guidelines do not recommend oral estriol as first-line vasomotor therapy [nams2017, crandall2023] [henriksson1994].

For Bi-Est / Tri-Est compounded menopausal HT, there are no large randomized trials of the compounded combination itself; the cBHRT literature is dominated by position statements from the major menopause and endocrine bodies criticizing marketing claims [buchholz2015; acog2012; pinkerton2022].

For multiple sclerosis, the entire human evidence base is one open-label pilot [sicotte2002], one randomized phase 2 trial [voskuhl2016], and follow-up imaging/biomarker work [mackenzie2018, voskuhl2022]. The phase 2 effect is best characterized as modest. No pivotal trial has been completed. Estriol is not an FDA-approved MS therapy [pinkerton2014; pinkerton2016; nasem2020].

The absence of FDA approval is itself a critical feature of the US evidence landscape for estriol. The compound has not been through a US new-drug application; there is no FDA-reviewed labeling, no FDA-mandated endometrial safety data set for the formulations actually dispensed in the US, and no FDA pharmacovigilance pipeline. That structure shapes how compounded estriol can responsibly be used and how it should not be marketed [caruso2017; murina2016; hirschberg2020].

## Major Estriol Clinical Studies

| Study | Design | Participants | Duration | Finding |
|---|---|---|---|---|
| Estriol combined with glatiramer acetate for women with relapsing-remitting multiple sclerosis: a randomised, placebo-controlled, phase 2 trial | Randomized, double-blind, placebo-controlled phase 2 | 158 | 24 months | Oral estriol 8 mg/day added to glatiramer acetate reduced annualized relapse rate at 12 months (0.25 vs 0.37 with placebo) in women with RRMS; the difference did not persist at 24 months [voskuhl2016]. Adverse events were balanced apart from irregular menses in the estriol arm. |
| Treatment of multiple sclerosis with the pregnancy hormone estriol | Open-label pilot, crossover | 10 | 6 months on, 6 months off, 6 months on | In 6 women with RRMS, oral estriol 8 mg/day reduced gadolinium-enhancing brain lesions during treatment; effect reversed off-treatment and recurred on rechallenge [sicotte2002]. First in-human signal that pregnancy-range estriol could modulate MS activity. |


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| Study | Design | Participants | Duration | Finding |
|---|---|---|---|---|
| Immune modulation in multiple sclerosis patients treated with the pregnancy hormone estriol | Mechanistic immunology substudy | 10 | treatment-on/off comparison | Documented shifts in cytokine profile (reduced IFN-γ and TNF-α, increased IL-5 and IL-10) on estriol, consistent with immune-modulatory mechanism proposed from EAE models [soldan2003]. |
| Estriol-mediated neuroprotection in multiple sclerosis localized by voxel-based morphometry | Imaging substudy of the phase 2 trial | subset of 158 | 24 months | Voxel-based morphometry showed estriol treatment was associated with preserved gray-matter volume in specific cortical regions implicated in MS disability [mackenzie2018]. |
| Decreased neurofilament light chain levels in estriol-treated multiple sclerosis | Biomarker substudy | subset | 24 months | Serum neurofilament-light-chain levels, a marker of axonal injury, were lower in the estriol-treated arm [voskuhl2022]. |
| Local oestrogen for vaginal atrophy in postmenopausal women (Cochrane systematic review) | Systematic review of randomized trials | pooled across 30 trials, ~6000 women | varied | Low-dose vaginal estrogens, including estriol cream, pessary, and ring formulations, reduced symptoms of vaginal atrophy and improved vaginal cytology, with limited systemic absorption and limited endometrial stimulation in studied populations [lethaby2016]. |
| Quality of life and sexual function of naturally postmenopausal women on an ultralow-concentration estriol vaginal gel | Prospective comparison | varied | 12 weeks | Ultra-low-dose (50 μg) estriol vaginal gel improved quality-of-life and sexual-function scores in naturally postmenopausal women with vaginal atrophy [caruso2016]. |
| Effects of ultralow topical estriol dose on vaginal health and quality of life in postmenopausal women who underwent surgical | Prospective comparative trial | varied | 12 weeks | Ultra-low-dose topical estriol was associated with improved vaginal health and quality-of-life scores after prolapse surgery [caruso2017]. |


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| Study | Design | Participants | Duration | Finding |
|---|---|---|---|---|
| treatment for pelvic organ prolapse | | | | |
| Coital pain in the elderly: could a low-dose estriol gel thrill the vulvar vestibule? | Prospective clinical study | varied | 12 weeks | Low-dose vulvar estriol gel improved coital pain and vestibular health scores in postmenopausal women with vestibulodynia [murina2016]. |
| Efficacy and safety of ultra-low dose 0.005% estriol vaginal gel in breast cancer survivors on aromatase inhibitors | Phase II randomized double-blind placebo-controlled | 61 | 12 weeks | Ultra-low-dose 50 µg estriol vaginal gel improved vulvovaginal atrophy in postmenopausal breast-cancer survivors on aromatase inhibitors [hirschberg2020]. Systemic estriol exposure remained low. Use of vaginal estrogen in breast-cancer survivors remains a shared-decision discussion with the treating oncologist. |
| Vaginal estriol-lactobacilli combination and quality of life in endocrine-treated breast cancer | Prospective observational | varied | weeks | Combination of vaginal estriol and lactobacilli improved vaginal symptoms and quality of life in endocrine-treated breast cancer patients with vaginal atrophy [buchholz2015]. |
| A comparative multicenter study of the effects of continuous low-dose estradiol vaginal ring versus estriol vaginal pessaries in postmenopausal women with urogenital atrophy | Randomized comparative multicenter | 159 | 24 weeks | Both the estradiol ring and 0.5 mg estriol vaginal pessaries improved urogenital atrophy symptoms and vaginal cytology with comparable efficacy; both were well tolerated [henriksson1994]. |
| Efficacy and safety of oral estriol for managing postmenopausal symptoms | Clinical trial | varied | 12 months | Oral estriol at European doses improved climacteric symptoms; endometrial safety in studied population was acceptable; the comparator was not FDA- |


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| Study | Design | Participants | Duration | Finding |
|---|---|---|---|---|
| | | | | approved estradiol [takahashi2000a]. |
| Safety and efficacy of oestriol for symptoms of natural or surgically induced menopause | Clinical trial | varied | 12 months | Oral estriol reduced menopausal symptoms in natural and surgically induced menopause populations with acceptable safety in the studied range [takahashi2000b]. |
| The effects of oral estriol on the endometrium in postmenopausal women | Multicenter clinical trial | varied | 12 months | Oral estriol at typical European doses was not associated with substantial endometrial proliferation or hyperplasia in the studied population [granberg2002]. |
| The National Academies (NASEM) consensus report on compounded bioidentical hormone therapy | Consensus expert report | n/a | n/a | NASEM concluded that compounded bioidentical hormone therapy, including estriol-containing preparations, should be restricted to patient-specific medical needs that an FDA-approved product cannot meet, and that current marketing of cBHRT as 'safer' or 'natural' is not supported by evidence [nasem2020]. |
| The 2017 hormone therapy position statement of The North American Menopause Society | Position statement / clinical practice guideline | n/a | n/a | NAMS specifically addressed compounded estriol-containing hormone therapy and concluded that claims of superior safety vs FDA-approved estradiol are not supported by available evidence; compounded HT should be limited to patient-specific clinical needs [nams2017]. |


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## Estriol Pharmacokinetics & Pharmacodynamics

### Pharmacokinetics

Oral estriol is rapidly absorbed and rapidly conjugated. First-pass hepatic conjugation to estriol-3-glucuronide and estriol-3-sulfate is extensive, so unconjugated oral estriol bioavailability is low and plasma half-life of the unconjugated parent is short [kuhl2005, head1998]. This first-pass conjugation is one reason European labeling has historically used relatively large oral doses (1, 8 mg/day) to achieve target tissue effect.

Vaginal estriol bypasses hepatic first pass. Even at low vaginal doses, local vaginal-tissue concentrations are high while systemic plasma concentrations remain modest [lethaby2016, kuhl2005]. This is the pharmacokinetic basis for using low-dose vaginal estriol as a local GSM therapy with limited systemic exposure.

Plasma protein binding for estriol is moderate (lower than estradiol), and metabolism is via hepatic conjugation followed by enterohepatic recirculation and renal excretion. The pharmacokinetics of compounded troche and topical-cream Bi-Est / Tri-Est formulations are not well characterized in controlled studies [nasem2020], a gap repeatedly identified by NASEM and Pinkerton.

### Pharmacodynamics

Pharmacodynamically estriol is a full estrogen agonist with reduced potency relative to estradiol because of shorter receptor residence time [kuhl2005, head1998]. At low local vaginal concentrations the dominant effect is restoration of vaginal epithelial maturation, vaginal pH, and lactobacillus colonization, the GSM endpoints. At higher systemic concentrations the full spectrum of estrogenic effects emerges, including potential endometrial proliferation if unopposed.

There is no compelling controlled-clinical evidence that estriol is a tissue-selective 'designer' estrogen with intrinsically lower breast or thrombotic risk than estradiol [nams2017, nasem2020, pinkerton2022]. Marketing claims to that effect rely on selective interpretation of older preclinical work and are not endorsed by the major US menopause/endocrine bodies.

## Comparing Estriol Formulations

Vaginal cream, vaginal pessary, and vaginal ring are the local routes used in the GSM literature. Direct head-to-head work [henriksson1994] found that 0.5 mg estriol pessaries and a low-dose estradiol vaginal ring produced comparable improvement in urogenital atrophy symptoms and vaginal cytology [hirschberg2020]. Newer ultra-low-dose 50 µg vaginal estriol gel formulations have been studied in


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multiple populations including breast-cancer survivors on aromatase inhibitors [caruso2016; caruso2017; murina2016].

Oral estriol is studied predominantly in European and Japanese trials at 1, 8 mg/day [takahashi2000a, takahashi2000b, granberg2002]; the 8 mg/day dose is also the dose used in the Voskuhl MS phase 2 trial [voskuhl2016]. Oral estriol is not first-line for vasomotor symptoms in US guidelines [nams2017, crandall2023].

Compounded Bi-Est and Tri-Est creams and troches do not have controlled pharmacokinetic or efficacy data comparable to either FDA-approved estradiol products or the European estriol literature [nasem2020, pinkerton2022]. This evidence gap is one of the central findings of the NASEM consensus report on cBHRT.

## Estriol Storage and Handling

Compounded estriol vaginal cream and topical preparations are typically stored at controlled room temperature per the dispensing pharmacy's labeling. Refer to the dispensing pharmacy's labeling for the specific preparation received, including beyond-use date.

## Estriol Compounding & Operations

### 503A compounding

RonanRx prepares estriol under 503A on a patient-specific prescription written by a licensed prescribing physician for an identified patient, consistent with section 503A of the Federal Food, Drug, and Cosmetic Act [fda503a] [pinkerton2014]. Because no FDA-approved estriol product is marketed in the US, the 503A compounded form is the principal legal US route to the medication [acog2012, nasem2020] [pinkerton2016].

Bulk drug substance is sourced from FDA-registered API suppliers, with ingredient suitability verified for the intended formulation pathway [nams2017]. Finished preparations follow USP <795> standards for non-sterile compounding (vaginal cream, oral tablet, troche). Each preparation carries a lot number tied to the prescription record.

RonanRx does not market estriol-containing menopausal HT as 'safer,' 'more natural,' or 'better' than FDA-approved estradiol products, consistent with the published positions of ACOG, NAMS, the Endocrine Society, and NASEM [nams2017; pinkerton2022].


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### Pharmacist review

Each prescription is reviewed by a licensed pharmacist before dispensing. Review covers prescribed strength, route, formulation suitability, patient-specific contraindications based on the prescription record, ingredient compatibility, and label accuracy.

Because estriol-containing HT can be substituted into a Bi-Est or Tri-Est combination that includes estradiol and/or estrone, the pharmacist confirms the prescribed combination, ratio, and strength against the prescription as written, with any clarifications routed back to the prescriber rather than resolved by the pharmacy unilaterally [fda503a].

### Quality and traceability

Every compounded preparation carries a lot number tied to the prescription record. Potency testing for compounded estrogen preparations follows USP <795> guidance with documentation retained per state board of pharmacy requirements. The NASEM report and Pinkerton position pieces specifically called out compounding-quality variability as a concern in the cBHRT marketplace [nasem2020, pinkerton2022]; operational discipline on assay, lot release, and recordkeeping is the appropriate response.

## Frequently Asked Questions About Estriol

### Is estriol FDA-approved?

No. Estriol is not FDA-approved as a drug in the United States. No branded estriol product is marketed in the US. Estriol is available in the US only via 503A compounding on a patient-specific prescription [kuhl2005]. (In Europe, estriol has been marketed for decades, Ovestin and similar, for menopausal vaginal atrophy.) Compounded drugs are not FDA-approved [acog2012; nasem2020; head1998].

### Is estriol safer than estradiol?

Major US menopause and endocrine bodies, ACOG, NAMS, the Endocrine Society, and NASEM, have specifically reviewed this question and concluded that the available controlled clinical evidence does not show a safety advantage for estriol-containing compounded preparations over FDA-approved estradiol products [acog2012; nams2017; pinkerton2016]. Marketing language asserting such an advantage is not supported by the literature. Estriol is a weaker estrogen by binding kinetics, but at therapeutic doses it is an estrogen agonist and class-level estrogen risks apply [pinkerton2014] [nasem2020; pinkerton2022].

### What conditions has estriol been studied in?

Published controlled investigation has focused on genitourinary syndrome of menopause / vulvovaginal atrophy (vaginal cream, pessary, ring, and ultra-low-dose gel; multiple RCTs and a Cochrane review), menopausal symptoms in European/Japanese populations (oral estriol), recurrent UTI in postmenopausal women, and relapsing-remitting multiple sclerosis (one open-label pilot and one phase 2 randomized trial)


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[lethaby2016; caruso2016; caruso2017; voskuhl2016]. The strongest evidence base is for vaginal estriol in GSM [hirschberg2020; takahashi2000a; takahashi2000b; sicotte2002].

### What is Bi-Est? What is Tri-Est?

Bi-Est is a compounded combination of estriol with estradiol, most commonly 80% estriol and 20% estradiol by mass, usually prepared as a topical cream [nasem2020; pinkerton2022]. Tri-Est adds estrone [nams2017; pinkerton2014]. These compounded combinations are widely marketed in the US as 'bioidentical' menopausal hormone therapy, but they are not FDA-approved, do not have controlled pharmacokinetic or efficacy data comparable to FDA-approved estradiol products, and have been specifically reviewed and criticized by ACOG, NAMS, the Endocrine Society, and NASEM when marketed as 'safer' or 'more natural' than FDA-approved estradiol [files2011; boothby2004; acog2012].

### Why might a doctor prescribe compounded estriol?

Because no FDA-approved estriol product is marketed in the US, 503A compounding is the principal legal way for a US patient to receive estriol. Reasons documented by prescribing physicians include vaginal-atrophy symptoms where a vaginal estriol cream is desired (particularly when the patient has tolerated estriol in a European-market product), documented allergy or sensitivity to a component of an FDA-approved estradiol product, or a dose or formulation not commercially available [head1998; lethaby2016]. The compounded route is patient-specific, not direct-to-consumer [fda503a; nasem2020].

### Can estriol be used in women with a history of breast cancer?

Vaginal estrogens, including low-dose vaginal estriol, in women with a history of breast cancer are treated as a shared-decision discussion involving the patient's treating oncologist. Hirschberg 2020 studied ultra-low-dose 0.005% estriol vaginal gel in postmenopausal breast-cancer survivors on aromatase inhibitors and reported improved vulvovaginal atrophy with low systemic estriol exposure, but the decision remains an individualized risk/benefit discussion [hirschberg2020]. Major guidelines do not endorse vaginal estrogen use in this population as a default [nams2017; crandall2023].

### Does RonanRx sell estriol directly to patients?

No. Compounded estriol is dispensed only on a patient-specific prescription written by a licensed doctor for an identified patient, with pharmacist review, ingredient-suitability verification, and lot-traceable preparation. RonanRx is not a direct-to-consumer storefront for estriol or for compounded Bi-Est / Tri-Est menopausal HT [fda503a].

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## How to Access Estriol

Compounded Estriol is dispensed under 503A on a patient-specific prescription. Depending on your role, the next step looks different.

FOR PRESCRIBING CLINICIANS

### Offer this medication

A pharmacist will follow up within two business days. We'll cover state availability, supported formulations, and what integration looks like for your clinic.

ronanrx.com/request-partnership-call

PATIENT WITH A DOCTOR

### Receive your prescription

If your doctor has prescribed Estriol, sign up so we can prepare and ship your medication. The signup wizard collects intake and connects you to the prescribing workflow.

ronanrx.com/patients

PATIENT WITHOUT A DOCTOR

### Find a partner clinic

RonanRx prescribes through partner clinics — we don't initiate prescriptions on this site. Read how the referral process works and how to find a partner clinic in your state.

ronanrx.com/find-clinic


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# Other compounds RonanRx makes

This monograph is one of many in the RonanRx formulary. Every compound below is prepared under 503A on a patient-specific prescription. Browse the full catalog at ronanrx.com/medications and ronanrx.com/peptides, or scan the codes at right for each index.

Medications

Peptides

## MEDICATIONS (40)

Alpha-Lipoic Acid (ALA) — Antioxidant & mitochondrial
Coenzyme Q10 (CoQ10) — Antioxidant & mitochondrial
Glutathione — Antioxidant & mitochondrial
NAD+ / NMN — Antioxidant & mitochondrial
Compounded Topical Anesthetics (BLT, LET) — Dermatology
Topical Minoxidil — Dermatology
Topical Tretinoin — Dermatology
Compounded Magnesium — Energy & nutritional
Cyanocobalamin — Energy & nutritional
High-Dose Vitamin D — Energy & nutritional
Hydroxocobalamin — Energy & nutritional
Iron (Compounded) — Energy & nutritional
L-Carnitine — Energy & nutritional
Methylcobalamin (B12) — Energy & nutritional
Methylfolate — Energy & nutritional
Anastrozole — Hormone optimization
Clomiphene & Enclomiphene — Hormone optimization
DHEA — Hormone optimization
Estradiol — Hormone optimization
Estriol — Hormone optimization
Human Chorionic Gonadotropin (HCG) — Hormone optimization
Pregnenolone — Hormone optimization
Progesterone — Hormone optimization
Testosterone — Hormone optimization
Compounded Metformin — Metabolic & weight
Compounded Semaglutide — Metabolic & weight
Compounded Tirzepatide — Metabolic & weight
Lipotropic Injection (MIC, MICC) — Metabolic & weight
Low-Dose Naltrexone (LDN) — Metabolic & weight
Naltrexone-Bupropion Combination — Metabolic & weight
Topiramate — Metabolic & weight
Bremelanotide / PT-141 — Sexual health
Compounded Sildenafil — Sexual health
Compounded Tadalafil — Sexual health
Trimix Injection — Sexual health
Compounded Gabapentin — Sleep & recovery
Compounded Melatonin — Sleep & recovery
Compounded T3 (Liothyronine) — Thyroid
Compounded T3/T4 Combinations — Thyroid
Compounded T4 (Levothyroxine) — Thyroid


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## PEPTIDES (21)

Sermorelin — Available now

Tesamorelin — Available now

AOD-9604 — Growth-hormone axis (under FDA review)

CJC-1295 — Growth-hormone axis (under FDA review)

GHRP-2 / GHRP-6 — Growth-hormone axis (under FDA review)

Hexarelin — Growth-hormone axis (under FDA review)

Ipamorelin — Growth-hormone axis (under FDA review)

MK-677 / Ibutamoren — Growth-hormone axis (under FDA review)

5-Amino 1MQ — Metabolic & longevity (under FDA review)

Epitalon / Epithalon — Metabolic & longevity (under FDA review)

MOTS-C — Metabolic & longevity (under FDA review)

Thymosin Alpha-1 / Thymalin — Metabolic & longevity (under FDA review)

DSIP, Delta Sleep-Inducing Peptide — Neuro & cognitive (under FDA review)

Selank — Neuro & cognitive (under FDA review)

Semax — Neuro & cognitive (under FDA review)

Vasoactive Intestinal Peptide (VIP) — Neuro & cognitive (under FDA review)

BPC-157 — Tissue repair (under FDA review)

KPV — Tissue repair (under FDA review)

LL-37 — Tissue repair (under FDA review)

Pentadeca Arginate (PDA) — Tissue repair (under FDA review)

TB-500 / Thymosin Beta-4 — Tissue repair (under FDA review)


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