WOMEN'S BIOIDENTICAL HORMONE REPLACEMENT THERAPY

Estradiol · Estriol · Progesterone · Testosterone · DHEA

Prescriber Reference Guide · The Medicine Shoppe, York PA

Perimenopause · Menopause · Hormone Optimization · Custom-Compounded · Lab-Guided · Rx Required

Program Overview

Compounded bioidentical hormone replacement therapy (BHRT) uses hormones that are molecularly identical to those produced endogenously by the female body -- derived from plant precursors (diosgenin from yam and soy) and synthesized to the same molecular structure as endogenous estradiol, estriol, progesterone, testosterone, and DHEA. Compounding allows the prescriber to individualize hormone type, dose, ratio, and delivery form based on the patient's laboratory values, symptom profile, and clinical history -- something no commercial one-size-fits-all product can offer. This guide provides a reference for prescribers compounding BHRT at The Medicine Shoppe.

Key Clinical Advantages of Compounded BHRT

- Individualized dosing -- doses titrated to lab values (serum or salivary) and symptom response, not standardized to a population average
- Hormone selection flexibility -- prescribe the specific hormones indicated for the individual patient; combine estradiol + estriol + progesterone + testosterone + DHEA in any clinically appropriate combination
- Delivery form options -- oral capsules, topical creams, vaginal creams, troches, sublingual drops; route matched to patient preference and pharmacokinetic goals
- Excipient control -- formulated without dyes, fillers, or allergens found in commercial products; critical for sensitive patients
- Estriol availability -- estriol is not available in any FDA-approved commercial product in the US; compounding is the only source for patients who clinically benefit from E3
- Combination preparations -- multiple hormones in a single application reduce patient burden and improve adherence

Bioidentical vs. Conventional HRT -- Key Distinctions

The term 'bioidentical' refers to molecular structure, not source or regulatory status. FDA-approved bioidentical options exist (estradiol patches, gels, progesterone capsules) but are limited in dose and form. Compounded BHRT extends this further with individualized dosing, additional hormone options (estriol, DHEA), and custom delivery forms. Prescribers should understand the distinctions:

	FDA-Approved HRT	Compounded BHRT
Molecular Structure	Varies -- includes bioidentical (estradiol, progesterone) and non-bioidentical (conjugated equine estrogens, medroxyprogesterone acetate)	Bioidentical -- identical molecular structure to endogenous hormones
Dosing	Fixed commercial doses	Individualized to lab values and symptoms
Estriol (E3)	Not available	Available via compounding only
Hormone Combinations	Limited fixed combinations	Any clinically appropriate combination
Delivery Forms	Limited commercial forms	Oral, topical, vaginal, sublingual, troche -- per prescriber
Excipient Control	Manufacturer-determined	Prescriber can specify; allergen/irritant-free available
Regulatory Status	FDA-approved with package insert labeling	Compounded per state pharmacy law and USP standards; not FDA-approved as a finished drug
Evidence Base	Extensive RCT data (WHI, KEEPS, ELITE)	Pharmacokinetic and clinical data; limited RCT data specific to compounded preparations

Hormone Profiles -- Mechanisms & Clinical Roles

Estradiol (E2)

Physiology	The dominant, most potent endogenous estrogen in premenopausal women. Produced primarily by ovarian granulosa cells. Binds estrogen receptors (ER-alpha and ER-beta) in virtually every tissue -- uterus, breast, bone, brain, cardiovascular system, skin, and urogenital tract.
Menopause Decline	Ovarian E2 production ceases at menopause; adrenal aromatization of androgens accounts for residual low-level production. The abrupt decline in E2 drives vasomotor symptoms, urogenital atrophy, bone loss, cognitive changes, and cardiovascular risk shifts.
Clinical Benefits	Vasomotor symptoms (hot flashes, night sweats) -- most effective treatment available; bone density preservation; mood and cognitive support; urogenital tissue maintenance; improved sleep quality; cardiovascular benefits when initiated in early menopause (timing hypothesis)
Compounded Forms	Topical cream (most common; avoids hepatic first-pass), oral capsule, vaginal cream, sublingual drop; concentration per prescriber specification; typical topical range 0.5-2 mg/day
Monitoring	Serum estradiol; symptom response; endometrial protection confirmation (progesterone co-prescription in women with intact uterus is mandatory)

Estriol (E3)

Physiology	The weakest of the three endogenous estrogens; predominant estrogen of pregnancy (produced by placenta). Has lower ER-alpha binding affinity than estradiol -- weaker systemic estrogenic activity with more selective action at urogenital ER-beta receptors. Not commercially available in the US in any FDA-approved product.
Clinical Role	Primarily used for urogenital atrophy, vaginal dryness, and local vulvovaginal tissue support. The lower systemic potency relative to E2 makes it preferred for vaginal/vulvar applications, particularly in patients where minimizing systemic estrogen exposure is a priority. Also used topically in some facial and skin aging protocols.
Bi-Est Formulations	Commonly compounded as Bi-Est (combination of estradiol and estriol in a fixed ratio -- typically 80/20 or 70/30 E2:E3 by percentage). Bi-Est provides systemic estrogen replacement (E2 component) combined with urogenital tissue benefit (E3 component) in a single preparation.
Evidence	Cochrane and clinical evidence strongly supports vaginal estriol for GSM/atrophic vaginitis. Evidence for systemic estriol as primary replacement is more limited than for estradiol; used as adjunct or in Bi-Est combinations by integrative/functional medicine prescribers.
Typical Formulation	Vaginal cream: estriol 0.5-1 mg/g; topical cream as part of Bi-Est: E2/E3 ratio per prescriber; all concentrations customizable

Progesterone

Physiology	Endogenous progesterone is produced by the corpus luteum in the luteal phase of the menstrual cycle and by the placenta during pregnancy. It opposes estrogen stimulation of the endometrium, supports sleep via GABA-A receptor neurosteroid activity (as allopregnanolone metabolite), and has anxiolytic and mood-stabilizing effects.
Critical Role: Endometrial Protection	In women with an intact uterus, estrogen therapy without adequate progestogen causes endometrial hyperplasia and increases endometrial carcinoma risk. Progesterone is mandatory in any estrogen-containing BHRT regimen for women who have not had a hysterectomy. This is non-negotiable.
Bioidentical vs. Synthetic Progestins	Medroxyprogesterone acetate (MPA, Provera) -- the synthetic progestin in conventional HRT -- has different receptor activity than natural progesterone and has been associated with increased breast cancer risk in the WHI study. Micronized bioidentical progesterone (Prometrium, or compounded equivalent) has a more favorable risk profile in multiple observational studies and does not appear to carry the same breast risk.
Sleep & Mood Benefits	Progesterone's conversion to allopregnanolone provides GABA-A receptor positive allosteric modulation -- producing anxiolytic, sedative, and sleep-promoting effects. Many BHRT patients report significant improvement in sleep quality and anxiety with progesterone. Oral route (bedtime) maximizes the neurosteroid benefit; topical route has lower allopregnanolone conversion.
Compounded Forms	Oral capsule (preferred for sleep/mood benefit and endometrial protection); topical cream (lower systemic levels -- adequate for symptom management but endometrial protection is less well-established; do not rely on topical progesterone alone for endometrial protection); vaginal suppository
Typical Doses	Oral: 100-200 mg at bedtime; topical cream: 20-100 mg/day; per prescriber based on clinical indication and monitoring

Testosterone

Physiology	Women produce testosterone in the ovaries and adrenal glands at approximately 1/10th male levels. Testosterone declines with age and drops precipitously with oophorectomy or adrenal insufficiency. Androgen receptors are expressed in the brain, muscle, bone, skin, clitoris, and throughout the genitourinary tract.
Clinical Benefits in Women	Libido and sexual desire (most evidence-supported indication); energy and vitality; muscle tone and body composition; cognitive clarity and focus; clitoral and genital sensitivity; mood and sense of wellbeing; bone density support (modest)
Evidence	Multiple RCTs demonstrate benefit of testosterone for hypoactive sexual desire disorder (HSDD) in post-menopausal women (Davis et al., Shifren et al.). An international consensus panel (2019) concluded testosterone is effective and safe for HSDD in post-menopausal women. Use in premenopausal women is less well-studied but clinically used for androgen deficiency, especially in those with SHBG elevation from oral contraceptives.
Compounded Forms	Topical cream (most common; applied to inner arm, thigh, or vulvar area); oral capsule (less preferred due to hepatic metabolism); sublingual
Typical Doses	Topical: 0.5-2 mg/day (significantly lower than male doses); start low and titrate to symptom response and lab values; avoid virilizing doses
Monitoring	Serum total and free testosterone, SHBG at baseline and 6-8 weeks after initiation; monitor for virilization (acne, hair growth, clitoral changes); maintain levels in upper female physiologic range

DHEA (Dehydroepiandrosterone)

Physiology	DHEA is the most abundant circulating adrenal steroid and serves as the primary precursor for sex hormone synthesis in peripheral tissues (intracrinology). DHEA and its sulfate (DHEA-S) decline progressively with age -- falling ~80% between ages 25 and 75. Peripheral conversion to androgens and estrogens occurs in target tissues based on local enzyme expression.
Clinical Applications	Adrenal support and energy; mood and wellbeing (DHEA receptors in brain); libido and sexual function (via androgen conversion); immune modulation; bone density support; menopausal symptom contribution. Intravaginal DHEA (prasterone/Intrarosa) is FDA-approved for dyspareunia -- the only FDA-approved DHEA product.
Compounded DHEA	Compounded oral DHEA capsules allow precise low-dose titration below commercially available OTC supplement doses; compounded vaginal DHEA suppositories/cream provide local intracrine androgen/estrogen conversion in urogenital tissue for GSM without significant systemic absorption.
Typical Doses	Oral: 5-25 mg/day (much lower than typical OTC doses; titrate to DHEA-S lab levels and symptoms); vaginal: 6.5-10 mg/day (equivalent to FDA-approved prasterone dose); concentration per prescriber
Monitoring	Serum DHEA-S at baseline and 6-8 weeks; maintain DHEA-S in upper-normal range for age; monitor for androgenic side effects at higher doses

Delivery Forms & Pharmacokinetics

Form	Pharmacokinetics & Advantages	Best For
Topical Cream	Transdermal absorption bypasses hepatic first-pass metabolism -- delivers hormone directly to systemic circulation without hepatic modification. Avoids oral estrogen's hepatic effects (SHBG elevation, clotting factor induction). Steady absorption with consistent daily application. Level and timing of peak vary by skin site and individual.	Estradiol, testosterone (preferred routes); avoids hepatic first-pass; preferred when liver health is a concern or when minimizing SHBG elevation is important
Oral Capsule	Undergoes hepatic first-pass metabolism -- oral progesterone converts to neuroactive metabolites (allopregnanolone) that provide sleep/anxiolytic benefit; oral estradiol has more hepatic estrogenic effect. Convenient once-daily dosing.	Progesterone (bedtime -- maximizes neurosteroid benefit); DHEA; some testosterone protocols; not preferred route for estradiol (hepatic first-pass increases clotting factors and SHBG)
Vaginal Cream	Local delivery to vaginal and vulvar tissue with minimal systemic absorption. Achieves high local tissue concentrations for urogenital indications without systemic hormonal exposure.	Estriol (vaginal atrophy, GSM); low-dose estradiol for local urogenital effect; DHEA for intracrine urogenital conversion; progesterone vaginal use for local uterine effect
Sublingual Drop	Absorbed directly through oral mucosa -- bypasses GI first-pass. Faster onset than oral capsule. Variable absorption; patient technique-dependent.	Estradiol or testosterone when rapid onset or first-pass avoidance is desired; useful for patients with GI absorption concerns
Combination Formula	Multiple hormones in a single preparation -- reduces number of daily applications. Can combine E2+E3 (Bi-Est), or estradiol+testosterone, or other combinations per clinical need.	Patients on multiple hormones seeking simplified regimen; improves adherence; prescriber specifies all ingredients and concentrations

Laboratory Assessment & Monitoring

Lab-guided prescribing distinguishes individualized BHRT from empirical hormone therapy. The following represents a standard monitoring framework; individual prescribers may adjust based on clinical context.

Baseline Labs (Before Initiating BHRT)

Estrogen Panel	Serum estradiol (E2); estriol (E3) if clinically relevant; FSH (confirms menopausal status -- FSH >40 mIU/mL generally confirms menopause in appropriate clinical context)
Progesterone	Serum progesterone (follicular phase or menopausal baseline); useful for establishing pre-treatment level
Androgens	Total testosterone, free testosterone, SHBG, DHEA-S; calculated free testosterone if SHBG is elevated

Thyroid	TSH at minimum; free T3, free T4, thyroid antibodies if symptomatic or history of thyroid disease -- thyroid dysfunction commonly mimics and overlaps with menopausal symptoms
Metabolic	Fasting glucose or HbA1c; lipid panel; CMP; CBC
Cancer Screening	Up-to-date mammogram; Pap/HPV testing per ACOG guidelines; endometrial biopsy if clinically indicated (unexplained bleeding, prolonged anovulation history)
Bone Density	DEXA scan in post-menopausal women or those with risk factors; establishes baseline for HRT bone protection monitoring
Blood Pressure / BMI	Document at baseline; relevant to cardiovascular risk assessment for HRT initiation decisions

Follow-Up Monitoring

6-8 Weeks Post-Initiation	Serum estradiol, testosterone (if prescribed), DHEA-S (if prescribed); symptom reassessment; dose adjustment as needed; assess for side effects
3-6 Months	Full hormone panel; symptom and quality of life reassessment; endometrial assessment if indicated (bleeding patterns with progesterone)
Annual	Mammogram; Pap/HPV per guidelines; lipid panel; metabolic panel; hormone levels; bone density per ISCD/NAMS guidelines; reassess risk-benefit of ongoing HRT
Progesterone Adequacy	In women with intact uterus on estrogen, confirm adequate progesterone coverage; unexplained uterine bleeding warrants endometrial biopsy regardless of progesterone use
Testosterone Monitoring	Total and free testosterone, SHBG at 6-8 weeks after initiation; maintain free testosterone in upper normal female range; monitor for virilization at each visit
DHEA-S Target	Maintain serum DHEA-S in the upper quartile of the age-appropriate normal range; avoid supraphysiologic levels

Risk-Benefit Framework

The 2002 WHI study generated significant concern about HRT safety that has since been substantially refined by re-analysis and subsequent research. The current evidence-based position, reflected in NAMS, Endocrine Society, and ACOG guidelines, supports individualized HRT for appropriate candidates -- particularly when initiated within 10 years of menopause or before age 60 (the timing hypothesis / window of opportunity).

Breast Cancer Risk

WHI Re-analysis	The WHI showed a small increased breast cancer risk with combined estrogen + MPA (synthetic progestin) -- not with estrogen alone (which showed a neutral or slightly reduced risk in hysterectomized women). The progestin type matters significantly.

Bioidentical Progesterone	Multiple observational studies (E3N cohort, KEEPS) suggest bioidentical progesterone does not carry the same breast risk as synthetic progestins (MPA). This is a key distinguishing factor in the BHRT risk discussion, though long-term RCT data specific to compounded regimens are limited.
Timing Hypothesis	HRT initiated within 10 years of menopause or before age 60 is associated with cardiovascular benefit and lower overall mortality in multiple analyses. HRT initiated more than 10 years post-menopause or after 60 carries different risk profile -- not contraindicated but requires more careful individualized assessment.
Baseline Risk Context	For a woman at average breast cancer risk, the absolute increase in breast cancer risk from combined HRT is small (comparable to or less than the risk associated with obesity, alcohol use, or nulliparity). Risk-benefit must be individualized.

Cardiovascular Considerations

Timing Hypothesis	Estrogen has cardioprotective effects in younger, recently menopausal women -- supports endothelial function, lipid profile, and insulin sensitivity. The KEEPS and ELITE trials support cardiovascular benefit when initiated early. Delayed initiation (>10 years post-menopause) in women with subclinical atherosclerosis may increase acute plaque risk.
Thromboembolism	Oral estrogen increases VTE risk via hepatic first-pass effects on clotting factors and SHBG. Transdermal estrogen does not appear to increase VTE risk in observational studies -- preferred route in patients with VTE risk factors, obesity, or thrombophilia.
Route Preference	Topical/transdermal estradiol is cardiovascularly preferred over oral estrogen for most patients -- avoids hepatic first-pass clotting factor induction while providing systemic estrogen benefit

Absolute Contraindications to Estrogen-Containing BHRT

- Unexplained vaginal bleeding (evaluate before initiating)
- Known or suspected estrogen-receptor-positive breast cancer (discuss individualized risk with oncologist for local vaginal estrogen)
- Active VTE or arterial thromboembolic disease (recent MI, stroke, PE) -- transdermal route may be considered after stabilization with specialist input
- Known thrombophilia -- consider transdermal route if HRT is indicated; avoid oral estrogen
- Active liver disease with hepatic impairment -- avoid oral estrogen; transdermal may be used with hepatologist input
- Endometrial cancer history -- individualized assessment; unopposed estrogen is contraindicated; combined regimens require specialist input

Common BHRT Protocols

The following represents common prescribing patterns; all doses are individualized based on lab values, symptoms, and clinical judgment. These are starting frameworks, not fixed protocols.

Perimenopausal Woman (Intact Uterus)

Estradiol	0.5-1 mg/day topical cream (adjust up to 1.5-2 mg/day based on symptom response and serum levels; target E2 in physiologic premenopausal range 50-200 pg/mL for symptom control)
Progesterone	100-200 mg oral at bedtime (mandatory with intact uterus; provides endometrial protection and sleep/mood benefit); or cyclic progesterone 200 mg days 1-14 of calendar month if still cycling
Testosterone	0.5-1 mg/day topical if libido, energy, or cognitive symptoms are prominent; titrate to free testosterone in upper normal female range
DHEA	5-10 mg/day oral if DHEA-S is in lower quartile for age; reassess at 6-8 weeks

Post-Menopausal Woman (Intact Uterus)

Estradiol	1-2 mg/day topical cream or Bi-Est (E2:E3 in 80:20 ratio) at equivalent dose; target serum E2 50-100 pg/mL for symptom control with lowest effective dose
Estriol (Vaginal)	0.5-1 mg/g vaginal cream 2-3x weekly for urogenital atrophy symptoms; can be combined with systemic estradiol or used alone for local indication
Progesterone	100-200 mg oral at bedtime nightly (continuous regimen preferred in post-menopausal women on continuous estrogen; avoids withdrawal bleeding)
Testosterone	0.5-1.5 mg/day topical for libido, energy, cognitive symptoms; monitor free T and SHBG
DHEA	5-15 mg/day oral or 6.5-10 mg/day vaginal for GSM component; per DHEA-S levels

Post-Menopausal Woman (Post-Hysterectomy)

Estradiol	1-2 mg/day topical cream; progesterone optional (no endometrial risk; some prescribers include for sleep/mood benefit); target symptom relief with lowest effective dose
Testosterone	0.5-1.5 mg/day topical; often the most impactful hormone in post-oophorectomy women with severe androgen deficiency
DHEA	Per DHEA-S levels; vaginal DHEA if urogenital symptoms are prominent; oral if systemic adrenal support is indicated
Progesterone (Optional)	100 mg oral at bedtime for sleep and mood benefit even without uterus; evidence supports neurosteroid benefit independent of endometrial protection

Formulation & Dispensing

Dosage Forms	Topical cream, oral capsule, vaginal cream, sublingual drops, troches -- all available; prescriber specifies form per clinical indication and patient preference
Hormones Available	Estradiol (E2), estriol (E3), Bi-Est (E2+E3 combinations), progesterone, testosterone, DHEA -- individually or in combination preparations
Custom Concentrations	All hormone concentrations individualized to prescriber specification based on lab values and clinical goals
Combination Preparations	Multiple hormones compounded in a single preparation (e.g., Bi-Est topical cream; estradiol + testosterone topical; oral progesterone capsule containing DHEA) -- reduces patient burden
Excipient Control	PG-free, paraben-free, dye-free formulations available; base selection per prescriber and patient needs
Quantity	30-day supply standard; 60- or 90-day available
Pricing	Cash pay -- contact pharmacy for current pricing by formulation
BUD / Storage	Per USP compounding standards; most topical preparations room temperature; labeled on each preparation

Ordering & Contact Information

All BHRT preparations require a valid prescription specifying hormone(s), dose, delivery form, and dosing instructions. Patients fill directly at our pharmacy. The compounding pharmacist is available to discuss formulation questions and base selection.

How to Order

- By phone -- call (717) 846-0500; ask for the compounding pharmacist; have patient name, DOB, hormone(s), dose(s), delivery form, and quantity ready; pharmacist available to assist with formulation decisions
- By fax -- send prescription to (717) 845-8767; list each hormone with dose and concentration; specify delivery form (cream, capsule, vaginal, etc.) and any base/excipient preferences
- E-prescribe -- select 'Compound' as medication type; specify all hormones, concentrations, and delivery form in the Sig/Comments field (e.g., 'Bi-Est 1 mg/g [80:20 E2:E3] topical cream -- apply 0.5 mL to inner arm daily'; 'Progesterone 100 mg oral capsule -- 1 cap at bedtime')

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