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The Truth About Bioidentical Hormone Therapy

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Confusion and unsubstantiated claims surround the custom-compounded bioidentical hormone therapy products used to treat menopausal symptoms, such as hot flashes. This review attempts to dispel some of the confusion.

What Is Bioidentical Hormone Therapy?

Bioidentical hormone therapy (BHT) refers to exogenous hormones that are biochemically similar to those produced endogenously by the ovaries or elsewhere in the body.[1] They are generally derived from soy and yams, but the plant product needs to be chemically altered to become a therapeutic agent for humans (eg, estrone, estradiol, estriol, progesterone, and testosterone).[2] Claims by compounding pharmacies that BHT is "natural" and "identical" to the hormones made in the body are not true.[3] Custom-made HT formulations that are compounded for an individual woman according to a health care provider's prescription are not subject to government regulations or tested for safety. There are, however, HT products regulated and approved by the Food and Drug Administration (FDA) that contain hormones chemically identical to those produced by women.

What Is the Difference Between Compounded and FDA-approved BHT?

Custom compounding of HT may combine several hormones (eg, estradiol, estrone, and estriol) and use nonstandard routes of administration (eg, subdermal implants, suppositories). Some of the hormones used are not government approved (estriol) or monitored, and sometimes the compounded therapies contain nonhormonal ingredients (eg, dyes, preservatives) that some women cannot tolerate.[4] In addition, compounders do not have to:

- Test for efficacy or safety.
- Provide product information about proven benefits and risks.
- Give proof of batch and dose standardization or purity.

By way of comparison, there are 17β-estradiol and progesterone products that have been well tested and are regularly inspected. Estradiol is available in oral, patch, gel, ring, lotion, and mist formulations. Micronized progesterone is available as oral or vaginal products. These products have been rigorously studied in clinical trials and are regulated by the government. They are sold with package inserts and product information. (See Table for a list of FDA-approved bioidentical HT products.) Another hormone, testosterone (shown to improve sexual desire), is not currently available as an FDA-approved bioidentical product.

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Many misconceptions surround the BHT products custom compounded for menopausal symptom relief. Unsubstantiated claims include that BHT promotes weight loss, prevents Alzheimer's disease and breast cancer, and provides control of the aging process.

Here are some unconfirmed statements that need to be dispelled about BHT.

Compounded BHT—Busted

Claim: There is good scientific data to support the safety and efficacy of compounded BHT.
Truth: No large, long-term studies have been conducted to determine the effectiveness, safety, or adverse effects of compounded BHT. No data have been submitted to the FDA to demonstrate that estriol is safe and effective. The FDA stated in 2008 that pharmacies should not compound products containing estriol unless the prescriber has submitted a valid investigational new drug application.[5,6]

Additionally, custom-compounded BHT does not inform patients of the "black box" warning carried on all FDA-approved HT products about increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary embolism, and deep vein thrombosis in postmenopausal women. Efficacy claims by self-proclaimed experts, marketers, and popular literature are often false and misleading, creating a population of misinformed women.[7]

Claim: Custom-compounded BHT adheres to quality control regulations.
Truth: Because compounding pharmacies are not regulated by the FDA nor are their products tested for quality, purity, and potency, BHT preparations can vary substantially from batch to batch.[2,8] Women might overdose or underdose on compounded BHT, and they might be exposed to unidentified risks. Compounding pharmacies buy the hormones from distributors. It is not known how many of the hormones are imported from other countries.

Table. FDA-approved Bioidentical Hormone Therapy Products

Composition	Product Name
Oral 17β-estradiol	Estrace Various generics
Oral estradiol acetate	Femtrace
17β-estradiol matrix patch	Alora Climara Esclim Fempatch Menostar Vivelle Vivelle-Dot Various generics
17β-estradiol reservoir patch	Estraderm
17β-estradiol transdermal gel	EstroGel Elestrin Divigel
17β-estradiol topical emulsion	Estrasorb
17β-estradiol transdermal spray	Evamist
17β-estradiol vaginal cream	Estrace vaginal cream
17β-estradiol vaginal ring	Estring
Estradiol acetate vaginal ring	Femring
Estradiol hemihydrates vaginal tablet	Vagifem Vagifem LD
Estradiol valerate injection	Delestrogen
Estradiol cypionate injection	Depot-estradiol
Oral micronized progesterone	Prometrium
Vaginal progesterone cream	Crinone*
Vaginal progesterone ovules	Endometrin*

*FDA approved for infertility, not menopausal hormone therapy.
Complete information available on the NAMS website at www.menopause.org/bioidenticalcharts.pdf.[15]

Claim: Salivary testing accurately reflects a midlife woman's hormone levels.
Truth: Many proponents of compounded BHT promote the testing of estrogen levels in a woman's saliva for prescrib-

ing "individualized" HT. There is no scientific basis for using saliva testing to adjust hormone levels.[9] Free serum hormone concentrations in a midlife woman's body change from day to day depending on diet, time of day, the specific hormone being tested, and other variables.[10] The dosing of compounded progesterone is particularly difficult to assess because the levels in serum, saliva, and tissue are markedly different.[2] It is not necessary to test hormone levels to treat symptoms.

FOCUSPOINT➤

For most women suffering from menopause-related symptoms, commercially available and approved hormone therapy will provide appropriate therapy without the risks of unpredictable custom preparations.

Claim: Compounded progesterone is adequate to protect the uterus from estrogen.
Truth: The absorption of transdermal compounded progesterone cream is variable and unpredictable. Serum levels of transdermal progesterone were shown in three studies to be insufficient to protect against estrogenic stimulation of the endometrium for women with a uterus.[10-12] There were also mixed results in randomized controlled trials of treatment of hot flashes.

Claim: Compounding pharmacies that make BHT should be closed down.
Truth: This statement is not true. The FDA has no interest in eliminating appropriate pharmacy compounding and focuses instead on the subset of inappropriate compounders who mislead the public.[13] The FDA believes that traditional compounding pharmacists provide a valuable medical service to patients who have not been able to find a commercial product that meets their individual needs. But the majority of symptomatic menopausal women should be able to find an FDA-approved product from the large variety in type of delivery and doses available.

Conclusion

For most women suffering from menopause-related symptoms, commercially available and approved HT will provide appropriate therapy without the risks of unpredictable custom preparations. According to the FDA and NAMS, use of BHT is justified when a woman cannot tolerate some of the ingredients in an approved product, when she needs a lower dose than is available, or she has specific medical needs. There are currently no peer-reviewed scientific data from randomized controlled trials to suggest that compounded HT is safer or more effective than conventional drugs.[4,14] Neither estriol nor topical progesterone cream has been shown to reduce the risk of osteoporosis or breast cancer or to prevent estrogen-induced endometrial hyperplasia—claims made by certain compounding pharmacies and self-proclaimed experts.

The FDA and NAMS advocate that BHT products should include a patient package insert identical to that required for government-approved products. This package information delineates the contraindications and warnings required by the FDA in class labeling for HT. In the absence of efficacy and safety data for BHT, the generalized benefit-risk ratio data of commercially available HT products should apply equally to BHT, along with additional risks intrinsic to unregulated compounding.

It is the responsibility of a practitioner to provide adequate education to each woman about the risks and benefits of any type of HT including the lack of quality control and scientific data for custom-compounded products and the unique risks these products pose. There

is no scientific evidence to support the claims of increased safety or efficacy for compounded BHT.

In the past 12 months, Dr Pinkerton has served as consultant for Endoceutics, Noven, Novogyn, and Pfizer and received research support for multicenter clinical trials from Bionovo, Depomed, and Endoceutics. Previous clinical trial support was received from Pfizer.

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For a **PATIENT HANDOUT** on bioidentical hormone therapy, see page 49.