



## **Non-Patch, Transdermal Estrogen Products Such as Divigel® Are Effective Hormone Therapy Alternatives to Oral Estrogen**

### ***Manuscript Also Reviews Quality Control Issues With Compounded Bioidentical Hormones***

**MAPLE GROVE, Minnesota** (January 27, 2010) Clinical and experimental evidence suggests that non-patch, transdermal estrogen therapies, such as [Divigel®](#) (estradiol gel) 0.1%, prescribed for the management of moderate to severe hot flashes, including night sweats, associated with menopause are effective alternatives to oral estrogen and compounded bioidentical hormones.<sup>1</sup> A review of the evidence was recently published in the February issue of the [Journal of Women's Health](#), authored by Nina Carroll, MD, of [Beth Israel Deaconess Medical Center and Brigham and Women's Hospital](#). The [Journal of Women's Health](#) is the official peer-reviewed journal of the [American Medical Women's Association](#) (AMWA).

“There is a great deal of misinformation being conveyed to women about bioidentical estrogen, much of which is being fueled by popular books that have a positive spin on aging, but sometimes err in the scientific information that they present on hormones in menopause,” said Dr. Carroll. “This misinformation generates many questions to clinicians about unproven approaches to the medical management of menopause. This article serves as a timely medical source and is designed to enhance clinical knowledge of hormone therapy options with a focus on FDA-approved transdermal estrogen currently available for the treatment of symptoms associated with menopause.”

## **About the Manuscript**

The article addresses a wide spectrum of issues surrounding the treatment of menopausal symptoms including variability in estradiol dosing and the differences between bioidenticals that are FDA-approved, and non-FDA-approved compounded bioidentical formulations. Dr. Carroll elaborates on the risks and benefits of oral and transdermal hormone therapies with a focus on five non-patch, transdermal estradiol therapies currently available in the United States. She also discusses the misconceptions surrounding custom-mixed (compounded) estrogen and FDA-approved estrogen.

“The article’s intent is also to present information about the lack of quality control and the variance in potency and bioequivalence that may occur with estrogen that is custom-mixed or compounded at pharmacies,” said Dr. Carroll. “We provide details on two studies by the [Food and Drug Administration’s Center for Drug Evaluation and Research](#) that suggest that the potential problems with the quality of compounded drugs, including estrogen, may be directly related to the compounding process.” In 2005, ACOG issued an opinion stating there was “no scientific evidence supporting the claims of increased efficacy or safety of individualized hormone therapy prepared by compounding pharmacies.”<sup>8</sup>

## **About Transdermal Delivery Systems**

Transdermal estrogen avoids first-pass metabolism, a process where the amount of a drug taken in is reduced before it reaches systemic circulation because a portion is metabolized in the liver. Avoiding first-pass metabolism allows for lower doses of hormones and establishes more consistent and more physiologic estrogen and metabolite blood levels. To achieve therapeutic levels, oral hormones require higher doses of estrogen than transdermals due to the first pass metabolism in the liver.<sup>2,6</sup>

Worldwide, the most commonly used transdermal delivery (TDD) systems for administering estradiol are patches and gels. Within the last few years, non-patch formulations of transdermal estrogen, such as [Divigel](#)<sup>®</sup>, have been developed that share the advantages of transdermal therapy but avoid the inconveniences of the patch, such as skin reactions to adhesives, disadhesion and visibility.<sup>1</sup> Studies have shown no difference in absorption, bioavailability, or peak concentrations between patches and gels, and administration of estradiol by non-patch transdermal therapies has been shown to provide consistent levels of serum estradiol.<sup>4,5</sup>

## **Current Estrogen Prescribing Recommendations**

Current recommendations for hormone therapy from the [U.S. Food and Drug Administration](#) (FDA), the [North American Menopause Society](#) (NAMS), and the [American College of Obstetricians and Gynecologists](#) (ACOG) suggest the use of the lowest effective dose for the shortest duration of time,

consistent with treatment goals, benefits and risks for the individual woman regardless of the delivery method.<sup>1</sup>

### **About the *Journal of Women's Health* and AMWA**

The [\*Journal of Women's Health\*](#) is a consistent source of information to meet the challenges of providing optimum healthcare for women. This authoritative peer-reviewed journal publishes the latest clinical and research papers on the medical health issues that affect women throughout their lifespan. The [\*Journal of Women's Health\*](#) is the core resource for cutting-edge advancements and clinical applications on new diagnostic procedures, therapeutic protocols for the management of diseases in women, and innovative research in gender-based biology that impacts diagnosis and therapy. The [American Medical Women's Association](#) (AMWA) is an organization of women physicians, medical students and other persons dedicated to serving as the unique voice for women's health and the advancement of women in medicine. The full manuscript entitled, "*A Review of Transdermal Non-Patch Estrogen Therapy for the Management of Menopausal Symptoms*" is available at [www.liebertpub.com](http://www.liebertpub.com).

### **About Divigel<sup>®</sup>**

[Divigel<sup>®</sup>](#) is a bioidentical transdermal gel and is FDA approved for the treatment of moderate-to-severe vasomotor symptoms (hot flashes) associated with menopause. The estrogen in [Divigel<sup>®</sup>](#) is derived from plant sources and is identical to the primary estrogen produced by a woman's ovaries before menopause. [Divigel<sup>®</sup>](#) is a quick-drying gel that is odorless when dry and is available in convenient, individual-use packets. One packet of gel is applied daily to the upper thigh on an area that measures approximately 5 x 7 inches; the smallest application area compared to all other available gel or lotion estrogen products. After the gel is applied, estradiol absorbs directly into the bloodstream without having to pass first through the liver. [Divigel<sup>®</sup>](#) offers the lowest FDA-approved dose of estradiol in any gel, lotion or spray (0.25 mg estradiol). [Divigel<sup>®</sup>](#) is available in three dosage strengths offering dosing flexibility to suit a woman's individual needs.<sup>9-13</sup>

[Divigel<sup>®</sup>](#) was approved by the U.S. Food and Drug Administration (FDA) in June 2007.

### **Important Safety Information for Patients**

**The following are not all the possible risks for [Divigel<sup>®</sup>](#). Please see the full Prescribing Information and talk to your healthcare provider.**

Estrogens increase the chance of getting cancer of the uterus (womb). Report any unusual vaginal bleeding right away while you are taking estrogens. Vaginal bleeding after menopause may be a warning

sign of cancer of the uterus. Your healthcare provider should check any unusual vaginal bleeding to find out the cause. In general, the addition of a progestin is recommended for women with a uterus to reduce the chance of getting cancer of the uterus.

Do not use estrogens, with or without progestins, to prevent heart disease, heart attacks or strokes. Using estrogens, with or without progestins, may increase your chance of getting heart attacks, strokes, breast cancer and blood clots.

Do not use estrogens, with or without progestins, to prevent dementia. Using estrogens, with or without progestins, may increase your risk of dementia.

Do not use estrogen products, including [Divigel](#)<sup>®</sup>, if you have unusual vaginal bleeding, currently have or have had certain cancers, had a stroke or heart attack in the past year, currently have or have had blood clots, currently have or have had liver problems, are allergic to any [Divigel](#)<sup>®</sup> ingredients or think you may be pregnant.

The most common side effects for all estrogen products are headache, breast pain, irregular vaginal bleeding or spotting, stomach/abdominal cramps and bloating, nausea and vomiting, and hair loss. Less common but serious side effects include breast cancer, cancer of the uterus, stroke, heart attack, blood clots, dementia, gallbladder disease and ovarian cancer.

In [Divigel](#)<sup>®</sup> clinical trials, the most common side effects were inflammation of the nasal passages and pharynx, upper respiratory tract infection, vaginal yeast infection, breast tenderness and vaginal bleeding. Call your healthcare provider right away if you have any symptoms that concern you.

Estrogen products should be used at the lowest dose possible for your treatment and only as long as needed. You and your healthcare provider should talk regularly about whether you still need treatment with [Divigel](#)<sup>®</sup>. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

For more information, call 1-800-654-2299 or visit [www.divigel.com](http://www.divigel.com)

### **Upsher-Smith Laboratories, Inc.**

[Upsher-Smith Laboratories, Inc.](#) is a rapidly growing pharmaceutical company that manufactures and markets both prescription and consumer products. Privately held since 1919, the company strives to recognize the unmet healthcare needs of our customers. Upsher-Smith prides itself in providing safe,

effective, and economical therapies to the ever-challenged healthcare environment. For additional information about Upsher-Smith, visit [www.upsher-smith.com](http://www.upsher-smith.com).

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