



Newly Published Menopause Study: “Bioidentical” and FDA-Approved Divigel® (estradiol gel) 0.1 Percent Safe and Effective Treatment for Moderate to Severe Hot Flashes Associated with Menopause

Data Shows Reduction in Frequency and Severity in Hot Flashes in as Early as 14 Days

MAPLE GROVE, MN (February 17, 2009) Upsher-Smith Laboratories, Inc. announced today the publication of results of a Phase III study demonstrating that Divigel® low-dose transdermal estradiol gel 0.1% is an effective treatment for relief of moderate to severe hot flashes associated with menopause. The objective of the study was to evaluate the efficacy and safety of three doses of Divigel® 0.1%, 1.0 mg, 0.5 mg, and, 0.25 mg/day, including the lowest approved dose of estradiol gel or lotion available for the treatment of vasomotor symptoms.¹⁻⁴ Data showed a statistically significant reduction in frequency and severity of hot flashes as early as week two in patients receiving Divigel®. The results were published in the January/February edition of *Menopause: Journal of the North American Menopause Society* (NAMS).

About the Study

A total of 488 postmenopausal women were evaluated in a 12-week study comparing placebo with estradiol gel 0.1% at doses of 1.0, 0.5, and 0.25 mg/day, with estimated daily deliveries of 0.027, 0.009, and 0.003 mg of estradiol, respectively. Primary endpoints were the change from baseline in daily frequency and severity of moderate to severe vasomotor symptoms. Change from baseline in the signs of vulvar and vaginal atrophy (vaginal pH and percentage of superficial cells) was also assessed. Treatment with estradiol gel 0.1% showed statistically significant reductions in frequency and severity of vasomotor symptoms from baseline compared with placebo, as early as Week 2, that were maintained throughout treatment. Signs of vulvar and vaginal atrophy were also significantly improved from baseline with all three doses of estradiol gel 0.1% compared with placebo.

“The development of Divigel[®] expands the bioidentical options for the effective treatment of the symptoms of menopause and offers women the lowest FDA-approved dose of estrogen therapy for hot flashes,” Dr. Richard Hedrick, Jr., key investigator, Hawthorne OB/GYN Associates. “Divigel[®] also offers dosing flexibility with availability of three different strengths (0.25 mg estradiol/day, 0.5 mg estradiol/day and 1.0 mg estradiol/day) giving physicians greater ability to individualize treatment for each woman.”

About Divigel®

Divigel® is indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause. The estrogen in Divigel® is derived from plant sources and is identical to the primary estrogen produced by a woman's ovaries before menopause. Certain older oral estrogen therapies contain conjugated estrogens derived from the urine of pregnant mares. Divigel® 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 an area that measures approximately 5 x 7 inches on the thigh, the smallest application area compared to all other available gel or lotion estrogen products.¹⁻⁴ After the gel is applied, it absorbs directly into the bloodstream without having to pass through the liver.

Divigel® 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®. Please read the full Patient Information leaflet and talk to your healthcare provider.

Estrogens increase the chance of getting cancer of the uterus. 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 (womb). 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[®], 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[®] 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[®] 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[®].

For more information, call 1-800-654-2299 or visit www.divigel.com.

Orion Corporation (OMX: ORNAV, ORNBV) has a licensing agreement with Upsher-Smith Laboratories for the development of Divigel® in the United States. Orion is one of the leading pharmaceutical companies in northern Europe through its development, manufacturing and marketing of pharmaceuticals, active pharmaceutical ingredients and diagnostic tests for global markets. The core therapeutic areas in Orion's product and research strategy are central nervous system disorders, cardiology, critical care and hormonal and urological therapies.

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.

References: 1. Divigel® [package insert]. Minneapolis, MN: Upsher-Smith Laboratories, Inc.; 2007. 2. Estrasorb® [package insert]. Bristol, TN: Graceway Pharmaceuticals, LLC; 2008. 3. EstroGel® [package insert]. Herndon, VA: Ascend Therapeutics, Inc.; 2007. 4. Elestrin™ [package insert]. Lincolnshire, IL: BioSante Pharmaceuticals, Inc.; 2007.

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