Important Safety Information for Healthcare Providers Estrogens should not be used in women with undiagnosed abnormal vaginal bleeding; known, suspected, or history of breast cancer; known or suspected estrogen-dependent neoplasia; active or history of deep vein thrombosis (DVT) or pulmonary embolism; active or recent arterial thromboembolic disease; liver dysfunction or disease; known hypersensitivity to Divigel® ingredients; or known or suspected pregnancy. **Estrogens increase the risk of endometrial cancer.** Close clinical surveillance of all women taking estrogens is important. Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of abnormal vaginal bleeding. There is no evidence that the use of "natural" estrogens results in a different endometrial risk profile than synthetic estrogens at equivalent doses. Long-term continuous administration of estrogen, with or without progestin, has also shown increased risk of breast and ovarian cancers. **Cardiovascular and other risks.** Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. The Women's Health Initiative (WHI) studies reported increased risks of stroke and DVT in postmenopausal women (50 to 79) during 6.8 and 7.1 years of treatment, respectively, with daily oral conjugated estrogens (CE) 0.625 mg alone, relative to placebo, and increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and DVT in postmenopausal women (50 to 79) during 5.6 years of treatment with daily oral CE 0.625 mg and medroxyprogesterone acetate (MPA) 2.5 mg, relative to placebo. The WHI Memory Study (WHIMS) reported increased risk of developing probable dementia in postmenopausal women 65 or older during 5.2 years of treatment with daily oral CE 0.625 mg alone and during 4 years of treatment with daily oral CE 0.625 mg and MPA 2.5 mg, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. These risks should be assumed to be similar for other combinations and dosage forms of estrogens and progestins. The less common but serious risks reported with estrogen therapy include certain cardiovascular disorders, certain malignant neoplasms, dementia, gallbladder disease, hypercalcemia and visual abnormalities. The most frequently reported adverse events in Divigel® clinical trials were nasopharyngitis, upper respiratory tract infection, vaginal mycosis, breast tenderness and metrorrhagia. Estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

This safety information is not all-inclusive. Please see Brief Summary, including black box and other warnings.

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

Confident coverage morning, noon, and night*

Divigel®

(estradiol gel) 0.1%

0.25 mg 0.5 mg 1 mg

www.divigel.com

While hot flashes can happen at any time, those that occur at night may interfere with sleep, and may in turn affect a woman's ability to manage daily activities.[1,2] Divigel® is indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause.[3]

Right dose for the right patient

With three dosing options including 0.25 g/day (0.25 mg), the lowest approved dose of estradiol gel for vasomotor symptoms, Divigel® allows for tailored, flexible dosing.[3]

24-hour relief

87% reduction (vs 48% with placebo) in frequency of moderate to severe hot flashes, including night sweats, for patients treated with Divigel® 1.0 g/day at week 12.[†3]

Convenient therapy

Once-daily application, even before bedtime, provides all-day and all-night estradiol coverage.[3]

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