INDICATION & IMPORTANT SAFETY INFORMATION

Divigel® (estradiol gel) 0.1% is indicated for the treatment of moderate to severe vasomotor symptoms due to menopause.

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS, PROBABLE DEMENTIA and BREAST CANCER

See Full Prescribing Information for complete Boxed Warning

Estrogen-Alone Therapy

- **There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens**
- **Do not use estrogen-alone therapy for the prevention of cardiovascular disease or dementia**
- **The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age)**
- **The WHI Memory Study (WHIMS) estrogen-alone ancillary study of the WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age or older**
- **Only daily oral 0.625 mg CE was studied in the estrogen-alone substudy of the WHI. Therefore, the relevance of the WHI findings regarding adverse cardiovascular events and dementia to lower CE doses, other routes of administration, or other estrogen-alone products is not known.**

Estrogen Plus Progestin Therapy

- **Do not use estrogen plus progestin therapy for the prevention of cardiovascular disease or dementia**
- **The WHI estrogen plus progestin substudy reported increased risks of DVT, pulmonary embolism (PE), stroke and myocardial infarction (MI) in postmenopausal women (50 to 79 years of age)**
- **The WHIMS estrogen plus progestin ancillary study of WHI reported an increased risk of developing probable dementia in postmenopausal women 65 years of age and older**
- **The WHI estrogen plus progestin substudy reported increased risks of invasive breast cancer**
- **Only daily oral 0.625 mg CE and 2.5 mg MPA were studied in the estrogen plus progestin substudy. Therefore, the relevance of the WHI findings regarding adverse cardiovascular events, dementia and breast cancer to lower CE plus other MPA doses, other routes of administration, or other estrogen plus progestin products is not known.**

Prescribe estrogens with or without progestins at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Divigel is contraindicated in women with undiagnosed abnormal genital bleeding; breast cancer or history of breast cancer, estrogen-dependent neoplasia; active DVT, PE), or history of these conditions; active arterial thromboembolic disease or a history of these conditions; known anaphylactic reaction, angioedema or hypersensitivity to Divigel, hepatic impairment or disease; or protein C, protein S, or antithrombin deficiency, or other known thrombolitic disorders.

Estrogens increase the risk of gallbladder disease.

Discontinue Divigel if hypercalcemia or sudden partial or complete loss of vision occur. Consider discontinuation of Divigel if there is a substantial increase in blood pressure or if pancreatitis occurs. Discontinue Divigel in women with hepatic impairment if there is a recurrence of cholestatic jaundice.

Monitor thyroid function in women on thyroid replacement therapy.

The most common adverse reactions (incidence ≥5 percent and greater than placebo) are metrorrhagia, breast tenderness, vaginal mycosis, nasopharyngitis, and upper respiratory tract infection.

Start therapy with the 0.25 grams dosage strength applied once daily on the skin of either the right or left upper thigh. Adjust the dose up to a maximum of 1.25 grams, as needed.

Alcohol-based gels are flammable. Patients should avoid fire, flame or smoking until the gel has dried.

You may report suspected adverse reactions to Vertical Pharmaceuticals, LLC at 1-800-444-5164, or to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Full Prescribing Information, including Boxed Warning and Patient Counseling Information. For more information, call 1-800-444-5164 or visit www.divigel.com.