Premarin Tablets (conjugated estrogens) - Drug Summary

Wyeth Pharmaceuticals Inc.

Related Drug Information

Premarin Tablets (conjugated estrogens)

BOXED WARNING

Estrogens increase the risk of endometrial cancer. Perform adequate diagnostic measures, including endometrial sampling, to rule out malignancy in postmenopausal women w/ undiagnosed persistent or recurring abnormal genital bleeding. Should not be used for the prevention of cardiovascular (CV) disease or dementia. Increased risks of MI, stroke, invasive breast cancer, pulmonary embolism (PE), and deep vein thrombosis (DVT) in postmenopausal women (50-79 yrs of age) reported. Increased risk of developing probable dementia in postmenopausal women ≥65 yrs of age reported. Should be prescribed at the lowest effective dose and for the shortest duration consistent w/ treatment goals and risks.

THERAPEUTIC CLASS

Estrogen

DEA CLASS

RX

ADULT DOSAGE & INDICATIONS

Postmenopausal Osteoporosis

Prevention:
Initial: 0.3mg qd continuously or cyclically (eg, 25 days on, 5 days off)
Titrate: Adjust subsequent dose based on clinical and bone mineral density responses

Use lowest effective dose and for the shortest duration consistent w/ treatment goals and risk

Menopausal Vasomotor Symptoms

Moderate to Severe:
Initial: 0.3mg/day continuously or cyclically (eg, 25 days on followed by 5 days off)
Titrate: Subsequent dose adjustment may be made based on response

Use lowest effective dose for the shortest duration; reevaluate periodically

Menopausal Vulvar/Vaginal Atrophy

Moderate to Severe:
Initial: 0.3mg/day continuously or cyclically (eg, 25 days on followed by 5 days off)
Titrate: Subsequent dose adjustment may be made based on response

Use lowest effective dose for the shortest duration; reevaluate periodically

Hypoestrogenism

Female Hypogonadism:
0.3 or 0.625mg qd cyclically (eg, 3 weeks on and 1 week off)
Titrate: Adjust dose based on severity of symptoms and response of the endometrium

Female Castration/Primary Ovarian Failure:
Usual: 1.25mg qd cyclically
Titrate: Adjust dose based on severity of symptoms and response

Use lowest effective dose and for the shortest duration consistent w/ treatment goals and risk

Metastatic Breast Cancer

Palliative Treatment in Appropriately Selected Women and Men:

10mg tid for a minimum of 3 months

Use lowest effective dose and for the shortest duration consistent w/ treatment goals and risk

Prostate Carcinoma

Palliative Treatment of Advanced Androgen-Dependent Carcinoma:
1.25-2.5mg (two 1.25mg tabs) tid

Use lowest effective dose and for the shortest duration consistent w/ treatment goals and risk

ADMINISTRATION

Oral route

May take w/o regard to meals

HOW SUPPLIED

Tab: 0.3mg, 0.45mg, 0.625mg, 0.9mg, 1.25mg

CONTRAINDICATIONS

Undiagnosed abnormal genital bleeding; known/suspected/history of breast cancer except in appropriately selected patients being treated for metastatic disease; known/suspected estrogen-dependent neoplasia; active/history of DVT/PE/arterial thromboembolic disease (eg, stroke, MI); liver impairment/disease; known protein C, protein S, antithrombin deficiency, or other known thrombophilic disorders; known/suspected pregnancy.

WARNINGS/PRECAUTIONS

D/C immediately if stroke, DVT, PE, and MI occurs or is suspected. Caution in patients w/ risk factors for arterial vascular disease and/or venous thromboembolism. If feasible, d/c at least 4-6 weeks before surgery of the type associated w/ an increased risk of thromboembolism, or during periods of prolonged immobilization. May increase risk of ovarian cancer and gallbladder disease requiring surgery. May lead to severe hypercalcemia in patients w/ breast cancer and bone metastases; d/c and take appropriate measures if hypercalcemia occurs. Retinal vascular thrombosis reported; if visual abnormalities or migraine occurs, d/c pending examination. If examination reveals papilledema or retinal vascular lesions, d/c permanently. Anaphylaxis and angioedema involving tongue, larynx, face, hands, and feet requiring medical intervention reported; d/c if anaphylactic reaction w/ or w/o angioedema occurs. Cases of malignant transformation of residual endometrial implants reported in women treated post-hysterectomy w/ estrogen-alone therapy; consider addition of progestin for women known to have residual endometriosis post-hysterectomy. May elevate BP and thyroid-binding globulin levels. May elevate plasma TGs leading to pancreatitis in patients w/ preexisting hypertriglyceridemia; consider discontinuation if pancreatitis occurs. Caution w/ history of cholestatic jaundice associated w/ past estrogen use or w/ pregnancy; d/c in case of recurrence. May cause fluid retention; caution w/ cardiac/renal dysfunction. Caution w/ hypoparathyroidism; estrogen-induced hypocalcemia may occur. May exacerbate symptoms of angioedema in women w/ hereditary angioedema. May exacerbate asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas; use w/ caution. May affect certain endocrine and blood components in lab tests.

ADVERSE REACTIONS

Abdominal pain, asthenia, back pain, headache, pain, depression, insomnia, dizziness, leukorrhea, breast pain, vaginal hemorrhage, vaginitis, flatulence, nausea, weight gain.

DRUG INTERACTIONS

CYP3A4 inducers (eg, St. John's wort, phenobarbital, carbamazepine, rifampin) may decrease levels, which may decrease therapeutic effects and/or change uterine bleeding profile. CYP3A4 inhibitors (eg, erythromycin, clarithromycin, ketoconazole) may increase levels, which may result in side effects. Women concomitantly receiving thyroid hormone replacement therapy may require increased doses of their thyroid replacement therapy; monitor thyroid function.

PREGNANCY AND LACTATION

Contraindicated in pregnancy, not for use in nursing.

MECHANISM OF ACTION

Estrogen; binds to nuclear receptors in estrogen-responsive tissues. Circulating estrogens modulate pituitary secretion of gonadotropins, luteinizing hormone, and follicle-stimulating hormone, through a negative feedback mechanism. Reduces elevated levels of these hormones in postmenopausal women.

PHARMACOKINETICS

Absorption: Administration of variable doses resulted in different parameters. **Distribution:** Largely bound to sex hormone-binding globulin and albumin; found in breast milk. **Metabolism:** Liver to estrone; estriol (major urinary metabolite); sulfate and glucuronide conjugation (liver); biliary secretion of conjugates into the intestine; hydrolysis; reabsorption. **Elimination:** Urine (parent compound and metabolites).

ASSESSMENT

Assess for undiagnosed abnormal genital bleeding, estrogen-dependent neoplasia, presence or history of breast cancer, active/history of DVT/PE/arterial thromboembolic disease, thrombophilic disorders, pregnancy/nursing status, any other conditions where treatment is contraindicated or cautioned, need for progestin therapy, and possible drug interactions.

MONITORING

Monitor for signs/symptoms of CV events, malignant neoplasms, dementia, gallbladder disease, hypercalcemia, visual abnormalities, anaphylaxis, angioedema, BP and serum TG elevations, fluid retention, exacerbation of endometriosis and other conditions, and other adverse reactions. Perform annual breast exam; schedule mammography based on age, risk factors, and prior mammogram results. Monitor thyroid function in women on thyroid replacement therapy. In cases of undiagnosed persistent or recurring genital bleeding, perform adequate diagnostic measures (eg, endometrial sampling) to rule out malignancies. Periodically reevaluate to determine the need of therapy.

PATIENT COUNSELING

Inform of the risks/benefits of therapy. Inform of the importance of reporting vaginal bleeding to physician as soon as possible. Inform of possible serious adverse reactions and of possible less serious but common adverse reactions of estrogen therapy.

STORAGE

20-25°C (68-77°F); excursions permitted to 15-30°C (59-86°F).

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