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ESTRADIOL
(es-tra-dye-ole)
 Estrace
estradiol acetate
 Estrace
estradiol cypionate
 Depo-Estradiol
estradiol valerate
 Oestrace
estradiol topical emulsion
 Estrace
estradiol topical gel
 Desigel, Drostan, Estrate
estradiol transdermal spray
 Estrasote
estradiol transdermal system
 Avion, Climara, Estracote, Estraderm, Menostar, Viscoderm, Visilone
estradiol vaginal tablet
 Vaginar
estradiol vaginal ring
 Femring, Estring
Classification
 Therapeutic: hormones
 Pharmacologic: estrogens
 Pregnancy Category X

Indications
PO, IM, Topical, Transdermal: Replacement of estrogen (HRT) to diminish moderate to severe vasomotor symptoms of menopause and of various estrogen deficiency states including: Female hypogonadism, Ovariectomy, Primary ovarian failure. Treatment and prevention of postmenopausal osteoporosis (unvaginal dose forms). PO Insensible loss postmenopausal breast or prostate carcinoma. Vag: Management of atrophic vaginitis that may occur with menopause (low dose), and hormone systemic symptoms of menopause (higher dose). Concurrent use of progesterone is recommended during cyclical therapy to decrease the risk of endometrial carcinoma in patients with an intact uterus.

Action
Estrogens promote growth and development of female sex organs and the maintenance of secondary sex characteristics in women. Metabolic effects include reduced blood cholesterol, protein synthesis, and sodium and water retention. Therapeutic Effects: Restoration of hormonal balance in various deficiency states, including menopause. Treatment of hormone-sensitive tumors.

Pharmacokinetics
Absorption: Well absorbed after oral administration. Heavily absorbed through skin and mucous membranes.
Distribution: Widely distributed. Crosses the placenta and enters breast milk.
Metabolism and Excretion: Mostly metabolized by the liver and other tissues. Enterohepatic recirculation occurs, and more absorption may occur from the GI tract.
Half-life: Gel: 36 hr.

TIME/ACTION PROFILE (estrogenic effects)

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>unknown</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>IM</td>
<td>unknown</td>
<td>unknown</td>
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<tr>
<td>TD</td>
<td>unknown</td>
<td>unknown</td>
<td>3–4 days (Estraderm), 7 days (Climara)</td>
</tr>
<tr>
<td>Topical</td>
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<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>Vaginal tablet</td>
<td>unknown</td>
<td>unknown</td>
<td>3–4 days</td>
</tr>
</tbody>
</table>

Contraindications/Precautions
 Contraindicated in: History of anaphylaxis or angioedema to estradiol, Thromboembolic disease (e.g., DVT, PE, MI, stroke), Protein C, protein S, or antithrombin III deficiencies; Pregnancy; Lactation.

Caution: History of breast cancer, endometrial cancer, or endometriosis; History of breast or uterine cancer; History of deep vein thrombosis or pulmonary embolism; Diabetes; Hyperlipidemia; Thrombocytopenia; Arterial disease; History of thrombotic events; History of ascites or edema; History of tamoxifen resistance; History of pelvic or breast surgeries; History of obesity; History of smoking.

Adverse Reactions
CNS: Headache, depression, dizziness, mood changes, migraine, nervousness, sleep disturbances.
CV: Edema, venous thromboembolism.
ENDO: Menstrual disturbances, breast tenderness.
GI: Nausea, vomiting, bloating, constipation, diarrhea.
GU: Vaginitis, dyspareunia, urinary urgency, dysmenorrhea, amenorrhea.
Metab: Weight gain.
Musculoskeletal: Arthralgia.
Skin: Rash, pruritus.
Other: Weight gain, fluid retention, breast tenderness.

References
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Deficiency or other thrombophilic disorder; History of breast cancer; History of estrogen-dependent cancer; Hepatic impairment; Undiagnosed vaginal bleeding; OB: Positive evidence of fetal risk.

Use Cautiously in:

Underlying cardiovascular disease; Severe hepatic or renal disease; May q the risk of endometrial carcinoma; History of porphyria; History of hereditary angioedema; Lactation: Usually compatible with breast feeding (AAP).

Adverse Reactions/Side Effects

CNS:

headache, dizziness, lethargy.

EENT:

intolerance to contact lenses, worsening of myopia or astigmatism.

CV:

MI, THROMBOEMBOLISM, edema, hypertension.

GI:

nausea, weight changes, anorexia, appetite, jaundice, vomiting.

GU:

women — amenorrhea, dysmenorrhea, breakthrough bleeding, cervical erosions, loss of libido, pyometra, endometrial atrophy. Dose: only data on prostate cancer available. If appropriate, administer transdermal estrogen. Men — erectile dysfunction, testicular atrophy.

Derm:

oily skin, acne, pigmentation, urticaria.

Endo:

gynecomastia (men), hyperglycemia.

F and E:

hypercalcemia, sodium and water retention.

MS:

leg cramps.

Misc:

breast tenderness.

Interactions

Drug-Drug:

May alter requirement for warfarin, oral hypoglycemic agents or insulins. Barbiturates or rifampin may effect

Drug-Diet:

May increase risk of adverse CV reactions.

Route/Dosage

Estrogens should be used in the lowest doses for the shortest period of time consistent with desired therapeutic outcome.

Symptoms of Menopause, Atrophic Vaginitis, Female Hypogonadism, Ovarian Failure/Osteoporosis

PO (Adults): 0.45–2 mg daily or in a cycle.

IM (Adults): 1–5 mg monthly (estradiol cypionate) or 10–20 mg (estradiol valerate) monthly.

Topical Emulsion (Estrasorb) (Adults): Apply two 1.74 g pouches (4.35 mg estradiol) daily.

Gel (Adults): Apply contents of one pouch (Divigel) or one actuation from pump (EstroGel, Elestrin) daily.

Spray (EvaMist) (Adults): 1 spray daily, may be to 2–3 sprays daily.

Transdermal (Adults): almen — 25–50 mcg/24 hr transdermal patch applied twice weekly. Estraderm — 50–mcg/24 hr transdermal patch applied once weekly. Vivelle-Dot — 25–50 mcg/24 hr transdermal patch applied twice weekly. Alora — 25–50 mcg/24 hr patch applied q 7 days. Progestin may be administered for 10–14 days of each month.

Vag (Adults): cream—2–4 g (0.2–0.4 mg estradiol) daily for 1–2 wk, then 1 to 1–3 g/yr for 1–2 wk. Ret maintenance dose of 1 g q 3–4 times weekly for 1 mo, then off for 1 wk; then repeat cycle. Vaginal mucus has been measured: Tip of vaginal cuff (gelling) — 12.4 mg, (released 50 mcg estradiol/24 hr) 3 mo or 24.8 mg (released 100 mcg estradiol/24 hr) 3 mo (gelling requires concurrent progestogens).

NURSING IMPLICATIONS

Assessment

● Monitor intake and output ratios and weekly weight. Report significant discrepancies or steady weight gain.

● Menopause:

Assess frequency and severity of vasomotor symptoms.

● Lab Test Considerations:

May cause q HDL, phospholipids, and triglycerides and p serum LDL and total cholesterol concentrations.

● May cause q serum glucose, sodium, cortisol, prolactin, prothrombin, and factor VII, VIII, IX, and X levels. May p serum bilirubin, pyridoxine, antithrombin III, and uric acid concentrations.

● May cause false interpretations of thyroid function tests, false p in norepinephrine platelet-induced aggregability, and false q in metyrapone tests.

● May cause hypercalcemia in patients with metastatic bone lesions.

Potential Nursing Diagnoses

Sexual dysfunction (Indications)
CONTINUED

Implementation

● Do not confuse Alora with Aldara.

● PO: Administer with or immediately after food to reduce nausea.

● Vag: Manufacturer provides applicator with cream. Dose is marked on the applicator. Wash applicator with mild soap and warm water after each use.

● Transdermal: When switching from PO form, begin transdermal therapy 1 wk after the last dose or when symptoms reappear.

● Topical: In a comfortable position, apply Estrasorb to clean, dry skin of thighs. Place two pouches on each leg. Allow application sites to dry completely before covering with clothing to prevent transfer. Wash hands with soap and water to remove residual estradiol.

● Apply Divigel individual-use once-daily packets of quick-drying gel to an area measuring 5 inches by 7 inches (size of 2 palm prints) on the thigh. Do not wash area for at least 1 hr after gel has dried.

● Spray EvaMist on inside of forearm at the same time each day. Do not massage or rub the spray into the skin. Allow to dry for 2 min before dressing and at least 1 hr before washing. Never spray EvaMist around breast or vagina. Do not use more than 56 doses, even if fluid remains in pump.

● Intramuscular (IM): Injection has oil base. Roll syringe to ensure even dispersion. Administer deep IM. Avoid IV administration.

Patient/Family Teaching

● Instruct patient on correct method of administration. Instruct patient to take medication at least 1 hr before next dose. If a dose is missed, apply if more than 12 hr before next dose; if less than 12 hr, omit dose and return to regular schedule. Do not double doses.

● Explain dose schedule and maintenance routine. Discontinuing medication suddenly may cause withdrawal bleeding.

● If nausea becomes a problem, advise patient that eating solid food often provides relief.

● Advise patient to report signs and symptoms of fluid retention (swelling of ankles and feet, weight gain), thromboembolic disorders (pain, swelling, tenderness to extremities, headache, chest pain, blurred vision), mental depression, or hepatic dysfunction (yellowed skin or eyes, pruritus, dark urine, light-colored stools) to health care professional.

● Advise patient to notify health care professional of medication regimen before treatment or surgery.

● Caution patient that cigarette smoking during estrogen therapy may cause increased risk of serious side effects, especially for women over age 35.

● Caution patient to use sunscreen and protective clothing to prevent increased pigmentation.

● Instruct patient to stop taking medication and notify health care professional if pregnancy is planned or suspected.

● Emphasize the importance of routine follow-up physical exams, including BP, breast, abdomen, and pelvic examinations; Pap smear every 6–12 mo, and mammograms every 12 mo or as directed. Health care professional will evaluate possibility of discontinuing medication every 1–6 mo. If on continuous (not cyclical) therapy or without concurrent progestins, endometrial biopsy may be recommended, if uterus is intact.

● Inform patient that estrogen should not be used in case of carcinomas of the breast.

● Instruct patient to take medication and notify health care professional of medication regimen for periodontal disease.

● Advise patient to notify health care professional of medication regimen before treatment or surgery.

● Caution patient that cigarette smoking during estrogen therapy may cause increased risk of serious side effects, especially for women over age 35.

● Caution patient to use sunscreen and protective clothing to prevent increased pigmentation.

● Advise patient treated for osteoporosis that exercise has been found to arrest and reverse bone loss. Patient should discuss any exercise limitations with health care professional before beginning program.

● Advise patient that estrogen should not be used in case of carcinomas of the breast.

● Instruct patient to take medication and notify health care professional if pregnancy is planned or suspected.

● Emphasize the importance of routine follow-up physical exams, including BP, breast, abdomen, and pelvic examinations; Pap smear every 6–12 mo, and mammograms every 12 mo or as directed. Health care professional will evaluate possibility of discontinuing medication every 1–6 mo. If on continuous (not cyclical) therapy or without concurrent progestins, endometrial biopsy may be recommended, if uterus is intact.

● Instruct patient in the correct use of applicator. Patient should remain recumbent for at least 30 min after administration. May use sanitary napkin to protect clothing, but do not use tampons.

● Instruct patient to use applicator provided with vaginal tablet. Insert up to high up in the vagina as comfortable without using force.

● Vaginal Ring: Instruct patient to press ring into an oval and insert into the upper third of the vaginal vault. Exact position is not critical. Once ring is inserted, pa-
The patient should not feel anything. If discomfort is felt, ring is probably not in far enough; gently push farther into vagina. Leave in place continuously for 90 days. Ring does not interfere with sexual intercourse. If straining at defecation makes ring move to lower vagina, push up with finger. If expelled totally, rinse ring with lukewarm water and reinsert. To remove, hook a finger through the ring and pull it out.

**Transdermal:** Instruct patient to wash and dry hands first. Apply disc to intact skin on hairless portion of abdomen (do not apply to breasts or waistline). Press disc for 10 sec to ensure contact with skin (especially around edges). Avoid areas where clothing may rub disc loose. Change site with each administration to prevent skin irritation. Do not reuse site for 1 wk; disc may be reapplied if falls off.

Advise patient referred for MRI to discuss patch with referring healthcare professional and MRI facility to determine if removal of patch is necessary prior to test and for directions for replacing patch.

Protections: Caution patients to make sure children are not exposed to patch and do not come into contact with any skin area where the drug was applied. Women who cannot avoid contact with children should wear a garment with long sleeves to cover the application site.

**Evaluation/Desired Outcomes**

- Resolution of menopausal vasomotor symptoms.
- Decreased vaginal and vulvar itching, inflammation, or dryness associated with menopause.
- Normalization of estrogen levels in patients with ovariectomy or hypogonadism.
- Control of the spread of advanced metastatic breast or prostate cancer.
- Prevention of osteoporosis.

**Why was this drug prescribed for your patient?**