Bazedoxifene/conjugated estrogens

Therapeutic: bone resorption inhibitors, hormones
Pharmacologic: selective estrogen receptor modulators, estrogens

Pregnancy Category X

Indications
Treatment of moderate/severe vasomotor symptoms of menopause in female patients with an intact uterus. Prevention of postmenopausal osteoporosis in female patients with an intact uterus (supplemental calcium and vitamin D recommended if dietary intake is not adequate).

Action
Both bazedoxifene and conjugated estrogens bind to α and β estrogen receptors. Conjugated estrogens act as an agonist at these receptors. Bazedoxifene acts as an agonist in some tissues and an antagonist in other tissues, including the uterus. The combined effects of estrogen replacement while minimizing the risk of endometrial hyperplasia and prevention of postmenopausal osteoporosis.

Pharmacokinetics
Absorption: Bazedoxifene—6% absorbed following oral administration; conjugated estrogens—well absorbed following oral administration.
Distribution: Bazedoxifene—unk; conjugated estrogens—widely distributed, higher concentrations found in sex hormone target organs, enter breast milk.
Protein Binding: Bazedoxifene—98–99%.
Metabolism and Excretion: Bazedoxifene—undergoes extensive metabolism by UGT enzymes in the intestinal tract and liver, undergoes biliary excretion with enterohepatic recycling and elimination in feces (85%); conjugated estrogens—highly metabolized (CYP3A4 enzyme system), some metabolites are hormonally active; metabolites are renally eliminated.

Half-life: Bazedoxifene—50 hr; conjugated estrogens—17 hr (estrone).

TIME/ACTION PROFILE (effect on vasomotor symptoms†)

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†effects on osteoporosis were noted at 12–24 mos and lasted throughout treatment (5 yr).

Contraindications/Precautions
Contraindicated in: Undiagnosed/abnormal vaginal bleeding; Not recommended for use in hepatic or renal impairment or BMI ≥ 27 kg/m² (risk of endometrial hyperplasia); History of known/suspected breast cancer or other estrogen-dependent cancer; Active or past history of thromboembolism including stroke, myocardial infarction or pulmonary embolism; Known protein C, protein S or antithrombin deficiency or other thrombophilic disorders; Geri: not recommended for use in patients ≥ 75 yr; OB: May cause fetal harm, do not use during pregnancy or in women who may become pregnant; Lactation: Estrogens enter breast milk, should not be used in breastfeeding women.

Use Cautiously in: Risk factors for thromboembolic phenomenon including diabetes, family history, obesity or systemic lupus erythematosus; History of cholestatic jaundice associated with estrogen use; Hypothyroidism (may need ↓ dose of thyroid replacement); History of hereditary angioedema (estrogen may provoke); History of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus or hepatic hemangiomas (estrogen may exacerbate these conditions).

Adverse Reactions/Side Effects

CV: THROMBOEMBOLISM, ↑ blood pressure, edema.
EENT: retinal vascular thrombosis.
GI: cholestatic jaundice, diarrhea, dyspepsia, gall bladder disease, nausea, oropharyngeal pain, upper abdominal pain.
Derm: hot flashes.
F and E: hypocalcemia.
MS: muscle spasms, neck pain.

Interactions

Bazedoxifene

Drug-Drug: Concurrent use with UGT inducers including carbamazepine, phenobarbital, phenytoin and rifampin may ↓ levels and result in ↑ risk of endometrial hyperplasia (monitoring during long-term concurrent use is recommended).

Canadian drug name.

Genetic Implication. CAPI TALS indicate life-threatening, underlines indicate most frequent. Strikethrough discontinued.
Interactions

Conjugated estrogens

Drug-Drug: Concurrent use with CYP3A4 inhibitors including clarithromycin, erythromycin, itraconazole, ketoconazole or ritonavir may ↑ levels of conjugated estrogens and the risk of endometrial hyperplasia (monitoring during long-term concurrent use is recommended). Concurrent use with CYP3A4 inducers including carbamazepine, phenobarbital, and rifampin may ↓ effectiveness and alter normal bleeding patterns. Concurrent use of progestins, other estrogens or estrogen agonists/antagonists may alter the effectiveness or treatment and/or ↑ risk of adverse reactions and should be avoided.

Drug-Natural Products: Concurrent use with St. John’s wort may ↓ effectiveness and alter uterine bleeding patterns.

Drug-Food: Concurrent use with grapefruit juice may ↑ levels of conjugated estrogens and the risk of endometrial hyperplasia.

Route/Dosage

PO (Adults): One tablet daily (bazedoxifene 20 mg/conjugated estrogen 0.45 mg).

NURSING IMPLICATIONS

Assessment

● Assess for frequency and intensity of postmenopausal vasomotor symptoms (hot flashes).

● Assess BP before and periodically during therapy.

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

● Lab Test Considerations: May cause hypocalcemia.

● May cause ↑ HDL and triglycerides, and ↓ serum LDL concentrations.

● May cause ↑ prothrombin time, partial thromboplastin time, and platelet aggregation time. May ↑ factors II, VII, IX, X, fibrinogen; ↓ levels of fibrinogen and fibrinogen activity and plasminogen antigen and activity.

● May cause ↑ thyroid-binding globulin causing increased circulating total thyroid hormone; may require higher doses of thyroid replacement therapy.

● May cause impaired glucose tolerance.

Potential Nursing Diagnoses

Sexual dysfunction (Indications)

Implementation

● Supplemental calcium and/or vitamin D should be added if inadequate.

● PO: Administer once daily without regard to meals. Swallow tablets whole; do not crush, break, or chew.

Patient/Family Teaching

● Instruct patient to take medication as directed. Take missed doses as soon as remembered unless almost time for next dose; do not double doses. Advise patient to keeparium in original container to protect from moisture; avoid placing in pill boxes or organizers. Open only one blister pack and one tablet at a time; do not redate opened and discard after 60 days.

● Advise patient to avoid grapefruit juice during therapy.

● Instruct patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and to avoid concurrent use of Rx, OTC, and herbal products, especially progestins, additional estrogens, or additional estrogen agonists/antagonists without consulting health care professional; may increase risk of uterine cancer.

● Advise patient to report signs and symptoms of fluid retention (swelling of ankles and feet, weight gain), thromboembolic disorders (pain, swelling, tenderness in extremities, headache, chest pain, blurred vision), new breast lumps, changes in vision or speech, unusual and severe headache, severe pain in clavicular area with or without chest pain or breath, weakness, and fatigue, or abnormal signal bleeding to health care professional.

● Advise patient that cigarette smoking during estrogen therapy may increase risk of serious side effects, especially for women over age 55.

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

● Emphasize the importance of routine follow-up physical exams, including BP, breast, abdomen, and pelvic examinations; Pap smear exams every 6–12 mo; and mammogram every 12 mo or as directed. Health care professional will evaluate possibility of discontinuing medication every 3–6 mo.

● Advise patient to report pregnancy if pregnancy is planned or suspected or breast feeding. May cause fetal harm.

© 2015 F.A. Davis Company

CONTINUED
CONTINUED

bazedoxifene/conjugated estrogens

Evaluation/Desired Outcomes

- Reduction in frequency and intensity of moderate to severe hot flashes.
- Decreased risk of development of osteoporosis.
- Therapy should be used for the shortest time possible and need for therapy evaluated regularly.

Why was this drug prescribed for your patient?