

CENESTIN® helps you treat them as individuals.

CENESTIN therapy offers distinct patient benefits...

- Consistent estrogen release¹⁻³
- Plant-derived formulation
- Effective 0.45 mg low starting dose

CENESTIN® 0.45 mg, 0.625 mg, 0.9 mg, and 1.25 mg are indicated for the treatment of moderate-to-severe vasomotor symptoms associated with menopause. CENESTIN® 0.3 mg is only indicated for the treatment of vulvar and vaginal atrophy. The most frequently reported adverse events in CENESTIN clinical trials were headache and insomnia, which occurred with similar frequency in the placebo group.

In women with intact uteri, use of estrogen without progestin may increase the risk of endometrial cancer. Women with undiagnosed abnormal genital bleeding, known or suspected breast cancer, estrogen-dependent neoplasia, active deep vein thrombosis, thromboembolic disorders, active or recent arterial thromboembolic disease, or who are pregnant should not use estrogen.

Estrogens should not be used for the prevention of cardiovascular disease or dementia. Due to increased risk of cardiovascular and thromboembolic events and invasive breast cancer, estrogen with or without progestin should be prescribed at the lowest effective dose for the shortest duration.

Please see brief summary of prescribing information on adjacent page.

For more information, visit us at www.cenestin.com

References: 1. Data on file. Duramed Pharmaceuticals, Inc. 2. Stevens RE, Roy P, Phelps KV. J Clin Pharmacol. 2002;42:332-341. 3. Hess HM. Dowling TC, Schwartz MJ. Today's Ther Trends. 2003;21:85-96.

CENESTIN® and Duramed® are registered trademarks of Duramed Pharmaceuticals, Inc.

© 2005 Duramed Pharmaceuticals, Inc.

BRC05519

February 2005

Printed in US

Choose

Synthetic conjugated estrogens, A) Tablets
0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg

For consistent release.

Cenestin[®]

(synthetic conjugated estrogens, A) Tablets

R only

f Summary (See package brochure for full prescribing in Revised SEPTEMBER 2004 11000422:

11000422506

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 undiagnosed persistent or recurring abnormal vaginal bleeding. There is no evidence that the use of vitalural estrogence results in a different endometrial risk portile than synthetic estrogens at equivalent estrogen doses. (See WARNINGS, Malignant neoplasms, Endometrial cancer.)

CARDIOVASCULAR AND OTHER RISKS

WARNINGS, Cardiovascular disorders.)

The Women's Health Initiative (WHI study reported increased ricks of myocardial infarction, stoke, incasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50 to 79 years of ape) during 5 years of treatment with roat contiguated equine estrogens (CE 0.628 mg) combined with medrosyproje esterone acetate (MPA 2.5 mg) relative to placebo. (See CLINICAL PHARMACOLOGY, Clinical Studies.)

The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported increased risk of developing probable demential in postmenopausal women 65 years of age or older during 4 years of treatment with oral conjugated estrogens plus medroxyprogesterone acetate reliative to placebo. It is unknown whether this finding applies to younger postmenopausal women. (See CLINICAL PHARMACOLOGY, Clinical Studies.)

Other doses of oral conjugated estrogens with medroxyprogesterone acetate, and other combinations and dosage forms of estrogens and progestins were not studied in the WHI clinical traits and, in the absence of out progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Treatment goals and neks for the individual woman.

CONTRAINDICATIONS Cenestin should not be used in women with any of the following conditions:

1. Undiagnosed abnormal genital biseding. 2. Known, suspected, or history of cancer of the breast. 3. Known or suspected estrogen-dependent neopless. 4. Known or suspected pregnancy. There is no indication for Cenestin pregnancy. There appears to be tittle or no increased risk of thirt defects is notifier born to women who have used estrogens and progestins from oral contraceptives inadvertently during early pregnancy. (See PRECAUTIONS.)

infown hypersensitivity to its ingriedients. 8. Known or suspected pregnandy. There is no indication for Cenestin pregnancy. There appears to be tilted or no invasaed risk of birth detects in children bort to women who have contributed to the contributed of th

build be permanently utraductions.

General

Addition of a progestin when a woman has not had a hysterectomy. Studies of the addition of a progestin of a progestin when a woman has not had a hysterectomy. Studies of the addition of a progestin 10 or more days of a cycle of estrogen administration, or daily with estrogen in a continuous regimen, have covered a lowered incidence of endometrial hyperplasia than would be induced by estrogen treatment alone.

Endometrial hyperplasia may be a precursor to endometrial cancer. There are, however, possible risks that may be associated with the use of progestins with estrogens compared to estrogen-alone regimens. These include a possible increased risk of breast cancer.

2. Elevated blood pressure. In a small number of case reports, substantial increases in blood pressure have been attributed to idiosyncratic reactions to estrogens. In a large, randomized, placebo controlled clinical trial, a generalized effect of estrogens on blood pressure was not seen. Blood pressure should be monitored at regular.

Intervals with estrogen use.

3. Hypertrig/yceridemia. In patients with pre-existing hypertrig/yceridemia, estrogen therapy may be associated with elevations of plasma trig/ycerides leading to pancreatitis and other complications.

4. Impaired liver function and past history of cholestatic jaunatice. Estrogens may be poorly metabolized in patients with impaired liver function. For patients with a history of cholestatic jaunatice associated with past estogen use or with pregnarcy, caution should be designed use or with pregnarcy, caution should be dis-

continued.

5. Hypothyvoldism. Estrogen administration leads to increased thyvoid-binding globulin (TBG) levels. Patients with normal thyvoid function can compensate for the increased TBG by making more thyvoid hormone, thus maintaining feet 1, and 17, serum concentrations in the normal range. Patients dependent on thyvide hormone replacement therapy who are also receiving estrogens may require increased doses of their thyvidid replacement therapy. These patients should have their thyroid function monitored in order to maintain their free thyroid hormone levels in an acceptable range.

6. Fluid referration. Because estrogens may cause some degree of fluid retention, patients with conditions that might be influenced by this factor, such as a cardiac or renal dysfunction, warrant careful observation when estrogens are prescribed.

These patients should have their thyroid function monitored in order to maintain their free thyroids hormone levels in an acceptable range.

6. Fluid retention. Because estrogens may cause some degree of fluid retention, patients with conditions that might be influenced by this factor, such as a cardiac or renal dysfunction, warrant careful observation when estrogens are prescribed.

8. Ovarian cancer. The CEMPA substudy of WHI reported that estrogen plus progestin increased the risk of ovarian cancer. After an average bellow-up of 5.6 years, the relative risk for ovarian cancer for CEMPA versus placebow as 1.58 (95% confidence interval 0.7 — 3.24) but was not statistically significant. The absolute risk for CEMPA versus placebo was 1.58 (95% confidence interval 0.7 — 3.24) but was not statistically significant. The absolute risk for CEMPA versus placebo was 1.58 (95% confidence interval 0.7 — 3.24) but was not statistically significant. The absolute risk for CEMPA versus placebo was 4.2 versus 2.7 cases per 10,000 women-years. In some epidemiologic studies, have not found these associations.

7. The properties of the properties

the most common classification or prousely elements in some tax of probable demential occurred in the 54% of women that were olider than 70. [See WARNINGS, Dementia.]

ADVERSE FLACTIONS.

ADVERSE FLACTIONS.

ADVERSE FLACTIONS.

Because of including the MARNINGS and PRECAUTIONS.

Because of linical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials of approximating rates.

In a 12-week clinical trial that included 72 women treated with 0.625 mg and 2 × 0.625 mg Cenestin and 48 women realted with placeton, adverse events that occurred at a rate of 2.5 %s. are summarized below.

Cardiovascular System — Palpitation Diagnates, Dysepsia, Flatulence, Nausea, Vomiting Metabolic and Nutritional — Peripheral Edema Muscuicoskeletal System — Athritigia, Myalgia

Nervous System — Depression, Dizzinass, Hypertonia, Insomnia, Leg Cramps, Nervousness, Respiratory System — Sansh University, Stan and Appendages — Rash University, System — Sansh University, Stan and Appendages — Rash University, Stan — Sansh University,

If a subject experiences the same event more man once, the first occurrence is tabusated.

The following additional advorser reactions have been reported with estrogen and/or progestin therapy:

1. Genifourinary system. Changes in vaginal bleeding pattern and abnormal withdrawal bleeding or flow; break-through bleeding; spotting; dysweneorhea, increase in suce of uterine leiomymental vagentials, encluding reginal candidates; change in amount of cervical secretion; changes in cervical ectropion; ovarian cancer; endometrial hyperplasia; endometrial cancer.

2. Breasts. Tenderness, enlargement, pain, nipple discharge, galactorrhea; fibrocystic breast changes; breast nancer.

2. Breasts. Tenderness, enlargement, pain, nipple discharge, galactorrhea; librocystic breast changes; breast cancer.
description, stroke; increase in blood pressure.
4. Gastrointesthal.
Auseau, ownling; abdominal cramps, bloating; cholestate jaundice; increased incidence of gallbladder disease; pancreatitis, enlargement of hepatic hemangiomas.
5. Skin. Ohloams or melasma, which may persist when drug is discontinued; erythema multiforme; erythema nodosum, hemorrhagic eruption; loss of scalib hair; hisustiem; prurtus, reath.
5. Eyes. Tienet wescular thromboss; infoldrance to contact lense of the properties.
6. Eyes. Tienet wescular thromboss; infoldrance to contact lenses; mental depression; chorea; nervousness; mod disturbances; intrability, exacerbation of epilepsy, dementia.
8. Miscellaneous. Increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema; arthalpas: leg cramps; changes in libido; urticaria, angloedema; anaphylacticid/anaphylactic reactions; hypocalcomia; oxacerbation of asthma; increased righyberides.

Manufactured By: Duramed Pharmaceuticals, Inc. Subsidiary of Barr Pharmaceuticals, Inc. Pomona, New York 10970