Young Women Don't Know Much About IUDs

BY DIANA MAHONEY New England Bureau

ATLANTA — Knowledge of intrauterine devices among adolescent and young adult women is limited, according to a study presented at the annual meeting of the North American Society for Pediatric and Adolescent Gynecology.

In a cross-sectional survey of 144 young women between the ages of 14 and 24 recruited from an adolescent gynecology

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 BRIEF SUMMARY OF PRESCRIBING INFORMATION
 (for full prescribing information and patient information, please visit our website at
 www.angeliq-us.com)

Estrogens with or without progestins should not be used for the prevention of cardid ar disease or dementia. (See WARNINGS, Cardiovascular disorders and Dementia.

ar disease or dementia. (See WARNINGS, Cardiovascular disorders and Dementia.) The Women's Health Initiative (WHI) study reported increased risks of myocardial inflarction, stroke, invasive breast cancer, pulmonary embloil, and deep vein thromotosis in post-menopausal women (50 to 79 years of age) during 5 years of treatment with noral conjugat-ed equine estrogens (5C to .652mg) combined with medroxyprogesterone acetate (MPA 2.5mg) relative to placebo (see CLINICAL PHARMACOLOGY, Clinical Studies and WARN-INGS, Cardiovascular disorders and Malignant meoplasms, Breast cancer.) The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported increased risk of developing probable dementia in postmenopausal women (5e years of treatment with onal conjugated estrogens plus medroxyprogesterone acetate, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. See CLINICAL PHARMACOLOGY

conjugatel estrogens plus medroxyprogesterone acetate, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women (See CLINICAL PHARMACDL-OGC, Clinical Sulfies, WARMINGS, Dementia and PHEAUTIONS, Genetine Usa.) Other doess of oral conjugatel estrogens with medroxyprogesterone acetate, and other combinations and dosage forms of estrogens and progestims were not studied in the WHI clinical trials, and, in the absence of comparable data, these risks should be assumed to be similar. Because of these risks, estrogens with or without progestims should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

MOLATIONS AND USAGE MARELID is included in women who have a uterus for the: 1. Treatment of moderate to severe vaso-motor symptoms associated with the menopause. 2. Treatment of moderate to severe symptoms of whar and variant atrophys associated with the menopause. When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered.

of symptoms of vulvar and vaginal arophy, topical vaginal products should be considered. **CONTRAINDICATIONS** Progestogenselserogens should not be used in individuals with any of the following conditions: 1. Undiagnosed abnormal gential bleeding. 2. Known, suspected, or history of cancer of the treast. 3. Known or suspected estrogen-dependent mepolasia. 4. Advie deep vein thrombosis, pulmonary embolism or history of these conditions. 5. Active or recent (e.g., within the past signal article afformobenobic disease (e.g., stroke, mycoardial infraction). 6. Renal insufficien-cy. 7. Liver dysfunction or disease. 8. Adrenal insufficiency. 9. **ANGELIQ** should not be used in patients with known hypersensitivity to its ingredients. 10. Known or suspected argengany. There is no indication for **ANGELIQ** in pregnancy. There appears to be liftle or no increased risk of birth detects in children born to women who have used estrogens and progesting from oral con-traceptives inadvertently during early pregnancy. (See **PECEUTIONS**).

WARNINGS ANGELIQ contains 0.5 mg of the progestin drospirenone that has antialdosterone activity, including the potential for hyperkalemia in high-risk patients. ANGELIQ should not be used in patients with conditions that predispose to hyperkalemia (i.e. renal insufficiency, hepatic dystunction, and adrenal insufficiency). Use caution when prescribing ANGELIQ to women who regularly take other medications that are instructions, such as NSANS, potasisum-sparing diurelise, potasisum supplements, ADE inhibitors, angiotensin-II receptor antagonists, and heparin. Consider checking serum potassi-um levels during the first treatment cycle in high-risk patients. See BOXED WARNINGS.

See BOXED WÄRNINGS. 1. Cardiovascular disorders Estrogen and estrogen/progestin therapy has been associated with an increased risk of cardiovascular events such as myocardial infarction and stroke, as well as venous thrombosis and pulmonary embolism (venous thromboembolism or VTE). Should any of these occur or be suspected, estrogens should be discontinued immediately. Risk factors for cardiovascular disease (e.g., hypertension, diabetes mellitus, tobacco use, hyper-cholesteriorilan; and obesity) and/or venous thromboembolism (e.g., personal history or tamily history of VTE, obseity, and systemic lugue enthematosus) should be managed appropriately. a. Coronary heard disease and stoke In the Women's Health Initiative study (WHI), an increase in the number of myocardial infarctions and strokes has been observed in women receiving oral GE compared to placebo. (See CLINICAL PHARMACOLOGY, Clinical Studies sections.)

Studies sections.) Compared to placebook (bit octional relations) and the section of the CMMPA substudy of WHI an increased risk of coronary heart disease (CHD) events (defined as non-tail mycardial infarction and CHD death) was observed in women receiving CEMIPA compared to women receiving placebo (37 vs 30 per 10,000 person years). The increase in risk was observed in are near a dipersisted. In the same substudy of WHI an increased risk of stroke was observed in women receiving CEMIPA compared to women receiving placebo (37 vs 21 per 10,000 person years). The increase in risk was observed after the first year and persisted. In postmenopausal women with documentat heart disease (n = 2.763, average age 66.7 years) a controlled cinical trial of secondary prevention of cardiovascular disease (Heart and Estrogen/Progestin Replacement Study; HERS) treatment with CEMIPA dia not reduce the overall rate of CHD events in postmenogausal women with seabilished coronary heart disease. There were more CHD events in the CEMIPA-treated group than in the placebo group in year 1, but not during the subsequent years.

placebo group in year 1, but not during the subsequent years. Two thousand three hundred and twendy one women from the original HERS trial agreed to par-ticipate in an open label extension of HERS, HERS II, Average follow-up in HERS II was an addi-tional 2.7 years. For a total of 6.8 years overalt. Rates of CHD events were comparable among women in the CEMPA group and the placebo group in HERS, HERS II, and overall.

Large does of estrogen (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown in a large prospective clinical tria in men to increase the risks of nonfatal myocardial infarction, pulmonary embolism, and thromohonheim).

thrombophients. **b. Venous thromboembolism (VTE)** In the Wornen's Health Initiative study (WHI), an increase in VTE has been observed in women receiving CE compared to placebo. (See **CLINICAL PHAR-**MACOLOGY and Clinical Studies sections.)

MACOLOGY and Clinical Studies sections.) In the CE/MPA substudy of WHI a 2-fold greater rate of VTE, including deep venous thrombosis and pulmonary emolism, was observed in women receiving CE/MPA compared to women receiving placebo. The rate of VTE was 34 per 10,000 woman-years in the CE/MPA group com-pared to 16 per 10,000 woman-years in the placebo group. The increase in VTE risk was observed during the first year and persisted. If fassible, estrogens should be discontinued at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of pro-longed immobilization.

in VTE has been observed in women in MACOLOGY and Clinical Studies sec

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ANGELIQ® TABLETS

INDICATIONS AND USAGE

clinic, gynecology outpatient clinics, and the community, more than half of the participants had never heard of an intrauterine device (IUD) and 97% had never used one, said Dr. Lisa Johnson of the adolescent medicine division of the Nassau (Bahamas) Department of Public Health.

The 20-minute, 44-item, semistructured interview assessed demographics, sexual history, contraceptive use and attitudes, and IUD knowledge and attitudes, Dr. Johnson said. The mean age of the respondents was 18.8 years. Nearly all (97%) of them were single, 58% were African American, and 39% were white. Approximately 84% of the group had ever been sexually active, with a mean age of 15.8 years at first sexual intercourse and a median of three lifetime partners. Among those who had ever had sex, 76% had ever been pregnant and 67% had ever had a sexually transmitted disease.

According to the survey results, 60% of the young women surveyed had never

3. Other binding proteins may be elevated in serum (i.e., corticosteroid binding globulin (CBG), sex hormone-binding globulin (CBG), leading to increased circulating corticosteroids and sex steroids, respectively. Free hormone concentrations may be decreased. Other plasma proteins may be increased (angiotensinogen/renin substrate, alpha-1-antitrypsin, ceruloplasmin).

Interaced (angularising)derivation sustaits, apriler i-aniutypsin, cerulopasmin). A. Increased plasma HDL and HDL 2 subfraction concentrations, reduced LDL cholesterol concentration, increased triglyceride levels. S. Impaired glucose tolerance. A. Reduced response to metyrapone test. E. CARCINOGENESIS, MUTAGENESIS, AND IMPAIRMENT OF FERTILITY

Long-term continuous administration of estrogen, with and without progestin, in women with and without a uterus, has shown an increased risk of endometrial cancer, breast can-cer, and ovarian cancer. (See **BOXED WARNINGS**, **WARNINGS** and **PRECAUTIONS**.)

with and without a uterus, has shown an increased risk of endometrial cancer, breast can-cer, and ovarian cancer. (see **BOXE WARNINGS**, **WARNINGS** and **PRECAUTIONS**.). Long-term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, utens, cenvix, vagina, testis, and liver. (See **BOXED WARNINGS**, **CONTRAINDICATIONS**, and **WARNINGS** sections.) In a 24 month oral carcinogenicity study in mice dosed with 10 mg/kg/dg drospirenone alone or 1 + 0.01, 3 + 0.03 and 10 + 0.1 mg/kg/dg drospirenone and ething testis, and to 10.3 times the exposure (AUC of drospirenone) of women taking a 1 mg dose, there was an increase in carci-nomas of the hardrain galan in the group that received the high dose of drospirenone alone. In a similar study in rate given 10 mg/kg/dg drospirenone and ething testing at 0.03, 4 . 0.03 and 10 + 0.1 mg/kg/dg drospirenone and tehing testadio. 23 to 51 2 tims the exposure of women tak-ing a 1 mg dose, there was an increased incidence of being and total (being nam diagnat) addr-and gland phechormooftomas in the provuor reaving the high dose of drospirenone. Drospirenone was not mutagenci: in a number of *in vitro* (Ames, Chinese Hardset Lung gene mutation and chro-mosomal damage in human hymblocytes) and *in vitro* (mouse micronucleus) genotoxicity tests. **Drospirenone** increased unscheduled DNA synthesis in rat heptacytes and formed adducts with rodent liver DNA but not with human liver DNA. (See WARNINGS section.) **C. NURSING MOTHERS**. Estrogen administration to nursing mothers has been shown to chercase the quarkity and quality of the mik. Zeetexteb amounts of estrogens have been iden-tified in the mik of mothers receiving this furg. Caution should be exercised when **ANGELID** satiministration of an ural contraceptive containing drospirenone about 0.02% of the

is administered to a nursing woman. After administration of an oral contraceptive containing drospirenone about 0.02% of the drospirenone dose was excreted into the breast milk of postpartum women within 24 hours. This results in a maximal daily dose of about 3 mog drospirenone in an infant. H. FEDIATRIC USE F ANGELUB is not indicated in children. I. GERUATRIC USE There have not been sufficient numbers of geriatric patients involved in clin-ical studies utilizing ANGELUB to determine whether those over 65 years of age differ from younger subjects in their response to ANGELUB.

younger subjects in their response to **ANGEU**. In the Women's Health Initiative Memory Study, including 4,532 women 65 years of age differ from followed for an average of 4 years, 82% (n. e. 3/27) were 65 to 74 while 19% (n. e. 300) were 75 and over. Most women (80%) had no prior hormone therapy use. Women treated with conjugat-ed estrogens plus medroxyprogesterone actuate were reported to have a two-fold increase in the risk of developing probable dementa. Architerier's disease was the most common classification of prob-able dementa in both the conjugated estrogens plus medroxyprogesterone acetate group and the placebo group. Ninety present of the cases of probable dementa occurred in the 54% of women who were older than 70. (See WARINIGS, Dementia.) ADVERSE FRACTIONS See BOXED WARININGS

See BOXED WARNINGS, WARNINGS, AND PRECAUTIONS.

See BUXED WARNINGS, WARNINGS, AND PHECAUTIONS. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical tri-als of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates. The following are adverse events reported with **ANGELQ** occurring in >5% of subjects:

Table 4. Adverse Events Regardless of Drug Relationship Reported

at a Frequency of >5% in a 1-year Double-blind Clinical Trial		
ADVERSE EVENT	E2 1 MG (N=226) n (%)	ANGELIQ (N=227) n (%)
BODY AS A WHOLE		
Abdominal pain	29 (12.8)	25 (11)
Pain in extremity	15 (6.6)	19 (8.4)
Back pain	11 (4.9)	16 (7)
Flu syndrome	15 (6.6)	16 (7)
Accidental injury	15 (6.6)	13 (5.7)
Abdomen enlarged	17 (7.5)	16 (7)
Surgery	6 (2.7)	12 (5.3)
METABOLIC & NUTRITIONAL DISORI	DERS	
Peripheral edema	12 (5.3)	4 (1.8)
NERVOUS SYSTEM		
Headache	26 (11.5)	22 (9.7)
RESPIRATORY SYSTEM		
Upper respiratory infection	40 (17.7)	43 (18.9)
Sinusitis	8 (3.5)	12 (5.3)
SKIN AND APPENDAGES		
Breast pain	34 (15.0)	43 (18.9)
UROGENITAL		
Vaginal hemorrhage	43 (19.0)	21 (9.3)
Endometrial disorder	22 (9.7)	4 (1.8)
Leukorrhea	14 (6.2)	3 (1.3)
e following additional adverse reaction	ns have been reported wit	n estrogen and or estro

gen/progestin therapy: 1. Genitourinary system Changes in vaginal bleeding pattern and abnormal withdrawal bleed-ing or flow, breakthrough bleeding, spotting, dysmenorrhea, increase in size of uterine leiomy-omata, vaginitis, including vaginal candidiasis, 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 cancer.

increased incidence of gall bladder disease, pancreatilis, enlargement of hegatic hemangiomas. 5. Skin Chlosma or melsama, which may persist when drug is discontinued, enythema multi-forme, erythema nodosum, hemorrhagic eruption, loss of scalp hair, hirsutism, prurtus, rash. 6. Eyes Retinal vascular thrombosis, intiderance to contact lenses. 7. Central nervous system Headache, migrarian (atiziness, mental depression, chorea, nerv-ousness, mood disturbances, irritability, exacerbation of epilepsy, dementia. 8. Miscellaneous Increase or decrease in weight, reduced carbohydrate tolerance, aggra-ation of porphyria, debma, arthraligais, leg caramys, changes in libido, anaphylactioid/ana-phylactic reactions including urticaria and angioedema, hypocalcemia, exacerbation of asthma, increaser tindiverdies.

dirospiretione itas animimeradornocou properties. Serious ill effects have not been reported following acute ingestion of large doses of pro-gestir/ostrogen-containing oral contraceptives by young children. Overdosage may cause nausea and withdrawal beeding may occur in females. Manufactured in Germany Anufactured in Germany Bayer HealthCare Pharmaceuticals 6007000 3288396 September 2005

'agreed" or "strongly agreed" that they would consider a birth control method that resulted in less painful (93%) and lighter (91%) periods and gave them control over when to stop (85%) and start it (80%), Dr. Johnson said. In addition, 61% reported being "willing" or "very willing" to use a birth control method that causes irregular vaginal bleeding if it was 99% effective at preventing pregnancy, she said.

heard of an IUD, yet a majority of them

However, only 30% of the respondents said they would consider a birth control method that involved placing a small plastic object in the uterus and only 27% said they would be interested in a device that had to be placed and removed by a health care provider, she noted.

An analysis of the survey responses

After the IUD demonstration, knowledge scores were increased significantly; nearly 65% of the young women liked the idea of an IUD for themselves.

showed that those who had heard of IUDs were significantly more likely to be older and sexually active compared with those who had not heard of them, and they were more likely to be white, Dr. Johnson said. "There was no association

between knowledge of IUDs and ever being pregnant, parity, ever having a sexually transmitted disease, or number of sexual partners," she said.

Following participation in the survey, each of the young women was given a 2minute description and demonstration of IUDs, followed by a test of knowledge about the birth control method. "After the IUD demonstration, knowledge scores were significantly increased," said Dr. Johnson. "Nearly 65% of the young women liked the idea of an IUD for themselves, while 12% were neutral and 24% said they disliked the idea," she reported.

Those who liked the IUDs for themselves were significantly more likely to be sexually active than those who did not or who were neutral, Dr. Johnson reported. "There was no association between liking IUDs and age, race, ever being pregnant, parity, ever having a sexually transmitted disease or number of sexual partners,' she said.

Among the young women who liked the idea of an IUD, the most appealing characteristics were that it did not require them to remember to use it every day, that it would not affect their ability to have children in the future, and that it did not need to be remembered with each sex act, Dr. Johnson said.

The findings suggest that "young women may not be getting sufficient information on all of the contraceptive options available to them, particularly IUDs," said Dr. Johnson. "Clinicians should discuss IUDs as an option with these patients and demonstrate how they are used in order for [patients] to make an informed decision about contraception."

CLINICAL PHARMACOLOGY, Clinical Studies). The results from observational studies are gener-ally consistent with those of the WHI clinical trial and report no significant variation in the risk of breast cancer among different estrogens or progestins, doese, or routes of administration. The CEVIMPs subuty of WHI reported an increased risk of breast cancer in women who took CE/MPA for a mean follow-up of 5.6 years. Observational studies have also reported an increased risk for estrogensynopestin combination therapy, and a smaller increased strik for generation therapy and a samelar increased increased with duration of use. From observational studies, the risk append to return to baseline in about five years after stopping treatment. In addition, observational studies suppest that the risk or breast cancer was greater, and became apparent anier, with estrogen/progestin tombination the appendix scompared to be stopped and the stopped progesting the stopped treatment. In addition, a baseline the appendix scompared to be stopped and became apparent anier, with estrogen/progesting that the risk of the stopped progesting on the stopped program to the stopped program to be appendix the stopped program to be stopped approximation and the stopped program to be appendix the stopped program to be stopped and became apparent anier, with estrogen/progesting approximation the stopped program to be stopped approximation and the stopped program to be stopped approximation the stopped program to be appendix the stopped program to be stopped approximation and the stopped program to be stopped program to be appendix the stopped program to be stopped program to be appendix the stopped program to be stopped program to be appendix the stopped program to be stopped program to be stopped program to be appendix the stopped program to be stopped program to be appendix the stopped program to be stopped program to be appendix the stopped program to be stopped program to be stopped program to be stopped program to be appe

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prior mammogram results. 3. Dementia In the estrogen alone Women's Health Initiative Memory Study (WHIMS), a sub-subuy of WHI. 294 Thysterechomical women aged 65 to 79 years were randomized to CE or placa-bo. In the estrogen plus progestin WHIMS substudy. 4,532 postmenopausal women aged 65 to 79 years were randomized to CE/MPA or placebo. In the estrogen alone substudy, after an average follow-up of 5.2 years, 28 women in the estro-gen alone group and 19 women in the placebo group were diagnosed with probable dementia The relative risk of probable dementia for estrogen alone versus placebo was 149 (95% CI.08.32-66). The absolute risk of probable dementia for estrogen alone versus placebo was 37 versus 25 cases per 10,000 women-years. It is unknown whether these findings apply to yurger postmenopausal women. (See CLINCAL PHARMACDLOBY, Clinical Studies and PRE-CAUTIONS, Seriatric USe.)

CAUTIONS, Geriatric Use.) After an average follow-up of 4 years. 40 women being treated with CE/MPA (1.8%, n = 2,229) and 21 women in the placebo group (0.9%, n = 2,303) revised diagnoses of probable dementia. The relative risk for CE/MPA versus placebo was 2.05 (95% confidence interval 1.21 – 3.48), and was similar for women with and without histories of menopausal hormoone use before WHIMS. The absolute risk of probable dementia for CE/MPA versus placebo was 4.5 versus 22 cases per 10,000 women-years, and the absolute excess risk for CE/MPA was 23 cases per 10,000 women-years. It is unknown whether these infinings apply to younger postmenopausal women. (See CLINCAL PHARMACOLORY, Clinical Studies and PECAL/DTONS, Cerratire Use.) A solibated relates 4.9 × 1.4 × 1.4 histories of menopausal

women. (See CLINICAL PHARMACULUSY, Clinical Studies and PHECAUTURUS, Genatric Use.) 4. Gallbalder disease A 2: to 4: to 40 increase in the risk of gallbalder disease requiring sur-gery in postmenopausal women receiving estrogens has been reported. 5. Hypercalcemia Estrogen administration may lead to severe hypercalcemia in patients with breast cancer and bore metastases. If hypercalcemia cours, use of the drug should be stopped and appropriate measures taken to reduce the serum calcium level. 6. Visual admormalities Retinu accular thrombosis has been reported in patients receiving estrogens. Discontinue medication pending examination if there is sudden partial or complete loss or vision, or a sudden onset of propriosis, diplopia, or morigane. If examination reveals papilledema or retinal vascular lesions, estrogens should be permanently discontinued. Derce LITOME. PRECAUTIONS

A. GENERAL

Addition of a progestin when a woman has not had a hysterectomy unders of the addition of a progestin for 10 or more days of a cycle of estrogen administration daily with estrogen in a continuous regimen, have reported a lowered incidence of endome-al hyperplasia than would be induced by estrogen treatment alone. Endometrial hyperplasia sy 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.

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 estrogen therapy on blood pressure was not seen. Blood pressure should be monitored at regular intervals with estrogen use. Hypertriglyceridemia In patients with pre-existing hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis and

appring to executions. **4. Impaired liver function and past history of cholestatic jaundice** Estrogens may be poor-her metabolized in natients with impaired liver function. For patients with a history of cholestatic

Impaired liver function and past history of cholestatic jaundice. Estrogens may be poorly metabolized in patients with impaired liver function. For patients with a history of cholestatic jaundice associated with as atteringen use or with pregnanor, caution should be exceeded and in the case of recurrence, medication should be discontinued.
 He clearance of drospirence was decreased in patients with moderate hepatic impairment.
 Hypolhyroidism Estrogen administration leads to increased thyroid-binding globulin (TBG) version patients with normal thyroid function can compensate for the increased TBG by making more thyroid hormone, thus maintaining free 14 and 13 serum concentrations in the normal range. Patients dependent on thyroid hormone replacement therapy who are also receiving estrogens and regulate larged.
 Fluid retention Because estrogen and estrogen/progestin therapy may cause some degree patients should have their thyroid function and testogen/progestin therapy may cause some degree fuluid retention, patients with conditions that might be influenced by this factor, such as a cardiac or renal dystunction, warrant careful observation when estrogens are prescribed.
 Hypopatermia Estorgen should be used with caution in individuals with sover bypocatemia.
 Hypopatermia As an aldosterone antagonist, drospirenone may increase the possibility of hyponatremia. As an aldosterone antagonist, drospirenone may increase the possibility of hyponatremia. As an aldosterone antagonist, drospirenone was on such as not storigens for avain as a cardiacor or enal dystunction, wars as a storigen sources. The esterogen alone, in patients with a note storgen should be used with a storgen should so was not statistically significant. The absolute risk for CAMPA versus placebow as s 36 (5%) condinece interact 07 – 324) but was not statistically significant. The absolute risk for CAMPA versus placebowas 4.2 versus 2.7 cases per disoridare for the or how roome

10. Exacerbation of endometriosis Endometriosis may be exacerbated with administra-0. Exacerbation of other conditions. Estrogens may cause an exacerbation of asthma, dia-ters mellius, epilepsy, migraine, porphyria, systemic lupus erythernatosus, and hepatic hernan-iomas, and should be used with caution in women with these conditions.
. PATIENT INFORMATION Physicians are advised to discuss the PATIENT INFORMATION after with patients for whom they prescribe ANGELIQ.

C. LABORATORY TESTS Estrogen administration should be initiated at the lowest dose for the approved indication and then guided by clinical response, rather than by serum hor-

D. DHOG/ABUMA UNY TEST IN TEACTURES 1. Accelerate dorbrombin time, andia thromboplastin time, and platelet aggregation time; increased platelet count; increased factors II, VII antigen, VIII antigen, VIII coaguant activity, IX, XII, VII- decreased antibrombin III, decreased antibrombin VIII corressed levels of fabrino-gen and fibrinogen activity; increased plasminogen antigen and activity. 2. Increased thyroid-binding globulin (TBG) levels leading to increased circulating total thyroid hommone, as measured by profician-bound oddine (VIB). Tal levels (by column or by radioim-munoassay) or T3 levels by radioimmunoassay. T3 resin uptate is decreased, reflecting the ele-vated TBG. Free T4 and free T3 concentrations are unaltered. Patients on thyroid replacement therapy may require higher doses of thyroid hommone.

2. Malignant neoplasms a. Endometrial cancer. The use of unopposed estrogens in women with intact uteri has been associated with an increased risk of endometrial cancer. The reported endometrial cancer risk among unopposed estrogen users is about 2- to 12-fold greater than in non-users, and appears dependent on duration of treatment and on estrogen dose. Noot studies show no sig-nificant increased risk associated with use of estrogens for less than one year. The greatest risk appears associated with prolonged use, with increased risks of 15- to 24-fold for five to trey years or and this risk has been shown to persist for at least 8 to 15 years after estro-gent fitterary is discontinued. mone levels (e.g., estradiol, FSH). D. DRUG/LABORATORY TEST INTERACTIONS

gen merapy is discontinued. Clinical surveillance of all women taking estrogen/progestin combinations 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 natural estrogene results in a different endometrial risk pro-file than synthetic estrogens of equivalent estrogen dose. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Buoinformaticance: **b. Breast cancer** The use of estrogens and progestins by postmenopausal women has been reported to increase the risk of breast cancer. The most important randomized clinical trial provid-ing information about this issue is the Women's Health Initiative (WHI) substudy of CEMPA (see



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ureas: cnanges, preast cancer. 3. Cardivascular: Deep and superficial venous thrombosis, pulmonary embolism, throm-bophlebitis, myocardial infraction, stroke, increase in blood pressure. 4. Gastrointestinal Nausea, vorniting, abdominal cramps, bloating, cholestatic jaundice, increased indicate of gall bladder disease, pancreating, enlargement of hepatic hemangiomas.

reases of ANEELIQ overdose, monitor serum concentrations of potassium and sodium since trospirenone has antimineralocorticoid properties.