

# Health Policy Changes in Store With New Congress

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Senior Editor

The changes in leadership brought about by the November mid-term elections are likely to result in significant shifts in the way Congress approaches health policy issues, according to several experts.

One change many physicians are hoping the new Democratic leadership will make is to fix the Medicare physician payment

formula. Under the current payment formula, physicians are facing a 5% payment cut in January. "For the immediate future, we are asking that they cancel the cut and give physicians a positive [payment increase] to reflect inflation, which is slightly over 2%," Dr. Cecil Wilson, chair of the American Medical Association board of trustees, said in an interview.

Such an immediate fix would not address the underlying problem, which is that the physician fee schedule relies on the

flawed Sustainable Growth Rate (SGR).

"Congress needs to do a permanent fix to this problem," said Dr. Wilson, an internist in Winter Park, Fla. "We will be working very hard on that for this coming year, to ask that they get rid of this formula and move to one that reflects the increased cost of providing care."

Ron Pollack, executive director of Families USA, a liberal consumer group based in Washington, voiced optimism that the new Congress would look at the payment

formula. "I think the Democrats probably do want to deal with that—whether it will be on a year-by-year basis or on a more permanent basis, I don't know," he said in an interview. "But I do think the Democrats are inclined to get that fixed."

Malpractice reform could be another story, Mr. Pollack said.

"The one and perhaps only way that is going to move forward will be if there is significant compromise," he said.

"[The strategy of] placing caps on dam-

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### 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 "natural" estrogens results in a different endometrial risk profile than synthetic estrogens of equivalent estrogen dose. (See **WARNINGS, Malignant neoplasms, Endometrial cancer.**)

### CARDIOVASCULAR AND OTHER RISKS

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

The estrogen-alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years of treatment with oral conjugated estrogens (CE 0.625 mg) per day relative to placebo. (See **CLINICAL STUDIES** in full Prescribing Information and **WARNINGS, Cardiovascular disorders**.)

The estrogen-plus-progestin substudy of the WHI reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50 to 79 years of age) during five years of treatment with oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) per day relative to placebo. (See **CLINICAL STUDIES** in full Prescribing Information and **WARNINGS, Cardiovascular disorders and Malignant neoplasms, Breast cancer.**)

The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with CE 0.625 mg alone and during four years of treatment with CE 0.625 mg combined with MPA 2.5 mg, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. (See **CLINICAL STUDIES** in full Prescribing Information and **WARNINGS, Dementia and PRECAUTIONS, Geriatric Use.**)

Other doses of conjugated estrogens and medroxyprogesterone acetate, and other combinations and dosage forms of estrogens and progestins, 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 progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

### INDICATIONS AND USAGE

Premarin therapy is indicated in the:

1. Treatment of moderate to severe vasomotor symptoms associated with the menopause.
  2. Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with the menopause. When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered.
  3. Treatment of hypogonadism due to hypogonadism, castration or primary ovarian failure.
  4. Treatment of breast cancer (for palliation only) in appropriately selected women and men with metastatic disease.
  5. Treatment of advanced androgen-dependent carcinoma of the prostate (for palliation only).
  6. Prevention of postmenopausal osteoporosis. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and for whom non-estrogen medications are not considered to be appropriate. (See **CLINICAL STUDIES** in full Prescribing Information.)
- The mainstays for decreasing the risk of postmenopausal osteoporosis are weight-bearing exercise, adequate calcium and vitamin D intake, and when indicated, pharmacologic therapy. Postmenopausal women require an average of 1500 mg/day of elemental calcium. Therefore, when not contraindicated, calcium supplementation may be helpful for women with suboptimal dietary intake. Vitamin D supplementation of 400-800 IU/day may also be required to ensure adequate daily intake in postmenopausal women.

### CONTRAINDICATIONS

Estrogens should not be used in individuals with any of the following conditions:

1. Undiagnosed abnormal genital bleeding.
2. Known, suspected, or history of cancer of the breast except in appropriately selected patients being treated for metastatic disease.
3. Known or suspected estrogen-dependent neoplasia.
4. Active deep vein thrombosis, pulmonary embolism or a history of these conditions.
5. Active or recent (e.g., within past year) arterial thromboembolic disease (e.g., stroke, myocardial infarction).
6. Liver dysfunction or disease.
7. Premarin tablets should not be used in patients with known hypersensitivity to their ingredients.
8. Known or suspected pregnancy. There is no indication for Premarin in pregnancy. There appears to be little or no increased risk of birth defects in children born to women who have used estrogen and progestins from oral contraceptives inadvertently during pregnancy. (See **PRECAUTIONS.**)

### WARNINGS

#### See **BOXED WARNINGS.**

#### 1. Cardiovascular disorders

Estrogen and estrogen-plus-progestin therapy have 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 arterial vascular disease (e.g., hypertension, diabetes mellitus, tobacco use, hypercholesterolemia, and obesity) and/or venous thromboembolism (e.g., personal history or family history of VTE, obesity, and systemic lupus erythematosus) should be managed appropriately.

#### a. Stroke and coronary heart disease

In the estrogen-alone substudy of the Women's Health Initiative (WHI) study, a statistically significant increased risk of stroke was reported in women receiving CE 0.625 mg daily compared to women receiving placebo (44 vs. 32 per 10,000 women-years). The increase in risk was demonstrated in year one and persisted. (See **CLINICAL STUDIES** in full Prescribing Information.)

Also, in the estrogen-alone substudy of WHI, no overall effect on coronary heart disease (CHD) events (defined as non-fatal MI, silent MI, or death, due to CHD) was reported in women receiving estrogen alone compared to placebo. (See **CLINICAL STUDIES** in full Prescribing Information.)

In the estrogen-plus-progestin substudy of WHI, a statistically significant increased risk of stroke was reported in women receiving CE/MPA 0.625 mg/2.5 mg daily compared to women receiving placebo (31 vs. 24 per 10,000 women-years). The increase in risk was demonstrated after the first year and persisted.

Also, in the estrogen-plus-progestin substudy of WHI, no statistically significant increase of CHD events was reported in women receiving CE/MPA compared to women receiving placebo (39 vs. 33 per 10,000 women-years). An increase in relative risk was demonstrated in year one, and a trend toward decreasing relative risk was reported in year 2 through 5. In postmenopausal women with documented heart disease (n=2,763, average age 66.7 years) a controlled clinical trial of secondary prevention of cardiovascular disease (Heart and Estrogen/progestin Replacement Study; HERS) treatment with CE/MPA 0.625 mg conjugated estrogens/2.5 mg medroxyprogesterone acetate daily demonstrated no cardiovascular benefit. During an average follow-up of 4.1 years, treatment with CE/MPA did not reduce the overall rate of CHD events in postmenopausal women with established

coronary heart disease. There were more CHD events in the CE/MPA-treated group than in the placebo group in year one, but not during the subsequent years. Two thousand three hundred and twenty-one women from the original HERS trial agreed to participate in an open-label extension of HERS, HERS II. Average follow-up in HERS II was an additional 2.7 years, for a total of 6.8 years overall. Rates of CHD events were comparable among women in the CE/MPA group and the placebo group in the HERS, the HERS II, and overall. Large doses 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 trial in men to increase the risk of nonfatal myocardial infarction, pulmonary embolism, and thrombophlebitis.

#### b. Venous thromboembolism (VTE)

In the estrogen-alone substudy of WHI, the risk of VTE (DVT and pulmonary embolism [PE]), was reported to be increased for women taking conjugated estrogens (28 vs. 21 per 10,000 women-years), although only the increased risk of DVT reached statistical significance (21 vs. 15 per 10,000 women-years). The increase in VTE risk was demonstrated during the first year. (See **CLINICAL STUDIES** in full Prescribing Information.)

In the estrogen-plus-progestin substudy of WHI, a statistically significant 2-fold greater rate of VTE was reported in women receiving CE/MPA compared to women receiving placebo (35 vs. 17 per 10,000 women-years). Statistically significant increases in risk for both DVT (26 vs. 13 per 10,000 women-years) and PE (18 vs. 8 per 10,000 women-years) were also demonstrated. The increase in VTE risk was demonstrated during the first year and persisted. If feasible, 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 prolonged immobilization.

#### 2. Malignant neoplasms

##### a. Endometrial cancer

The use of unopposed estrogens in women with intact uterus has been associated with an increased risk of endometrial cancer. The reported endometrial cancer risk among unopposed estrogen users with an intact uterus is about 2- to 12-fold greater than in non-users, and appears dependent on duration of treatment and on estrogen dose. Most studies show no significant increased risk associated with the 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 ten years or more, and this risk has been shown to persist for at least 8 to 15 years after estrogen therapy is discontinued.

Clinical surveillance of all women taking estrogen-plus-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 estrogens results in a different endometrial risk profile than synthetic estrogens of equivalent estrogen dose. Adding a progestin to postmenopausal estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer.

##### b. Breast cancer

In some studies, 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 providing information about this issue is the Women's Health Initiative (WHI). (See **CLINICAL STUDIES** in full Prescribing Information.) The results from observational studies are generally consistent with those of the WHI clinical trial.

Observational studies have also reported an increased risk of breast cancer for estrogen-plus-progestin combination therapy, and a smaller increased risk for estrogen-alone therapy, after several years of use. For both findings, the excess risk increased with duration of use, and appeared to return to baseline over about five years after stopping treatment (only the observational studies have substantial data on risk after stopping). In these studies, the risk of breast cancer was greater, and became apparent earlier, with estrogen-plus-progestin combination therapy as compared to estrogen-alone therapy. However, these studies have not found significant variation in the risk of breast cancer among different estrogens or among different estrogen-plus-progestin combinations, doses, or routes of administration.

In the estrogen-alone substudy of WHI, after an average of 6.8 years of follow-up, CE (0.625 mg daily) was not associated with an increased risk of invasive breast cancer (RR 0.77, 95% nCI 0.59-1.01).

In the estrogen-plus-progestin substudy, after a mean follow-up of 5.6 years, the WHI substudy reported an increased risk of breast cancer. Prior use of estrogen alone or estrogen-plus-progestin combination hormone therapy was reported by 26% of the women. The relative risk of invasive breast cancer was 1.24 (95% nCI 1.01-1.54), and the absolute risk was 41 vs. 33 cases per 10,000 women-years, for estrogen-plus-progestin compared with placebo, respectively. Among women who reported prior use of hormone therapy, the relative risk of invasive breast cancer was 1.86, and the absolute risk was 46 vs. 25 cases per 10,000 women-years, for estrogen-plus-progestin compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.09, and the absolute risk was 40 vs. 36 cases per 10,000 women-years for estrogen plus progestin compared with placebo. In the WHI trial, invasive breast cancers were larger and diagnosed at a more advanced stage in the estrogen-plus-progestin group compared with the placebo group. Metastatic disease was rare, with no apparent difference between the two groups. Other prognostic factors, such as histologic subtype, grade and hormone receptor status did not differ between the groups. The use of estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. All women should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations. In addition, mammography examinations should be scheduled based on patient age, risk factors, and prior mammogram results.

#### 3. Dementia

In the estrogen-alone Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, a population of 2,947 hysterectomized women aged 65 to 79 years was randomized to CE (0.625 mg daily) or placebo. In the estrogen-plus-progestin WHIMS substudy, a population of 4,532 postmenopausal women aged 65 to 79 years was randomized to CE/MPA (0.625 mg/2.5 mg daily) or placebo.

In the estrogen-alone substudy, after an average follow-up of 5.2 years, 28 women in the estrogen-alone group and 19 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE alone vs. placebo was 1.49 (95% nCI 0.83-2.66). The absolute risk of probable dementia for CE alone. Placebo was 37 vs. 25 cases per 10,000 women-years.

In the estrogen-plus-progestin substudy, after an average follow-up of four years, 40 women in the estrogen-plus-progestin group and 21 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for estrogen plus progestin vs. placebo was 2.05 (95% nCI 1.21-3.48). The absolute risk of probable dementia for CE/MPA vs. placebo was 45 vs. 22 cases per 10,000 women-years.

When data from the two populations were pooled as planned in the WHIMS protocol, the reported overall relative risk for probable dementia was 1.76 (95% nCI 1.19-2.60). Since both substudies were conducted in women aged 65 to 79 years, it is unknown whether these findings apply to younger postmenopausal women. (See **BOXED WARNINGS and PRECAUTIONS, Geriatric Use.**)

#### 4. Gallbladder Disease

A 2- to 4-fold increase in the risk of gallbladder disease requiring surgery in postmenopausal women receiving estrogens has been reported.

#### 5. Hypercalcemia

Estrogen administration may lead to severe hypercalcemia in patients with breast cancer and bone metastases. If hypercalcemia occurs, use of the drug should be stopped and appropriate measures taken to reduce the serum calcium level.

#### 6. Visual abnormalities

Retinal vascular thrombosis has been reported in patients receiving estrogens. Discontinue medication pending examination if there is sudden partial or complete loss of vision, or a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, estrogens should be discontinued.

### PRECAUTIONS

#### A. General

##### 1. Addition of a progestin when a woman has not had a hysterectomy

Studies of the addition of a progestin for 10 or more days of a cycle of estrogen administration, or daily with estrogen in a continuous regimen, have reported 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; adverse effects on lipoprotein metabolism (e.g., lowering HDL, raising LDL) and impairment of glucose tolerance.

#### 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 during estrogen use.

#### 3. Hypertriglyceridemia

In patients with pre-existing hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis and other complications. In the HOPE study, the mean percent increase from baseline in serum triglycerides after one year of treatment with Premarin 0.625 mg, 0.45 mg, and 0.3 mg compared with placebo were 34.3, 30.2, 25.1, and 10.7, respectively. After two years of treatment, the mean percent changes were 47.6, 32.5, 19.0, and 5.5, respectively.

#### 4. 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 past estrogen use or with pregnancy, caution should be exercised, and in the case of recurrence, medication should be discontinued.

#### 5. Hypothyroidism

Estrogen administration leads to increased thyroid-binding globulin (TBG) levels. Patients with normal thyroid function can compensate for the increased TBG by making more thyroid hormone, thus maintaining free T<sub>4</sub> and T<sub>3</sub> serum concentrations in the normal range. Patients dependent on thyroid hormone replacement therapy who are also receiving estrogens may require increased doses of their thyroid 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 retention

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

#### 7. Hypocalcemia

Estrogens should be used with caution in individuals with severe hypocalcemia.

#### 8. Ovarian cancer

The estrogen-plus-progestin substudy of WHI reported that after an average follow-up of 5.6 years, the relative risk for ovarian cancer for estrogen plus progestin vs. placebo was 1.58 (95% nCI 0.77 - 3.24), but was not statistically significant. The absolute risk for estrogen plus progestin vs. placebo was 4.2 vs. 2.7 cases per 10,000 women-years. In some epidemiologic studies, the use of estrogen-only products, in particular for 10 or more years, has been associated with an increased risk of ovarian cancer. Other epidemiologic studies have not found these associations.

#### 9. Exacerbation of endometriosis

Endometriosis may be exacerbated with administration of estrogen therapy. Malignant transformation of residual endometrial implants have been reported in women treated post-hysterectomy with estrogen-alone therapy. For patients known to have residual endometriosis post-hysterectomy, the addition of progestin should be considered.

#### 10. Exacerbation of other conditions.

Estrogen therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas and should be used with caution in patients with these conditions.

#### B. Patient Information

Physicians are advised to discuss the contents of the **PATIENT INFORMATION** leaflet with patients for whom they prescribe Premarin.

#### C. Laboratory Tests

Estrogen administration should be initiated at the lowest dose for the treatment of postmenopausal moderate-to-severe vasomotor symptoms and moderate-to-severe symptoms of postmenopausal vulvar and vaginal atrophy and then guided by clinical response rather than by serum hormone levels (e.g., estradiol, FSH). Laboratory parameters may be useful in guiding dosage for the treatment of hypogonadism due to hypogonadism, castration and primary ovarian failure.

#### D. Drug/Laboratory Test Interactions

1. Accelerated prothrombin time, partial thromboplastin time, and platelet aggregation time; increased platelet count; increased factors II, VII antigen, VIII coagulant activity, IX, X, XII, VII-X complex, and beta-thromboglobulin; decreased levels of anti-factor Xa and antithrombin III; decreased antithrombin III activity; increased levels of fibrinogen and fibrinogen activity; increased plasminogen antigen and activity.
2. Increased thyroid binding globulin (TBG) levels leading to increased circulating total thyroid hormone levels as measured by protein-bound iodine (PBI), T<sub>4</sub> levels (by column or by radioimmunoassay) or T<sub>3</sub> levels by radioimmunoassay. T<sub>3</sub> resin uptake is decreased, reflecting the elevated TBG. Free T<sub>4</sub> and free T<sub>3</sub> concentrations are unaltered. Patients on thyroid replacement therapy may require higher doses of thyroid hormone.
3. Other binding proteins may be elevated in serum, i.e., corticosteroid binding globulin (CBG), sex hormone binding globulin (SHBG), leading to increased total 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).
4. Increased plasma HDL and HDL<sub>2</sub> cholesterol subtraction concentrations, reduced LDL cholesterol concentrations, increased triglyceride levels.
5. Impaired glucose tolerance.
6. Reduced response to metyrapone test.

#### E. Carcinogenesis, Mutagenesis, Impairment of Fertility

(See **BOXED 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, uterus, cervix, vagina, testis, and liver.

#### F. Pregnancy

Premarin should not be used during pregnancy. (See **CONTRAINDICATIONS.**)

#### G. Nursing Mothers

Estrogen administration to nursing mothers has been shown to decrease the quantity and quality of the milk. Detectable amounts of estrogens have been identified in the milk of mothers receiving this drug. Caution should be exercised when Premarin is administered to a nursing woman.

#### H. Pediatric Use

Estrogen therapy has been used for the induction of puberty in adolescents with some forms of pubertal delay. Safety and effectiveness in pediatric patients have not otherwise been established.

Large and repeated doses of estrogen over an extended time period have been shown to accelerate epiphyseal closure, which could result in short stature if treatment is initiated before the completion of physiologic puberty in normally developing children. If estrogen is administered to patients whose bone growth is not complete, periodic monitoring of bone maturation and effects on epiphyseal centers is recommended during estrogen administration.

Estrogen treatment of prepubertal girls also induces premature breast development and vaginal modification, and may induce vaginal bleeding. In boys, estrogen treatment may modify the normal pubertal process and induce gynecomastia. (See **INDICATIONS AND USAGE and DOSAGE AND ADMINISTRATION.**)

#### I. Geriatric Use

Of the total number of subjects in the estrogen-alone substudy of the Women's Health Initiative (WHI) study, 46% (n=4,943) were 65 years and over, while 7.1% (n=767) were 75 years and over. There was a higher relative risk (CE vs. placebo) of stroke in women less than 75 years of age compared to women 75 years and over.

In the estrogen-alone Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, a population of 2,947 hysterectomized women, aged 65 to 79 years, was randomized to CE (0.625 mg daily) or placebo. After an average follow-up of 5.2 years, the relative risk (CE vs. placebo) of probable dementia was 1.49 (95% nCI 0.83-2.66). The absolute risk of developing probable dementia with estrogen alone was 37 vs. 25 cases per 10,000 women-years with placebo.

Of the total number of subjects in the estrogen-plus-progestin substudy of the Women's Health Initiative study, 44% (n=7,320) were 65-74 years of age, while 6.6% (n=1,095) were 75 years and over. There was a higher relative risk (CE/MPA vs. placebo) of non-fatal stroke and invasive breast cancer in women 75 and over compared to women less than

75 years of age. In women greater than 75, the increased risk of non-fatal stroke and invasive breast cancer observed in the estrogen-plus-progestin combination group compared to the placebo group was 75 vs. 24 per 10,000 women-years and 52 vs. 12 per 10,000 women-years, respectively.

In the estrogen-plus-progestin WHIMS substudy, a population of 4,532 postmenopausal women aged 65 to 79 years, was randomized to CE/MPA (0.625 mg/2.5 mg daily) or placebo. In the estrogen-plus-progestin group, after an average follow-up of four years, the relative risk (CE/MPA vs. placebo) of probable dementia was 2.05 (95% nCI 1.21-3.48). The absolute risk of developing probable dementia with CE/MPA was 45 vs. 22 cases per 10,000 women-years with placebo.

Seventy-nine percent of the cases of probable dementia occurred in women that were older than 70 for the CE group, and 82 percent of the cases of probable dementia occurred in women who were older than 70 in the CE/MPA group. The most common classification of probable dementia in both the treatment groups was Alzheimer's disease.

When data from the two populations were pooled as planned in the WHIMS protocol, the reported overall relative risk for probable dementia was 1.76 (95% nCI 1.19-2.60). Since both substudies were conducted in women aged 65 to 79 years, it is unknown whether these findings apply to younger postmenopausal women. (See **BOXED WARNINGS and WARNINGS, Dementia.**)

With respect to efficacy in the approved indications, there have not been sufficient numbers of geriatric patients involved in studies utilizing Premarin to determine whether those over 65 years of age differ from younger subjects in their response to Premarin.

### ADVERSE REACTIONS

#### See **BOXED WARNINGS, WARNINGS, and PRECAUTIONS.**

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 trials 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.

During the first year of a 2-year clinical trial with 2,333 postmenopausal women between 40 and 65 years of age (88% Caucasian), 1,012 women were treated with conjugated estrogens and 332 were treated with placebo. Table 6 summarizes adverse events that occurred at a rate of  $\geq 5\%$ .

TABLE 6. NUMBER (%) OF PATIENTS REPORTING  $\geq 5\%$  TREATMENT EMERGENT ADVERSE EVENTS

Body System Adverse event	— Conjugated Estrogens Treatment Group —			
	0.625 mg (n=348)	0.45 mg (n=338)	0.3mg (n=326)	Placebo (n=332)
Any adverse event	323 (93%)	305 (90%)	292 (90%)	281 (85%)
Body as a Whole				
Abdominal pain	56 (16%)	50 (15%)	54 (17%)	37 (11%)
Accidental injury	21 (6%)	41 (12%)	20 (6%)	29 (9%)
Asthenia	25 (7%)	23 (7%)	25 (8%)	16 (5%)
Back pain	49 (14%)	43 (13%)	43 (13%)	39 (12%)
Flu syndrome	37 (11%)	38 (11%)	33 (10%)	35 (11%)
Headache	90 (26%)	109 (32%)	96 (29%)	93 (28%)
Infection	61 (18%)	75 (22%)	74 (23%)	74 (22%)
Pain	5			

age awards probably makes it difficult to move this forward. On the other hand, to the extent that alternative conflict resolution systems are established that substantially reduce litigation and provide more people with access to grievance mechanisms short of legal proceedings, that certainly has a chance of movement," Mr. Pollack said.

Michael Cannon, director of health policy studies at the Cato Institute, a libertarian think tank in Washington, was even more negative. Malpractice reform "is not going anywhere and that's a welcome development, because the Constitution does not give Congress any authority to play any role in that area," he said. "The Republicans never recognized that, but the Democrats, in this instance, are in favor of letting the states deal with that issue, and they are not interested in any federal malpractice reforms."

Covering the uninsured is another area that could move to the front burner under the Democrats, Dr. Wilson said.

**Another thing the Democrats will consider doing is to close up the 'doughnut hole,' the coverage gap beneficiaries have when their drug bills exceed a certain amount.**

"We now know that [the uninsured] are more likely to get sicker and die sooner" than those with insurance, he said. "We'll be trying to increase the visibility of that problem."

One definite health care priority for Rep.

Nancy Pelosi (D-Calif.), who will become Speaker of the House in January, will be to get rid of a prohibition in the Medicare prescription drug coverage law that bans the Centers for Medicare and Medicaid Services from negotiating prices directly with pharmaceutical companies.

"We can and we must make the Medicare prescription drug plan fairer and more cost effective," Rep. Pelosi said in a statement regarding that issue.

Removal of that prohibition would be a welcome change, according to Mr. Pollack. By bargaining directly with drug companies, the Department of Veterans Affairs "has achieved much lower prices than the lowest prices charged by all Medicare Part D plans," he said in a statement, noting that the median price difference was 46%.

Mr. Cannon had quite a different take on the idea. "Democrats are attracted to price controls because it allows them to provide a benefit for current generations through lower-cost drugs, while imposing a cost on future generations, which is fewer new drugs being developed" due to declining revenues for pharmaceutical companies, he said.

Another thing the Democrats will consider doing with the Part D plan is to close up the "doughnut hole," the gap in coverage beneficiaries have when their drug bills exceed a certain amount. Rep. Pelosi has said she plans to do this using the savings achieved through letting Medicare negotiate drug costs directly.

Analysts are anticipating a new direction in health policy in the new Congress because the presumed new chairs of the

committees and subcommittees dealing with health care are considered quite liberal.

This group includes Rep. Charles Rangel (D-N.Y.), expected to head the Ways and Means Committee; Rep. John Dingell (D-Mich.), expected to head the Energy and Commerce Committee; Rep. George Miller (D-Calif.), expected to head the Education and Workforce Committee; and Rep. Fortney H. "Pete" Stark (D-Calif.), expected to head the Ways and Means health subcommittee.

"It's going to be very interesting to see how these folks approach health care," said Mr. Cannon, noting that Rep. Dingell

has introduced legislation for a single-payer health care system every year since 1955. "We will see if they just try to go for moderate Democratic ideas ... or if they really follow their hearts and try to kill health savings accounts, or launch some sort of Clinton-like initiative that aims to provide coverage for everyone. They're not moderates, and they're not shrinking violets. They don't seem like the kind who are going to take orders; they seem to want to run their own show."

The upcoming reauthorization of the State Children's Health Insurance Program (SCHIP), a federal/state program to provide health insurance to children in

families with income too high for Medicaid but too low to be able to afford private insurance coverage, is one example of legislation the Democrats could put their stamp on, according to Mr. Pollack.

"Due to its broad, bipartisan support, SCHIP no doubt will be reauthorized," he said. "However, since approximately 9 million children continue to be uninsured, the real question before the Congress is whether the reauthorization process will expand health coverage and provide adequate SCHIP funding for those children who don't have coverage and whose families can't afford it. A simple reauthorization will be a major disappointment." ■

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**Your patients rely on you to provide the best care possible. Weigh the risks of tubal ligation against the minimally invasive *Essure*<sup>®</sup> procedure.**

**Examine the facts:**  
The FDA has encouraged your patients to ask you for alternatives to laparoscopic procedures.<sup>1</sup> *Are you offering them a non-incisional alternative to tubal ligation?*

The President of ACOG\* has emphasized patient safety: "The public is demanding it; hospitals and accrediting authorities are demanding it; and we should be demanding of ourselves."<sup>2</sup> *If you aren't offering the Essure procedure to your sterilization patients, are you putting their safety first?*

Patients are excited about the benefits of the *Essure* procedure. *Your patients are moving forward. Are you?*

**Start now by taking advantage of:**

- Complimentary training
- Preceptored cases
- Online tools at [www.essureMD.com](http://www.essureMD.com)

**Choose the *Essure* procedure over tubal ligation.**

Do your patients justice by emailing [justice@conceptus.com](mailto:justice@conceptus.com) today to learn about training on the *Essure* procedure.

**essure<sup>®</sup>**  
Permanent Birth Control  
[www.EssureMD.com](http://www.EssureMD.com)

1. <http://www.fda.gov/cdrh/medicaldevicesafety/stamp/trocar.html>  
2. [http://www.acog.org/from\\_home/publications/press\\_releases/nr05-10-06-1.cfm](http://www.acog.org/from_home/publications/press_releases/nr05-10-06-1.cfm)  
\* This statement does not imply endorsement of the *Essure* procedure  
Please see Prescribing Information Summary on adjacent page  
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