

Does Red Clover Work?

**Q** I've seen advertisements for red clover as a treatment for menopausal symptoms. Is it an effective alternative to hormone replacement therapy (HRT)?

**A** Red clover (*Trifolium pratense*) is a medicinal herb originally used by American Indians to treat whooping cough, gout, and cancer. It's also taken as a cancer treatment in many other parts of the world, and it's found in herbal preparations for skin irritation.

Recently, red clover extracts have been promoted for relief of menopausal symptoms, namely hot flashes and vaginal dryness. Proponents claim that its effectiveness comes from its *isoflavone* (also known as phytoestrogen) content. In the body, these plant chemicals mimic or counter the effects of estrogen, and they are thought to be responsible for soy's beneficial effect on hot flashes. Red clover contains high concentrations of four major iso-

flavones: *formononetin*, *biochanin A*, *daidzein*, and *genistein*. Promensil (a proprietary extract of red clover isoflavones) and other red clover preparations are being marketed for long-term use as a "natural" form of HRT.

A group of researchers from George Washington University and Columbia University recently reviewed the scientific evidence for red clover's effects in the September issue of *Menopause: The Journal of The North American Menopause Society*. They found two good clinical trials in which menopausal women were randomly given either red clover extracts or a placebo for three months. In both trials, women kept diaries of their symptoms and study clinicians examined smears of vaginal cells to assess any estrogen-like effect on the vagina. The women also underwent pelvic ultrasounds to assess the thickness of the endometrium, the lining of the uterus. Neither

trial found red clover to be better than a placebo for hot flashes or vaginal dryness. The researchers also found no beneficial effect on serum cholesterol.

Red clover is on the FDA's GRAS (generally recognized as safe) list, but its long-term use has never been studied. We don't know what impact it might have over time on endometrial or breast tissue. Also, some species of clover contain *coumarins*, compounds that reduce blood-clotting capabilities. Any woman taking blood-thinning drugs such as warfarin (Coumadin), heparin, clopidogrel (Plavix), pentoxifylline (Trental), or even aspirin, should check with her doctor before using red clover extracts.

Considering red clover's unproven effects and possible risks, you'd be better off spending your money on soy, which has a modest effect on menopausal symptoms, or estrogen, which has by far the strongest effect. ❖

Are Standard Doses of HRT Equivalent?

**Q** Whenever I read about the effects of hormone replace therapy (HRT), the researchers always seem to use 0.625 mg of Premarin. I'm taking 1 mg of Estrace daily. How does this compare to the standard dose of Premarin?

**A** In common clinical practice, physicians consider the doses you mentioned of these two forms of estrogen to be roughly equivalent. Premarin is by far the most widely used estrogen product in the United States. To date, most clinical studies of HRT have used this brand of conjugated equine estrogens (CEE). Consequently, we know more about its effects than those of other forms of HRT. However, different estrogens may act at different

strengths in different body tissues. For example, 0.625 mg of CEE is roughly comparable to 1.0 mg of 17beta-estradiol when measuring its effects on liver function. But when it comes to bone density, 0.5 mg of estradiol has about the same effect as the standard 0.625 mg of CEE.

Thus, it's hard to be precise about dosing equivalencies for the various estrogens. With that reservation in mind, the table at right shows the doses of commonly used oral estrogens that have approximately the same effects as 0.625 mg of Premarin. All are available in lower doses as well. ❖

Approximately Equivalent Oral Estrogen Doses for Menopausal Use

Type of Estrogen	Standard Dose
Conjugated equine estrogens (CEE) (Preamarin)	0.625 mg
Synthetic conjugated estrogens (Cenestin)	0.625 mg
17beta-estradiol (Estrace, various generics)	1.0 mg
Estropipate (Ortho-Est, Ogen, various generics)	0.625 mg
Esterified estrogens (Estratab, Menest)	0.75 mg

(Source: *The North American Menopause Society, 2000*)

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